ORAU-30021

707758

ORAU/ORNL COMMITTEE ON HUMAN STUDIES
BUSINESS FILE
(FILE 1)

REPOSITORY OAK RIDGE INSTITUTE FOR SCIENCE & EDUCATION, MEDICAL SCIENCES DIV.

COLLECTION ORAU/ORNL COMMITTEE OF HUMAN STUDIES

BOX No. VANCE ROAD FACILITY, Rm. 202A

FOLDER Doc No. #30021 File 1 of 2

1032475

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
5600 ROCKVILLE PIKE
BETHESDA, MD. 20014

July 1, 1966

TO : Heads of Institutions Receiving Public Health Service Grants

FROM : Surgeon General, Public Health Service

SUBJECT: Revised procedures for clinical research and investigation involving human subjects

On February 8, 1966, I issued a policy statement relating to investigations involving human beings, including clinical research, pointing out the need for group review to protect the rights and welfare of the human subjects involved. The original policy involved only the support of research and research training. The application of this policy has been extended to all grants and awards of the Public Health Service in the support of research, training, or demonstration projects, including the projects supported through general research support and those of fellows and trainees. The policy is not applicable to grants in support of construction, alterations, renovations, or research resources -- it is obviously applicable to the Public Health Service projects using these facilities and resources.

Experience gained in administering this policy has led to revision and clarification of procedure. The major procedural revision is one for assurance agreements between each grantee institution and the Public Health Service which will obviate the necessity for providing detailed assurance with each application. Attached to this memorandum is a statement of revised policy and procedure (Policy and Procedure Order 129) which has been issued at my instruction.

The Public Health Service will continue its study of the issues of investigations involving human subjects. As experience shows the need for revised or augmented policy or procedures, these will be developed. I shall be pleased to receive suggestions and information from officials and investigators of grantee institutions to assist the Service in the conduct of its study.

I trust that these revisions, reflective of the advice I have received from many of you, will facilitate your discharge of this important obligation.

William H. Stewart

William H. Stewart, M.D.

Attachment

1032476

U. S. Public Health Service
Division of Research Grants
Bethesda, Maryland 20014

PPO #129, Revised
POLICY
July 1, 1966

SUBJECT : Investigations Involving Human Subjects, including Clinical Research: Requirements for Review to Insure the Rights and Welfare of Individuals

APPLICABILITY : All Public Health Service Grants and Awards

EFFECTIVE DATE: Immediately

SUPERSEDES : PPO #129, February 8, 1966
PPO #129 Supplement, April 7, 1966

I. BACKGROUND:

Culminating several years of study by various Public Health Service staff and advisory groups, the National Advisory Health Council passed the following resolution on December 3, 1965:

> "Be it resolved that the National Advisory Health Council believes that Public Health Service support of clinical research and investigation involving human beings should be provided only if the judgment of the investigator is subject to prior review by his institutional associates to assure an independent determination of the protection of the rights and welfare of the individual or individuals involved, of the appropriateness of the methods used to secure informed consent, and of the risks and potential medical benefits of the investigation."

II. POLICY:

The Surgeon General accepted the resolution of the National Advisory Health Council and promulgated the following policy statement on February 8, 1966:

> "No new, renewal, or continuation research or research training grant in support of clinical research and investigation involving human beings shall be awarded by the Public Health Service unless the grantee has indicated in the application the manner in which the grantee institution will provide prior review of the judgment of the principal investigator or program director by a committee of his institutional associates. This review should assure an independent determination: (1) of the rights and welfare of the individual or individuals involved, (2) of the appropriateness of the methods used to secure informed consent, and (3) of the risks and potential medical benefits of the investigation. A description of the committee of the associates who will provide the review shall be included in the application."

1032477

III. REVISED POLICY:

By decision of the Surgeon General, the application of this policy has been extended to all grants and awards of the Public Health Service in the support of research, training, or demonstration projects, including the projects supported through general research support and those of fellows and trainees. The policy is not applicable to grants in support of construction, alterations, renovations, or research resources -- it is obviously applicable to [illegible] projects using these facilities and resources.

This policy will be included in all pertinent grant program policy and instruction statements, and will be among the conditions of award agreed upon by grantee institutions and the Public Health Service. The policy applies to all investigations involving human subjects, including clinical research.

A. Assignment of Responsibility

Safeguarding the rights and welfare of human subjects involved in research supported by PHS grants is the responsibility of the institution to which the grant is awarded. The institution must assure the Public Health Service that in the case of investigations and activities supported directly by the PHS, it will provide group review and decision, maintain surveillance, and provide advice for investigators on safeguarding the rights and welfare of human subjects. The institution also has the responsibility to provide whatever professional attention or facilities may be required for the safety and well-being of human subjects. The institution shall be responsible for developing the administrative mechanism for review, surveillance, and advice; however, the PHS requires that, prior to inception of each course of investigation, objective decisions be made on the three points cited in the Surgeon General's policy statement (above) by an appropriate committee of associates of the investigator having no vested interest in the specific project involved. The grantee institution may utilize staff, consultants, or both to carry out the review. Any group responsible for review should possess not only specific scientific competence to comprehend the scientific content of the investigations reviewed, but also other competencies pertinent to the judgments that need to be made.

The grantee is required to make and keep written records of the group reviews and decisions on the use of human subjects and to obtain and keep documentary evidence of informed consent relating to investigations carried out with the assistance of PHS financial support.

B. Time of Review

While this policy requires that review be conducted prior to the use of human beings as subjects, there are advantages to both the PHS and the grantee in having the review conducted prior to application for PHS support. The PHS encourages the institution to do so, if the review can be accomplished without causing unreasonable delay in the application process and if the application is of a type that normally contains a reviewable scientific protocol.

IV. PROCEDURAL REVISIONS -- ASSURANCES OF APPLICANTS AND GRANTEES:

Upon issuance of this policy statement, the PHS will require necessary assurances from the grantee institutions which sponsor investigations involving human subjects, including clinical research. These assurances will cover both the general principles of safeguarding human rights and welfare in the conduct of research and the specific points of the Surgeon General's policy. The assurance should provide explicit information on the policy and procedure it employs for review and decision on the propriety of plans of research involving human subjects. The descriptions will include the competencies represented in the committees of associates utilized for review, the sources of consultants (if used), the administrative mechanisms by which surveillance is provided for projects involving human subjects -- particularly to deal with changes in protocol or emergent problems of investigations, the means of guidance and advice provided for investigators, and the manner in which the institution will assure itself that the advice of the committee of associates will be followed. Copies of documents of institutional policies on these issues should be attached to the memorandum of assurance. An example of an acceptable assurance is attached.

Assurances can be provided which apply only to individual major components of universities or other large institutions in those instances where assurances covering the total institution are impracticable or inadvisable.

Each assurance and its attachments shall be transmitted to the Public Health Service, in care of the Chief, Division of Research Grants. When the Public Health Service has reviewed and accepted the assurance, the Chief, Division of Research Grants, shall so notify both the responsible official of the grantee institution involved and all Public Health Service extramural research program offices.

Each grantee institution shall report currently any changes in its policies, its procedures, or the competencies represented on its committee of associates.

... each application that includes or is likely to include investigations involving human subjects, including clinical research, the applicant institution should make reference to the certification as follows:

"The investigations encompassed by this application have been or will be approved by the committee of associates of the [illegible] grantee(s) in accordance with this institution's [illegible] on clinical research dated _____."

Until an institution-wide assurance has been accepted by the PHS, the institution can fulfill requirements of this policy for individual studies by submitting an assurance with each application for PHS financial support, stating that prior to inception of investigations, the requirements of section III. A. of this Policy and Procedure Order will be followed. The statement must also describe the composition of the group which will conduct the review.

This interim procedure will be acceptable until November 1, 1966. After that date no new, supplemental, renewal, or continuation application for a Public Health Service grant or award to support investigations involving human subjects will be accepted for review unless the PHS has approved an institution-wide assurance.

Nothing in the institution-wide assurance or in the interim policy procedure used in some cases until November 1, 1966, should inhibit PHS staff, advisory groups, or consultants (1) from identifying concern for the welfare of human subjects, and communicating this concern to the grantee institution, or (2) from recommending disapproval of the application if the gravity of the hazards and risks so indicate.

In the case of awards to U.S. citizens receiving fellowships for training abroad, special conditions or circumstances relating to the place at which the training is being provided may upon occasion justify modification of these requirements. Requests from the sponsor for approval of such modifications must be reviewed by the Office of International Research, NIH, and approved by the PHS bureau chief concerned.

Attachment

ORIGINATING OFFICE: Office of the Surgeon General, PHS

APPROVED BY: Grants Policy Officer, OSG

Ernestine Allen

Date: July 1, 1966

Index: Clinical Research
Human Subjects, Investigations Involving
Individual , Rights and Welfare of

1032480

ple of an Acceptable Assurance

Institutional Assurance on

Investigations Involving Human Subjects,

Including Clinical Research

The (name of institution) agrees with the principles of the Public Health Service policy (identified as Policy and Procedure Order 129 dated July 1, 1966) with regard to investigations involving human subjects, including clinical research. This institution agrees that review independent of the investigator is necessary to safeguard the rights and welfare of human subjects of research investigations and assures the Public Health Service that it will establish and maintain advisory groups competent to review plans of investigation involving human subjects, prior to initiation of investigations, to insure adequate safeguard. Group reviews and decisions will be carried out in reference to (1) the rights and welfare of the individuals involved, (2) the appropriateness of the methods used to obtain informed consent, and (3) the risks and potential medical benefits of the investigations.

The institution also agrees to exercise surveillance of PHS-supported projects using human subjects for changes in protocol which may alter the investigational situation with regard to the criteria cited above. The institution further assures the Public Health Service that it will provide advice and consultation to investigators on matters of employing human subjects in investigation, and also that it will provide whatever professional attention or facilities may be required to safeguard the rights and welfare of human subjects involved in investigation. Records of group review and decision on the use of human subjects and of informed consent will be developed and kept by the institution.

Attached as part of this statement are copies of policy and procedure of this institution with regard to use of human subjects in investigation, as well as a description of the groups utilized to review projects for enforcement of these policies and the manner in which the institution will assure itself that the advice of the committee of associates is followed.

Signature: _____

Title: _____

Date: _____

Attachments

1032481

The attached statement of Public Health Service policy and procedure, identified as PPO #129, Revised, July 1, 1966, requires that each institution receiving support from the Public Health Service for projects that include the investigation of human subjects send to us, and have approved, an institution-wide statement of assurance concerning investigations that involve human subjects.

We shall accordingly need for your institution an institutional statement of agreement which covers in substance the points of the sample statement attached to the Public Health Service policy issuance of July 1, 1966 (#129), and which bears the signature of the official authorized to sign for the institution.

We shall also need as attachments to this statement a description of the following:

1. The requirements at your institution for the following --

   a. Group review and decision on the adequacy of provisions for protecting the rights and welfare of the subjects, on the appropriateness of the methods used to secure the informed consent of the subjects, and on the risks and potential medical benefits of the investigation (please see section III A on page 2 and section IV on page 3)

   b. Bringing to the attention of the committee of associates changes in investigative protocol, which may affect the subjects, before such changes are made, and emergent problems of investigation, which may affect the subjects, when such problems occur

   c. Conveying the advice of the committee of associates to the investigator concerned

   d. Assuring the institution that the investigator follows the advice of the committee of associates (please see section IV on page 3)

2. The competencies represented in the committee of associates (please see section III A on page 2 and section IV on page 3)

3. The sources of consultants, if employed (please see section IV on page 3)

4. Provision of facilities and professional attention necessary for the health and safety of the subjects (please see section III A on page 2)

1032482

Attachment 1

[illegible] LIST OF REVIEW OF ASSURANCE
ACCEPTABLE AND UNACCEPTABLE [illegible]

PLEASE INITIAL AT RIGHT OF EACH INSTRUCTION YOU WISH TO GIVE

[illegible]	[illegible]	
[illegible]	Accept, provided no medical or surgical procedures	
	To not review because:	
[illegible]	Human subjects not involved	
	Involves no risks or stress or welfare of subjects	
	Institution not responsible or responsible for [illegible]	
	[illegible] of assurance	
	[illegible] of surgical procedure [illegible]	
	[illegible] additional information about:	
	Requirements of the institution for group review and decision on re:	
R/A	All three below	
R/A1	The adequacy of provisions for protecting the rights and welfare of the subjects	
R/A2	The appropriateness of the methods used to secure the informed consent of the subjects	
R/A3	The risks and potential medical benefits of the investigation	
	Requirements of the institution for re:	
	All three below (surveillance)	
B/1	Bringing to the attention of the committee of associates changes in investigative protocol, which may affect the subjects, before such changes are made, and emergent problems of investigation, which may affect the subjects, when such problems occur	
B/2	Conveying the advice of the committee of associates to investigator	
B/3	Assuring the institution that the investigator follows the advice of the committee of associates	
B/4	Competencies represented in the committee of associates	
B/5	Sources of consultance, if employed	
B/6	Provision of facilities and professional attention necessary for the health and safety of the subjects	
B/7	The applicability of the statement (to whole institution? to which components? etc. -- see comments below)	

6 - comments on reverse side.

1032483

5. The applicability of your statement, i.e., whether to the institution as a whole or to a specified component of the institution (please see section IV on page 3)

Your early reply will help us hasten the review.

1032484

File Copy

THE POLICY OF VANDERBILT UNIVERSITY ON INVESTIGATIONS INVOLVING HUMAN SUBJECTS

In accordance with the recent directive of the Surgeon General of the United States Public Health Service, Vanderbilt University has taken steps to clarify and consolidate its policies regarding investigations on human subjects. The elements of these policies are as follows:

1. For all investigations involving human subjects, prior review and endorsement by an independent committee of peers is required.
2. Prior informed consent shall be obtained from the participating subjects.

To implement these policies, the University has appointed a Committee on Clinical Investigation which will provide prior review and continuing surveillance on all clinical investigations involving human subjects, regardless of the source of support. Before such projects are undertaken, a written proposal must be submitted to the Committee on Clinical Investigation; if changes in experimental approach are made in the course of the project, the investigator will seek prior approval of the Committee on Clinical Investigation.

It is understood that the investigator will take diligent steps to inform the subject of his legal guardian (or both) of the nature and possible risks of the procedure. Documentation of the informed consent will be kept in accordance with the procedures approved by the Committee on Clinical Investigation.

These policies are designed to underscore the institution's attention to the inherent dignity and rights of man within a climate of intellectual vigor and scientific excellence.

Rob Roy Purdy
Senior Vice Chancellor
Vanderbilt University

R. Batson

Randolph Batson, M.D.
Director of Medical Affairs, [redacted]
School of Medicine

1032485

CLINICAL INVESTIGATION PROPOSAL

Date: _____

TITLE: _____

Principal Investigator or Project Director: _____

Grant No: _____ Period Requested: _____

Type of Grant: Research [ ]; Training [ ]; Other: _____

New [ ]; Competing Renewal [ ]; Continuation [ ]

For continuation grants, under Section A, B and C, indicate only changes in procedures involving human subjects.

A. List type(s) of subjects to be studied:

Below each group of patients or volunteers, indicate the investigational procedures to be carried out on that group (see example attached).

1032486

INFORMED CONSENT

D. The consent form which is approved for inclusion in the Medical Records of patients in Vanderbilt University Hospital is attached. If this consent form is not to be used in all of the proposed studies, an explanation of the methods to be used in obtaining informed consent must be included on a separate sheet headed METHOD FOR OBTAINING AND DOCUMENTING INFORMED CONSENT.

E. 1. Radioisotopes will be adminstered to human volunteers:

Yes/ / No / /

2. If "Investigational New Drugs" are to be administered to human volunteers, a copy of the appropriate F.D.A. application accompanies this proposal if this has been filed.

If investigational drugs not so covered are used in the study, a copy of the appropriate F.D.A. application will be submitted to the Committee on Clinical Investigation prior to use of such agent.

3. Written evidence of informed consent will be obtained in all investigations involving human subjects.

4. If changes in the experimental approach are to be made in the future I will seek prior approval of the Committee on Clinical Investigation in writing.

_____

Principal Investigator

or

Program Director

1032487

EXAMPLE OF INFORMATION NEEDED IN SECTION A

A. List type(s) of subjects to be studied. Below each group of patients or volunteers, list the investigational procedures to be carried out in that group:

1. Adult Patients with Paroxysmal Nocturnal Hemoglobinuria.
   a. Therapy with androgen, vitamin E, transfusion and/or iron.
   b. Blood, urine and stool collections.
   c. Bone marrow examination.
   d. Ferrokinetic studies.
2. Normal Adult Volunteers. (Medical Center Personnel)
   a. Blood collections.
3. Volunteer Investigators.
   a. Blood collections.
   b. Ferrokinetic studies.
4. Adult Patients with Other Hematologic Diseases. (Patient Controls)
   a. Blood collections.
5. Prisoner Volunteers.
   a. Ferrokinetic studies.
   b. Blood collections.
6. Volunteers in Pediatric Age Group.
   a. Blood collections.

1032488

B. The intra-University transmittal form which accompanies each USPHS grant proposal contains the following statement which is signed by the Department Chairman:

"In studies involving human subjects, the rights and welfare of the individuals and the risks and potential medical benefits have been reviewed. No new studies or changes in the present protocol will be undertaken in human subjects without prior approval of the Vanderbilt Committee on Clinical Investigation."

1032489

Procedures for the Implementation of Vanderbilt's Policy on Investigations Involving Human Subjects

I. The preceding attached statement of Vanderbilt's Policy on Investigations involving Human Subjects will be sent to all faculty members of the School of Medicine and to all Deans and Departmental Chairmen in the University following the acceptance of this policy by the United States Public Health Service.

II. Vanderbilt University Committee on Clinical Investigation:

The following are the academic positions of the members of the Vanderbilt University Committee on Clinical Investigation:

Chairman of the Committee:

Associate Professor of Medicine and Pharmacology (Clinical Pharmacology)

Secretary of the Committee:

Director, Office for Sponsored Research (School of Medicine)

Associate Professor of Psychology

Associate Professor of Medicine (Staff of the Thayer Veterans Administration Hospital)

Assistant Professor of Pediatrics (Cardiovascular Research)

Associate Professor of Surgery

Associate Professor of Medicine and Radiology

Associate Professor of Physiology

Professor of Pharmacology (Psychopharmacology Research, associated with Central State Psychiatric Hospital)

Associate Professor of Medicine (Antibiotic and Infectious Disease Research)

Professor of Medicine (Staff of Nashville General Hospital)

Professor of Philosophy (Research in Medical Ethics)

Where required, consultations are requested by the Committee from individuals who can contribute special knowledge regarding the scientific merit and the risks of proposed investigations.

1032490

VANDERBILT UNIVERSITY MEDICAL CENTER

Consent for Clinical Research Study

TITLE OF PROJECT: _____

PROJECT DIRECTOR: _____ Date _____

This is to certify that I _____ hereby agree to participate as a volunteer in a program of investigation under the supervision of Dr. _____.

The studies have been defined and fully explained by Dr. _____ _____ and I understand that the studies will involve the following special procedures:

_____

_____

_____

_____

_____

_____

_____

_____ _____
Volunteer's Signature (or parent or guardian) Date

I, the undersigned, have defined and fully explained the studies involved to the above volunteer.

_____ _____
Investigator's Signature Date

1032491

III. Relation of Other Committees to the Committee on Clinical Investigation:

Radioisotope Committee: The Radioisotope Committee provides prior review and approval of all projects in which radioisotopes are used in human subjects. For such projects, therefore, approval of both committees is required, and the administrative mechanism for review of projects by the Vanderbilt Committee on Clinical Investigation automatically brings these investigations before the Radioisotope Committee. One member of the Radioisotope Committee is also a member of the Committee on Clinical Investigation. The Radioisotope Committee is assisted in its functions by a full-time Radiation Safety Officer, Dr. Sam H. Lott.

Advisory Committee to the Clinical Research Center: A considerable proportion of the clinical research at Vanderbilt University Hospital is conducted on the 21-bed multi-categorical Clinical Research Center. From its inception, the Advisory Committee of the Clinical Research Center has provided prior review of projects carried out on the Center, and has considered the scientific merits of the projects and the risks and rights of the subjects involved as integral parts of the process of review and approval. An attending physician makes rounds on all patients on the multi-categorical center three times weekly; during the time that he is attending on the Center, he is an ex-officio member of the Advisory Committee and thereby keeps the committee in touch with the day-to-day operation of the Center and the conduct of projects thereon. One member of the Clinical Research Center Advisory Committee is also a member of the University Committee on Clinical Investigation.

Sub-committee on Non-medical Projects in the University: To assist and consult with the Committee on Clinical Investigation in the review of University projects arising outside of the medical school which are primarily in the areas of psychology, sociology and engineering, a sub-committee composed of two psychologists, one sociologist, one engineer and one philosopher has been appointed. This group reviews and comments on these projects before they are submitted to the Committee on Clinical Investigation for final review and approval.

Committees in Vanderbilt Affiliated Hospitals: A Committee on Clinical Investigation has been in operation for some time at the Veterans Administration Hospital. This committee provides prior review on studies involving human subjects within that hospital. One member of the Veterans Administration Hospital committee is also a member of the Vanderbilt Committee on Clinical Investigation. A similar committee has been established at the Central State Psychiatric Hospital and one of the members of this committee is also a member of the Vanderbilt Committee on Clinical Investigation. These committees in Vanderbilt-affiliated Hospitals provide prior review and surveillance of projects in their respective institutions and cooperate with the University Committee on Clinical Investigation in these activities. Their review mechanisms do not, however, substitute for those of the University Committee.

1032492

IV. Procedures for Review and Approval of Projects by the Committee:

A. All investigations involving human subjects must be reviewed and approved by the Committee prior to initiation. Proposals are submitted to the Secretary, Committee on Clinical Investigation, Office of the Director of Medical Affairs. Applications must be favorably recommended by the Committee before submission to granting agencies.

B. Method of Review: The Clinical Investigation proposal form which is employed for all project proposals to the Committee on Clinical Investigation is attached. These proposals with the requested supporting information are reviewed by the members of the Committee individually prior to the Committee meeting, and considered by the Committee in session. For all projects where the Committee may wish further information, the investigator is interviewed personally by the Committee in session. In each project review, the risks are weighed and the precautions of the investigator to prevent risk are reviewed. The potential of the investigation to produce medical benefits and to advance scientific knowledge are considered, and recommendations regarding improvement in the experimental design may be made to the investigator.

In projects where the risk and indications vary considerably depending upon the condition of the patient, a condition for the approval of the project is that the departmental chairmen accept the responsibility for insuring appropriate independent consultation on the individual patients prior to the investigation.

For all projects involving the use of investigational drugs, the proposals to the Food and Drug Administration for investigating or sponsoring these agents are reviewed.

At the end of the Clinical Investigation proposal, the investigator signs a statement which reiterates his compliance with the University's policy that "If changes in the experimental approach are to be made in the future, I will seek prior approval of the Committee on Clinical Investigation in writing."

C. Methods for obtaining and documenting informed consent: For all projects, the methods for obtaining and documenting informed consent will be reviewed by the Committee on Clinical Investigation. Only those which are in accord with the policies of the University and the United States Public Health Service will be approved.

V. Role of the Department Chairmen in the School of Medicine in the Implementation of the Policy.

A. The executive faculty of the Vanderbilt University School of Medicine (which includes the Chairmen of all Departments in the Medical School) has unanimously approved the Vanderbilt policy on investigations involving human subjects, and affirmed the departmental chairman's responsibility for the implementation of this policy by the members of their department.

File Copy

ORM P-8A

MEMORANDUM

TO Dr. Kaiseley

DATE December 20, 1966

SUBJECT Human Experimentation

COPIES TO Dr. Edwards

I am enclosing copy of Dr. Dunham's letter with attachments about clinical research and investigation involving human subjects. We will need to get something together on this before the next BioMedical Directors' Meeting -- which is February 13-14, 1967.

Gould A. Andrews

pe

1032494

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON, D.C. 20545

December 14, 1966

Dr. Gould Andrews
Director, Medical Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37831

Dear Dr. Andrews:

Following the lead of the Surgeon General in instituting a code of ethics for human experimentation, it seems appropriate that we in the Atomic Energy Commission assure ourselves that our own house is in order. I should, therefore, like to propose that we consider at our next Program Directors' meeting procedures that each of you are following at your respective institutions and compare them with Public Health Service requirements.

Enclosed is a copy of the Surgeon General's statement as well as the check list which Public Health Service staff uses to evaluate the institution's compliance.

Sincerely yours,

C. L. Dunham

C. L. Dunham, M.D., Director
Division of Biology and Medicine

Enclosure:
As stated above

1032495

OPTIONAL FORM NO. 10
MAY 1962 EDITION
GSA GEN. REG. NO. 27

5010-107

UNITED STATES GOVERNMENT

Memorandum

TO : Dr. Charles L. Dunham, Director
Division of Biology and Medicine

DATE: MAY 13 1966

FROM : Bertram H. Schur
Associate General Counsel

SUBJECT: USE OF HUMAN VOLUNTEERS IN BIOMEDICAL RESEARCH

This is in reference to a proposed memorandum to bring to the attention of the General Manager the contemplated new AEC biomedical research project involving the use of human volunteers. As we understand it, convicts, college students, and other individuals, twenty one years of age or older, will be invited to volunteer, and monetary consideration will be paid for their services. These individuals will ingest or be injected with promethium-147 or plutonium-237. This program will be conducted for AEC by the Hanford Occupational Health Foundation. You have asked for our views.

From the legal standpoint, there are two areas of potential risk which should be considered in the use of human volunteers in experiments:

1. Risk of adverse effects from the radiation experiments properly carried out; for example, the risk that the intended dosage of 0.1 roentgens might cause some pathological condition in certain individuals.

2. Risk of injury from negligent conduct in the course of the experiment; for example, the risk that an experimenter might be negligent in the operation of the radiation source and give dosage of 1.0 rather than 0.1 roentgens causing injury to the volunteer.

It is our opinion that each volunteer should sign a written, witnessed agreement in which he or she states that he or she is in sound mental and physical condition and is participating in the experiment on his or her own volition, that he or she understands that what is being done is for experimental purposes and not for the treatment or diagnosis of the individual, and that he or she understands the nature, procedures, and probable effects of the experiment. In addition, the agreement should set forth the nature and purpose of the experiment, the procedure to be used (including a description of the individual volunteer's participation or use in the experiment), the known possible risks, if any, and the arrangements, if necessary, for possible termination of the experiment or research (e.g. if the volunteer later desires to withdraw from the experiment). It would be advisable if the agreement also negated any inference that the paid volunteers are employees of the contractor for purposes of the experiment. The agreement should be signed only after the volunteer has had an

0324qb

Buy U.S. Savings Bonds Regularly on the Payroll Savings Plan

opportunity to ask questions. Assuming complete understanding and no unequal bargaining factors (e.g. pressure on prisoners to submit), such an agreement would protect against liability for unauthorized invasion of the person.

The consent form may also contain language absolving the contractor and the AEC from responsibility for injuries to a volunteer resulting from the experiment. This would probably be binding on the volunteer if no negligence occurs. It is doubtful, however, that the clause can be so drawn as to be binding on the volunteer if negligence causes the injury. Not only is the law uncertain on this point, but we cannot be sure as to what law will apply. (Developments in the field of conflicts of law have been such that it is not clear whether the law of the State of Washington would be applied in every case; for example, a volunteer residing in some other state when his injury first becomes apparent might contend that that other state has the most significant contacts with the claim and that its law should be applied.)

Whether or not language absolving the contractor and the AEC from liability - either with or without mentioning negligence - should be incorporated in the consent form is a matter of policy. It may well be that the Commission would prefer not to attempt to add any special provisions designed to eliminate or minimize possible liability. In this regard, it should be borne in mind that the consent agreement itself, without specially added language, would probably be considered as tantamount to a disclaimer of liability for injuries resulting from the experiment properly carried out - that is, where no negligence occurs.

We understand that the contractor has no special view with respect to the obtainment of any special disclaimer agreements, and, also, that liability insurance is available at a reasonable premium; presumably, the contractor and RLOO are exploring the advisability of obtaining such insurance.

cc: Chester G. Brinck, RLOO
Dr. Wm. T. Doran, Jr., OS

1032497

Report of Meeting to Consider Establishment of Committee on Human Use

April 6, 1967

Present: Dr. Robert Heyssel, Dr. Robert Lange, Dr. Lowell Edwards, and Dr. Gould Andrews

A meeting was held at the Medical Division on April 6, 1967, to discuss the establishment of a committee on clinical investigation which would serve to advise and monitor the Medical Division program in relation to the ethics of research in human beings and the suitability, from this viewpoint, of research going on at the Medical Division. It was pointed out that this committee would be a replacement for more informal arrangements that had previously existed in the Medical Division. The desire to have two outside consultants - Dr. Lange and Dr. Heyssel - had been stimulated by a suggestion from the Atomic Energy Commission which followed the meeting of their Advisory Committee in November, 1966. It had been pointed out by the Advisory Committee and the Commission that they did not wish to imply any criticism of our past practices, but that because of the widespread concern over ethics of human experimentation, and the possibility that some criticism, either valid or not, might arise, they believed it would be desirable to have some outside, disinterested consultants who were familiar with what we were doing, and who had passed on each individual research proposal.

Corrected Draft

A rather general discussion was held. We considered at some length the function of the committee. It was our opinion that the committee would serve to review research proposals and decide whether or not they were justifiable from the viewpoint of any risk that might be involved in studies done on human

Medical Division wanted some consultation on the suitability of a study in an individual patient it might be quite reasonable to seek telephone discussion on this.

Scope of the Committee's Work:

It was decided that the committee should concern itself with all studies done in human beings, whether these subjects are patients in the research hospital or normal volunteers of some type.

Approval of the Previously Prepared ORAU Medical Division Document on Human Volunteers and the Function of the ORAU Isotopes Committee:

Dr. Lange and Dr. Heyssel are in agreement with the document as presented. It was pointed out by Dr. Heyssel that there are certainly some risks in using employees, and that careful protection should be given to employees used as research subjects. Students are quite unsuitable for most research procedures unless the risk is nil since they are not really free to refuse to participate. Dr. Heyssel has serious reservations about using prisoners in research because here too it is very difficult to establish a situation which is free of any suggestion of coercion.

Future Meetings:

It was decided that we would try to have another meeting, perhaps in May or June, and begin to review research proposals. We decided that we should eventually review all of the significant human research at the Medical Division, including those projects that are already under way, with highest priority to review of any studies that might be of questionable suitability or subject to criticism.

Gould Andrews
Acting Secretary

1032499

If approved by the chairman of the Medical Division, or considered worthy of serious consideration by the Committee on Human Studies, copies will be sent to Dr. Lange, Dr. Heyssel, and other members of the committee previous to the meeting of the committee. At the time of the meeting, further questions may be asked of the investigator and then the committee will either approve or disapprove the research proposal.

What is to be Considered by the Committee?

The committee is to review all research at the ORAU Medical Division involving human patients in which there is believed to be a significant risk to the patients or a significant possibility that criticism might be leveled at the scientists for their manner of doing studies in human beings. The decision about whether or not a specific investigative procedure involves any risk and therefore requires action by the committee would rest with the Medical Division. The Medical Division should bring to the committee's attention by name and brief description those experiments in human beings believed to have negligible risk, i.e., a systematic survey of hemoglobin and hematocrit values in thyroid patients. Considerable discussion was held about the suitability of undertaking a rather unconventional form of treatment in a single seriously ill patient, partly with the objective of immediate benefit to the patient and partly as a preliminary research effort that might be the basis for a future controlled investigation. Here the group felt that considerable leeway rests with the physician who is responsible for the patient's care. Ordinarily the Committee on Human Studies would not be involved with decisions concerning a single patient but rather with policy matters or research on groups of patients. However, if circumstances were such that the staff of the

1032500

have the approval of both of the outside consultants. In the event that one consultant objects to a research proposal, if there is otherwise considerable support for it, other consultation would be sought. It is our impression that in most instances the committee would be able to reach an essentially unanimous opinion on each research proposal.

Relation of the Committee on Human Studies to the Existing Radioisotope Committee at ORAU Medical Division

It was our opinion that the new committee would not replace the existing radioisotope committee. Proposed studies involving radioisotopes would need to be approved first by the ORAU Isotopes Committee and then by the Committee on Human Studies. Minor changes in research involving radioisotopes could be approved by the Isotopes Committee without further ratification by the Committee on Human Studies. Copies of the minutes of the Isotopes Committee will be sent to Dr. Lange and Dr. Heyssel.

Function of the Committee on Human Studies

The Committee on Human Studies would have meetings called by the chairman at whatever frequency seemed necessary - perhaps two or three times per year. Certain problems not requiring a full meeting of the committee could be handled by telephone communications, preferably by a three-way hook-up with Dr. Lange and Dr. Heyssel. New research proposals would be written up by the senior investigator. A form for this was developed, based upon the one used at the University of Tennessee in Knoxville with suitable modifications. After the form is filled out, the proposal will be evaluated by the administrative office of ORAU Medical Division.

1032501

beings. If no risk is involved, the committee would not make any effort to evaluate the research proposal from the point of view of its scientific value. However, if there are significant hazards, the committee would need to evaluate the scientific merit of the proposal and balance it against the possible risks.

Name of the Committee

We chose the title, "Committee on Human Studies."

a. Composition of the Committee

It was decided to have, in addition to Dr. Lange and Dr. Heyssel, three members of the Medical Division staff on the committee. These would probably include one Ph.D. and two M.D.s. Andrews would be one of the Medical Division members and Edwards would sit in on the meetings without being an active member of the committee. We discussed at some length the fact that the people from the Medical Division would probably be involved to some degree with any research that was under consideration, and decided that in spite of this possible problem the proposed composition of the committee would be satisfactory.

b. Officers of the Committee

The committee would need a chairman, who would probably be from the Medical Division, and a secretary who would be one of the consultants. Dr. Lange has agreed to serve as secretary for at least an initial period.

Decisions of the Committee

It was our concensus that the decisions of the committee would probably need to be unanimous to allow a research proposal to go forward, or at least to

Ruth, Please put a file
Gilardi
for V

Members of the Human Use Committee

March 14, 1967

Planned Study of Sodium-22 Retention in Normal Humans

File, Dr. Bergner

There will be a meeting of the Human Use Committee Friday, March 17, at 2:00 p.m. in Dr. Kniseley's office.

Agenda:
Consideration of proposal to use sodium-22 in human volunteers.

Ralph M. Kniseley

to:
Dr. Edwards
Dr. Lushbaugh
Dr. Kniseley
Mr. Cloutier
Dr. Hayes
Mr. Harmon ✓

1032503

File Cabt : see page 9 et seq.

FDA Responsibility in Radiopharmaceutical Research

Bryant L. Jones, M.D.
Division of Oncology and Radiopharmaceuticals
Office of New Drugs
Bureau of Medicine
Food and Drug Administration

Dear Cindy:
No need for me to comment. It's getting closer.
Dave

Gentlemen. It is certainly an honor to be with you today and to be included among the notable guest lecturers at this outstanding course in radioisotopes techniques and Nuclear Medicine. It was but a few brief months ago when I sat in open-mouthed wonder, as a member of class number 20, as CDR. Tom Mitchell spun his complex web of exponential equations and Dr. Van Hove held us intrigued with his multi-dot puzzles. My presence here today, however, is not to mystify, and I have not been asked to submit questions for your final examination. My purpose in accepting this invitation is to clarify some popular misconceptions about the Food and Drug Administration. To delineate its responsibilities and the relationships that exist between the medical profession, drug research, and government.

As an agency, the Food and Drug Administration has been in existence for more than sixty years, in fact, since June 30, 1906, when President Theodore Roosevelt signed the Federal Food and Drugs Act. There is no doubt that such a law was necessary to protect the health and welfare of the public. Most of you are aware of the story of Dr. Harvey

---

For presentation at 21st class in Radioisotope Techniques and Nuclear Medicine for Medical Officers, U.S. Naval Medical School, National Naval Medical Center, Bethesda, Maryland, May 18, 1967.

1032504

Washington Wiley and his volunteer "poison squad" who proved the lethal qualities of boric acid which was generally used as a commercial food preservative. Perhaps you may have read Upton Sinclair's book, THE JUNGLE, which exposed the unscrupulous practices of the meat packing industry. In those days one couldn't be too sure whether one's breakfast sausage was made of pork or mascerated rat carcasses. A less well known hazard was that of Mrs. Winslow's Soothing Syrup for teething babies. Its principle soothing ingredient was morphine. Coffee contained a share of adulterants in the form of oats, peas, beans, and barley corn to say nothing of chicory, brown bread, charcoal, red slate, bark, and date stones. To please the eye, it contained more colors than an artist's palate such as Sheele's green, iron oxide, yellow ochre, chrome yellow, burnt umber, Venetian red, Tumeric, and Prussian blue.

The early twentieth century was a lusty time in the nation's history and the tiny Bureau of Chemistry charged with the responsibility under the first Act with less than 50 people on the staff had very rough going. Indeed, the present Food and Drug Administration with nearly 5,000 employees and eighteen district offices scattered over the country is little more equipped for its monumental tasks and responsibilities.

The abuses were rampant but concern was expressed by only a few dedicated people, consumer protection groups, and legislators. Once again the power of the press and tragedy combined to arouse an apathetic public. In 1933, F. J. Schlink's book, 100,000,000 Guinea Pigs,

1032505

revealed the hidden horrors lurking in simple widely used commodities. About this time one entrepreneur used diethylene glycol (today's permanent automobile antifreeze) as a diluent for the new wonder drug sulfanilimide. This concoction took 107 lives, most of them children, and gave emotional impetus to drug safety aspect of the Food, Drug, and Cosmetic Act of 1938, the basic law under which we operate today.

More of course was needed. Beyond safety is effectiveness and reliability. You, as physicians, must be assured that not only is a drug "safe" within the limits of its approved use, but that it does what it is supposed to do as stated in the labeling. The principal label being the package insert. Once again it fell upon the few to overcome formidable opposition by industry and by many segments of the medical profession. Again tragedy lent emotional impetus and on the crest of the thalidomide catastrophy, the Kefauver-Harris Amendments of 1962 unanimously passed Congress in October of 1962.

But what is the FDA and what does it do? The FDA is a regulatory agency. It regulates all aspects of the pharmaceutical business from the gathering of raw material to the administration of the final product by a physician to a patient. Its primary responsibility is to insure that the final product is of the highest quality and that it is effective in the treatment of the disease for which it is prescribed. The Act, as we commonly refer to it, as it now is written states that a "New Drug" cannot be distributed interstate for use in man without approval by the Food and Drug Administration.

1032506

And what is a new drug? A new drug is one which is not generally recognized by qualified experts as being safe and effective for the use proposed. If there is any uncertainty about a new drug status, the FDA will furnish judgement on request.

One of the general misconceptions is that a drug is old because it has been around for a long time, or that it is innocuous because it is sold over the counter. Not so.

A drug may be "new" without necessarily being a new substance. For example, if aspirin tablets were labeled or promoted as a seasickness remedy, they would be considered a "new drug." Even an accepted remedy, used for years, if manufactured in a new form such as a timed-release capsule, is considered to be a new drug requiring evaluation by the FDA. Clinical investigation may be required to show that the active substance is released in a slow and sustained manner, and that the capsule is safe and effective as claimed.

In order to allow for clinical investigation, some means had to be provided whereby drugs could be evaluated for safety and efficacy, prior to the time of a New Drug Application approval. The Act provides an exemption from the regulations as long as certain criteria are met. It is this exemption which has created the furor in scientific circles. It is this provision of the Act which critics in industry and medicine use to charge the government with curtailing investigations and discouraging good people from entering the investigational new drug field. Experience has now proven otherwise.

1032507

There are now about 25,000 investigators on file and we can discern no drop in the quantity of published professional literature on new drugs. If anything, the quality of the scientific papers and the investigational programs is improved. Clinical investigation is now coming of age, it has a higher degree of sophistication with more actual protection for the physicians and for the sponsors when the regulations are observed. There is a degree of order and responsibility where only a minimum existed before. The simple fact of requiring a researcher to file an investigational plan or protocol showing a rational approach to his experimentation upon human patients which will be closely scrutinized by a body of disinterested experts gives pause for close self-examination of his proposals. But let us look at the requirements of the law in more detail.

Before a new drug may be tested on human beings, a sponsor -- which may be a pharmaceutical firm, a research institution, or a physician in private practice -- must supply to the Food and Drug Administration the information specified as a "Notice of Claimed Investigational Exemption for a New Drug," an IND or form 1571. This IND form is contained in the Investigational Drug Regulations and may be obtained upon request.

An IND requires the inclusion of a variety of information.

a. The complete identity and composition of a drug must be stated along with the source and sufficient manufacturing data to insure that appropriate standards are followed to insure safety.

1032508

b. An IND must contain all the information available to the sponsor derived from preclinical studies, including studies made on laboratory animals, and any clinical studies and experience with the drug from which the sponsor has concluded that it is reasonably safe to initiate clinical trial. Initially, the FDA is concerned with safety.

The FDA generally requires as a minimum: that acute toxicity be determined in two species of animals, that results of administration of the drug for two to four weeks be observed in at least two species, and that the route of administration be the same as that to be used in the human trial. Additional animal studies are usually necessary.

c. A description of the investigations to be undertaken must be included. This is the plan of study or protocol and it must state the numbers of patients to be studied and the duration of study.

d. The information regarding the training and experience of the investigators must be included. The investigators are required to submit to the sponsors completed forms FD 1572 for clinical pharmacology studies or form FD 1573 for clinical trial.

These two forms are similar and in essence require an investigator to state all details of his training and experience which qualify him to conduct the proposed investigations. The medical

or research facility where the investigations are to be conducted must be stated and any expert committees or panels responsible for approving the experimental project must be identified.

Accurate records for drug accountability must be maintained in addition to careful clinical records. These records must be kept for two years after termination of the investigation and made available upon request to the sponsor and to the FDA. The investigator must agree to submit regular reports at appropriate intervals not to exceed one year, and to report emergency or alarming reactions immediately. Investigators are also obliged under the law to obtain informed consent from patients or their legal representatives (unless in his professional judgement it would be contrary to the best interests of the patient).

An investigator must also certify that the investigational drug will be administered only to subjects under his personal supervision or under the supervision of specifically named investigators responsible to him.

e. Sponsors are in turn then obliged to transmit all the data generated by the investigators to the FDA. Emergency reports of severe unexpected untoward reactions to them must be promptly transmitted to the FDA and their progress reports made at regular intervals not to exceed one year.

At any time, a plan of investigation may be modified by submitting a supplement, new investigators may be added and old ones deleted. From this, one may readily see that the investigational drug program is a vigorous one requiring close cooperation between industry, government, and the medical profession at all stages.

Once an IND has been filed with the FDA, an investigator may proceed with his study. He need not wait for "approval" or any other type of sanction except in certain extenuating circumstances which I will mention in a moment. The FDA does reserve the right to terminate or otherwise halt any investigation at any time for certain stated causes which are listed as follows:

1) Evidence of significant hazard.
2) Convincing evidence that the drug is ineffective.
3) Submission of false data.
4) Omission of material information.
5) Unsatisfactory manufacturing practices.
6) Failure to conduct the investigation in accordance with the plan submitted by the sponsor.
7) Commercialization of the drug.
8) Failure to submit progress reports at intervals not exceeding one year.
9) Failure to report serious or potentially serious adverse reactions.
10) Failure to meet requirements for patient consent.

The special preclearance approval for clinical trial, which I mentioned previously, presently applies to:

a. Investigations of hallucinogenic drugs, such as LSD.

b. Investigations of drugs so toxic that their use may be justified only under special conditions, such as DMSO.

c. Reinstitution of drug investigations which had been terminated by the Commissioner.

A program can hardly be called restrictive which asks only that the government be informed of research activity as it is proposed and as it is conducted. It is a great protection to patients and physicians alike to have an interested agency alert to the dangers of drug research and ready and able to act.

At this point I could extend this discussion into other aspects of FDA work, particularily into the procedures of approving a New Drug Application, an NDA; of the special programs of antibiotic and insulin certification; and of the surveillance of New Drugs on the market, but I do not consider these areas germaine to the interests of this class at this time. Rather, in my remaining time, I would like to focus on the particular problems as they exist in the field of radiopharmaceuticals. Most of you may have heard that radiopharmaceuticals are exempt from the new drug regulations because they are under the province of the Atomic Energy Commission. That is not true. The responsibility for the investigational programs of radiopharmaceuticals rests with the FDA. However, by order of the Commissioner of Food and Drugs published

as 28 Federal Register 183, January 8, 1963, there is a provision as follows:

"That, ~ 130.3 (28 F.R. 179) shall not apply to radioactive drugs, until further notice, provided the radioactive new drugs for investigational use are being shipped in complete conformity with the regulations issued by the Atomic Energy Commission."

Aah ha! First you say it ain't and then you say it is. You're right. There is confusion and that brings me to the primary purpose of my discussion this afternoon.

The exemption to the "Exemption of New Drugs for Investigational Use" applies only to the investigational uses of radiopharmaceuticals and in particular only to those radiopharmaceuticals that are reactor produced. A manufacturer should have an approved NDA (New Drug Application) before commercial distribution is undertaken. This requirement is not being universally applied at the moment because under the AEC regulations a firm may sell radiopharmaceuticals while in the investigational stage, and firms hide behind this loophole. If the exemption were lifted tomorrow, many firms would not be able to supply radiopharmaceuticals even though they are on the AEC list of well-established isotopes and uses.

In the memorandum of understanding between the FDA and AEC only radiopharmaceuticals that are reactor produced are exempt. Cyclotron or linear accelerator produced radioactive nuclides are not exempt from the provisions of the New Drug Regulations.

Perhaps the most serious oversite not recognized by investigators (and I believe that I am safe in making this statement) is that every institution or facility operating under a broad license from the AEC, which is developing new procedures and clinical methods, is in violation of the new drug regulations because they are using new chemicals and compounds which are new drugs in their own right.

Let me give you an example. Technetium 99m sodium pertechnetate obtained by eluting a molybdenum 99 generator which was reactor-produced may be considered exempt from the New Drug Regulations as long as it is shipped and used in conformity with the AEC regulations. However, it may be reacted with hydrogen sulfide gas or rhenium in form of potassium perrhenate to form a sulfur or rhenium colloid which may be used for liver scanning. The sulfur colloid and the rhenium colloid are not exempt under the AEC regulations. These drugs are new drugs in their own right and any investigator using them should have an IND on file with the FDA or be a participating investigator covered by a properly sponsored and filed IND.

Recently I had the privilege of touring the Brookhaven National Laboratories. They very proudly reviewed the clinical usefulness of technetium as a scanning agent, and rightly so. But I counted seven, what shall I say, illegal or unauthorized procedures. Technetium sulfide colloid for liver, spleen, and bone marrow scanning. Technetium iron ascorbate and technetium thiocyanate. Technetium macroaggregate for lung scan and technetium serum albumin. These latter two products,

incidently, are under the control of the Division of Biologics Standards of the United States Public Health Service. The FDA regulations apply to biologicals but the DBS must license a company to sell them. The IND's are filed with and reviewed by this sister agency.

There are unending examples. Boron compounds, the same boron that Dr. Wiley was concerned with, are being administered to patients. There is some evidence that boron accumulates to a higher degree in gliomas than in normal brain tissue. When it is administered, the patient is subjected to a thermal neutron flux and any tissue containing boron is irridated by alfa particles. Boron is just as poisoness today as it was sixty years ago.

We at the FDA feel that radiopharmaceuticals should be handled in the same manner as are any other drugs and that the radiation only constitutes an additional hazard. We feel that there is no basic difference between reactor and accelerator produced nuclides and that it is confusing to have different sets of rules and regulations and responsible agencies. We feel that the hazards of pharmacological research cannot be ignored because of concern for the radiation hazard. We look forward to the further notice in the Federal Register which will remove reactor produced radiopharmaceuticals from the exemption of the New Drug Regulations. We look forward to a vigorous participation in pharmaceutical research where government, industry, and the medical profession can utilize the sparkling atom for the benefit of mankind.

1032515

File Mr. Harmon

A meeting of the Human Use Committee of the Oak Ridge Institute of Nuclear Studies met on 15 September 1967.

The following members were present: Robert Heyssel, K. C. Goh, Gould Andrews, Lowell Edwards, Edward Balish, and Robert D. Lange.

The following new proposals and recommended actions were discussed:

1. Immunotherapy of Acute Leukemia.

This project invoked a great deal of discussion about possible risks to the recipient of irradiated malignant cells. The members of committee approved the plans for at least a few more studies since the risks are most certainly minimal, but recommended that possible other methods for obtaining specifically sensitized malignant cells be explored.

Dr. R. L. Hayes was present for the discussion of the following two projects.

2. Clinical Trial of $^{113}In^{m}$ as a Kidney and Bone Scanning Agent.

After discussion, the proposal was approved after appropriate clearances have been made.

3. Clinical Trial of ^{68}Ga-Labeled Hydrous Ferric Oxide Colloid for Bone Marrow Scanning.

After discussion, the proposal was approved after appropriate clearances have been made.

The following on-going studies were presented and discussed:

1. Marrow Grafting following Total Body Irradiation.

2. Use of Small Tracer Doses of Rare Elements in Human Volunteers.

3. Use of Radiolodine in Surgical Removal of Thyroid Cancers.

The continuation of these three programs was approved.

Submitted by

Robert D. Lange, M. D.

RDL:bt

1032516

Medical Division

Oak Ridge Associated Universities

HUMAN USE COMMITTEE

I. Committee's Mission

To receive, evaluate, approve, and monitor proposals for new uses of radioisotopes in human beings. This committee will replace the earlier, less formal, arrangement that has been operating.

II. Committee Membership

The committee, appointed by the Division Chairman, consists of Dr. Edwards, Dr. Lushbaugh, Mr. Cloutier, Dr. Kniseley, Dr. Hayes, and Mr. Harmon - ex officio. A member of the Health Physics group - Mr. Cloutier or his delegate - must be present or represented by his document. Of the other four voting members, at least three persons should be present, one of whom may be replaced by the Division Chairman. Changes in the committee membership will be made as required by the Division Chairman.

III. Protocol for a Proposal for a New Use

A. A written proposal should be submitted in advance of any meeting for study by each committee member.
B. The following outline should be used:
    1. Question that the research might answer
    2. Radioisotope
    3. Chemical form
    4. Route of administration
    5. Proposed dosage (chemical and radioisotopic)
    6. Experimental protocol:
        a. Number and selection of subjects
        b. Duration of studies
        c. Types and frequency of assays
C. To make an evaluation of the proposal, the following information must accompany it.
    1. Animal distribution data and calculation of radiation dose to whole body and critical organs
    2. Related and pertinent human data
    3. Appraisal of chemical radiation and infectious hazards

IV. Guidelines for Dosage and Selection of Subjects

A. Each proposal will be evaluated for radiation dose in light of NCRP Handbook 69 guidelines.
B. Recruitment of volunteers must fall within policies established in the Division.

V. Approval of protocol will consist of a concise written summary of its extent signed by the participating members, and will reflect complete committee concurrence.

Corrected draft approved by members September, 1966

1032517

OAK RIDGE ASSOCIATED UNIVERSITIES
Oak Ridge, Tennessee

Patient Admittance Agreement

The Oak Ridge Institute of Nuclear Studies (ORINS) Medical Research Hospital is operated by Oak Ridge Associated Universities (ORAU) for the U. S. Atomic Energy Commission (AEC) for the conduct of certain clinical research programs. These programs are mainly in areas allied to the application of radiation and radioisotopes to medicine and other health sciences.

I understand that I have been accepted as a patient for admission to the hospital, or as an outpatient, because my physical condition has been determined by the hospital staff to make me a suitable patient for a currently active clinical research project.

I further understand that while a patient at the research hospital examinations, treatments, and tests may be prescribed which are experimental in nature and I hereby consent to such examinations, treatments, or tests. Notwithstanding the above, I reserve the right to a full explanation of any such proposed examination, test, or treatment and the right to withdraw my consent. I further reserve the right to withdraw completely should I find that I am unable to continue.

I further understand that I can remain in the research hospital only so long as I am needed for research purposes, and that I must be discharged when my participation in a study is completed and when, in the opinion of the hospital staff, my medical condition permits. In such event, I understand that ORAU, its officers, employees, and agents, cannot assume responsibility for any continued medical care.

The above statements have been explained to me by the member of the Medical Division staff named below. I understand and accept the statements.

I have not been influenced in making this agreement by any representations or statements regarding improvement in my physical condition or the probable results of any treatments received, but instead expressly assume all risks incident to my hospitalization, care, and treatment.

Patient's signature	Medical Division staff member's signature
Parent or guardian's signature	Date

1032518

OAK RIDGE ASSOCIATED UNIVERSITIES
Oak Ridge, Tennessee

Summary Sheet

Name _____ Hospital Number _____

Diagnoses	Code

Operations	Date	Code

Radiation Therapy (Type, Dose, Site, Date)

_____

_____

_____

Radioisotopes (Nuclide, Compound, Dose, Route, Date)

_____

_____

_____

_____

Date of Admission _____ Return Date _____

Date of Discharge _____ Outpatient ☐ Inpatient ☐

Hospital Days _____

Death Date _____ _____

Physician

Autopsy: ORINS ☐ No ☐

Elsewhere _____ _____

Chief, Clinical Services

Admission Number ☐

1032519

SUMMARY SHEET MED-23(2-67)

OAK RIDGE ASSOCIATED UNIVERSITIES
Oak Ridge, Tennessee

Consent to Experimental Treatment

I authorize the performance upon _____
(myself or name of patient)
of the following treatment: _____

_____

_____
(State nature of treatment)

The nature and purpose of the treatment, possible alternative methods of treatment, the risks involved, and the possibilities of complications have been explained to me. I understand that this treatment is not the usual treatment for my disorder and is therefore experimental and remains unproven by medical experience so that the consequences may be unpredictable.

DATE: _____ _____
(Patient or person authorized to consent for patient)

WITNESS: _____

_____

I have talked with _____ about
Name
the proposed course of treatment to be given _____
Name
including the following:* _____

_____

_____ _____
Physician Date

*Physician should indicate experimental drugs, radioisotopes, radiation therapy, and/or possible placebo or sham therapy.

1032520

OAK RIDGE ASSOCIATED UNIVERSITIES

Oak Ridge, Tennessee

Authorization for the Administration of Radioactive Substance

I hereby authorize the staff of the ORINS Medical Division to administer to _____ the following radioactive substance _____ (Nuclide) _____ (Chemical)

_____ (Dose) _____ (Route of administration).

The purpose of this procedure has been explained to me as being:

_____

_____

_____

Its relevance to my condition, the risks and any possible alternatives have been explained to me.

_____
Name of patient

_____
Date

1032521

AUTHORIZATION FOR THE ADMINISTRATION OF RADIOACTIVE SUBSTANCE MED-148(2-67)

OAK RIDGE ASSOCIATED UNIVERSITIES
Oak Ridge, Tennessee

Consent to Operation

PATIENT _____ AGE _____

DATE _____ TIME _____ A.M. / P.M. PLACE _____

1. I hereby authorize the medical staff of the ORINS Medical Division, or such physician as they may designate, to perform upon _____ (state name of patient or myself) the following operation: _____

_____.

If in the course of the operation any unforeseen condition arises calling for procedures in addition to or different from those now authorized, I further request and authorize him to do whatever he deems advisable.

2. The nature and purpose of the operation, possible alternative methods of treatment, the risks involved, and the possibility of complications have been fully explained to me, I acknowledge that no guarantee or assurance has been made as to the results that may be obtained.

3. I consent to the administration of anesthesia by or under the direction of a staff member of the ORINS Medical Division or such other qualified person as he may designate. I further consent to the use of such anesthetics as he may deem advisable with the exception of _____ (if none, so state).

4. I consent to the disposal by authorities of the ORINS Medical Division of any tissues or parts which may be removed.

5. I consent to the taking and publication of any photographs in the course of this operation for the purpose of advancing medical education and science.

6. For the purpose of advancing medical education and science, I also consent to the admittance of observers to the operating room.

I CERTIFY THAT I HAVE READ AND FULLY UNDERSTAND THE FOREGOING CONSENT TO OPERATION, THAT THE EXPLANATIONS THEREIN REFERRED TO WERE MADE, AND THAT ALL BLANKS OR STATEMENTS REQUIRING INSERTION OR COMPLETION WERE FILLED IN AND INAPPLICABLE PARAGRAPHS, IF ANY, WERE STRICKEN BEFORE I SIGNED.

Signature of Patient _____

Signature of Patient's Spouse _____

When the patient is a minor or incompetent to give consent:

Signature of person authorized to give consent _____

Relationship to Patient _____

WITNESS: _____

1032522

I have talked with _____
(patient's name or person consenting)
about the contemplated operation and have explained the risk involved.*

Remarks: _____

_____

_____

_____
Physician

_____
Date

*If sterilty, blindness, or loss of hearing is a possibility, please describe briefly the explanation given to the patient.

1032523

OAK RIDGE ASSOCIATED UNIVERSITIES
Oak Ridge, Tennessee

Request for Autopsy

NAME OF DECEASED _____ Age ____ Hosp. No. _____

MARITAL STATUS OF DECEASED IS: (Circle word that applies)

SINGLE MARRIED WIDOWED SEPARATED (But not divorced) DIVORCED

TIME OF DEATH _____
Month Day Year Hour

1. I hereby certify that I assume custody of the body of the above-designated deceased for purpose of burial, and assume responsibilities connected therewith.

2. I hereby authorize the Pathologist of the Oak Ridge Institute of Nuclear Studies, an operating unit of Oak Ridge Associated Universities, and such person or persons as he may designate, to perform an autopsy on the body of my _____
(State relationship of deceased to signer.)

I authorize him, too, to have present at that autopsy such persons as he may deem proper.

3. The autopsy here authorized may be either a complete or partial autopsy. Such organs and tissues may be removed as the physician performing the autopsy considers necessary for study subsequent to the autopsy, to accomplish the purposes of the autopsy, to eliminate undesirable radioactivity, or for therapeutic purposes. The tissues removed may be retained or disposed of after examination. (If the nature and extent of this autopsy or the right to remove parts of the body are to be limited in any way, those LIMITATIONS SHOULD BE CLEARLY STATED BELOW). In the absence of any stated limitations, it is to be understood that the pathologist by whom the operation is performed is to be the sole judge of the nature and extent of the autopsy. He is specifically authorized to examine the cranial contents and the extremities, if such examination is necessary to complete study of the case.

LIMITATIONS (Specify): _____

_____

4. After the autopsy, the body should be released to: _____

_____

5. I FURTHER CERTIFY THAT I HAVE READ AND UNDERSTAND ALL THE FOREGOING.

DATE _____ SIGNATURE _____

ADDRESS _____

WITNESSES:

1. _____

2. _____

1032524

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8411

_____
Date

I, _____, hereby give my permission
Name

for the _____, _____,
Name of Hospital or Physician City

_____, to release any medical information to the Oak
State

Ridge Associated Universities, Medical Division, which the Medical Division may request.

_____
Patient's Signature

Witness: _____

_____

1032525

Justification vs. Risk Declared Key Factors in Clinical Research

Special to the House Physician Reporter

GHENT, Belgium—Legal risks in clinical investigation can be minimized if the researcher limits the use of subjects to "situations in which there is a maximum of scientific justification and a minimum of risk."

This was stressed here recently by Bernard D. Hirsh, LL B., director of the American Medical Association law division, who spoke at the First World Meeting on Medical Law. Physicians, he added, have a duty to obtain consent from a person who has the authority to give it before treatment that legally might be considered assault. This rule probably would be strictly applied for adults who participate in experiments without the expectation of medical benefit, he asserted.

Mr. Hirsh

He noted, however, that it would be of questionable legality to use children or mentally incompetent persons in such experiments, even if the parent or guardian consented.

Mr. Hirsh admitted that the answer to the question of how much information a physician must furnish to a patient to avoid legal liability is complex, because it arises out of two separate and distinct legal obligations.

One is the necessity to obtain valid consent; the other is that the physician should act with the highest degree of good faith to protect the interest of the patient.

"Thus it appears," said Mr. Hirsh, "that the clinical investigator must always provide an investigative subject with an adequate explanation and information regarding the risks that may occur."

Unless they are to receive needed medical treatment, he continued, persons lacking the "capacity to consent," such as children and the mentally incompetent, should not be used for clinical investigation merely because they are available. However, in investigations where it is essential to use such persons, "it seems unlikely that public policy would entirely foreclose clinical investigation," Mr. Hirsh declared.

He predicted the eventual development of "some legal mechanism to provide authorization under appropriate limitations and safeguards" for those who lack the capacity to give informed consent.

1032526

Decrease Reported in Number Of Medical School Applicants

Special to the House Physician Reporter

EVANSTON, Ill.—For the second year in a row, the total number of medical school applicants has decreased, according to a recent announcement by the Association of American Medical Colleges.

For 1966-67, 18,250 persons applied for admission to the first-year class of U.S. medical schools. However, it was noted, the recent trend toward more applications per person continued with an average of 4.8 per applicant for the year. The resulting total of 87,627 medical school applications represent a new high.

Slightly More Places

One-half of the total medical school applicants were accepted to the first-year class, including 348 persons who did not matriculate. The first-year medical school enrollment consisted of 8,775 new entrants and 216 students either repeating or completing the first year of medical school after a previous enrollment.

According to the AAMC, the number of first-year places in 1966-67 rose significantly for the first time in the past three years to a record high that provided slightly more places for new entrants this year than the one preceding.

Of the applicants for first-year places, there was a slight rise over the past year in MCAT scores.

Even rejected applicants did better on the MCAT this year than previously, suggesting that an increasing number of these people might have qualified for medical school if additional places had been available.

"This consideration," it was noted, "together with the projected increases in the number of applicants in the immediate future, indicate the potential for significant expansion of medical school enrollment without compromising high admission standards for medical students."

[redacted]

or

1032527

VOLUNTEER'S RELEASE

Bone Marrow Procedure

Oak Ridge Associated Universities Only

I, _____, the undersigned, do hereby acknowledge that I have on this day, of my own free will and accord, volunteered to the Oak Ridge Associated Universities (hereinafter referred to as "Association") one bone marrow specimen by needle aspiration.

I understand that this procedure is for research purposes only and that it is not treatment of any physical infirmities, known or unknown. No known benefit to me will result directly from this procedure.

The nature and demands of obtaining the bone marrow specimen by needle aspiration have been explained to me, and I understand and accept the hazards involved.

It is understood that I am to be paid the sum of $25.00 by the Association in consideration of which I do hereby release and discharge the Association, its officers, employees, successors and assigns, from all claims, actions, and causes of action, at law or in equity, which I do now or may hereafter have against the Association, resulting from or growing out of the sale of said bone marrow or its removal from my body. It is further understood and agreed that I am to retain no control whatsoever over the said specimen or the use thereof.

Dated This _____Day of _____, 19___.

WITNESS: VOLUNTEER:

_____ (Signature) _____ (Signature)

I have carefully explained the nature, demands and foreseeable risks of the procedure to the above named Volunteer.

PHYSICIAN:

_____ (Date) _____ (Signature)

1032528 1/69

OAK RIDGE ASSOCIATED UNIVERSITIES

WHOLE BLOOD PROCUREMENT, RELEASE, & PAYMENT AUTHORIZATION

I, the undersigned, do hereby acknowledge that I have on this day, of my own free will and accord, delivered and sold to the Oak Ridge Associated Universities (hereinafter referred to as ("Association") _____cc's of my own blood, by direct vein aspiration.

It is understood that I am to be paid the below specified sum by the Association in consideration of which I do hereby release and discharge the Association, its successors and assigns, from all claims, actions and causes of action, at law or in equity, which I do now or may hereafter have against the Association, resulting from or growing out of the sale of said blood or its removal from my body. It is further understood and agreed that I am to retain no control whatsoever over the said blood or the use thereof.

____	0 - 100 cc	$5.00
____	101 - 200 cc	10.00
____	201 - 300 cc	15.00
____	301 - 400 cc	20.00
____	401 - above	25.00

This _____ day of _____, 1970.

_____ _____

Name (Please Print) Signature of Donor

_____

Mail Check To

_____

City State Zip

Witnesses:

_____

_____

Account to Charge:_____

_____

BLOOD RECEIVED BY

_____

DIVISION APPROVAL

_____

1032529

MAY 19 1969

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
WASHINGTON, D.C. 20201

May 1, 1969

TO : Heads of Institutions Receiving Public Health Service Grants from:
Consumer Protection and Environmental Health Service
Health Services and Mental Health Administration
National Institutes of Health

FROM : Director, Division of Research Grants, National Institutes of Health

SUBJECT: Protection of the Individual as a Research Subject

During the 3 years since the announcement of Public Health Service policy concerning research involving human subjects, there has been a continuing study of the effectiveness of the policy and of the adequacy of its procedures. This study has been carried out in the light of comments by Public Health Service staff and representatives of the grantee institutions involved. The policy has also been discussed with individuals who have expressed an interest in its impact on the health and welfare of man--both as an individual who serves as a research subject, and as a member of the community which benefits from the products of this research.

The review confirmed the utility of the policy, but recommended changes in the policy statement to provide better understanding of the requirements. The enclosed publication replaces all previous policy statements on this subject and is effective immediately. The new requirement that "...applications and contract proposals should, whenever possible, be given institutional review and approval prior to their submission to the Public Health Service" and the companion requirement that an institution "...submit with the application, or as soon after submission of the application as possible..." a certification that this review and approval has taken place will be liberally interpreted during the first effective months of the new policy. However, no grant involving human subjects and lacking a certificate of institutional review and approval will be awarded after December 31, 1969.

The following list identifies other changes in policy or in emphasis:

...The policy is applicable to all research involving human subjects supported through grants, awards, or contracts by the National Institutes of Health, the Health Services and Mental Health Administration, and the Consumer Protection and Environmental Health Service.

...A subject is considered to be any human being exposed to any research procedure as the result of the availability of Public Health Service funds.

1032530

...A research procedure is one which goes beyond the diagnostic and therapeutic needs of the subject as determined by his attending professional and the institutional review committee.

...Applicability of the policy is discussed in terms of the hazards inherent in a wide range of medical, social, and behavioral projects.

...Emphasis is placed on the fact that research may be supported not only by research and research training grants, and by research fellowships, but also by biomedical sciences support grants, demonstration grants, and other types of grants and awards not specifically associated with research.

...There is a reminder that institutional review committees should consider not only the form of a consent but also the substance of the information to be given to the subject.

...There is an explicit prohibition against implementing with Public Health Service funds any project, or proposed change in a project, not approved by the institutional committee.

...The scientist proposing a project should be informed of the reasons for any adverse actions taken by the institutional committee.

...The institution sponsoring a grant or contract is responsible for review of a project even though a portion, or all, of the research may be conducted by a cooperating institution.

...Reference is made to the desirability for legal competence on institutional committees.

The Public Health Service will continue its study of the issues involved in the protection of the individuals who serve as research subjects and of the effectiveness of this policy. The policy is administered by the Division of Research Grants on behalf of the Consumer Protection and Environmental Health Service, the Health Services and Mental Health Administration, and the National Institutes of Health. Procedures previously accepted as meeting the assurance requirements of the earlier issuance (PPO #129, revised July 1, 1966) will be considered to meet the requirements of the new policy, unless review by the grantee institution, or by this office, indicates that changes are necessary.

Comments or inquiries regarding the interpretation of application of the policy may be addressed to the Director, Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

Eugene A. Confrey

Eugene A. Confrey, Ph.D.

Enclosure

0032531

7= for Ley

EXAMPLE OF AN ACCEPTABLE STATEMENT OF COMPLIANCE
AS REQUIRED BY THE SURGEON GENERAL'S ISSUANCE OF MAY 1, 1969*

Policy and Procedures of Marimar University Concerning Investigations Involving Human Subjects

I. Ethical Policy. The Faculty and Board of Trustees of this University have officially adopted the code of medical and general ethics, promulgated by the World Medical Association as the Declaration of Helsinki.

II. Administrative Review. All applications for funds from the Public Health Service must be submitted through the Office of Research and Special Projects of this University. Here they are reviewed chiefly for completeness, budget accuracy, and for compliance with PHS policy. For any proposal involving the use of human subjects the applicant is required to inform this Office whether he has submitted copies to the Faculty Research Committee (described below). This Office is required to call to the Committee's attention any projects not so submitted which appear to involve human subjects.

III. Membership of Review Committee. The Membership of the Faculty Research Committee consists of the Chairmen of all academic Departments and the principal administrative officers; the Chairman of the Committee is the Assistant Dean of the Graduate School in charge of sponsored research. The degrees and areas of specialization of the incumbents are listed overleaf (not included with this example). The Faculty Chaplain, Fr. Brown, and Mr. Ephriam Tutt, our legal officer, may be called as consultants.

IV. Initial Review by Committee. All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects must be submitted to the Faculty Research Committee prior to submission to the PHS, and in the exact form to be used for submission. Regardless of the nature or degree of risk anticipated, the applicant must present in writing, and be prepared to defend in person before the Committee, detailed information on the following points:

1. The possible risks to the rights and welfare of human subjects, including the rights of privacy, freedom from undue harassment, and confidentiality of data, and a description of the provisions made to minimize these risks.

2. Methods used to acquire informed consent, with special emphasis on their appropriateness to the particular situation inherent in the study plan.

3. The relative risks of the project as compared to the probable benefits to the subjects and to society.

1032532

For each application the Committee will either certify that these points have been properly dealt with and declare that the project may be submitted to the PHS, or recommend to the President of the University that submission be delayed until specific deficiencies (spelled out in writing) are adequately dealt with.

Members of the Committee who are in any way directly involved in the work covered by any project being considered will be replaced by appropriate substitutes during the pertinent discussion.

The Committee's findings will be transmitted in writing to the President, the appropriate departmental chairman, and the applicant. No funds shall be released by the Comptroller until the President has concurred with these recommendations. The applicant's administrative superior shall maintain normal supervision of the project activities in the light of the Committee's report.

V. Continuing Review by Committee. The Faculty Research Committee meets quarterly. Investigators in charge of projects involving human subjects are required to submit to each of these sessions status reports in which are presented any emergent problems. The Chairman will maintain a project log summarizing the Committee discussions on these reports. If a report in delinquent, the Chairman will contact the investigator to ascertain the status of the study protocol. If at any time the Committee is dissatisfied with the conduct of the project, or with the cooperation of the investigator, they shall immediately report this to the President and recommend that financial support of the project be withheld until the deficiencies are corrected.

If a responsible investigator plans a change in study protocol, he will submit the proposed changes to the Committee for their approval, before putting them into practice.

VI. Provisions to Protect the Health and Safety of Human Subjects. This University has a 20 bed health unit staffed by 4 part-time M.D.'s. Serious cases are referred to the Washington County Hospital.

VII. Applicability of this Assurance. This assurance applies to this University, its extension campuses in Mayberry and Tarbox, and its Institute for Human Relations in Colesville.

*This example was drafted in the Institutional Relations Section, Division of Research Grants, National Institutes of Health. It refers to no existing institution and is intended only as a guide for use in developing acceptable statements of compliance.

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8411

Institutional Assurance on Research Involving Human Subjects

The Oak Ridge Associated Universities will comply with the principles of the Public Health Service policy with regard to research involving human subjects which requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. It assures the Public Health Service that it will establish and maintain advisory groups competent to review research plans involving human subjects, prior to the initiation of this research, in order to insure adequate safeguards. Group reviews and decisions will be carried out in reference to (1) the rights and welfare of the individuals involved, (2) the appropriateness of the methods used to obtain informed consent, and (3) the risks and potential benefits of the proposed research.

The institution agrees to a continuing exchange of information and advice between the review group and the investigator or director, particularly to deal with proposed changes in research design, and with emergent problems which may alter the investigational situation with regard to the criteria cited above. The institution will assure itself that its policies and the advice of its review groups are followed. It will also provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects involved in research. Records of group review and decision on the use of human subjects and of informed consent will be developed and kept by the institution.

Signed [signature], M.D.

Title Chairman, Medical Division

Date May 29, 1969

Enclosures (Implementing Guidelines)

1032534

Medical Division

Oak Ridge Associated Universities

Oak Ridge, Tennessee

ORAU GUIDELINES FOR RESEARCH ON HUMAN SUBJECTS

Revised July 1969

I. Ethical Policy

The staff of the Medical Division and the Committee on Human Studies of Oak Ridge Associated Universities have officially adopted the code of ethics adopted by the World Medical Association, known as the Declaration of Helsinki. We accept as amplification of this document, the statement of the British Medical Research Council.

II. Administrative Review

All applications for funds to conduct research involving human subjects must be submitted through the office of the Executive Director of ORAU. For any proposal involving research in human subjects, the applicant is required to state in writing whether the proposed program has been submitted to the Committee on Human Studies.

III. Membership of the Committee

The Committee includes two outside consultants familiar with the type of research done at ORAU and having no personal participation in the projects discussed. Other members of the Committee are the chairman of the Medical Division, four members of the Division's scientific staff, and a lawyer who is head of legal services for ORAU. The chief of clinical services at ORAU is an ex officio member.

IV. Initial Review by Committee

All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects must be presented to and approved by the Committee on Human Studies prior to submission for funding, and in the exact form to be used for submission. Regardless of the nature or degree of risk anticipated, the applicant must present in writing, and be prepared to defend in person before the Committee, detailed information on the following points:

1. The possible risks to the rights and welfare of human subjects, including the rights of privacy, freedom from undue harassment, and confidentiality of data, and a description of the provisions made to minimize these risks.

1032535

2. Methods used to acquire informed consent, and the form in which it is stated, with special emphasis on the appropriateness to the particular situation inherent in the study plan.

3. The relative risks of the project as compared to the probable benefits to the subjects and to society.

For each application the Committee will either certify that these points have been properly dealt with and declare that the project may be submitted for funding, or recommend to the Executive Director of ORAU that submission be delayed until specific deficiencies (spelled out in writing) are adequately dealt with.

Members of the Committee who are in any way directly involved in the work will not participate during the pertinent discussion.

Approval of the Committee members reviewing the application must be unanimous. In the event that only one member of the Committee disapproves of a proposal, one or more additional outside consultants especially qualified and approved by the majority of the Committee will be asked to review the problem. If they concur, the research may go forward over the dissent of the one member of the regular committee.

The Committee's findings will be transmitted in writing to the Executive Director and to the Chairman of the Medical Division and the applicant. No funds shall be released by the ORAU Fiscal Services Department until the Executive Director has concurred with these recommendations. The applicant's administrative superior shall maintain continuing review of the project activities in the light of the Committee's report.

V. Continuing Review by Committee

The Committee meets twice yearly or at such additional times as called by the chairman. Investigators in charge of projects on human subjects are required to submit at each of these sessions status reports in which are presented any emergent problems. If a report is delinquent, the Executive Director of ORAU will contact the investigator to ascertain the status of the study protocol. If at any time the Committee is dissatisfied with the conduct of the project, or with the cooperation of the investigator, they shall immediately report this to the Executive Director and recommend that financial support of the project be withheld until the deficiencies are corrected.

1032536

If a responsible investigator plans a change in study protocol, he will submit the proposed changes to the Committee for their approval, before putting them into practice.

VI. Provisions to Protect the Health and Safety of Human Subjects

The ORAU Medical Division has a 26-bed clinical facility with modern equipment, including a surgical suite. It is staffed with at least four full-time permanent staff physicians devoting most of their time to clinical research and patient care, plus seven other physicians in various positions (pathology, division chairman, etc.) plus a variable number of temporary physician trainees. Special consultant services from Knoxville and from medical schools participating in ORAU are sought when needed. The nearby facilities of the Oak Ridge Hospital of the Methodist Church are available to our unit.

VII. Applicability of this Assurance

Although at the present time all research involving human subjects is localized at the Vance Road site of the Medical Division of Oak Ridge Associated Universities, the same provisions would apply to other research sites of the Medical Division, and to the other divisions and offices of ORAU, should human research be undertaken at these sites.

1032537

REVIEW AND ACTION

Committee on Human Studies

Oak Ridge Associated Universities

Medical Division

Principal Investigator:_____ Identifying No._____

Project Title:_____

_____

Comments:

Approved:_____(date)

Disapproved:_____(date)

_____
Secretary, Committee on Human Studies

Adopted 4-67 1032538

To: Committee on Human Studies

Oak Ridge Associated Universities

Medical Division

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

(Three copies required. Use reverse side of these forms if additional space is needed.)

Date_____

I. Senior Investigator: _____

Co-Investigators: _____

_____

_____

Title of Project: _____

_____

_____

II. Objectives of Experiment: (Use additional blank pages if needed.)

Adopted 4-67

1032539

III. Methods of Procedure:

Brief description of methods, all medications including name and dose range, number and types of subjects anticipated, time for single session, total number of sessions, total duration of study, methods used to screen subjects, etc. (Use additional blank pages if needed.)

IV. Possible hazards and their evaluation:

1032540

V. Radioisotopes and New Drugs:

If the study involves radioisotopes, indicate action of the ORAU Medical Division Isotope Committee. If new drugs are involved, indicate that appropriate application to FDA has been made.

VI. Responsibility of Senior Investigator:

The principal investigator will follow the procedures of the ORAU Medical Division Committee on Human Studies in obtaining "informed consent" from the subject under study. The investigator recognizes that he retains the primary responsibility for safeguarding the interests of the participants under study. Any significant changes in methods of procedure or of the development of unexpected risks will be brought to the attention of Committee on Human Studies.

Starting Date_____ Signatures: _____
Investigator

_____
Investigator

_____
Investigator

MEDICAL DIVISION REVIEW

VII. The application described above has been subjected to review and has been approved.

_____
Chairman

_____
Date

1032541

FORM P-4

File for Dr. Andrews July 10 meeting

MEMORANDUM

TO Senior Staff - Medical Division DATE May 29, 1969

SUBJECT GUIDELINES FOR RESEARCH INVOLVING HUMAN SUBJECTS

COPIES TO Dr. Pollard; Files

1. The Medical Division since its opening has sought to safeguard the rights and safety of its patients who participate in research studies. In recent years more formalized procedures for institutions have emerged, in part stimulated by the policy statements of the NIH.

2. The Medical Division formally established a "Committee on Human Studies" in 1967, charged with initial and continuing review assignments.

3. Attached is a Guideline, and an Application for the Use of Humans as Experimental Subjects which must be reviewed and approved by the Committee before such new experimental projects can be activated.

4. We request that any planned projects which have not yet been reviewed be submitted to the Division Office by July 1 so that the Committee members can study the proposal before its meeting July 10.

R. M. Kniseley

RMK:fed

Attached
Guidelines - Research on Human Subjects
Statement by Medical Research Council
Curriculum Vitae of Committee Members
Review and Action
Application
Institutional Assurance..
Declaration of Helsinki

1032542

PART ONE OF A GENERAL INSTITUTIONAL ASSURANCE

The (name of institution) will comply with the policy for the protection of human subjects participating in projects and activities supported directly or indirectly by grants, contracts, or awards from the Department of Health, Education, and Welfare. In fulfillment of its assurance:

This institution will establish and maintain a committee competent to review projects and activities that involve human subjects. The committee will be assigned responsibility to determine for each project and activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.

The risks to subjects are outweighed by the potential benefits to him, or by the importance of the knowledge to be gained.

The procedures for obtaining informed consent are adequate and appropriate.

This institution will provide for committee reviews to be conducted objectively and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interest.

This institution will encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

This institution will provide whatever facilities and professional attention are required to safeguard the rights and welfare of human subjects.

This institution will maintain appropriate and informative records of committee reviews of applications and active projects, of briefings of subjects for obtaining informed consent, and other documentation that may pertain to the selection, participation, and protection of subjects, and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

This institution will periodically reassure itself through appropriate administrative overview that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with its assurance as accepted by the Department of Health, Education, and Welfare.

Official signing for the Institution

Signature _____

Title _____

Date _____

Enclosure: Implementing Guidelines, Part Two of a General Institutional Assurance

SPECIAL INSTITUTIONAL ASSURANCE IN CONNECTION WITH SINGLE PROJECTS INVOLVING HUMAN SUBJECTS

(0) The (name of institution) will comply with the policy for the protection of human subjects participating in projects or activities supported by grants, contracts, and awards made by the Department of Health, Education, and Welfare. This policy requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. An initial review of the application for a grant, contract, or award identified as _____ submitted by this institution on behalf of _____ indicates that:

(1) In the opinion of this committee the risks to the rights and welfare of the subjects in this project or activity are:

The committee states that adequate safeguards against these risks have been provided.

(2) In the opinion of the committee the potential benefits of this activity to the subjects outweigh any probable risks. This opinion is justified by the following reasons:

(3) In the opinion of the committee the following informed consent procedures will be adequate and appropriate:

(4) The committee agrees to arrange for a continuing exchange of information and advice between itself and the investigator or director, particularly to deal with proposed changes in project or activity design, and with emergent problems which may alter the investigational situation with regard to the criteria cited above. This exchange will be implemented through:

This institution will provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects.

(Exhibit X1-40-2 continued)

(5) The signatures, names, occupations, or titles of the members of the committee are listed below.

Name	Occupation or Title
Name	Occupation or Title
Name	Occupation or Title
Name	Occupation or Title

(6) Official signing for Institution

Name	Title	Date

(see instructions)

EXCERPT
CHAPTER 1-40
PROTECTION OF HUMAN SUBJECTS

1-40-20 POLICY

Safeguarding the rights and welfare of human subjects involved in projects and in other activities supported by grants, contracts, and awards from the Department of Health, Education, and Welfare is the responsibility of the institution which receives or is accountable to the DHEW for the funds awarded for the support of the project or activity. Grants, contracts, and awards involving human subjects at risk will not be made to an individual unless he is affiliated with or sponsored by an institution which can and will assume this responsibility.

In order to provide for the adequate discharge of this institutional responsibility, it is the policy of the Department that no grant, contract, or award for a project or activity involving human subjects at risk shall be made until assurance that the project or activity will be subject to initial and continuing review by an appropriate institutional committee has been officially presented to and accepted by the DHEW. This review shall assure that the rights and welfare of the subjects involved are adequately protected, that the risks to an individual are outweighed by the potential benefits to him or by the importance of the knowledge to be gained, and that the methods to be used to obtain informed consent are adequate and appropriate. 1/ The institution must also provide with each proposal involving human subjects a certification that it has been or will be reviewed prior to the proposed starting date in accordance with the terms of the institution's assurance.

Since the welfare of subjects is a matter of concern to the Department of Health, Education, and Welfare as well as to the institution, no grant, contract, or award involving human subjects shall be made unless the application for such support has been reviewed and approved by an appropriate professional committee within the responsible organizational component of the Department. This review must establish that the project or activity, as described in the application, will not interfere with or impair the rights and welfare of the subjects, nor involve risks that outweigh either potential benefits to the subjects or the expected value of the knowledge sought, nor deny the rights of the subject to adequate and appropriate informed consent. The committee may recommend to the awarding agency, and the awarding agency may require, the imposition of specific grant, contract, and award terms providing for the protection of human subjects, including requirements for informed consent.

1/ In the United States, adherence to the regulations of the Food and Drug Administration (21 CFR 130.37) governing consent in projects involving investigative new drugs (IND) is required by law.

EXCERPT

1-40-40 GRANTEE IMPLEMENTATION

A. Negotiation of Assurances

An institution applying to DHEW for a grant, contract, or award involving human subjects must provide written assurance that it will abide by DHEW policy. The assurance shall embody a statement of compliance with DHEW requirements for initial and continuing committee review of grant, contract, and award supported activities and a set of implementing guidelines including identification of the committee, and its review procedures, or in the case of special assurances concerned with single projects or activities, a report of initial findings and proposed continuing review procedures.

Assurances will not be accepted from institutions or institutional components which do not have control over the expenditure of DHEW grant, contract, and award funds unless they are an active part of a cooperative project or activity.

An assurance will be accepted only after review and approval by the Division of Research Grants, NIH.

B. Types of Assurance

Assurances may be one of two types:

1. General Assurance.

   A general assurance describes the review and implementation procedures applicable to any and all DHEW supported activities within an institution, regardless of the number, location, or types of its organizational components. (See Exhibit X1-40-1.) General assurances will be required from institutions having a significant number of concurrent DHEW projects or activities.

2. Special Assurance.

   A special assurance will, as a rule, describe those review and implementation procedures applicable to a single project or activity. (See Exhibit X1-40-2.) Special assurances may also be negotiated in modified forms to meet unusual requirements either of the awarding agency or of the institution receiving a grant, contract, or award. Special assurances are not to be solicited from institutions which have on file an accepted general assurance.

1032547

C. Minimum Requirements for General Assurances

1. Statement of Compliance.

A formal statement of compliance with DHEW policy must be executed by an appropriate institutional official.

2. Implementing Guidelines.

The institution must include as part of its assurance implementing guidelines that specifically provide for:

a. The statement of principles that will assist the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may be an appropriate existing code or declaration or one formulated by the institution itself. It is to be understood that no such principles supersede DHEW policy or applicable law.

b. A committee or committee structure which will conduct initial and continuing reviews. Committee members shall be identified by name, occupation or position, and by other pertinent indications of experience and competence in areas pertinent to the areas of review such as earned degrees, board certifications, licensures, memberships, etc.

The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of projects and activities commonly conducted at the institution. The committee's membership, maturity, experience, and expertise should be such as to justify respect for its advice and counsel. No member of an institutional committee shall be involved in either the initial or continuing review of a project or activity in which he has a professional responsibility, except to provide information requested by the committee. In addition to possessing the professional competence to review specific projects, the committee should be able to determine acceptability of the application in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. This may require the committee to include persons whose primary concerns lie in these areas rather than in the conduct of research, development, and service programs of the types supported by the DHEW.

c. The procedures which the institution will follow in carrying out its initial and continuing review of applications and projects.

d. ~~The~~ procedures ~~which~~ the committee will follow to provide advice and counsel to project and program directors ~~with regard to the committee's actions~~, and the requirements for reporting to the committee any emergent problems or proposed procedural changes.

e. ~~The~~ procedures which the institution will follow to maintain an active and effective committee and ~~to implement its recommendations~~.

D. Minimum Requirements for Special Assurances

An acceptable special assurance covering a single project or activity consists of a properly completed statement of compliance, similar to that illustrated by Exhibit X1-40-2. This shall identify the specific grant, contract, or award concerned by its number, if known, by its full title, and by the name of the project or program director, principal investigator, fellow, or other person immediately responsible for the conduct of the project or activity. The assurance shall be signed by a committee of not fewer than three members and executed by an appropriate institutional official. The committee shall describe in general terms those risks to the subject that it recognizes as inherent in the project or activity. Consent procedures to be used should be identified. Any consent statement to be signed, heard, or read by the subject or responsible third parties should be attached. The assurance should outline the circumstances under which the director or investigator will be required to inform the committee of proposed changes in the project or activity, or of emergent problems, involving human subjects. The assurance should also indicate whether the director or investigator will be required to submit written reports, appear for interview, or be visited by the committee or committees to provide for continuing review. It should also indicate the intervals at which such review will take place.

E. 1. Timing and Certification of Institutional Review--General Assurances

All proposals and applications involving human subjects submitted by institutions with accepted general assurances should, whenever possible, be given institutional review and approval prior to submission to the DHEW. The proposal or application should be appropriately marked in the spaces provided on forms, or the

following statement should be typed on the lower or right hand margin of the page bearing the name of the institutional official authorized to sign or execute applications or proposals for the institution.

"HUMAN SUBJECTS - REVIEWED ON _____(date)_____."

(This date should be no more than 90 days prior to the date on which the application or proposal was signed or executed.)

If it will be necessary to delay the review, the application should be appropriately marked in the spaces provided on forms or the following statement should be typed in the lower or right hand margin of the page bearing the name of the institutional official authorized to sign or execute applications or proposals for the institution.

"HUMAN SUBJECTS - REVIEW PENDING ON _____(date)_____."

(This date must be earlier than the proposed starting date of the project.)

These statements will be accepted as certification that the grant, contract, or award as described in the application has been or will be reviewed in accordance with DHEW policy and the institution's assurance.

If the application or proposal is not certified and review by DHEW indicates that human subjects are involved, the awarding agency will request certification from the institution prior to completion of processing and award.

If the application or proposal is certified, but the pending review date is later than the date on which the awarding agency wishes to make an award, the agency will request certification from the institution prior to completion of processing and award.

If certification is not received, the application as prepared will be considered incomplete, and no award will be made.

If an application, at the time it is submitted to the DHEW does not describe a project or activity involving or likely to involve human subjects, no certification should be submitted. However, in those instances where funds are awarded in response to the application and it later becomes appropriate to use all or parts

of these funds in projects or activities which will involve human subjects, such use must be reviewed and approved in accordance with the institutional assurance prior to the use of subjects:

----Where support is provided by project grants or contracts, review and approval of such changes must be certified to the awarding agency or contracting agency, together with a description of the proposed change in the project plan or contract workscope. Subjects should not be used prior to receipt of approval from agency staff or from the project officer concerned.

----Where support is provided by a mandatory grant or institutional grant, in which cases the institution determines within broad guidelines the project or activities supported, including the use of human subjects (i.e., general research support grants, clinical research center projects), review must be carried out in accordance with the institutional assurance. Certification for individual projects need not be forwarded to the awarding agency.

----Whenever the committee is uncertain as to whether a change should or should not be reported, the question should be referred to the agency concerned.

All certifications are subject to verification by DHEW representatives authorized to examine institutional and committee records.

2. Timing and Certification of Institutional Review--Special Assurances

When a special assurance is submitted, it provides certification for the initial grant, contract, or award year concerned. No additional documentation is required. If the terms of the grant or contract provide for additional years of support, with annual negotiation of budgets, the noncompeting renewal application or proposal shall be certified in the manner described in the preceding section (1-40-40 E.1.).

W. F. Start a file

Mr. Harmon

FORM P-4

MEMORANDUM

TO Senior Staff - Medical Division DATE May 29, 1969

SUBJECT GUIDELINES FOR RESEARCH INVOLVING HUMAN SUBJECTS

COPIES TO Dr. Pollard; Files

1. The Medical Division since its opening has sought to safeguard the rights and safety of its patients who participate in research studies. In recent years more formalized procedures for institutions have emerged, in part stimulated by the policy statements of the NIH.

2. The Medical Division formally established a "Committee on Human Studies" in 1967, charged with initial and continuing review assignments.

3. Attached is a Guideline, and an Application for the Use of Humans as Experimental Subjects which must be reviewed and approved by the Committee before such new experimental projects can be activated.

4. We request that any planned projects which have not yet been reviewed be submitted to the Division Office by July 1 so that the Committee members can study the proposal before its meeting July 10.

R

R. M. Kniseley

RMK:fed

1032552

GUIDELINES

Research on Human Subjects

Oak Ridge Associated Universities

Medical Division

1. Principles

The Medical Division proposes to follow the code of standards of the Medical Research Council published 18 July 1964 in the British Medical Journal (attached) entitled Responsibility in Investigations on Human Subjects. The approach to informed consent will follow those guidelines (attached form).

2. Description of Review Committee

(a) Name: Committee on Human Studies

(b) Composition: Two outside consultants not involved in Medical Division research; Dr. Gould Andrews, Chairman of the Medical Division; two M.D. staff members; one Ph.D. staff member; Lawyer, Head Legal Services, Oak Ridge Associated Universities; and Dr. C. L. Edwards, Chief of Clinical Research, as ex officio member.

(c) Membership 1969. (See attached curriculum vitae)

3. Description of Review Procedures

(a) Scope. The committee should concern itself with all studies done in human beings, whether patients in the research hospital or normal volunteers of some type. The committee is to review all research at the ORAU Medical Division in which there is believed to be a significant risk to the patients or a significant possibility that criticism might be leveled at the scientists for their manner of doing studies in human beings. The decision about whether or not a specific investigative procedure involves any risk and therefore requires action by the committee would rest with the Medical Division. The Medical Division should bring to the committee's attention by name and brief description those experiments in human beings believed to have negligible risk, i.e., a systematic survey of hemoglobin and hematocrit values in thyroid patients. As to the suitability of undertaking a rather unconventional form of treatment in a single seriously ill patient, partly with the objective of immediate benefit to the patient and partly as a preliminary research effort that might be the basis for a future controlled investigation, considerable leeway rests with the physician who is responsible for the patient's care. Ordinarily the Committee on Human Studies would not be involved with decisions concerning a single patient but rather with policy matters or

research on groups of patients. However, if circumstances were such that the staff of the Medical Division wanted some consultation on the suitability of a study in an individual patient it might be quite reasonable to seek telephone consultation.

(b) The senior investigator who proposes a research project shall submit an Application for the Use of Humans as Experimental Subjects (See attached form.)

(c) The Chairman will circulate the proposal to the Committee after review by the Division Office. The committee members should request answers to questions that arise in advance of the meeting where possible.

(d) Unanimous concurrence by committee members must be obtained to allow a proposal to go forward. If there is dissent, additional outside consultation would be sought.

(e) Proposed studies involving new radioisotopes would first be presented to and approved by the ORAU Isotope Committee.

1032554

To: Committee on Human Studies

Oak Ridge Associated Universities

Medical Division

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

(Three copies required. Use reverse side of these forms if additional space is needed.)

Date_____

I. Senior Investigator: _____

Co-Investigators: _____

_____

_____

Title of Project: _____

_____

_____

II. Objectives of Experiment: (Use additional blank pages if needed.)

Adopted 4-67

1032555

III. Methods of Procedure:

Brief description of methods, all medications including name and dose range, number and types of subjects anticipated, time for single session, total number of sessions, total duration of study, methods used to screen subjects, etc. (Use additional blank pages if needed.)

IV. Possible hazards and their evaluation:

1032556

V. Radioisotopes and New Drugs:

If the study involves radioisotopes, indicate action of the ORAU Medical Division Isotope Committee. If new drugs are involved, indicate that appropriate application to FDA has been made.

VI. Responsibility of Senior Investigator:

The principal investigator will follow the procedures of the ORAU Medical Division Committee on Human Studies in obtaining "informed consent" from the subject under study. The investigator recognizes that he retains the primary responsibility for safeguarding the interests of the participants under study. Any significant changes in methods of procedure or of the development of unexpected risks will be brought to the attention of Committee on Human Studies.

Starting Date_____ Signatures: _____
Investigator

_____
Investigator

_____
Investigator

MEDICAL DIVISION REVIEW

VII. The application described above has been subjected to review and has been approved.

_____
Chairman

_____
Date

1032561

GUIDELINES

Research on Human Subjects

Oak Ridge Associated Universities

Medical Division

1. Principles

The Medical Division proposes to follow the code of standards of the Medical Research Council published 18 July 1964 in the British Medical Journal (attached) entitled Responsibility in Investigations on Human Subjects. The approach to informed consent will follow those guidelines (attached form).

2. Description of Review Committee

(a) Name: Committee on Human Studies

(b) Composition: Two outside consultants not involved in Medical Division research; Dr. Gould Andrews, Chairman of the Medical Division; two M.D. staff members; one Ph.D. staff member; Lawyer, Head Legal Services, Oak Ridge Associated Universities; and Dr. C. L. Edwards, Chief of Clinical Research, as ex officio member.

(c) Membership 1969. (See attached curriculum vitae)

3. Description of Review Procedures

(a) Scope. The committee should concern itself with all studies done in human beings, whether patients in the research hospital or normal volunteers of some type. The committee is to review all research at the ORAU Medical Division in which there is believed to be a significant risk to the patients or a significant possibility that criticism might be leveled at the scientists for their manner of doing studies in human beings. The decision about whether or not a specific investigative procedure involves any risk and therefore requires action by the committee would rest with the Medical Division. The Medical Division should bring to the committee's attention by name and brief description those experiments in human beings believed to have negligible risk, i.e., a systematic survey of hemoglobin and hematocrit values in thyroid patients. As to the suitability of undertaking a rather unconventional form of treatment in a single seriously ill patient, partly with the objective of immediate benefit to the patient and partly as a preliminary research effort that might be the basis for a future controlled investigation, considerable leeway rests with the physician who is responsible for the patient's care. Ordinarily the Committee on Human Studies would not be involved with d[illegible]ns concerning a single patient but rather with policy matters or

0032558

research on groups of patients. However, if circumstances were such that the staff of the Medical Division wanted some consultation on the suitability of a study in an individual patient it might be quite reasonable to seek telephone consultation.

(b) The senior investigator who proposes a research project shall submit an Application for the Use of Humans as Experimental Subjects (See attached form.)

(c) The Chairman will circulate the proposal to the Committee after review by the Division Office. The committee members should request answers to questions that arise in advance of the meeting where possible.

(d) Unanimous concurrence by committee members must be obtained to allow a proposal to go forward. If there is dissent, additional outside consultation would be sought.

(e) Proposed studies involving new radioisotopes would first be presented to and approved by the ORAU Isotope Committee.

1032559

Responsibility in Investigations on Human Subjects

Statement by Medical Research Council

Under this heading the Medical Research Council include in their Annual Report for 1962–63 (Cmnd. 2382, H.M.S.O., 1964, price 16s. 6d. net) a statement on investigations on human beings which is intended to serve as a guide to medical men engaged in this kind of work. It is a statement of such importance that we reproduce it here in full.

During the last 50 years medical knowledge has advanced more rapidly than at any other period in its history. New understandings, new treatments, new diagnostic procedures, and new methods of prevention have been, and are being, introduced at an ever-increasing rate; and if the benefits that are now becoming possible are to be gained these developments must continue.

Undoubtedly the new era in medicine upon which we have now entered is largely due to the marriage of the methods of science with the traditional methods of medicine. Until the turn of the century the advancement of clinical knowledge was in general confined to that which could be gained by observation, and means for the analysis in depth of the phenomena of health and disease were seldom available. Now, however, procedures that can safely, and conscientiously, be applied to both sick and healthy human beings are being devised in profusion, with the result that certainty and understanding in medicine are increasing apace.

Yet these innovations have brought their own problems to the clinical investigator. In the past, the introduction of new treatments or investigations was infrequent, and only rarely did they go beyond a marginal variation on established practice. To-day far-ranging new procedures are commonplace, and such are their potentialities that their employment is no negligible consideration. As a result, investigators are frequently faced with ethical and sometimes even legal problems of great difficulty. It is in the hope of giving some guidance in this difficult matter that the Medical Research Council issue this statement.

A distinction may legitimately be drawn between procedures undertaken as part of patient-care which are intended to contribute to the benefit of the individual patient, by treatment, prevention, or assessment, and those procedures which are undertaken either on patients or on healthy subjects solely for the purpose of contributing to medical knowledge and are not themselves designed to benefit the particular individual on whom they are performed. The former fall within the ambit of patient-care and are governed by the ordinary rules of professional conduct in medicine; the latter fall within the ambit of investigations on volunteers.

Important considerations flow from this distinction.

Procedures Contributing to the Benefit of the Individual

In the case of procedures directly connected with the management of the condition in the particular individual, the relationship is essentially that between doctor and patient. Implicit in this relationship is the willingness on the part of the subject to be guided by the judgment of his medical attendant. Provided, therefore, that the medical attendant is satisfied that there are reasonable grounds for believing that a particular new procedure will contribute to the benefit of that particular patient, either by treatment, prevention, or increased understanding of his case, he may assume the patient's consent to the same extent as he would were the procedure entirely established practice. It is axiomatic that no two patients are alike and that the medical attendant must be at liberty to vary his procedures according to his judgment of what is in his patients' best interests. The question of novelty is only relevant to the extent that in reaching a decision to use a novel procedure the doctor, being unable to fortify his judgment by previous experience, must exercise special care. That it is both considerate and prudent to obtain the patient's agreement before using a novel procedure is no more than a requirement of good medical practice.

The second important consideration that follows from this distinction is that it is clearly within the competence of a parent or guardian of a child to give permission for procedures intended to benefit that child when he is not old or intelligent enough to be able himself to give a valid consent.

A category of investigation that has occasionally raised questions in the minds of investigators is that in which a new preventive, such as a vaccine, is tried. Necessarily, preventives are given to people who are not, at the moment, suffering from the relevant illness. But the ethical and legal considerations are the same as those that govern the introduction of a new treatment. The intention is to benefit an individual by protecting him against a future hazard; and it is a matter of professional judgment whether the procedure in question offers a better chance of doing so than previously existing measures.

In general, therefore, the propriety of procedures intended to benefit the individual—whether these are directed to treatment, to prevention, or to assessment—are determined by the same considerations as govern the care of patients. At the frontiers of knowledge, however, where not only are many procedures novel but their value in the particular instance may be debatable, it is wise, if any doubt exists, to obtain the opinion of experienced colleagues on the desirability of the projected procedure.

Control Subjects in Investigations of Treatment or Prevention

Over recent years the development of treatment and prevention has been greatly advanced by the method of the controlled clinical trial. Instead of waiting, as in the past, on the slow accumulation of general experience to determine the relative advantages and disadvantages of any particular measure, it is now often possible to put the question to the test under conditions which will not only yield a speedy and more precise answer but also limit the risk of untoward effects remaining undetected. Such trials are, however, only feasible when it is possible to compare suitable groups of patients and only permissible when there is a genuine doubt within the profession as to which of the two treatments or preventive regimes is the better. In these circumstances it is justifiable to give to a proportion of the patients the novel procedure on the understanding that the remainder receive the procedure previously accepted as the best. In the case when no effective treatment has previously been devised then the situation should be fully explained to the participants and their true consent obtained.

Such controlled trials may raise ethical points which may be of some difficulty. In general, the patients participating in them should be told frankly that two different procedures are being assessed and their co-operation invited. Occasionally, however, to do so is contraindicated. For example, to awaken patients with a possibly fatal illness to the existence of such doubts about effective treatment may not always be in their best interest; or suspicion may have arisen as to whether a

1032560

particular treatment has any effect apart from suggestion, and it may be necessary to introduce a placebo into part of the trial to determine this. Because of these and similar difficulties it is the firm opinion of the Council that controlled clinical trials should always be planned and supervised by a group of investigators and never by an individual alone. It goes without question that any doctor taking part in such a collective controlled trial is under an obligation to withdraw a patient from the trial, and to institute any treatment he considers necessary, should this, in his personal opinion, be in the better interests of his patient.

Procedures not of Direct Benefit to the Individual

The preceding considerations cover the majority of clinical investigations. There remains, however, a large and important field of investigations on human subjects which aim to provide normal values and their variation so that abnormal values can be recognized. This involves both ill persons and "healthy" persons, whether the latter are entirely healthy or patients suffering from a condition that has no relevance to the investigation. In regard to persons with a particular illness, such as metabolic defect, it may be necessary to know the range of abnormality compatible with the activities of normal life or the reaction of such persons to some change in circumstances, such as an alteration in diet. Similarly it may be necessary to have a clear understanding of the range of a normal function and its reaction to changes in circumstances in entirely healthy persons. The common feature of this type of investigation is that it is of no direct benefit to the particular individual and that, in consequence, if he is to submit to it he must volunteer in the full sense of the word.

It should be clearly understood that the possibility or probability that a particular investigation will be of benefit to humanity or to posterity would afford no defence in the event of legal proceedings. The individual has rights that the law protects and nobody can infringe those rights for the public good. In investigations of this type it is therefore always necessary to ensure that the true consent of the subject is explicitly obtained.

By true consent is meant consent freely given with proper understanding of the nature and consequences of what is proposed. Assumed consent or consent obtained by undue influence is valueless, and, in this latter respect, particular care is necessary when the volunteer stands in special relationship to the investigator, as in the case of a patient to his doctor, or a student to his teacher.

The need for obtaining evidence of consent in this type of investigation has been generally recognized, but there are some misunderstandings as to what constitutes such evidence. In general, the investigator should obtain the consent himself in the presence of another person. Written consent unaccompanied by other evidence that an explanation has been given, understood, and accepted, is of little value.

The situation in respect of minors and mentally subnormal or mentally disordered persons is of particular difficulty. In the strict view of the law parents and guardians of minors cannot give consent on their behalf to any procedures which are of no particular benefit to them and which may carry some risk of harm. Whilst English law does not fix any arbitrary age in this context, it may safely be assumed that the Courts will not regard a child of 12 years or under (of 14 years or under for boys in Scotland) as having the capacity to consent to any procedure which may involve him in an injury. Above this age the reality of any purported consent which may have been obtained is a question of fact, and as with an adult the evidence would, if necessary, have to show that irrespective of age the person concerned fully understood the implications to himself of the procedures to which he was consenting.

In the case of those who are mentally subnormal or mentally disordered the reality of the consent given will fall to be judged by similar criteria to those which apply to the making of a will, contracting a marriage, or otherwise taking decisions which have legal force as well as moral and social implications. Where true consent in this sense cannot be obtained, procedures which are of no direct benefit and which might carry a risk of harm to the subject should not be undertaken.

Even when true consent has been given by a minor or a mentally subnormal or mentally disordered person, considerations of ethics and prudence still require that, if possible, the assent of parents or guardians or relatives, as the case may be, should be obtained.

Investigations that are of no direct benefit to the individual require, therefore, that his true consent to them shall be explicitly obtained. After adequate explanation, the consent of an adult of sound mind and understanding can be relied upon to be true consent. In the case of children and young persons the question whether purported consent was true consent would in each case depend upon facts such as the age, intelligence, situation, and character of the subject, and the nature of the investigation. When the subject is below the age of 12 years, information requiring the performance of any procedure involving his body would need to be obtained incidentally to and without altering the nature of a procedure intended for his individual benefit.

Professional Discipline

All who have been concerned with medical research are aware of the impossibility of formulating any detailed code of rules which will ensure that irreproachability of practice which alone will suffice where investigations on human beings are concerned. The law lays down a minimum code in matters of professional negligence and the doctrine of assault. But this is not enough. Owing to the special relationship of trust that exists between a patient and his doctor, most patients will consent to any proposal that is made. Further, the considerations involved in a novel procedure are nearly always so technical as to prevent their being adequately understood by one who is not himself an expert. It must therefore be frankly recognized that, for practical purposes, an inescapable moral responsibility rests with the doctor concerned for determining what investigations are, or are not, proposed to a particular patient or volunteer. Nevertheless, moral codes are formulated by man, and if, in ever-changing circumstances of medical advance, their relevance is to be maintained, it is to the profession itself that we must look, and in particular to the heads of departments, the specialized Societies, and the editors of medical and scientific journals.

In the opinion of the Council, the head of a department where investigations on human subjects take place has an inescapable responsibility for ensuring that practice by those under his direction is irreproachable.

In the same way the Council feel that, as a matter of policy, bodies like themselves that support medical research should do everything in their power to ensure that the practice of all workers whom they support shall be unexceptionable and known to be so.

So specialized has medical knowledge now become that the profession in general can rarely deal adequately with individual problems. In regard to any particular type of investigation, only a small group of experienced men who have specialized in this branch of knowledge are likely to be competent to pass an opinion on the justification for undertaking any particular procedure. But in every branch of medicine specialized scientific societies exist. It is upon these that the profession in general must mainly rely for the creation and maintenance of that body of precedents which shall guide individual investigators in case of doubt, and for the critical discussion of the communications presented to them on which the formation of the necessary climate of opinion depends.

1032561

Finally, it is the Council's opinion that any account of investigations on human subjects should make clear that the appropriate requirements have been fulfilled, and, further, that no paper should be accepted for publication if there are any doubts that such is the case.

The progress of medical knowledge has depended, and will continue to depend, in no small measure upon the confidence which the public has in those who carry out investigations on human subjects, be these healthy or sick. Only in so far as it is known that such investigations are submitted to the highest ethical scrutiny and self-discipline will this confidence be maintained. Mistaken, or misunderstood, investigations could do incalculable harm to medical progress. It is our collective duty as a profession to see that this does not happen and so to continue to deserve the confidence that we now enjoy.

1032562

June 18, 1969

Dr. Seymour Bress
Liaison Officer
Institutional Relations Section
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Bress:

We appreciate the comments in your June 9 letter and the sample of an "Acceptable Statement of Compliance." We would like to reassure you that, on the points where our guidelines were silent, in practice we do share the determination to protect the individuals who are our research subjects.

Our Committee, at its next meeting (July 10), will reconsider the earlier guidelines, with a view to specifically correcting those deficiencies you feel now exist. We will be in touch with you after that meeting.

Sincerely yours,

Gould A. Andrews, M.D.

GAA:fb

cc:
Dr. Balish
Dr. Edwards
Dr. Goh
Mr. Koons
Dr. Nelson
Dr. Brill
Dr. Lange

1032563

See Below

June 2, 1969

Meeting of the Committee on Human Studies

File

There will be a meeting of the Committee on Human Studies at the Medical Division of ORAU on July 10, 1969, at 10:30 a.m., in the second Floor Conference Room.

Agenda: (1) Review new proposals for human experimentation.
(2) Consider adoption of a code of standards.
(3) Set mechanisms for scheduling regular meetings and reviews.

Members of Committee
Dr. Dalich
Dr. Edwards
Dr. Ceh
Mr. Keene
Dr. Nelson
Dr. Andrews
Dr. A. B. Brill
Dr. Robert Lange

C. A. Andrews

cc: Mr. Herman

(1) Attach copy of Attachment No. 1 to Panel
(2) C.V.'s
(3) Statement
(4) Application

1032564

June 2, 1969

Dr. A. Bertrand Brill
Associate Professor of Medicine
and Radiology
Vanderbilt School of Medicine
Nashville, Tennessee 37203

Dear Randy:

As agreed upon last week, we have set the meeting of the Committee on Human Studies at the ORAU Medical Division for July 10, 1969, at 10:30 a.m., in the Second Floor Conference Room.

The agenda for the meeting is as follows:

(1) to review new proposals that involve human subjects,
(2) to consider adoption of a code of standards, and
(3) to set mechanisms for scheduling regular meetings and reviews.

You will receive an "official" request at a later date.

For your interest, we are enclosing a Xerox of "Responsibility in Investigations on Human Subjects," from the British Medical Research Council, and a preliminary "Guidelines," synthesized from our earlier Minutes.

Sincerely yours,

Gould A. Andrews, M.D.

GAA:fb

Enc. 4 C.R. pamphlet

1032565

June 2, 1969

Dr. Robert D. Lange
Assistant Director
U. T. Memorial Research Center
1924 Alcoa Highway
Knoxville, Tennessee 37920

Dear Bob:

As agreed upon last week, we have set the meeting of the Committee on Human Studies at the ORAU Medical Division for July 10, 1969, at 10:30 a.m., in the Second Floor Conference Room.

The agenda for the meeting is as follows:

(1) to review new proposals that involve human subjects,
(2) to consider adoption of a code of standards, and
(3) to set mechanisms for scheduling regular meetings and reviews.

You will receive an "official" request at a later date.

For your interest, we are enclosing a Xerox of "Responsibility in Investigations on Human Subjects," from the British Medical Research Council, and a preliminary "Guidelines," synthesized from our earlier minutes.

Sincerely yours,

Gould A. Andrews, M.D.

GAA:fb

Enc. 3

1032566

FORM P-4

MEMORANDUM

TO Senior Staff - Medical Division DATE May 29, 1969

SUBJECT GUIDELINES FOR RESEARCH INVOLVING HUMAN SUBJECTS

COPIES TO Dr. Pollard; Files

1. The Medical Division since its opening has sought to safeguard the rights and safety of its patients who participate in research studies. In recent years more formalized procedures for institutions have emerged, in part stimulated by the policy statements of the NIH.

2. The Medical Division formally established a "Committee on Human Studies" in 1967, charged with initial and continuing review assignments.

3. Attached is a Guideline, and an Application for the Use of Humans as Experimental Subjects which must be reviewed and approved by the Committee before such new experimental projects can be activated.

4. We request that any planned projects which have not yet been reviewed be submitted to the Division Office by July 1 so that the Committee members can study the proposal before its meeting July 10.

R. M. Kniseley

RMK:fed

Senior Staff
Guidelines
Application

Members of Committee
Guidelines
Application
Curriculum Vitae of Committee
British Med. Res. Council Reprint

Dr. Pollard
Guidelines, (2) statement by Medical Research Council, (3) Consent to Experiment Treatment, (4) curriculum vitae, (5) applicat (6) review and action, (7) ethics of human experimentation, (8) institutional assurance, (9) Declaration of Helsinki.

1032567

The committee on Human Studies met on 10 July, 1969.

The following members were present: Mr. Melvin A. Koons, and Drs. A. Bertrand Brill, Gould Andrews, Kong-oo Goh, Edward Balish, and Robert D. Lange.

The following new proposals were discussed and approved:

1. A Study of Infections in Cancer Patients. by Drs. Edward Balish and C. Lowell Edwards.

It was noted that not all patients would have small intestinal specimens obtained three times weekly and that only adults would have bowel sterilization procedures. The committee expressed concern that all patients should be informed that it was possible for them to withdraw without prejudice. A new consent form is to be prepared. The committee urged that the senior investigators keep a continued surveillance for possible drug reactions ~~and emergence of any drug reactions~~ and emergence of any drug resistant organisms. It was also emphasized that the committee be informed at each meeting about the results of this project.

2. Tumor Scanning with Gallium 67. Senior Investigator: C. L. Edwards.

The committee noted with favor that cooperative studies were being carried out with established investigators. It was noted that ORAU was legally responsible for material sent out for human use.

3. Study of Granulocytic Kinetics in Myeloproliferative Diseases. Senior Investigator: Helen Vodopick.

Dr. Vodopick was present for this discussion.

The project was approved. The only question was in regard to which "consent form" would be used.

The next meeting of the committee was tentatively scheduled for September 18, 1969.

Submitted by

Robert D. Lange, M.D.

RDL:cak

1032568

Committee on Human Studies

Minutes of Meeting - July 10, 1969

A meeting of the Committee on Human Studies was held on July 10, 1969. The morning session met in the second floor conference room of the Medical Division and the afternoon session was held in the Administration Building conference room. Present were: Dr. Robert Lange, Dr. A. Bertrand Brill, Mr. Melvin Koons, Dr. Kong-oo Goh, Dr. Edward Balish, and Dr. Gould Andrews. Also attending was Dr. C. Lowell Edwards, who is an ex officio member. Dr. Bill Nelson was absent.

During the early part of the meeting an extensive discussion was held about the scope of the Committee's review. In all circumstances, much responsibility rests with the individual physician investigator. It was decided that special studies on an individual patient would not normally require the Committee's action but that when a "project" was established it should be looked at. Even projects that seem to involve no significant risk should come, at least briefly, to the Committee's attention. The Committee felt that the procedure should be the same for all projects regardless of source of funding.

The Committee agreed, however, that in the periods between meetings, interim, tentative approval could be established for new projects if this did not conflict with rules of funding agencies. This would be done by action of the Oak Ridge members of the Committee alone when the chairman judged the studies to involve no significant risk; when there was some possible risk, interim approval would be sought by telephoning, in addition, Dr. Brill and Dr. Lange. In all such instances the project would come up for review at the next regular meeting of the whole Committee.

It was requested that each research proposal include samples of the forms that would be used to obtain patients' consent.

The Committee developed a formal statement of policy to fulfill the requirements of NIH and chose to adopt it as a general policy for all research.

Dr. Lange agreed to record action on specific research proposals.

It was tentatively decided to hold the next meeting on Thursday, September 18, 1969.

Submitted by

Gould A. Andrews, M.D.

pe

1032569

Medical Division

Oak Ridge Associated Universities

Oak Ridge, Tennessee

ORAU GUIDELINES FOR RESEARCH ON HUMAN SUBJECTS

Revised July 1969

I. Ethical Policy

The staff of the Medical Division and the Committee on Human Studies of Oak Ridge Associated Universities have officially adopted the code of ethics adopted by the World Medical Association, known as the Declaration of Helsinki. We accept as amplification of this document, the statement of the British Medical Research Council.

II. Administrative Review

All applications for funds to conduct research involving human subjects must be submitted through the office of the Executive Director of ORAU. For any proposal involving research in human subjects, the applicant is required to state in writing whether the proposed program has been submitted to the Committee on Human Studies.

III. Membership of the Committee

The Committee includes two outside consultants familiar with the type of research done at ORAU and having no personal participation in the projects discussed. Other members of the Committee are the chairman of the Medical Division, four members of the Division's scientific staff, and a lawyer who is head of legal services for ORAU. The chief of clinical services at ORAU is an ex officio member.

IV. Initial Review by Committee

All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects must be presented to and approved by the Committee on Human Studies prior to submission for funding, and in the exact form to be used for submission. Regardless of the nature or degree of risk anticipated, the applicant must present in writing, and be prepared to defend in person before the Committee, detailed information on the following points:

1. The possible risks to the rights and welfare of human subjects, including the rights of privacy, freedom from undue harassment, and confidentiality of data, and a description of the provisions made to minimize these risks.

1032570

2. Methods used to acquire informed consent, and the form in which it is stated, with special emphasis on the appropriateness to the particular situation inherent in the study plan.

3. The relative risks of the project as compared to the probable benefits to the subjects and to society.

For each application the Committee will either certify that these points have been properly dealt with and declare that the project may be submitted for funding, or recommend to the Executive Director of ORAU that submission be delayed until specific deficiencies (spelled out in writing) are adequately dealt with.

Members of the Committee who are in any way directly involved in the work will not participate during the pertinent discussion.

Approval of the Committee members reviewing the application must be unanimous. In the event that only one member of the Committee disapproves of a proposal, one or more additional outside consultants especially qualified and approved by the majority of the Committee will be asked to review the problem. If they concur, the research may go forward over the dissent of the one member of the regular committee.

The Committee's findings will be transmitted in writing to the Executive Director and to the Chairman of the Medical Division and the applicant. No funds shall be released by the ORAU Fiscal Services Department until the Executive Director has concurred with these recommendations. The applicant's administrative superior shall maintain continuing review of the project activities in the light of the Committee's report.

V. Continuing Review by Committee

The Committee meets twice yearly or at such additional times as called by the chairman. Investigators in charge of projects on human subjects are required to submit at each of these sessions status reports in which are presented any emergent problems. If a report is delinquent, the Executive Director of ORAU will contact the investigator to ascertain the status of the study protocol. If at any time the Committee is dissatisfied with the conduct of the project, or with the cooperation of the investigator, they shall immediately report this to the Executive Director and recommend that financial support of the project be withheld until the deficiencies are corrected.

1032571

If a responsible investigator plans a change in study protocol, he will submit the proposed changes to the Committee for their approval, before putting them into practice.

VI. Provisions to Protect the Health and Safety of Human Subjects

The ORAU Medical Division has a 26-bed clinical facility with modern equipment, including a surgical suite. It is staffed with at least four full-time permanent staff physicians devoting most of their time to clinical research and patient care, plus seven other physicians in various positions (pathology, division chairman, etc.) plus a variable number of temporary physician trainees. Special consultant services from Knoxville and from medical schools participating in ORAU are sought when needed. The nearby facilities of the Oak Ridge Hospital of the Methodist Church are available to our unit.

VII. Applicability of this Assurance

Although at the present time all research involving human subjects is localized at the Vance Road site of the Medical Division of Oak Ridge Associated Universities, the same provisions would apply to other research sites of the Medical Division, and to the other divisions and offices of ORAU, should human research be undertaken at these sites.

1032572

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

August 11, 1969

Gould Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

RNK

Dear Dr. Andrews:

We are pleased to inform you that the Public Health Service has reviewed and accepted the statement of assurance dated May 29, 1969, as amended August 1, 1969, submitted by the Oak Ridge Associated Universities, Inc., as being in compliance with the requirements contained in the Surgeon General's policy issuance of May 1, 1969, relating to investigations involving human subjects.

It is necessary that the Public Health Service be kept informed on a current basis of any changes in policies, procedures, or committee composition relating to this requirement.

We appreciate your cooperation in this matter. We welcome any comments or suggestions you may wish to make as we continue to try to clarify the ethical issues present in the pursuit of projects involving human subjects.

Sincerely yours,

Stephen P. Hatchett

Stephen P. Hatchett, Ph.D.
Acting Director
Division of Research Grants

1032573

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8411

Institutional Assurance on Research Involving Human Subjects

The Oak Ridge Associated Universities will comply with the principles of the Public Health Service policy with regard to research involving human subjects which requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. It assures the Public Health Service that it will establish and maintain advisory groups competent to review research plans involving human subjects, prior to the initiation of this research, in order to insure adequate safeguards. Group reviews and decisions will be carried out in reference to (1) the rights and welfare of the individuals involved, (2) the appropriateness of the methods used to obtain informed consent, and (3) the risks and potential benefits of the proposed research.

The institution agrees to a continuing exchange of information and advice between the review group and the investigator or director, particularly to deal with proposed changes in research design, and with emergent problems which may alter the investigational situation with regard to the criteria cited above. The institution will assure itself that its policies and the advice of its review groups are followed. It will also provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects involved in research. Records of group review and decision on the use of human subjects and of informed consent will be developed and kept by the institution.

Signed [signature] M.D.

Title Chairman, Medical Division

Date May 29, 1969

Enclosures (implementing Guidelines)

1032574

If a responsible investigator plans a change in study protocol, he will submit the proposed changes to the Committee for their approval, before putting them into practice.

VI. Provisions to Protect the Health and Safety of Human Subjects

The ORAU Medical Division has a 26-bed clinical facility with modern equipment, including a surgical suite. It is staffed with at least four full-time permanent staff physicians devoting most of their time to clinical research and patient care, plus seven other physicians in various positions (pathology, division chairman, etc.) plus a variable number of temporary physician trainees. Special consultant services from Knoxville and from medical schools participating in ORAU are sought when needed. The nearby facilities of the Oak Ridge Hospital of the Methodist Church are available to our unit.

VII. Applicability of this Assurance

Although at the present time all research involving human subjects is localized at the Vance Road site of the Medical Division of Oak Ridge Associated Universities, the same provisions would apply to other research sites of the Medical Division, and to the other divisions and offices of ORAU, should human research be undertaken at these sites.

1032575

August 1, 1969

Dr. Seymour Bress
Liaison Officer
Institutional Relations Section
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Bress:

As a follow-up to our June 18 reply to your letter of June 9, we are enclosing a revised "Guidelines for Research on Human Subjects" that has been adopted by Oak Ridge Associated Universities. The revision has incorporated the procedures that were not adequately delineated in our earlier draft. We trust that these will clear up the deficiencies that you felt existed.

We are also enclosing the certificate attesting to the review and approval of the grant application, "The Control of Infections in Cancer Patients," Edward Balish and C. Lowell Edwards, Principal Investigators.

Sincerely yours,

Gould Andrews, M.D.
Chairman
The Medical Division

GAA:fb

Enc.

1032576

Medical Division

Oak Ridge Associated Universities

Oak Ridge, Tennessee

ORAU GUIDELINES FOR RESEARCH ON HUMAN SUBJECTS

Revised July 1969

I. Ethical Policy

The staff of the Medical Division and the Committee on Human Studies of Oak Ridge Associated Universities have officially adopted the code of ethics adopted by the World Medical Association, known as the Declaration of Helsinki. We accept as amplification of this document, the statement of the British Medical Research Council.

II. Administrative Review

All applications for funds to conduct research involving human subjects must be submitted through the office of the Executive Director of ORAU. For any proposal involving research in human subjects, the applicant is required to state in writing whether the proposed program has been submitted to the Committee on Human Studies.

III. Membership of the Committee

The Committee includes two outside consultants familiar with the type of research done at ORAU and having no personal participation in the projects discussed. Other members of the Committee are the chairman of the Medical Division, four members of the Division's scientific staff, and a lawyer who is head of legal services for ORAU. The chief of clinical services at ORAU is an ex officio member.

IV. Initial Review by Committee

All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects must be presented to and approved by the Committee on Human Studies prior to submission for funding, and in the exact form to be used for submission. Regardless of the nature or degree of risk anticipated, the applicant must present in writing, and be prepared to defend in person before the Committee, detailed information on the following points:

1. The possible risks to the rights and welfare of human subjects, including the rights of privacy, freedom from undue harassment, and confidentiality of data, and a description of the provisions made to minimize these risks.

1032577

2. Methods used to acquire informed consent, and the form in which it is stated, with special emphasis on the appropriateness to the particular situation inherent in the study plan.

3. The relative risks of the project as compared to the probable benefits to the subjects and to society.

For each application the Committee will either certify that these points have been properly dealt with and declare that the project may be submitted for funding, or recommend to the Executive Director of ORAU that submission be delayed until specific deficiencies (spelled out in writing) are adequately dealt with.

Members of the Committee who are in any way directly involved in the work will not participate during the pertinent discussion.

Approval of the Committee members reviewing the application must be unanimous. In the event that only one member of the Committee disapproves of a proposal, one or more additional outside consultants especially qualified and approved by the majority of the Committee will be asked to review the problem. If they concur, the research may go forward over the dissent of the one member of the regular committee.

The Committee's findings will be transmitted in writing to the Executive Director and to the Chairman of the Medical Division and the applicant. No funds shall be released by the ORAU Fiscal Services Department until the Executive Director has concurred with these recommendations. The applicant's administrative superior shall maintain continuing review of the project activities in the light of the Committee's report.

V. Continuing Review by Committee

The Committee meets twice yearly or at such additional times as called by the chairman. Investigators in charge of projects on human subjects are required to submit at each of these sessions status reports in which are presented any emergent problems. If a report is delinquent, the Executive Director of ORAU will contact the investigator to ascertain the status of the study protocol. If at any time the Committee is dissatisfied with the conduct of the project, or with the cooperation of the investigator, they shall immediately report this to the Executive Director and recommend that financial support of the project be withheld until the deficiencies are corrected.

FORM P-4

MEMORANDUM

TO Dr. Kniseley DATE September 15, 1969

SUBJECT Human Studies Committee

COPIES TO

I had a call back on August 19 from Dr. Aposhian* as a result of my earlier call to Dr. Pelczar, and Dr. Aposhian suggested the following people as clinical pharmacologists who would be interested in human studies of a new drug:

Dr. John A. Oates (or someone he would recommend)
Vanderbilt University

Dr. Leon Goldberg
Emory University

Dr. Rubin Bressler
Duke University

G.A.A.

pe

*First name, Vasken

1032579

Studies

A meeting of the Human Use Committee of the Oak Ridge Institute of Nuclear Studies met on 15 September 1967.

The following members were present: Robert Heyssel, K.O.Goh, Gould Andrews, Lowell Edwards, Edward Balish, and Robert D. Lange.

The following new proposals and recommended actions were discussed:

1. Immunotherapy of Acute Leukemia.

This project invoked a great deal of discussion about possible risks to the recipient of irradiated malignant cells. The members of committee approved the plans for at least a few more studies since the risks are most certainly minimal, but recommended that possible other methods for obtaining specifically sensitized malignant cells be explored.

Dr. R. L. Hayes was present for the discussion of the following two projects.

2. Clinical Trial of $^{113}In^{m}$ as a Kidney and Bone Scanning Agent.

After discussion, the proposal was approved after appropriate clearances have been made.

3. Clinical Trial of ^{68}Ga-Labeled Hydrous Ferric Oxide Colloid for Bone Marrow Scanning.

After discussion, the proposal was approved after appropriate clearances have been made.

The following on-going studies were presented and discussed:

#1. Marrow Grafting following Total Body Irradiation. superseded by #13

2. Use of Small Tracer Doses of Rare Elements in Human Volunteers.

3. Use of Radioiodine in Surgical Removal of Thyroid Cancers.

The continuation of these three programs was approved.

Submitted by

Robert D. Lange, M.D.

RDL:ht

HUMAN STUDIES COMMITTEE MEETING

September 18, 1969

Members Present:

G. A. Andrews
Melvin E. Koons
Edward Balish
Randy Brill
John Storer
Bill Nelson
Robert Lange

The following other people participated:

Ralph Kniseley
Lowell Edwards
Francis Goswitz
Jere Bauer

The following projects were presented for committee action:

1. Studies of Total-Body Irradiation in Patients with Hematologic Disorders. Senior Investigator: C. L. Edwards. Co-Investigators: C. C. Lushbaugh, Helen Vodopick, Francis A. Goswitz, Bill Nelson, R. M. Kniseley, and G. A. Andrews. # 10

The committee approved this project but recommended the purchase of new dosimetry equipment for the METBI facility to allow continuous monitoring.

2. Blood Lymphocyte Survival and Distribution in Patients with Lymphoproliferative Disorders. Senior Investigator: Francis Goswitz. Co-Investigators: Helen Vodopick, C. C. Lushbaugh, and C. L. Edwards. # 11

This project evoked a good deal of discussion, mainly on the suitability of Cr^{51} and selenomethionine as a lymphocyte label. It was the feeling of the committee that as currently performed with 250 microcuries of Cr^{51} that no particular hazard existed for the patient with a malignant disease involving lymphocytes. However, the committee did not feel that it would be justified to use individuals with benign disorders or patients who had been exposed to total-body irradiation. It was further suggested that the

1032581

suitability of the isotopes be re-evaluated by the staff and only if the staff (Internal Research Committee) concurred in their suitability should the current studies be continued.

3. Scanning Tumors of the Retroperitoneal Lymph Nodes After Intralymphatic Injection of Radioactive Gallium.

The committee approved this project, but it was pointed out that the greatest danger may reside in the lymphangiogram procedure. The danger of performing the procedure in patients with pulmonary disease was noted.

Two projects were discussed in a preliminary fashion and were not presented for formal committee review. These projects were:

1. Dr. Jere Bauer discussed the possibility of engagement in a program of dialysis of blood against an enzyme. At this particular moment asparaginase is being considered as a possible enzyme. A great deal of animal work is needed before this can be presented as a definitive project.

2. Gould Andrews and John Storer discussed, in a preliminary fashion, the possible participation of the Medical Division in studies on radiation protective agents in collaboration with a group at Walter Reed Army Institute of Research. The compound showing the most promise has been given the code number WR-2721. While there seems to be no question about the ability of this drug to offer radiation protection in animals, pharmacologic data in animals and man is meager.

   Certain groups of patients were thought to be suitable for study if further data indicated feasibility. Among these groups were patients with incurable solid tumors and patients with skin metastases on which the material might be used topically. It was thought that patients in the total-body irradiation program should not be included.

Submitted by:

R D Lange

Robert D. Lange

1032582

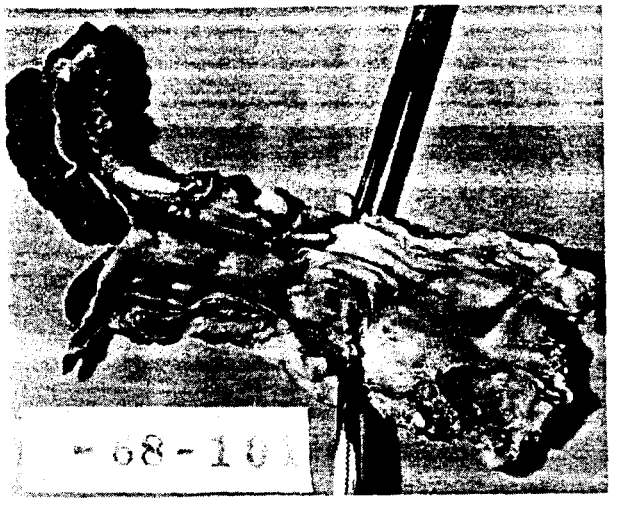


FIGURE 2. *Autopsy Specimen of the Inferior Vena Cava Five Years after Ligation and Death from Myocardial Infarction, Demonstrating No Areas of Constriction and a Completely Open Lumen.*

Clamps are on the renal veins. Note the hematoma about the right iliac vein.

DISCUSSION

Although I was aware of the work by Streuter suggesting recanalization of the inferior vena cava after catgut ligature, such an occurrence was considered highly improbable in the case presented above. Even though the vena cava opened sometime before death, at no time was there any improvement in the venous stasis of the lower extremity, indicating that the permanent changes from the previous thrombophlebitis were the basis for the continuing edema and ulceration.

Although a patent vena cava did not improve the lower extremities, it did provide a pathway for re-embolization, which may or may not have occurred. The absence of cor pulmonale suggests that the patient had not had major re-embolization.

LAW-MEDICINE NOTES

New Public Health Service Regulations on Human Experimentation

WILLIAM J. CURRAN, J.D., S.M.HYG.

AFTER three years of experience in administering the program, the United States Public Health Service has promulgated the first significant revision of its 1966 guidelines concerning the use of human subjects in Public Health Service-supported extramural research, demonstration, and training projects and contracts.[1]

The revised guidelines provide important clarification and amplification of the earlier provisions. In the main, however, they do not change the objectives or the basic philosophy of the program.[2] Protection of the welfare of research subjects continues to be the keynote of the entire program.

It is made clear that the guidelines apply to all research involving human subjects which is supported by any Public Health Service unit whether concerned with medical, behavioral or social studies. Research subjects include patients, normal volunteers, donors of body fluids, organs or tissues, and members of the general population involved in environmental and epidemiological studies.

Important further amplification is provided regarding the requirement of subject consent. It is indicated that consent can be obtained from parents, guardians or next of kin for minors and other legally incompetent persons. By implication, this would authorize research projects involving the use of children, mentally ill persons, or mentally retarded persons where legally valid consent is obtained. It is probable that local state law would govern the validity of such consent. A definition of the term "consent" is provided in the new regulations. It is said that consent is valid if the subject (or representative) is given "a fair explanation" of the procedures, their possible benefits and attendant hazards and discomforts, and the objectives of the research. The definition is quite similar to that in the Food and Drug Administration's regulations concerning the use of humans in the testing of new drugs.[3] The FDA also uses the term "fair explanation." The Public Health Service probably goes somewhat beyond FDA in requiring disclosure of "discomforts."

The most important procedural change in the guidelines requires that institutional (grantee) review committees approve all applications *before* submission to Public Health Service. Formerly, institutions had a choice of reviewing before or after submission as long as they reviewed and approved the protocol prior to the beginning of the actual research. Understandably, given the choice, the majority of institutions adopted the practice of reviewing only after a grant was actually awarded. The change is, however, a good one in terms of the administration of the program.[2] Under the previous practice, it was difficult to identify clearly where responsibility was placed to protect the welfare of subjects. The Public Health Service staff and advisory committees were concerned primarily with assessing the merits of the applications, though staff and committees did often raise questions concerning legal and ethical matters. There was ambiguity due to the fact that the institutional review committees might be considering these matters later and might alter the research protocols substantially or even refuse to allow the research to be conducted. Also, some pressure undoubtedly was felt by the institutional review committees to allow projects to proceed when they had already been awarded by the Public Health Service.

The procedural change on institutional review

1032583

enabled Public Health Service to clarify its own responsibility in this field. It states as follows:

> Since the welfare of the subject is a matter of concern to the Public Health Service as well as to the institution, PHS advisory groups, consultants, and staff will independently review all research involving human subjects, recommending unfavorable action on grants, contracts, or awards if the research presents unacceptable hazards.

One of the most attractive features of the original Public Health Service guidelines, however, is the high degree of self-regulation allowed to research institutions to police themselves in these matters through their own review committees. This system is continued and strengthened in these new provisions. In this regard the revised guidelines contain a major recommendation concerning the composition of review groups. It is suggested that "legal competence" would be desirable on the committees in order to help to make judgments regarding institutional regulations, relevant law and standards of professional practice. The beneficial union of medicine and law thus receives an important, and much appreciated, recognition.

References

1. United States Department of Health, Education, and Welfare, Public Health Service, Division of Research Grants. Protection of the Individual as a Research Subject. Washington, DC, Government Printing Office, 1969 (Publication No. 0-348-095)
2. For a detailed examination of the 1966 guidelines and their operation, see Curran WJ. Government regulation of the use of human subjects in medical research: The approach of two federal agencies. Daedalus 98:542-594, 1969
3. 32 Federal Register 3994 (March 11, 1967)

Massachusetts Physicians Art Society

171. *The Barn*

(Exhibited at Annual Meeting of the Massachusetts Medical Society, 1969)

Photograph

Hugh Tatlock, M.D.

Chief of Medicine, Colley Dickinson Hospital, Northampton, Massachusetts.

1032583 A

Draft
recvd 7 Oct
1969

Statement of Policy of the Donner Laboratory and the Lawrence Radiation Laboratory

COMMITTEE FOR SAFEGUARDS IN RESEARCH IN HUMAN SUBJECTS

Lawrence Radiation Laboratory, University of California, Berkeley
February 1967

Purpose of Committee

The Committee functions in an advisory capacity to the Director of the Donner Laboratory of the Lawrence Radiation Laboratory. When such research involves N.I.H. funds, a separate approval for the investigation must be obtained from the Berkeley Campus Advisory Committee on Safeguards in Research in Human Subjects. When the proposed research utilizes inpatients from institutions other than the Donner Laboratory, approval for the experiment from the extramural institution is obtained. The responsibility for seeking approval for a clinical research protocol is the function of the responsible investigator. Post-doctoral research fellows supported by the National Institutes of Health, whose research involves use of human subjects, are expected to present acceptable research protocols to both this Committee and to the Berkeley Campus Advisory Committee on Safeguards and Research on Human Subjects.

State of Present Policies

1. Prior to initiation of any investigation involving the use of humans, a protocol describing in detail the purpose, methods and possible hazards attendant to the experiment is to be submitted and approved by the above Committee. When such protocols involve experimental use of radionuclides in humans, they contain a detailed summary of available information relative to the distribution and metabolic fate of the given radioisotope-labeled material in the bodies of animals and of humans, together with estimates of initial radiation dose rate and of total radiation dose delivered to the whole human body and to each critical body organ. In judging acceptable doses, the Committee is guided by factors including the age, sex and life expectancy of the subject, the expectancy of producing

1032584

offspring, the probability of the procedure's therapeutic or diagnostic value in a present illness, the established controls or normal values for a particular procedure, and the overall balance of risk against scientific merit of the proposal. If the procedure involves the single administration of radionuclides not greater than the maximum permissible body burden (MPBB) for the general population (1/10 the occupational value as stated by the United States National Committee on Radiation Protection and Measurements) of a radionuclide with effective half life (T_{eff}) of a few weeks or less, the applicant can ordinarily expect Committee approval for use in a limited number of volunteer adult humans, as well as in patients.

If the procedure involves a single administration not greater than the occupational MPBB of a radionuclide with T_{eff} of a few hours or less, the applicant can ordinarily expect Committee approval for use in small numbers of volunteer normal adults judged unlikely to bear children in the future, or in patients with limited life expectancy or for whom the procedure offers diagnostic information. When subjects are given multiple doses of radionuclides in a single procedure or participate in multiple radioisotope procecures, the total dose received in the procedure as well as the cumulative previous radiation dose delivered to critical tissues should be estimated, and such estimates are submitted for review by the Committee.

2. The Committee reviews potentially hazardous physical procedures, specific to the protocol imposed on the human subject (other than those related to venepuncture for blood sampling and body excrement collection). Sterility and lack of phrogenicity of parenterally administered materials are insured. Investigators are expected to design their experimental protocols to be safe from any potentially hazardous mechanical procedures.

3. The Committee considers the chemical form of a material administered to a human subject in any experimental protocol as being acceptably safe when the material is either a normal body constituent which has no known toxicity when administered in the dose and by the route proposed in the experimental protocol, or a drug considered acceptable by the United States Food and Drug Administration

for clinical use when administered in the dose and by the route proposed in the given experimental protocol. When the chemical nature of the material to be used in any given experiment does not correspond to either of the two above mentioned categories and represents an experimental drug which has not yet received sanction for routine clinical use by the United States Food and Drug Administration, then all restrictions to the use of this drug imposed by the United States Food and Drug Administration are imcorporated in the requirements for the proposed experimental protocol.

4. Normal subjects volunteering for studies involving administration of radionuclides are over 21 years of age and are usually males. Normal female subjects may be studied when the physician is reasonably certain, after history and physical examination, that they are not pregnant at the time of the study. When circumstances are such that the individual investigator feels it is necessary to administer radiation or radionuclides to normal volunteer subjects who are under the age of 21 or to study a normal female subject during pregnancy, then each case is individually evaluated by the Committee.

5. Written informed consent must be obtained from each human subject as required by the Directors of the Laboratory.

6. Adequate written records must be kept, including written informed consent and the nature and quantity of radionuclides or other experimental materials administered to a given subject. The investigator is obligated to promptly inform the Director of the Laboratory of any difficulties adversely affecting the patient.

7. Confidentiality of information obtained from the subject must be assured.

8. All procedures in which radioisotopes are administered to humans are considered appropriate for review by the Committee.

9. Signed copies of approved protocols are returned to the author as an indication of approval by the Committee. The investigator is obliged to adhere to the approved protocol.

Committee Members:

James Born, LL.Bl, M.D., Assistant Director, Donner Laboratory, University of California, Berkeley, California.

Hardin B. Jones, Ph.D., Professor of Physiology and Medical Physics, Assistant Director of Donner Laboratory, University of California, Berkeley, California.

Howard Parker, M.D., Ph.D., Head of Medical Services Department, Donner Laboratory and Lawrence Radiation Laboratory, Berkeley, California.

William E. Siri, B.Sc., Physicist to the Donner Laboratory, University of California, Berkeley, California.

Harry S. Winchell, M.D., Ph.D., Associate Research Physician and Hematologist at Donner Laboratory, University of California, Berkeley, California. Chairman.

1032587

Addendum to the "Statement of policy of the Donner Laboratory and the Lawrence Radiation Laboratory Committee for Safeguards in Research in Human Subjects."

To insure that all materials administered to human subjects during the course of any experimental protocol are sterile and pyrogen free, the following requirements must be satisfied. The final product must be tested for sterility and pyrogens prior to initial administration of material to human subjects. Subsequent to the initiation of the experimental protocol, the final product must be tested for sterility and pyrogenicity at least once during every four month period. Records must be kept of all such sterility and pyrogen testing by the individual investigator and must be available for perusal by this Committee. Each time the protocol is modified or changed in any way, repeat testing of the final product for sterility and lack of pyrogenicity must be obtained prior to using said product in human subjects. It is recommended that where possible all components utilized in the preparation of the final product and all glassware used in containing these components be purchased certified sterile and pyrogen free.

The following criteria are proposed for limiting the radiation dose received by normal human volunteers receiving radioisotopes as part of any experimental protocol. These limitations do not apply to the use of radioisotopes in patients with disease processes in whom the data obtained from the study can be useful in evaluating said disease process. (The restrictions refer to radionuclides decaying by gamma, beta + and beta -, internal conversion and electron capture processes. Evaluation of alpha emitting or neutron emitting radionuclides are considered individually.)

1. Where the effective half-time of the radioisotope in the body is greater than six months, the maximum dose and dose rate to any tissue must be less than 1/100 of that recommended by the NCRP for radiation workers (e.g. intergral dose less than 50 mr per year).

2. Where the effective half-time within the body is less than six months but greater than one week, the maximum initial dose rate

to any tissue is less than 1/10th of that recommended by the NCRP for radiation workers (less than 0.5 r per year).

3. For radionuclides with a short effective half-life in the body (less than one week), the maximum dose to bone, bone marrow, lymph nodes, intestinal mucosa and gonads must be less than 0.5 r and the total dose to any tissue other than those noted above must be less than 5 r.

1032589

Protocol for Preparation of Report to Committee for Safeguards in Research in Human Subjects

Organize information in paragraphs according to the following headings.

a) State title of research proposal.

b) List responsible investigators.

c) Briefly summarize purpose of administering radionuclides to humans, source, number, sex and age distribution of human subjests and information given subjects concerning the nature and hazards of the study.

d) List isotopes used, modes of decay, physical t 1/2 biological t 1/2 (cite reference for biological t 1/2 when possible).

e) Summarize what is known about the distribution and local turnover rates of each material in the human body (i.e. estimate the function describing radionuclide concentration changes as a function of time in the target organ(s).

f) Show, in detail, calculation of maximal radiation dose rate, and cumulative radiation dose in critical organs (bone marrow, G.I. tract, gonads and organs of maximal localization). If distribution of the material used is approximately uniform, calculate whole body dose. (see attached forms for suggested methods for use in radiation dose calculation.)

g) Summarize procedures used to assure sterility and lack of pyrogenicity of materials to be administered to human subjects.

1032590

Sample

EXAMPLE OF AN ACCEPTABLE STATEMENT OF COMPLIANCE
AS REQUIRED BY THE SURGEON GENERAL'S ISSUANCE OF MAY 1, 1969*

Policy and Procedures of Marimar University Concerning Investigations Involving Human Subjects

I. Ethical Policy. The Faculty and Board of Trustees of this University have officially adopted the code of medical and general ethics, promulgated by the World Medical Association as the Declaration of Helsinki.

II. Administrative Review. All applications for funds from the Public Health Service must be submitted through the Office of Research and Special Projects of this University. Here they are reviewed chiefly for completeness, budget accuracy, and for compliance with PHS policy. For any proposal involving the use of human subjects the applicant is required to inform this Office whether he has submitted copies to the Faculty Research Committee (described below). This Office is required to call to the Committee's attention any projects not so submitted which appear to involve human subjects.

III. Membership of Review Committee. The Membership of the Faculty Research Committee consists of the Chairmen of all academic Departments and the principal administrative officers; the Chairman of the Committee is the Assistant Dean of the Graduate School in charge of sponsored research. The degrees and areas of specialization of the incumbents are listed overleaf (not included with this example). The Faculty Chaplain, Fr. Brown, and Mr. Ephriam Tutt, our legal officer, may be called as consultants.

IV. Initial Review by Committee. All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects must be submitted to the Faculty Research Committee prior to submission to the PHS, and in the exact form to be used for submission. Regardless of the nature or degree of risk anticipated, the applicant must present in writing, and be prepared to defend in person before the Committee, detailed information on the following points:

1. The possible risks to the rights and welfare of human subjects, including the rights of privacy, freedom from undue harassment, and confidentiality of data, and a description of the provisions made to minimize these risks.

2. Methods used to acquire informed consent, with special emphasis on their appropriateness to the particular situation inherent in the study plan.

3. The relative risks of the project as compared to the probable benefits to the subjects and to society.

1032591

For each application the Committee will either certify that these points have been properly dealt with and declare that the project may be submitted to the PHS, or recommend to the President of the University that submission be delayed until specific deficiencies (spelled out in writing) are adequately dealt with.

Members of the Committee who are in any way directly involved in the work covered by any project being considered will be replaced by appropriate substitutes during the pertinent discussion.

The Committee's findings will be transmitted in writing to the President, the appropriate departmental chairman, and the applicant. No funds shall be released by the Comptroller until the President has concurred with these recommendations. The applicant's administrative superior shall maintain normal supervision of the project activities in the light of the Committee's report.

V. Continuing Review by Committee. The Faculty Research Committee meets quarterly. Investigators in charge of projects involving human subjects are required to submit to each of these sessions status reports in which are presented any emergent problems. The Chairman will maintain a project log summarizing the Committee discussions on these reports. If a report in delinquent, the Chairman will contact the investigator to ascertain the status of the study protocol. If at any time the Committee is dissatisfied with the conduct of the project, or with the cooperation of the investigator, they shall immediately report this to the President and recommend that financial support of the project be withheld until the deficiencies are corrected.

If a responsible investigator plans a change in study protocol, he will submit the proposed changes to the Committee for their approval, before putting them into practice.

VI. Provisions to Protect the Health and Safety of Human Subjects. This University has a 20 bed health unit staffed by 4 part-time M.D.'s. Serious cases are referred to the Washington County Hospital.

VII. Applicability of this Assurance. This assurance applies to this University, its extension campuses in Mayberry and Tarbox, and its Institute for Human Relations in Colesville.

*This example was drafted in the Institutional Relations Section, Division of Research Grants, National Institutes of Health. It refers to no existing institution and is intended only as a guide for use in developing acceptable statements of compliance.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD. 20014
AREA CODE 301 TEL: 656-4000

June 9, 1969

Gould Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P.O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Andrews:

We have received and reviewed the procedures your institution plans to follow in reviewing projects involving human subjects. I am afraid, however, that the procedures you outlined are either silent or too narrowly construed on several points we believe are crucial to the protection of an individual as a research subject. For example:

1. Public Health Service policy requires that any project involving the use of human subjects must be reviewed and be subject to continuing review by your institutional committee. Your procedures permit the screening out of certain projects with "insignificant" risks to the subjects.

2. Your procedures do not explicitly state that the committee will review the project to determine (a) how the rights and welfare of the human subjects involved will be protected, (b) the appropriateness of the methods used to obtain informed consent, and (c) that the potential benefits of the proposed research will exceed the risks.

3. Your procedures are silent on the need for the committee to exercise continuing review of the project to confirm that the investigator has followed the advice of the committee, if any, and that he has not changed his approved protocol without prior advice of the committee.

4. Your procedures do not state that the investigator may not change his protocol without prior committee approval.

5. Your procedures do not indicate the emergency facilities available to the subjects should an emergency occur.

1032593

I have attached a copy of sample procedures we have drawn up in this office. It covers all of the points we are most concerned with and you may find it helpful in expanding your procedures to cover the items mentioned above.

If you have any questions about our policies in this area, please feel free to contact me.

Sincerely yours,

Seymour Bress
Liaison Officer
Institutional Relations Section
Division of Research Grants

Enclosures

1032594

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

File Ctl

August 11, 1969

Gould Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

RMK

Dear Dr. Andrews:

We are pleased to inform you that the Public Health Service has reviewed and accepted the statement of assurance dated May 29, 1969, as amended August 1, 1969, submitted by the Oak Ridge Associated Universities, Inc., as being in compliance with the requirements contained in the Surgeon General's policy issuance of May 1, 1969, relating to investigations involving human subjects.

It is necessary that the Public Health Service be kept informed on a current basis of any changes in policies, procedures, or committee composition relating to this requirement.

We appreciate your cooperation in this matter. We welcome any comments or suggestions you may wish to make as we continue to try to clarify the ethical issues present in the pursuit of projects involving human subjects.

Sincerely yours,

Stephen P. Hatchett

Stephen P. Hatchett, Ph.D.
Acting Director
Division of Research Grants

1032595

Mr. Harmon

Feb

MEETING OF COMMITTEE ON HUMAN STUDIES OF

Oak Ridge Associated Universities

Held 19 January, 1970 at Medical Division.

Members of Committee Present	Staff Members Present
G. A. Andrews	N. Gengozian
A. B. Brill	C. L. Edwards
Melvin Koons	Helen Vodopick
R. D. Lange	Karl Hubner
Wm. Nelson	
John Storer	
Tom Lincoln	

The Meeting was held to discuss the initiation of a project entitled:

Therapeutic Allogenic Transplantation of Human Bone Marrow.

Gould Andrews introduced the proposal and gave a brief historical background of the use of bonemarrow transplantation.

There was a great deal of discussion of the proposed project and many questions were raised. Among the questions were the advisability of using anti-lymphocyte-serum before additional animal studies were performed and also regarding consideration of the use of extracorporeal irradiation. There were questions regarding the method to be used for producing and obtaining the anti-lymphocyte-serum as well as a discussion of the selection of participants and dangers of fat embolism.

It was brought out that the AEC was very interested in the "informed consent" procedure and would need to be satisfied regarding the form to be signed.

There was a discussion of the safety factors involved in the use of the high dose facilities at U.T.A.E.C. and the possibility of purchasing an auxilliary power source was suggested.

1032596

There followed a discussion of the graft versus host reaction and it was pointed out that this was a real hazard.

Each of these foregoing questions were answered to the satisfact on of the committee.

At this point Drs. Andrews, Gengozian, Edwards, Vodopick and Hubner retired and the following motion was proposed by Dr. Storer, seconded by Dr. Brill and was passed unanimously by the remaining members of the committee:

> The committee approves the project as submitted contingent on the preparation of a release which meets all legal requirements. The committee further recommends that an independent evaluation of the extent of understanding of the release on the part of the patient or parent be made if feasible. It is suggested that a member of the clergy might make such an evaluation. The committee also expressed a wish that they be kept informed on the progress of this project.

Submitted by

R D Lange

Robert D. Lange, M.D.
Committee on Human Studies

1032597

FORM P-4A

MEMORANDUM

TO R. M. Kniseley DATE April 17, 1970

SUBJECT Committee on Human Studies

COPIES TO C. L. Edwards, J. H. Harmon, Melvin Koons, Bill Nelson
File

I just talked with Mel Koons and he said that he would be glad to continue to serve on our committee to review human applications of new procedures. His address is Law Department, ORNL, Building 9704-2 (Y-12 area), and his telephone extension is 3-7295.

G.A.A.

pe

1032598

OAK RIDGE NATIONAL LABORATORY
OPERATED BY
UNION CARBIDE CORPORATION
NUCLEAR DIVISION

POST OFFICE BOX X
OAK RIDGE, TENNESSEE 37830

Office of the Director

June 26, 1970

Dr. William G. Pollard
Executive Director
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Bill:

As you are perhaps aware, the Division of Biology and Medicine of the Atomic Energy Commission has officially adopted the NIH procedures for human experimentation. Jim Liverman, Associate Director for Biomedical and Environmental Sciences, has discussed with Ralph Kniseley the possibility that the ORAU Medical Division Committee on Human Studies could also handle the limited number of applications for such studies which the Oak Ridge National Laboratory might have. This letter is to request your formal agreement that this method of proceeding makes sense at this time, and to offer to provide our fair share of costs involved with the operation of your Committee.

Since it is necessary that we respond to John Totter's request by July 1, I would appreciate an early reply.

Sincerely yours,

ORIGINAL SIGNED BY
ALVIN M. WEINBERG

Alvin M. Weinberg

AMW:JLL:lmm

Attachment

cc: H. I. Adler
N. G. Anderson
R. F. Hibbs
R. M. Kniseley
T. A. Lincoln
J. L. Liverman
R. A. McNees
K. Z. Morgan
M. E. Ramsey
H. M. Roth

1032599

Institutional Assurance on Research Involving Human Subjects

The Oak Ridge National Laboratory will comply with the principles of the AEC policy with regard to research involving human subjects which requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. It assures the AEC that it has established and maintains advisory groups competent to review research plans involving human subjects, prior to the initiation of this research, in order to insure adequate safeguards. By agreement (see attachment), the Oak Ridge Associated Universities Committee on Human Studies will also review all ORNL proposals in this area. Group reviews and decisions will be carried out in reference to (1) the rights and welfare of the individuals involved, (2) the appropriateness of the methods used to obtain informed consent, and (3) the risks and potential benefits of the proposed research.

The institution agrees to a continuing exchange of information and advice between the review group and the investigator or director, particularly to deal with proposed changes in research design, and with emergent problems which may alter the investigational situation with regard to the criteria cited above. The institution will assure itself that its policies and the advice of its review groups are followed. It will also provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects involved in research. Records of group review and decision on the use of human subjects and of informed consent are developed and kept by the institution.

Signed Alvin M. Weinberg
Director

Date June 29, 1970

Attachment

1032600

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8411

July 1, 1970

Dr. Alvin M. Weinberg, Director
Oak Ridge National Laboratory
Oak Ridge, Tennessee

Dear Alvin:

It certainly makes good sense, as requested in your letter of June 26, 1970, to use a single committee on human experimentation for both ORAU and ORNL. I have checked with Gould Andrews and he assures me that he has already given his verbal approval to Dr. Lincoln and others to having you use our committee for this purpose. This letter records my concurrence with him in this approval and makes official the formal agreement of Oak Ridge Associated Universities for the use by Oak Ridge National Laboratory of our Committee on Human Studies in compliance with NIH procedures for human experimentation in ORNL.

The costs involved in meetings of this committee are so small that we do not feel an attempt to allocate them between ORNL and ORAU would be worth the effort. Simply have your people let either Gould Andrews or Ralph Kniseley know when you wish to use the committee and they will schedule it.

Sincerely,

Bill

William G. Pollard
Executive Director

WGP:ahp

cc: Gould A. Andrews, ORAU Medical Division
Roger Hibbs, Nuclear Division, Union Carbide
H. M. Roth, LUD, AEC

1032601

file
E Com on Human Studies

OAK RIDGE NATIONAL LABORATORY

OPERATED BY
UNION CARBIDE CORPORATION
NUCLEAR DIVISION

UNION CARBIDE

POST OFFICE BOX X
OAK RIDGE, TENNESSEE 37830

OFFICE OF THE DIRECTOR

July 14, 1970

Dr. John R. Totter, Director
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington, D. C. 20545

Dear John:

Human Experimentation

This letter is in response to your letter of May 15, 1970, requesting that we place on file with your Division an acceptable assurance as described beginning on page five of the booklet entitled, "Protection of the Individual as a Research Subject."

This reply is somewhat belated because we felt it would make more sense from an operational standpoint, since we have so few instances of human experimentation, to utilize the Committee that has been established by the Oak Ridge Associated Universities' Medical Division. Attached are exchanges of correspondence between W. G. Pollard, Executive Director, Oak Ridge Associated Universities, and me indicating the willingness of Dr. Pollard to have the ORAU Committee on Human Studies assure our compliance with the NIH procedures as were outlined in the above-cited booklet. In addition, I have filled out and signed an Institutional Assurance on Research Involving Human Subjects form which follows very much the format of that of the ORAU letter to you earlier.

I hope that this manner of handling is satisfactory to you. If you have additional questions, please contact J. L. Liverman who will see that the necessary changes, if any, are carried out.

Sincerely,

Alvin M. Weinberg
Director

AMW:JLL:bmr
Attachments

cc: H. I. Adler
N. G. Anderson
R. F. Hibbs
R. M. Kniseley
T. A. Lincoln
J. L. Liverman
R. A. McNees
K. Z. Morgan
M. E. Ramsey
H. M. Roth

1032602

file
C Com on Hum Studies

OAK RIDGE NATIONAL LABORATORY

OPERATED BY
UNION CARBIDE CORPORATION
NUCLEAR DIVISION

POST OFFICE BOX X
OAK RIDGE, TENNESSEE 37830

OFFICE OF THE DIRECTOR

July 14, 1970

Dr. John R. Totter, Director
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington, D. C. 20545

Dear John:

Human Experimentation

This letter is in response to your letter of May 15, 1970, requesting that we place on file with your Division an acceptable assurance as described beginning on page five of the booklet entitled, "Protection of the Individual as a Research Subject."

This reply is somewhat belated because we felt it would make more sense from an operational standpoint, since we have so few instances of human experimentation, to utilize the Committee that has been established by the Oak Ridge Associated Universities' Medical Division. Attached are exchanges of correspondence between W. G. Pollard, Executive Director, Oak Ridge Associated Universities, and me indicating the willingness of Dr. Pollard to have the ORAU Committee on Human Studies assure our compliance with the NIH procedures as were outlined in the above-cited booklet. In addition, I have filled out and signed an Institutional Assurance on Research Involving Human Subjects form which follows very much the format of that of the ORAU letter to you earlier.

I hope that this manner of handling is satisfactory to you. If you have additional questions, please contact J. L. Liverman who will see that the necessary changes, if any, are carried out.

Sincerely,

Alvin M. Weinberg
Director

AMW:JLL:bmr
Attachments

cc: H. I. Adler
N. G. Anderson
R. F. Hibbs
R. M. Kniseley
T. A. Lincoln
J. L. Liverman
R. A. McNees
K. Z. Morgan
M. E. Ramsey
H. M. Roth

1032603

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

July 8, 1971

Gould Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Andrews:

Your institution has on file with this office an assurance of compliance with Public Health Service policy on the protection of human subjects. The terms of that assurance are applicable to all PHS-supported activities at your institution which involve human subjects. A copy of our letter accepting your assurance is attached.

Recent changes in policy to govern specified programs of the Department of Health, Education, and Welfare (including the Public Health Service) will require review and possible renegotiation of your assurance. Revised assurances can take the form of either an institutional "general" assurance such as the one you now have to cover all supported activities, or "special" assurances to be provided for each project that involves human subjects.

We believe that your institution may qualify for the "special" assurance procedure, and encourage you to take advantage of this more direct instrument. This procedure has been devised primarily for those institutions receiving support for only an occasional or a few projects involving human subjects. Instructions will be provided for each new and renewal application as it is proceeding through DHEW review.

Noncompeting applications for continuation support may, if you wish, be certified for institutional committee review under your current assurance. In this case, for an interim period your institution may operate concurrently under both kinds of assurances as they apply to different projects. Alternatively you may request immediate conversion to the "special" assurance.

Enclosed is an excerpt from the DHEW policy describing "Minimum Requirements for Acceptable General and Special Institutional Assurances." Exhibit forms that apply to each type of assurance are also enclosed. Perhaps I should make it clear that a future reconversion from several "special" assurances to a "general" assurance is quite feasible.

1032604

If we receive no response to this letter within 60 days, we will assume that you will have no objection to use of the "special" assurance procedure at your institution. If you wish consideration for a "general" assurance, please respond with a listing of all projects involving human subjects, whether supported by DHEW or by other sources, that are under active review by your institutional committee.

Sincerely yours,

D. T. Chalkley

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants

2 Enclosures

1032605

GUIDELINES

Research on Human Subjects

Oak Ridge Associated Universities

Medical Division

1. Principles

The Medical Division proposes to follow the code of standards of the Medical Research Council published 18 July 1964 in the British Medical Journal (attached) entitled Responsibility in Investigations on Human Subjects. The approach to informed consent will follow those guidelines (attached form).

2. Description of Review Committee

(a) Name: Committee on Human Studies

(b) Composition: Two outside consultants not involved in Medical Division research; Dr. Gould Andrews, Chairman of the Medical Division; two M.D. staff members; one Ph.D. staff member; Lawyer, Head Legal Services, Oak Ridge Associated Universities; and Dr. C. L. Edwards, Chief of Clinical Research, as ex officio member.

(c) Membership 1969. (See attached curriculum vitae)

3. Description of Review Procedures

(a) Scope. The committee should concern itself with all studies done in human beings, whether patients in the research hospital or normal volunteers of some type. The committee is to review all research at the ORAU Medical Division in which there is believed to be a significant risk to the patients or a significant possibility that criticism might be leveled at the scientists for their manner of doing studies in human beings. The decision about whether or not a specific investigative procedure involves any risk and therefore requires action by the committee would rest with the Medical Division. The Medical Division should bring to the committee's attention by name and brief description those experiments in human beings believed to have negligible risk, i.e., a systematic survey of hemoglobin and hematocrit values in thyroid patients. As to the suitability of undertaking a rather unconventional form of treatment in a single seriously ill patient, partly with the objective of immediate benefit to the patient and partly as a preliminary research effort that might be the basis for a future controlled investigation, considerable leeway rests with the physician who is responsible for the patient's care. Ordinarily the Committee on Human Studies would not be involved with d[illegible]ns concerning a single patient but rather with policy matters or

0032606

See revised Aug 71

research on groups of patients. However, if circumstances were such that the staff of the Medical Division wanted some consultation on the suitability of a study in an individual patient it might be quite reasonable to seek telephone consultation.

(b) The senior investigator who proposes a research project shall submit an Application for the Use of Humans as Experimental Subjects (See attached form.)

(c) The Chairman will circulate the proposal to the Committee after review by the Division Office. The committee members should request answers to questions that arise in advance of the meeting where possible.

(d) Unanimous concurrence by committee members must be obtained to allow a proposal to go forward. If there is dissent, additional outside consultation would be sought.

(e) Proposed studies involving new radioisotopes would first be presented to and approved by the ORAU Isotope Committee.

Responsibility in Investigations on Human Subjects

Statement by Medical Research Council

Under this heading the Medical Research Council include in their Annual Report for 1962–63 (Cmnd. 2382, H.M.S.O., 1964, price 16s. 6d. net) a statement on investigations on human beings which is intended to serve as a guide to medical men engaged in this kind of work. It is a statement of such importance that we reproduce it here in full.

During the last 50 years medical knowledge has advanced more rapidly than at any other period in its history. New understandings, new treatments, new diagnostic procedures, and new methods of prevention have been, and are being, introduced at an ever-increasing rate; and if the benefits that are now becoming possible are to be gained these developments must continue.

Undoubtedly the new era in medicine upon which we have now entered is largely due to the marriage of the methods of science with the traditional methods of medicine. Until the turn of the century the advancement of clinical knowledge was in general confined to that which could be gained by observation, and means for the analysis in depth of the phenomena of health and disease were seldom available. Now, however, procedures that can safely, and conscientiously, be applied to both sick and healthy human beings are being devised in profusion, with the result that certainty and understanding in medicine are increasing apace.

Yet these innovations have brought their own problems to the clinical investigator. In the past, the introduction of new treatments or investigations was infrequent, and only rarely did they go beyond a marginal variation on established practice. To-day far-ranging new procedures are commonplace, and such are their potentialities that their employment is no negligible consideration. As a result, investigators are frequently faced with ethical and sometimes even legal problems of great difficulty. It is in the hope of giving some guidance in this difficult matter that the Medical Research Council issue this statement.

A distinction may legitimately be drawn between procedures undertaken as part of patient-care which are intended to contribute to the benefit of the individual patient, by treatment, prevention, or assessment, and those procedures which are undertaken either on patients or on healthy subjects solely for the purpose of contributing to medical knowledge and are not themselves designed to benefit the particular individual on whom they are performed. The former fall within the ambit of patient-care and are governed by the ordinary rules of professional conduct in medicine; the latter fall within the ambit of investigations on volunteers.

Important considerations flow from this distinction.

Procedures Contributing to the Benefit of the Individual

In the case of procedures directly connected with the management of the condition in the particular individual, the relationship is essentially that between doctor and patient. Implicit in this relationship is the willingness on the part of the subject to be guided by the judgment of his medical attendant. Provided, therefore, that the medical attendant is satisfied that there are reasonable grounds for believing that a particular new procedure will contribute to the benefit of that particular patient, either by treatment, prevention, or increased understanding of his case, he may assume the patient's consent to the same extent as he would were the procedure entirely established practice. It is axiomatic that no two patients are alike and that the medical attendant must be at liberty to vary his procedures, according to his judgment of what is in his patients' best interests. The question of novelty is only relevant to the extent that in reaching a decision to use a novel procedure the doctor, being unable to fortify his judgment by previous experience, must exercise special care. That it is both considerate and prudent to obtain the patient's agreement before using a novel procedure is no more than a requirement of good medical practice.

The second important consideration that follows from this distinction is that it is clearly within the competence of a parent or guardian of a child to give permission for procedures intended to benefit that child when he is not old or intelligent enough to be able himself to give a valid consent.

A category of investigation that has occasionally raised questions in the minds of investigators is that in which a new preventive, such as a vaccine, is tried. Necessarily, preventives are given to people who are not, at the moment, suffering from the relevant illness. But the ethical and legal considerations are the same as those that govern the introduction of a new treatment. The intention is to benefit an individual by protecting him against a future hazard; and it is a matter of professional judgment whether the procedure in question offers a better chance of doing so than previously existing measures.

In general, therefore, the propriety of procedures intended to benefit the individual—whether these are directed to treatment, to prevention, or to assessment—are determined by the same considerations as govern the care of patients. At the frontiers of knowledge, however, where not only are many procedures novel but their value in the particular instance may be debatable, it is wise, if any doubt exists, to obtain the opinion of experienced colleagues on the desirability of the projected procedure.

Control Subjects in Investigations of Treatment or Prevention

Over recent years the development of treatment and prevention has been greatly advanced by the method of the controlled clinical trial. Instead of waiting, as in the past, on the slow accumulation of general experience to determine the relative advantages and disadvantages of any particular measure, it is now often possible to put the question to the test under conditions which will not only yield a speedy and more precise answer but also limit the risk of untoward effects remaining undetected. Such trials are, however, only feasible when it is possible to compare suitable groups of patients and only permissible when there is a genuine doubt within the profession as to which of the two treatments or preventive regimes is the better. In these circumstances it is justifiable to give to a proportion of the patients the novel procedure on the understanding that the remainder receive the procedure previously accepted as the best. In the case when no effective treatment has previously been devised then the situation should be fully explained to the participants and their true consent obtained.

Such controlled trials may raise ethical points which may be of some difficulty. In general, the patients participating in them should be told frankly that two different procedures are being assessed and their co-operation invited. Occasionally, however, to do so is contraindicated. For example, to awaken patients with a possibly fatal illness to the existence of such doubts about effective treatment may not always be in their best interest; or suspicion may have arisen as to whether a

1032608

particular treatment has any effect apart from suggestion, and it may be necessary to introduce a placebo into part of the trial to determine this. Because of these and similar difficulties it is the firm opinion of the Council that controlled clinical trials should always be planned and supervised by a group of investigators and never by an individual alone. It goes without question that any doctor taking part in such a collective controlled trial is under an obligation to withdraw a patient from the trial, and to institute any treatment he considers necessary, should this, in his personal opinion, be in the better interests of his patient.

Procedures not of Direct Benefit to the Individual

The preceding considerations cover the majority of clinical investigations. There remains, however, a large and important field of investigations on human subjects which aim to provide normal values and their variation so that abnormal values can be recognized. This involves both ill persons and "healthy" persons, whether the latter are entirely healthy or patients suffering from a condition that has no relevance to the investigation. In regard to persons with a particular illness, such as metabolic defect, it may be necessary to know the range of abnormality compatible with the activities of normal life or the reaction of such persons to some change in circumstances, such as an alteration in diet. Similarly it may be necessary to have a clear understanding of the range of a normal function and its reaction to changes in circumstances in entirely healthy persons. The common feature of this type of investigation is that it is of no direct benefit to the particular individual and that, in consequence, if he is to submit to it he must volunteer in the full sense of the word.

It should be clearly understood that the possibility or probability that a particular investigation will be of benefit to humanity or to posterity would afford no defence in the event of legal proceedings. The individual has rights that the law protects and nobody can infringe those rights for the public good. In investigations of this type it is therefore always necessary to ensure that the true consent of the subject is explicitly obtained.

By true consent is meant consent freely given with proper understanding of the nature and consequences of what is proposed. Assumed consent or consent obtained by undue influence is valueless, and, in this latter respect, particular care is necessary when the volunteer stands in special relationship to the investigator, as in the case of a patient to his doctor, or a student to his teacher.

The need for obtaining evidence of consent in this type of investigation has been generally recognized, but there are some misunderstandings as to what constitutes such evidence. In general, the investigator should obtain the consent himself in the presence of another person. Written consent unaccompanied by other evidence that an explanation has been given, understood, and accepted, is of little value.

The situation in respect of minors and mentally subnormal or mentally disordered persons is of particular difficulty. In the strict view of the law parents and guardians of minors cannot give consent on their behalf to any procedures which are of no particular benefit to them and which may carry some risk of harm. Whilst English law does not fix any arbitrary age in this context, it may safely be assumed that the Courts will not regard a child of 12 years or under (of 14 years or under for boys in Scotland) as having the capacity to consent to any procedure which may involve him in an injury. Above this age the reality of any purported consent which may have been obtained is a question of fact, and as with an adult the evidence would, if necessary, have to show that irrespective of age the person concerned fully understood the implications to himself of the procedures to which he was consenting.

In the case of those who are mentally subnormal or mentally disordered the reality of the consent given will fall to be judged by similar criteria to those which apply to the making of a will, contracting a marriage, or otherwise taking decisions which have legal force as well as moral and social implications. Where true consent in this sense cannot be obtained, procedures which are of no direct benefit and which might carry a risk of harm to the subject should not be undertaken.

Even when true consent has been given by a minor or mentally subnormal or mentally disordered person, considerations of ethics and prudence still require that, if possible, the assent of parents or guardians or relatives, as the case may be, should be obtained.

Investigations that are of no direct benefit to the individual require, therefore, that his true consent to them shall be explicitly obtained. After adequate explanation, the consent of an adult of sound mind and understanding can be relied upon to be true consent. In the case of children and young persons the question whether purported consent was true consent would in each case depend upon facts such as the age, intelligence, situation, and character of the subject, and the nature of the investigation. When the subject is below the age of 12 years information requiring the performance of any procedure involving his body would need to be obtained incidentally to and without altering the nature of a procedure intended for his individual benefit.

Professional Discipline

All who have been concerned with medical research are aware of the impossibility of formulating any detailed code of rules which will ensure that irreproachability of practice which alone will suffice where investigations on human beings are concerned. The law lays down a minimum code in matters of professional negligence and the doctrine of assault. But this is not enough. Owing to the special relationship of trust that exists between a patient and his doctor, most patients will consent to any proposal that is made. Further, the considerations involved in a novel procedure are nearly always so technical as to prevent their being adequately understood by one who is not himself an expert. It must therefore be frankly recognized that, for practical purposes, an inescapable moral responsibility rests with the doctor concerned for determining what investigations are, or are not, proposed to a particular patient or volunteer. Nevertheless, moral codes are formulated by man, and if, in ever-changing circumstances of medical advance, their relevance is to be maintained, it is to the profession itself that we must look, and in particular to the heads of departments, the specialized Societies, and the editors of medical and scientific journals.

In the opinion of the Council, the head of a department where investigations on human subjects take place has an inescapable responsibility for ensuring that practice by those under his direction is irreproachable.

In the same way the Council feel that, as a matter of policy, bodies like themselves that support medical research should do everything in their power to ensure that the practice of all workers whom they support shall be unexceptionable and known to be so.

So specialized has medical knowledge now become that the profession in general can rarely deal adequately with individual problems. In regard to any particular type of investigation, only a small group of experienced men who have specialized in this branch of knowledge are likely to be competent to pass an opinion on the justification for undertaking any particular procedure. But in every branch of medicine specialized scientific societies exist. It is upon these that the profession in general must mainly rely for the creation and maintenance of that body of precedents which shall guide individual investigators in case of doubt, and for the critical discussion of the communications presented to them on which the formation of the necessary climate of opinion depends.

1032609

Finally, it is the Council's opinion that any account of investigations on human subjects should make clear that the appropriate requirements have been fulfilled, and, further, that no paper should be accepted for publication if there are any doubts that such is the case.

The progress of medical knowledge has depended, and will continue to depend, in no small measure upon the confidence which the public has in those who carry out investigations on human subjects, be these healthy or sick. Only in so far as it is known that such investigations are submitted to the highest ethical scrutiny and self-discipline will this confidence be maintained. Mistaken, or misunderstood, investigations could do incalculable harm to medical progress. It is our collective duty as a profession to see that this does not happen and so to continue to deserve the confidence that we now enjoy.

1032610

Committee on Human Studies — August, 1971

1. Gould A. Andrews, M.D, Chairman

2. Brill, A. Bertrand, M.D., Ph.D.
Associate Professor, Dept. of Medicine
Division of Nuclear Medicine & Physics
Vanderbilt University School of Medicine
Nashville, Tennessee 37203
FTS: 8,8, 749-5022
Ext.: 322-2394

3. Edwards, C. Lowell, M.D.
Chief of Clinical Services
ORAU Medical Division
Ext. 285

4. Koons, Mr. Melvin E.
Law Department (Y-12)
Union Carbide Corporation
Bldg. 9704-2
Ext. 3-5979

5. Lange, Robert D., M.D.
Assistant Director
U. T. Memorial Research Center & Hospital
1924 Alcoa Highway
Knoxville, Tennessee 37920
(8) (9) 971-3235

6. Lincoln, Thomas A., M.D.
Director
Health Division
ORNL
Bldg. 4500-N (Rm. K-122)
Ext. 3-6681

7. Nelson, Dr. Bill M.
Pathologist
ORAU Medical Division
Ext. 287

8. Storer, John B., M.D.
Scientific Director for Pathology & Immunology
Biology Division
Bldg. 9207 (Y-12 Area)
Ext. 3-5046

1032611

Name: Gould A. Andrews
Position: Internist, Division Chairman
School: University of Michigan, A.B., 1940
University of Michigan, M.D., 1943
Licensure: Tennessee
Board: Internal Medicine
Memberships: Society for Experimental Biology and Medicine; American Association for Cancer Research; American Thyroid Association; Society of Nuclear Medicine; Southern Society for Clinical Research; American Medical Association; American Association for the Advancement of Science; American Federation for Clinical Research; Fellow, American College of Physicians; American Society of Hematology (1968); Health Physics Society, East Tennessee Chapter; Tennessee Academy of Science; Tennessee Blood Club

Name: A. Bertrand Brill
Position: Associate Professor of Medicine and Radiology, Vanderbilt School of Medicine.
School: Grinnell, A.B., 1949
University of Utah, M.D., 1956
University of California, Berkeley, Ph.D., 1961
Licensure: Tennessee
Memberships: American Association for the Advancement of Science; Society of Nuclear Medicine; Radiation Research Society; American Thyroid Association
Other Indication of Experience and Competence:
Medical Director, Division of Radiological Health, U.S. Public Health Service, 1957-1964, Rockville, Maryland

Name: C. L. Edwards
Position: Chief of Clinical Research
School: Manchester College, A.B., 1950
Indiana University, M.D., 1954
Licensure: Tennessee, Indiana
Board: Internal Medicine
Memberships: Roane-Anderson County Medical Society; Tennessee Medical Association; American Medical Association; Society of Nuclear Medicine; American Association for the Advancement of Science; New York Academy of Sciences

1032612

Name: Melvin E. Koons
Position: Executive Assistant to President, Union Carbide Corporation Nuclear Division

School: University of North Dakota, B.A., 1955, Juris Doctor, 1961.
Admitted to Practice of Law:
North Dakota 1961; Tennessee 1964; Federal District Court, North Dakota, 1961; East Tennessee, 1964; U. S. Supreme Court, 1966
Memberships: American Bar Association, Public Contracts Section; Federal Bar Association, Government Contracts Committee, R & D Contracts Subcommittee; Tennessee Bar Association; North Dakota Bar Association, Ward County, North Dakota, Bar Association

Name: Robert Lange
Position: Research Professor; Assistant Director, University of Tennessee Memorial Research Center
School: Macalester College, B.A.
Washington University, M.D., 1944
Licensure: Tennessee, Minnesota, Missouri, Georgia
Board: Internal Medicine
Memberships: American Association for the Advancement of Science; American Medical Association; Knoxville Academy of Medicine Southern Society of Research; Central Society of Clinical Research; American College of Physicians; International Society of Hematology, etc.

Name: Thomas A. Lincoln
Position: Director, Health Division, ORNL

School: Macalester College, St. Paul, Minnesota, BA (Chemistry), 1946
U. of Minnesota, Minneapolis, Minnesota, BS 1947, BM 1949, MD 1950.
Rotating Internship, Ancker Hospital, St. Paul, Minn., 1949-50

Licensure: Tennessee, Minnesota
Board: American Board of Preventive Medicine, by examination, June 5, 1963
Memberships: Fellow Industrial Medical Association
Past President, Tenn. Industrial Medical Assn.
American Academy of Occupational Medicine
AMA
Past President, Roane Anderson Co. Medical Society.
Treas. Board of Directors, Oak Ridge Regional Mental Health Center

1032613

Name: Bill Nelson
Position: Research Pathologist
School: University of Kansas, A.B., 1948
University of Chicago, School of Medicine, M.D., 1952
Licensure: Tennessee
Board: American Board of Pathology
Memberships: American Medical Association; American Society of Clinical Pathologists; Reticuloendothelial Society; Society of Nuclear Medicine; Tennessee Association of Pathologists

Name: John B. Storer
Position: Scientific Director for Pathology and Immunology
Biology Division, ORNL
School: University of Chicago, M.D., 1947

Licensure: -

Board:

Memberships: American Association for Cancer Research
American Society for Experimental Pathology
Radiation Research Society
Society for Experimental Biology and Medicine
National Council on Radiation Protection and Measurements

1032614

Draft (R. M. Kniseley)
August 16, 1971

Suggested job description and duties of recording secretary of Committee on Human Studies

1. Record and transcribe detailed minutes of committee meetings.

2. Distribute promptly in draft form to committee members for corrections and revisions. Set a deadline for receipt of corrections.

3. Record and distribute Review & Action Form (revised August '71) to concerned investigators and committee members. · can be distributed

4. Set dates for Annual Meeting and interim called meetings.

5. Maintain a complete documentation of committee work, including phone consultations on new proposals or revisions.

6. Maintain a list of active projects which will be revised at the time of each meeting. This list will be distributed to all committee members as a part of the agenda for every called meeting.

7. Maintain a separate file of inactive, discontinued, or disapproved projects.

-more

1032615

8. Receive written applications to committee. Assign "identifying number" (in chronologic order). Check list of questions to be answered (from Review & Action form) on every application and ascertain an answer is included on each point (methods, hazards, reason for study, benefits from study, informed consent, etc.) before it is forwarded to committee members.

9. At time of meeting obtain from the committee an answer to each question on Review & Action Form (revised August '71).

10. Maintain a file of the several patient consent forms used in the Medical Division (see attached)*

*

1)	Consent to Experimental Treatment	Med-146 (2/67)
2)	Patient Admittance Agreement	Med-13 "
3)	Authorization for Administration of Radioactive Substance	Med-148 "
4)	Consent for Operation	Med-145 "
5)	Release of Medical Information	-
6)	Request for Autopsy	Med-139 (7/71)
7)	Bone Marrow Procedure (Volunteer Release)	Med Div 1/69
8)	Whole Blood Procurement, Release and Payment Authorization (Non Patient)	

1032616

RM P-4

MEMORANDUM

Keep indefinitely

TO Medical Division Senior Staff DATE August 31, 1971

SUBJECT Outpatients and Volunteer Subjects in Research Projects

COPIES TO File

As a follow-up to the last meeting of our Committee on Human Studies we are reviewing procedures and policies. We request senior staff members directly involved to be certain that these steps are taken for each patient or volunteer subject:

All persons who contribute blood samples, other specimens, or physiological data as part of a research project, or as a procedure in a consultation visit should -

a) receive a hospital number from Medical Records and supply identifying information

b) sign appropriate consent forms.

Gould A. Andrews

Gould A. Andrews, M.D.

Distribution:

Mr. Cloutier
Dr. Edwards
Dr. Gengozian
Mr. Gibbs
Dr. Goswitz
Mr. Harmon
Dr. Hayes
Dr. Hubner
Dr. Kingdon
Dr. Kniseley
Dr. Littlefield
Dr. Lushbaugh
Mr. Morris
Dr. Nelson
Dr. Porter
Dr. Ricks
Dr. Snyder
Mrs. Sutliff
Dr. Swartzendruber
Dr. Urso
Dr. Vodopick

10261

(19)

OAK RIDGE ASSOCIATED UNIVERSITIES

WHOLE BLOOD PROCUREMENT, RELEASE, & PAYMENT AUTHORIZATION

I, the undersigned, do hereby acknowledge that I have on this day, of my own free will and accord, delivered and sold to the Oak Ridge Associated Universities (hereinafter referred to as ("Association") _____cc's of my own blood, by direct vein aspiration.

It is understood that I am to be paid the below specified sum by the Association in consideration of which I do hereby release and discharge the Association, its successors and assigns, from all claims, actions and causes of action, at law or in equity, which I do now or may hereafter have against the Association, resulting from or growing out of the sale of said blood or its removal from my body. It is further understood and agreed that I am to retain no control whatsoever over the said blood or the use thereof.

____	0 - 100 cc	$5.00
____	101 - 200 cc	10.00
____	201 - 300 cc	15.00
____	301 - 400 cc	20.00
____	401 - above	25.00

This _____ day of _____, 1970.

_____ _____

Name (Please Print) Signature of Donor

_____

Mail Check To

_____

City State Zip

Witnesses:

_____

_____

Account to Charge:_____

_____

BLOOD RECEIVED BY

_____

DIVISION APPROVAL

_____

1032618

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

December 16, 1971

Gould Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Andrews:

Please refer to our letter of July 8, 1971.

Since we have received no response within the stipulated 60-day time period, we are hereby converting your institution's "general" assurance on the use of human subjects to the "special" mechanism described in our previous letter.

You will be provided instructions for submitting "special" assurances for any new or competing renewal applications that your institution may submit. For any currently active grants, the procedures described in your "general" assurance should continue to be followed until those grants terminate.

Sincerely yours,

D. T. Chalkley

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants

REC'D. MEDICAL DIVISION 12-20-71

1032619

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8411

December 22, 1971

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants
Department of Health Education and Welfare
National Institutes of Health
Bethesda, Maryland 20014

Dear Doctor Chalkley:

Thank you for your letter of the 16th. On reviewing the situation I am sorry that we did not apply for "general" assurance on the use of human subjects during the 60-day period stipulated in your letter of July 8. We now believe that if we are still eligible to do so, we would like to make such an application. One of the reasons we did not do so, in addition to our own enertia, was some confusion about the first sentence of the 3rd paragraph of your letter of July 8th in which you encouraged us to take advantage of the "special" assurance procedure. On rereading the correspondence I believe that perhaps in this sentence the word "special" should have been substituted by the word "general."

At any rate, we would like to apply for the general assurance if we can still do so. I am sorry for any inconvenience this may have caused you.

Sincerely,

Gould A. Andrews, M.D.
Chairman,
The Medical Division

GAA/pe

1032620

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

December 30, 1971 1716

Gould A. Andrews, M.D.
Chairman
Oak Ridge Associated Universities, Inc.
P.O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Andrews:

The critical line in our July 8, 1971, letter was the last: "If you wish consideration for a "general" assurance please respond with a listing of all projects involving human subjects, whether supported by DHEW or by other sources, that are under active review by your institutional committee."

Attached is a listing of all DHEW programs currently requiring review of projects involving human subjects. The Department has finally required use of this procedure by its grantees and contractors, the Department of Defense and the AEC are using it in special cases on an informal basis. The Food and Drug Administration requires use of the procedure for all investigational new drug studies carried out under exemptions from the labelling provisions of the Food, Drug, and Cosmetic Act.

If you are-or should be- reviewing a significant number of concurrent projects, we will be glad to renegotiate your assurance. The list first, please, and Happy New Year.

Sincerely yours,

D. T. Chalkley

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants

Enclosure

1032621

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PROGRAMS REQUIRING INSTITUTIONAL REVIEW OF GRANT AND CONTRACT
APPLICATIONS AND ACTIVITIES
FOR COMPLIANCE WITH
DHEW POLICY
PROTECTION OF HUMAN SUBJECTS

I. Office of Education

Bureau of Education for the Handicapped-all grants and contracts
National Center for Educational Research-all grants and contracts

II. Public Health Service (includes Food and Drug Administration, Health Services and Mental Health Administration, and National Institutes of Health)

Research Project Grants (except R09, R13 programs)
Program Projects and Center Grants (except P06, P07, P09 programs)
General Support (Research Related)
- General Research Support
- Health Sciences Advancement Awards
- Biomedical Sciences Support Grants

Fellowships (except F05, F15)
Research Career Awards
Research Training (except T07, T09, T13, T14, T15)
Research Contracts

III. Social and Rehabilitation Services

Aging Research and Development Grants (OAA Title IV)
Child Welfare Demonstration Grants (SSA Title IV)
Hospital Improvement Grants (HIP)
Hospital Staffing Grants (HIST)
Public Assistance Demonstration Grants (SSA Title XI, Section 1115)
Rehabilitation Research and Development Grants (VRA Title IV)
Rehabilitation Research and Training Grants (VRA Title IV) except as specifically exempted by Regional Mental Retardation Consultant
Rehabilitation Service Grants (VRA Title IV)
Rehabilitation SWEAT Grants (VRA Title IV)
Social Welfare Cooperative Research and Development Grants (SSA Title XI Sec 1110)

1032622

ATTACHMENT A
EXAMPLE OF A STATEMENT OF COMPLIANCE
PART ONE OF A GENERAL INSTITUTIONAL ASSURANCE

The (name of institution) will comply with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education, and Welfare. In fulfillment of its assurance:

This institution will establish and maintain a committee competent to review projects and activities that involve human subjects. The committee will be assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.
The risks to subjects are outweighed by potential benefits.
The informed consent of subjects will be obtained by methods that are adequate and appropriate.

This institution will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interests.

This institution will encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

This institution will provide for the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

This institution will maintain appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

This institution will periodically reassure itself through appropriate administrative overview that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with its assurance as accepted by the Department of Health, Education, and Welfare.

Official signing for the Institution

Signature _____

Title _____

Date _____

1032623

Enclosure: Implementing Guidelines, Part Two of a General Institutional Assurance

ATTACHMENT B

EXAMPLE OF A STATEMENT OF COMPLIANCE

SPECIAL INSTITUTIONAL ASSURANCE IN CONNECTION WITH
SINGLE PROJECTS INVOLVING HUMAN SUBJECTS

(0) The (name of institution) will comply with the policy for the protection of human subjects participating in projects or activities supported by grants and contracts made by the Department of Health, Education, and Welfare. This policy requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. An initial review of the application for a grant or contract identified as _____, submitted by this institution on behalf of _____ indicates that:

(1) In the opinion of this committee the risks to the rights and welfare of the subject in this project or activity are:

The committee states that adequate safeguards against these risks have been provided.

(2) In the opinion of the committee the potential benefits of this activity to the subjects outweigh any probable risks. This opinion is justified by the following reasons:

(3) In the opinion of the committee the following informed consent procedures will be adequate and appropriate. Documentation is attached.

(4) The committee agrees to arrange for a continuing exchange of information and advice between itself and the investigator or director, particularly to deal with proposed changes in project or activity design, or with emergent problems which may alter the investigational situation with regard to the criteria cited above. This exchange will be implemented through:

1032624

This institution will provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects.

(5) The signatures, names, and occupations or titles of the members of the committee are listed below.

Signature	Name	Occupation or Title

Date of Committee Approval _____

(6) Official signing for Institution _____
Signature

_____
Name

_____
Title

_____
Institution

_____
Address

_____

_____
Telephone Number

Date _____

1032625

(see instructions)

INSTRUCTIONS

An acceptable special institutional assurance consists of a properly completed formal statement of compliance with Department of Health, Education, and Welfare policy (see Attachment B), signed by a committee of not less than three members and by an official authorized to sign for the institution. The explanatory paragraphs which follow refer to the corresponding section of the attachment.

(0) This should identify the application for a grant, contract, or award by its identifying number, where known, or by its full title. The name should be that of the investigator, program director, fellow, or other individual immediately responsible for the conduct of the work.

(1) The committee should identify in general terms those risks that it recognizes as probable occurrences; i.e., "Aggravation of anxiety status through contact with interviewers," "Preservation of confidentiality of data," "Renal injury subsequent to multiple biopsy,""Possibility of side reactions to drugs," "Possible local hematosis and nerve injury associated with venipuncture."

(2) The committee should identify the benefits to the subject or to mankind in general that will accrue through the subject's participation in the project. This should be followed by a brief discussion, weighing the risks against the benefits.

(3) Consent procedures should be described and the minimum statement to be used should be attached. "Students responding to the attached advertisement will be interviewed." "The project outline will be submitted to the executive council of the P-TA." "Individual teachers will be asked to allow an observer in the rooms chosen." "Superintendents of several state mental hospitals will be approached. The attached statement to the next of kin

1032626

or guardian will be signed by the principal investigator and the superintendent." "The following special consent form will be signed by each subject and his or her spouse or next of kin before acceptance of the subject." "No prior consent will be sought. The following debriefing schedule will be followed within 30 minutes after completion of the test."

(4) This should indicate whether the investigator or director will be required to submit written reports, or to appear for interviews, or will be visited by the committee or committee representatives, and at approximately what intervals these steps will be carried out.

(5) No further explanation is necessary.

(The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of the project. The committee may be an existing one, or one especially appointed for the purpose. The institution may utilize staff, consultants, or both. The membership should possess not only broad competence to comprehend the nature of the project, but also other competencies necessary in the judgments as to acceptability of the project or activity in terms of institutional regulations, relevant law, standards of professional practice, and community acceptance. The committee's maturity and experience should be such as to justify respect for its advice and counsel.)

(No individual involved in the conduct of the project shall participate in its review, except to provide information to the committee.)

(Committee members should be identified in the assurance by name, positions, earned degrees, board certifications, licensures, memberships, and other indications of experience, competence, and interest.)

The completed assurance should be attached to the application, or returned directly to the office requesting its submission.

IMPLEMENTING GUIDELINES FOR RESEARCH ON HUMAN SUBJECTS
(In Compliance with PHS/DHEW Policy on Protection of Human Subjects)

Oak Ridge Associated Universities and Oak Ridge National Laboratory

Committee on Human Studies

(Revised January 1972)

A. Statement of Principles

The Committee on Human Studies for Oak Ridge Associated Universities and Oak Ridge National Laboratory has officially adopted the code of ethics adopted by the World Medical Association, known as the Declaration of Helsinki. It accepts as amplification of this document the statement of the British Medical Research Council. (Appendix I)

B. Membership of Committee

The committee shall include at least two outside consultants familiar with the type of research done at Oak Ridge and having no personal participation in the projects discussed. Other members shall be the Chairman of the Medical Division, two members of the scientific staff of ORNL, one member of the Medical Division's scientific staff, and a lawyer. The Chief of Clinical Services of the ORAU Medical Division will serve as an ex officio member.

C. Procedures in Carrying out Initial and Continuing Review of Applications and Projects

1. Initial Review

All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects must be presented to and approved by the Committee on Human Studies, whenever possible prior to submission for funding, and in the exact form used for submission. Regardless of the nature or degree of risk anticipated, the applicant must present in writing, and be prepared to defend in person before the committee, detailed information on the following points:

a. The possible risks to the rights and welfare of human subjects, including the rights of privacy, freedom from undue harassment, and confidentiality of data, and a description of the provisions made to minimize these risks.

1032629

FORM P-4

Ref for Dr. Andrews July 10 meeting

MEMORANDUM

TO Senior Staff - Medical Division DATE May 29, 1969

SUBJECT GUIDELINES FOR RESEARCH INVOLVING HUMAN SUBJECTS

COPIES TO Dr. Pollard; Files

1. The Medical Division since its opening has sought to safeguard the rights and safety of its patients who participate in research studies. In recent years more formalized procedures for institutions have emerged, in part stimulated by the policy statements of the NIH.

2. The Medical Division formally established a "Committee on Human Studies" in 1967, charged with initial and continuing review assignments.

3. Attached is a Guideline, and an Application for the Use of Humans as Experimental Subjects which must be reviewed and approved by the Committee before such new experimental projects can be activated.

4. We request that any planned projects which have not yet been reviewed be submitted to the Division Office by July 1 so that the Committee members can study the proposal before its meeting July 10.

R. M. Kniseley

RMK:fed

Attached
Guidelines - Research on Human Subjects
Statement by Medical Research Council
Curriculum Vitae of Committee Members
Review and Action
Application
Institutional Assurance..
Declaration of Helsinki

1032630

PART ONE OF A GENERAL INSTITUTIONAL ASSURANCE

The (name of institution) will comply with the policy for the protection of human subjects participating in projects and activities supported directly or indirectly by grants, contracts, or awards from the Department of Health, Education, and Welfare. In fulfillment of its assurance:

This institution will establish and maintain a committee competent to review projects and activities that involve human subjects. The committee will be assigned responsibility to determine for each project and activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.

The risks to subjects are outweighed by the potential benefits to him, or by the importance of the knowledge to be gained.

The procedures for obtaining informed consent are adequate and appropriate.

This institution will provide for committee reviews to be conducted objectively and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interest.

This institution will encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

This institution will provide whatever facilities and professional attention are required to safeguard the rights and welfare of human subjects.

This institution will maintain appropriate and informative records of committee reviews of applications and active projects, of briefings of subjects for obtaining informed consent, and other documentation that may pertain to the selection, participation, and protection of subjects, and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

This institution will periodically reassure itself through appropriate administrative overview that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with its assurance as accepted by the Department of Health, Education, and Welfare.

Official signing for the Institution

Signature _____

Title _____

Date _____

Enclosure: Implementing Guidelines, Part Two of a General Institutional Assurance

SPECIAL INSTITUTIONAL ASSURANCE IN CONNECTION WITH SINGLE PROJECTS INVOLVING HUMAN SUBJECTS

(0) The (name of institution) will comply with the policy for the protection of human subjects participating in projects or activities supported by grants, contracts, and awards made by the Department of Health, Education, and Welfare. This policy requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. An initial review of the application for a grant, contract, or award identified as _____ submitted by this institution on behalf of _____ indicates that:

(1) In the opinion of this committee the risks to the rights and welfare of the subjects in this project or activity are:

The committee states that adequate safeguards against these risks have been provided.

(2) In the opinion of the committee the potential benefits of this activity to the subjects outweigh any probable risks. This opinion is justified by the following reasons:

(3) In the opinion of the committee the following informed consent procedures will be adequate and appropriate:

(4) The committee agrees to arrange for a continuing exchange of information and advice between itself and the investigator or director, particularly to deal with proposed changes in project or activity design, and with emergent problems which may alter the investigational situation with regard to the criteria cited above. This exchange will be implemented through:

This institution will provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects.

(Exhibit X1-40-2 continued)

(5) The signatures, names, occupations, or titles of the members of the committee are listed below.

Name	Occupation or Title
Name	Occupation or Title
Name	Occupation or Title
Name	Occupation or Title

(6) Official signing for Institution

Name	Title	Date

(see instructions)

EXCERPT
CHAPTER 1-40
PROTECTION OF HUMAN SUBJECTS

1-40-20 POLICY

Safeguarding the rights and welfare of human subjects involved in projects and in other activities supported by grants, contracts, and awards from the Department of Health, Education, and Welfare is the responsibility of the institution which receives or is accountable to the DHEW for the funds awarded for the support of the project or activity. Grants, contracts, and awards involving human subjects at risk will not be made to an individual unless he is affiliated with or sponsored by an institution which can and will assume this responsibility.

In order to provide for the adequate discharge of this institutional responsibility, it is the policy of the Department that no grant, contract, or award for a project or activity involving human subjects at risk shall be made until assurance that the project or activity will be subject to initial and continuing review by an appropriate institutional committee has been officially presented to and accepted by the DHEW. This review shall assure that the rights and welfare of the subjects involved are adequately protected, that the risks to an individual are outweighed by the potential benefits to him or by the importance of the knowledge to be gained, and that the methods to be used to obtain informed consent are adequate and appropriate. 1/ The institution must also provide with each proposal involving human subjects a certification that it has been or will be reviewed prior to the proposed starting date in accordance with the terms of the institution's assurance.

Since the welfare of subjects is a matter of concern to the Department of Health, Education, and Welfare as well as to the institution, no grant, contract, or award involving human subjects shall be made unless the application for such support has been reviewed and approved by an appropriate professional committee within the responsible organizational component of the Department. This review must establish that the project or activity, as described in the application, will not interfere with or impair the rights and welfare of the subjects, nor involve risks that outweigh either potential benefits to the subjects or the expected value of the knowledge sought, nor deny the rights of the subject to adequate and appropriate informed consent. The committee may recommend to the awarding agency, and the awarding agency may require, the imposition of specific grant, contract, and award terms providing for the protection of human subjects, including requirements for informed consent.

1/ In the United States, adherence to the regulations of the Food and Drug Administration (21 CFR 130.37) governing consent in projects involving investigative new drugs (IND) is required by law.

1-40-40 GRANTEE IMPLEMENTATION

A. Negotiation of Assurances

An institution applying to DHEW for a grant, contract, or award involving human subjects must provide written assurance that it will abide by DHEW policy. The assurance shall embody a statement of compliance with DHEW requirements for initial and continuing committee review of grant, contract, and award supported activities and a set of implementing guidelines including identification of the committee, and its review procedures, or in the case of special assurances concerned with single projects or activities, a report of initial findings and proposed continuing review procedures.

Assurances will not be accepted from institutions or institutional components which do not have control over the expenditure of DHEW grant, contract, and award funds unless they are an active part of a cooperative project or activity.

An assurance will be accepted only after review and approval by the Division of Research Grants, NIH.

B. Types of Assurance

Assurances may be one of two types:

1. General Assurance.

   A general assurance describes the review and implementation procedures applicable to any and all DHEW supported activities within an institution, regardless of the number, location, or types of its organizational components. (See Exhibit X1-40-1.) General assurances will be required from institutions having a significant number of concurrent DHEW projects or activities.

2. Special Assurance.

   A special assurance will, as a rule, describe those review and implementation procedures applicable to a single project or activity. (See Exhibit X1-40-2.) Special assurances may also be negotiated in modified forms to meet unusual requirements either of the awarding agency or of the institution receiving a grant, contract, or award. Special assurances are not to be solicited from institutions which have on file an accepted general assurance.

C. Minimum Requirements for General Assurances

1. Statement of Compliance.

A formal statement of compliance with DHEW policy must be executed by an appropriate institutional official.

2. Implementing Guidelines.

The institution must include as part of its assurance implementing guidelines that specifically provide for:

a. The statement of principles that will assist the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may be an appropriate existing code or declaration or one formulated by the institution itself. It is to be understood that no such principles supersede DHEW policy or applicable law.

b. A committee or committee structure which will conduct initial and continuing reviews. Committee members shall be identified by name, occupation or position, and by other pertinent indications of experience and competence in areas pertinent to the areas of review such as earned degrees, board certifications, licensures, memberships, etc.

The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of projects and activities commonly conducted at the institution. The committee's membership, maturity, experience, and expertise should be such as to justify respect for its advice and counsel. No member of an institutional committee shall be involved in either the initial or continuing review of a project or activity in which he has a professional responsibility, except to provide information requested by the committee. In addition to possessing the professional competence to review specific projects, the committee should be able to determine acceptability of the application in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. This may require the committee to include persons whose primary concerns lie in these areas rather than in the conduct of research, development, and service programs of the types supported by the DHEW.

c. The procedures which the institution will follow in carrying out its initial and continuing review of applications and projects.

d. The procedures which the committee will follow to provide advice and counsel to project and program directors with regard to the committee's actions, and the requirements for reporting to the committee any emergent problems or proposed procedural changes.

e. The procedures which the institution will follow to maintain an active and effective committee and to implement its recommendations.

D. Minimum Requirements for Special Assurances

An acceptable special assurance covering a single project or activity consists of a properly completed statement of compliance, similar to that illustrated by Exhibit X1-40-2. This shall identify the specific grant, contract, or award concerned by its number, if known, by its full title, and by the name of the project or program director, principal investigator, fellow, or other person immediately responsible for the conduct of the project or activity. The assurance shall be signed by a committee of not fewer than three members and executed by an appropriate institutional official. The committee shall describe in general terms those risks to the subject that it recognizes as inherent in the project or activity. Consent procedures to be used should be identified. Any consent statement to be signed, heard, or read by the subject or responsible third parties should be attached. The assurance should outline the circumstances under which the director or investigator will be required to inform the committee of proposed changes in the project or activity, or of emergent problems, involving human subjects. The assurance should also indicate whether the director or investigator will be required to submit written reports, appear for interview, or be visited by the committee or committees to provide for continuing review. It should also indicate the intervals at which such review will take place.

E. 1. Timing and Certification of Institutional Review--General Assurances

All proposals and applications involving human subjects submitted by institutions with accepted general assurances should, whenever possible, be given institutional review and approval prior to submission to the DHEW. The proposal or application should be appropriately marked in the spaces provided on forms, or the

following statement should be typed on the lower or right hand margin of the page bearing the name of the institutional official authorized to sign or execute applications or proposals for the institution.

"HUMAN SUBJECTS - REVIEWED ON _____(date)_____."

(This date should be no more than 90 days prior to the date on which the application or proposal was signed or executed.)

If it will be necessary to delay the review, the application should be appropriately marked in the spaces provided on forms or the following statement should be typed in the lower or right hand margin of the page bearing the name of the institutional official authorized to sign or execute applications or proposals for the institution.

"HUMAN SUBJECTS - REVIEW PENDING ON _____(date)_____."

(This date must be earlier than the proposed starting date of the project.)

These statements will be accepted as certification that the grant, contract, or award as described in the application has been or will be reviewed in accordance with DHEW policy and the institution's assurance.

If the application or proposal is not certified and review by DHEW indicates that human subjects are involved, the awarding agency will request certification from the institution prior to completion of processing and award.

If the application or proposal is certified, but the pending review date is later than the date on which the awarding agency wishes to make an award, the agency will request certification from the institution prior to completion of processing and award.

If certification is not received, the application as prepared will be considered incomplete, and no award will be made.

If an application, at the time it is submitted to the DHEW does not describe a project or activity involving or likely to involve human subjects, no certification should be submitted. However, in those instances where funds are awarded in response to the application and it later becomes appropriate to use all or parts

of these funds in projects or activities which will involve human subjects, such use must be reviewed and approved in accordance with the institutional assurance prior to the use of subjects:

----Where support is provided by project grants or contracts, review and approval of such changes must be certified to the awarding agency or contracting agency, together with a description of the proposed change in the project plan or contract workscope. Subjects should not be used prior to receipt of approval from agency staff or from the project officer concerned.

----Where support is provided by a mandatory grant or institutional grant, in which cases the institution determines within broad guidelines the project or activities supported, including the use of human subjects (i.e., general research support grants, clinical research center projects), review must be carried out in accordance with the institutional assurance. Certification for individual projects need not be forwarded to the awarding agency.

----Whenever the committee is uncertain as to whether a change should or should not be reported, the question should be referred to the agency concerned.

All certifications are subject to verification by DHEW representatives authorized to examine institutional and committee records.

2. Timing and Certification of Institutional Review--Special Assurances

When a special assurance is submitted, it provides certification for the initial grant, contract, or award year concerned. No additional documentation is required. If the terms of the grant or contract provide for additional years of support, with annual negotiation of budgets, the noncompeting renewal application or proposal shall be certified in the manner described in the preceding section (1-40-40 E.1.).

Justification vs. Risk Declared Key Factors in Clinical Research

Special to the House Physician Reporter

GHENT, Belgium—Legal risks in clinical investigation can be minimized if the researcher limits the use of subjects to "situations in which there is a maximum of scientific justification and a minimum of risk."

This was stressed here recently by Bernard D. Hirsh, LL B., director of the American Medical Association law division, who spoke at the First World Meeting on Medical Law. Physicians, he added, have a duty to obtain consent from a person who has the authority to give it before treatment that legally might be considered assault. This rule probably would be strictly applied for adults who participate in experiments without the expectation of medical benefit, he asserted.

Mr. Hirsh

He noted, however, that it would be of questionable legality to use children or mentally incompetent persons in such experiments, even if the parent or guardian consented.

Mr. Hirsh admitted that the answer to the question of how much information a physician must furnish to a patient to avoid legal liability is complex, because it arises out of two separate and distinct legal obligations.

One is the necessity to obtain valid consent; the other is that the physician should act with the highest degree of good faith to protect the interest of the patient.

"Thus it appears," said Mr. Hirsh, "that the clinical investigator must always provide an investigative subject with an adequate explanation and information regarding the risks that may occur."

Unless they are to receive needed medical treatment, he continued, persons lacking the "capacity to consent," such as children and the mentally incompetent, should not be used for clinical investigation merely because they are available. However, in investigations where it is essential to use such persons, "it seems unlikely that public policy would entirely foreclose clinical investigation," Mr. Hirsh declared.

He predicted the eventual development of "some legal mechanism to provide authorization under appropriate limitations and safeguards" for those who lack the capacity to give informed consent.

1032640

1-27-72

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

January 17, 1972 1716

Mr. William G. Pollard
Executive Director
Oak Ridge Associated Universities
P.O. Box 117
Oak Ridge, Tennessee 37830

Dear Mr. Pollard:

One of the awarding units of the Department of Health, Education, and Welfare has recently called our attention to the fact that it is reviewing a proposal from your institution which involves the use of human subjects, 1 R01 CA 13042-01, "Regulation of Granulopoiesis," Dr. Helen V. Goswitz.

Safeguarding the rights and welfare of human subjects involved in activities supported by grants or contracts from the Department of Health, Education, and Welfare is the responsibility of the institution which receives or is accountable to the DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of the Department that no grant or contract for an activity involving human subjects shall be made unless the application for such support has been reviewed and approved by an appropriate institutional committee as well as by an appropriate professional committee within the responsible component of the Department.

The institution must submit to the Department of Health, Education, and Welfare, for its review, approval, and official acceptance, an assurance of its compliance with this policy.

In our letter of December 16, 1971, Dr. Gould A. Andrews, Chairman, was notified that your "general" assurance was being inactivated as far as new and competing renewal grants are concerned and that such grants would now be subject to the "special" assurance mechanism. The enclosed example should be completed, typed on your letterhead, and forwarded to this office.

A prompt and complete reply may avoid interruption in the processing of an application, or if it is already approved, a delay in the award of funds.

Sincerely yours,

Mark H. Conner, Ph.D.
Institutional Relations Section
Division of Research Grants

Enclosure

102641

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8411

January 28, 1972

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants
Department of Health, Education and Welfare
National Institutes of Health
Bethesda, Maryland 20014

Dear Doctor Chalkley:

We wish to request a "general" assurance and are here listing the projects under review by our committee:

1. Clinical Trials of $^{113}In^{m}$ as a Kidney and Bone Scanning Agent. (AEC)

2. Use of Radioiodine in Surgical Removal of Thyroid Cancers (AEC).

3. Study of Granulocyte Kinetics in Myeloproliferative Disorders. (AEC)

4. Tumor Scanning with Gallium-67 (AEC, NIH, ACS).

5. Studies of Total-Body Irradiation in Patients with Hematologic Disorders (AEC).

6. Scanning Tumors of Retroperitoneal Lymph Nodes after Intralymphatic Injection of Radioactive Gallium (AEC).

7. Therapeutic Transplantation of Allogeneic Human Bone Marrow. (AEC)

8. Histologic Changes in the Skin Related to the Graft-Versus-Host Reaction after Marrow Transplantation (AEC).

9. Changes in Blood Enzyme Levels Following Exercise and/or Total-Body Irradiation in Man (AEC, NASA).

10. Chromosomal Breakages in Fibroblasts from Women Taking Oral Contraceptives (NIH).

11. Regulation of Granulopoiesis (NIH). (New Project)

1032642

In addition to these projects, our committee has agreed to review proposals for the Oak Ridge National Laboratory. The following is under active consideration: Cytogenetic Analysis of Primary Spermatocytes of Irradiated Individuals.

Please let me know if further information is needed.

Sincerely,

Gould A. Andrews, M.D.
Chairman,
The Medical Division

GAA/pe

1032643

REVIEW AND ACTION

ORAU/ORNL Committee on Human Studies

Principal Investigator _____ Ident. No. _____

Project Title _____

_____

1. In the opinion of this committee the risks to the rights and welfare of the subjects in this project or activity are:

   The committee states that adequate safeguards against these risks have been provided.

2. In the opinion of the committee the potential benefits of this activity to the subjects outweigh any probable risks. This opinion is justified by the following reasons:

3. In the opinion of the committee the following informed consent procedures will be adequate and appropriate:

4. The committee seeks continuing communication with the investigator(s) on this project along the following lines:

5. Other committee comments:

Approve _____

Disapprove _____

_____
Chairman of Committee

_____
Date

1032644

(Revised January 1972)

Human Experimentation

Code of Ethics of the World Medical Association

A draft code of ethics on human experimentation drawn up by the World Medical Association was published in the British Medical Journal of 27 October 1962. The original draft of this was in English. A revised version was accepted as the final draft at the meeting of the World Medical Association in Helsinki in June 1964. The original of this draft was in French, of which the W.M.A.'s English version is printed below. It is to be known as the Declaration of Helsinki.

DECLARATION OF HELSINKI

It is the mission of the doctor to safeguard the health of the people. His knowledge and conscience are dedicated to the fulfilment of this mission.

The Declaration of Geneva of the World Medical Association binds the doctor with the words, "The health of my patient will be my first consideration"; and the International Code of Medical Ethics which declares that "Any act or advice which could weaken physical or mental resistance of a human being may be used only in his interest."

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to each doctor in clinical research. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Doctors are not relieved from criminal, civil, and ethical responsibilities under the laws of their own countries.

In the field of clinical research a fundamental distinction must be recognized between clinical research in which the aim is essentially therapeutic for a patient, and clinical research the essential object of which is purely scientific and without therapeutic value to the person subjected to the research.

I. Basic Principles

1. Clinical research must conform to the moral and scientific principles that justify medical research, and should be based on laboratory and animal experiments or other scientifically established facts.

2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

II. Clinical Research Combined with Professional Care

1. In the treatment of the sick person the doctor must be free to use a new therapeutic measure if in his judgment it offers hope of saving life, re-establishing health, or alleviating suffering.

If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient has been given a full explanation. In case of legal incapacity consent should also be procured from the legal guardian; in case of physical incapacity the permission of the legal guardian replaces that of the patient.

2. The doctor can combine clinical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that clinical research is justified by its therapeutic value for the patient.

III. Non-therapeutic Clinical Research

1. In the purely scientific application of clinical research carried out on a human being it is the duty of the doctor to remain the protector of the life and health of that person on whom clinical research is being carried out.

2. The nature, the purpose, and the risk of clinical research must be explained to the subject by the doctor.

3a. Clinical research on a human being cannot be undertaken without his free consent, after he has been fully informed; if he is legally incompetent the consent of the legal guardian should be procured.

3b. The subject of clinical research should be in such a mental, physical, and legal state as to be able to exercise fully his power of choice.

3c. Consent should as a rule be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject, even after consent is obtained.

4a. The investigator must respect the right of each individual to safeguard his personal integrity, especially if the subject is in a dependent relationship to the investigator.

4b. At any time during the course of clinical research the subject or his guardian should be free to withdraw permission for research to be continued. The investigator or the investigating team should discontinue the research if in his or their judgment it may, if continued, be harmful to the individual.

1032645

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

February 3, 1972 1716

Gould A. Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P.O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Andrews:

The list of projects under review by your committee, furnished with your letter of January 28, 1972, is quite impressive. We will reactivate your former Public Health Service assurance pending receipt of an assurance of compliance with the present DHEW policy.

Our request of January 17, 1972, to Mr. William G. Pollard, Executive Director, for a special assurance in connection with your pending proposal, 1 R01 CA 13042-01, "Regulation of Granuopoiesis," Dr. Helen V. Goswitz, may be disregarded. This proposal should be reviewed by your committee in accordance with the terms of your PHS assurance and certification of that review should be forwarded to the National Cancer Institute. You may use the enclosed form NIH 1611 for this purpose.

The requirements for compliance with Department of Health, Education, and Welfare policy are set forth in the enclosed letter. The revision of your PHS assurance should be submitted as soon as possible so that review may be completed prior to the July 1, 1972, deadline.

Sincerely yours,

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Reseearch Grants

Enclosure

1032646

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

February 3, 1972 1716

Gould A. Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P.O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Andrews:

Safeguarding the rights and welfare of human subjects involved in activities supported by grants or contracts from the Department of Health, Education, and Welfare is the responsibility of the institution which receives or is accountable to the DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of the Department that no grant or contract for an activity involving human subjects shall be made unless the application for such support has been reviewed and approved by an appropriate institutional committee as well as by an appropriate professional committee within the responsible component of the Department.

The institution must submit to the Department of Health, Education, and Welfare, for its review, approval, and official acceptance, an assurance of its compliance with this policy. The minimum requirements for a "General" assurance are:

1. A formal statement of compliance with DHEW policy executed by an appropriate institutional official. (See Attachment A, "Institutional Guide to DHEW Policy on Protection of Human Subjects," enclosed.)

2. A statement describing the implementing guidelines to be adopted by the applicant institution. (See pages 24 and 25 of the previously cited enclosure.)

Perhaps the enclosed example will guide you in preparing an acceptable statement on implementing guidelines. This example was drafted in this office, and refers to no existing institution. You may adapt it to fit your own local situation, although you are under no restriction to do so. Instead, you may wish to devise your own format.

1032647

As you will see from the example, what is required is a description of a group review system for proposals involving human subjects which will be applied to all projects, present and future, for which DHEW support may be sought. Thus, the information requested should not be restricted to control of an individual project but should describe a general and permanent institutional procedure.

A prompt and complete reply may avoid interruption in the processing of an application, or if it is already approved, a delay in the award of funds.

Sincerely yours,

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants

Attachments

1032648

FORM P-4

MEMORANDUM

TO Vodopick (Grant) File DATE Feb. 21, 1972

SUBJECT

COPIES TO

With reference to Dr. Chalkley's letter to Dr. Andrews, of February 3, 1972, Dr. Andrews said that Dr. Vodopick has submitted what was required.....

I presume this included form NIH 1611. (From GAA's office we are to submit the "compliance" form, and revised PHS assurance.)

Polly

1032649

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-3411

February 28, 1972

To Committee on Human Studies:

A. B. Brill
C. L. Edwards
M. E. Koons
R. D. Lange
T. A. Lincoln
B. M. Nelson
J. B. Storer

Attached are copies of the revised Guidelines, in compliance with the Public Health Service - Department of Health, Education, and Welfare, in line with recommendations of the Committee at the January 31 meeting.

Gould A. Andrews

Enclosure:

Guidelines
Declaration of Helsinki (Appendix I)
Review & Action Form (Appendix II)

1032650

IMPLEMENTING GUIDELINES FOR RESEARCH ON HUMAN SUBJECTS
(In Compliance with PHS/DHEW Policy on Protection of Human Subjects)

Oak Ridge Associated Universities and Oak Ridge National Laboratory

Committee on Human Studies

(Revised January 1972)

A. Statement of Principles

The Committee on Human Studies for Oak Ridge Associated Universities and Oak Ridge National Laboratory has officially adopted the code of ethics adopted by the World Medical Association, known as the Declaration of Helsinki. It accepts as amplification of this document the statement of the British Medical Research Council. (Appendix I)

B. Membership of Committee

The committee shall include at least two outside consultants familiar with the type of research done at Oak Ridge and having no personal participation in the projects discussed. Other members shall be the Chairman of the Medical Division, two members of the scientific staff of ORNL, one member of the Medical Division's scientific staff, and a lawyer. The Chief of Clinical Services of the ORAU Medical Division will serve as an ex officio member.

C. Procedures in Carrying out Initial and Continuing Review of Applications and Projects

1. Initial Review

All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects must be presented to and approved by the Committee on Human Studies, whenever possible prior to submission for funding, and in the exact form used for submission. Regardless of the nature or degree of risk anticipated, the applicant must present in writing, and be prepared to defend in person before the committee, detailed information on the following points:

a. The possible risks to the rights and welfare of human subjects, including the rights of privacy, freedom from undue harassment, and confidentiality of data, and a description of the provisions made to minimize these risks.

1032651

b. Methods used to acquire informed consent, and the form in which it is stated, with special emphasis on the appropriateness to the particular situation inherent in the study plan.

c. The relative risks of the project as compared to the probable benefits to the subjects and to society.

For each application the committee will either certify that these points have been properly dealt with and declare that the project may be submitted for funding, or recommend to the Executive Officer of ORAU or ORNL (whichever is applicable) that submission be delayed until specific deficiencies (spelled out in writing) are adequately dealt with.

Members of the committee who are in any way directly involved in the work will not participate in the decision to approve or disapprove the study.

Approval of the committee members reviewing the application must be unanimous. In the event that only one member of the committee disapproves of a proposal, one or more additional outside consultants especially qualified and approved by the majority of the committee will be asked to review the problem. If they concur, the research may go forward over the dissent of the one member of the regular committee.

The committee's findings will be transmitted in writing to the appropriate officer of the laboratory proposing the research and to the applicant. No funds shall be released until the executive officer has concurred with these recommendations. The applicant's administrative superior shall maintain continuing review of the project activities in the light of the committee's report.

2. Continuing Review

The committee will have a regular Annual Meeting (in February) and additional interim meetings as called by the chairman. Investigators in charge of projects on human subjects are required to submit at each annual meeting status reports in which are presented any emergent problems. If a report is delinquent, the chairman of the committee will contact the investigator to ascertain the status of the study protocol. If at any time the committee is dissatisfied with the conduct of the project, or with the cooperation of the investigator, they shall immediately report this to the appropriate executive officer and recommend that financial support of the project be withheld until deficiencies are corrected.

If a responsible investigator plans a change in study protocol, he will submit the proposed changes to the committee for approval before putting them into practice.

D. Procedures of the Committee to Provide Advice and Counsel to Investigators

On request, senior investigators will appear before the committee at its called meetings to answer any questions concerning a new proposal. The questions and replies will form part of the official minutes of the committee. These will be distributed to the concerned staff members together with recorded actions of the committee on a Review and Action Form. (Appendix II)

E. Requirements for Reporting any Emergent Problems or Proposed Procedural Changes to the Committee

All senior investigators with proposed or active projects will receive notice of committee meetings and on request will appear before the committee. At this time they shall present in writing any proposed changes in procedures and shall describe any new risks and benefits, and any methods for safe-guarding patients' rights and procedures for informed consent in advance of instituting these changes. At this time they shall also report in writing any emergent problems.

F. Procedures to Maintain an Active and Effective Committee

1. The chairman will ensure an active committee by calling, in addition to the regular Annual Meeting, at least one additional meeting each year.

2. The members will be enjoined to assess every ongoing project as well as new proposals.

3. Outside committee members will be paid a consultant's fee and travel expenses providing they are able to accept it.

4. Full committee Minutes to all members will be distributed promptly in draft form for corrections and review, so that the opinions and actions can be recorded accurately.

5. On a regular basis, at least annually, a full Medical Division professional staff meeting will be held to review our policies on human experimentation.

* * *

Ident. No._____

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date_____

Principal Investigator: _____

Co-Investigators: _____

_____

_____

_____

Title of Project: _____

_____

Use Following Format (Submit Original and 8 Copies)

I. Objectives of Experiment:

(Include statement why experiment must be done in humans, and expected benefits from the knowledge.)

II. Methods of Procedure:

Brief description of methods, all medications including name and dose range, number and types of subjects anticipated, time for single session, total number of sessions, total duration of study, methods used to screen subjects, etc.

III. Possible Hazards and their Evaluation:

IV. Radioisotopes and New Drugs

If the study involves radioisotopes, indicate action of the Isotopes Committee. If new drugs are involved, indicate that appropriate application to FDA has been made.

See page 2

1032654

Title of Project: _____

Ident. No. _____

V. Responsibility of Principal Investigator:

Include statement of your procedures for protecting rights of the patients and gaining informed consent.

The principal investigator will follow the procedures of the Committee on Human Studies in obtaining "informed consent" from the subjects under study. The investigator recognizes that he retains the primary responsibility for safe-guarding the interests of the participants under study. Any significant changes in methods of procedure or of the development of unexpected risks will be brought to the attention of the Committee on Human Studies.

Starting Date_____

Signatures: _____Principal Investigator

_____ Co-Investigator

_____ "

_____ "

_____ "

_____ "

DIVISION REVIEW:

The application described above has been reviewed and approved.

Official signing for the institution:

Signature_____

Title _____

Institution_____

Date _____

1032655

REVIEW AND ACTION

ORAU/ORNL Committee on Human Studies

Principal Investigator _____ Ident. No. _____

Project Title _____

_____

1. In the opinion of this committee the risks to the rights and welfare of the subjects in this project or activity are:

   The committee states that adequate safeguards against these risks have been provided.

2. In the opinion of the committee the potential benefits of this activity to the subjects outweigh any probable risks. This opinion is justified by the following reasons:

3. In the opinion of the committee the following informed consent procedures will be adequate and appropriate:

4. The committee seeks continuing communication with the investigator(s) on this project along the following lines:

5. Other committee comments:

Approve _____

Disapprove _____

_____
Chairman of Committee

_____
Date

1032656

(Revised January 1972)

Human Experimentation

Code of Ethics of the World Medical Association

A draft code of ethics on human experimentation drawn up by the World Medical Association was published in the British Medical Journal of 27 October 1962. The original draft of this was in English. A revised version was accepted as the final draft at the meeting of the World Medical Association in Helsinki in June 1964. The original of this draft was in French, of which the W.M.A.'s English version is printed below. It is to be known as the Declaration of Helsinki.

DECLARATION OF HELSINKI

It is the mission of the doctor to safeguard the health of the people. His knowledge and conscience are dedicated to the fulfilment of this mission.

The Declaration of Geneva of the World Medical Association binds the doctor with the words, "The health of my patient will be my first consideration"; and the International Code of Medical Ethics which declares that "Any act or advice which could weaken physical or mental resistance of a human being may be used only in his interest."

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to each doctor in clinical research. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Doctors are not relieved from criminal, civil, and ethical responsibilities under the laws of their own countries.

In the field of clinical research a fundamental distinction must be recognized between clinical research in which the aim is essentially therapeutic for a patient, and clinical research the essential object of which is purely scientific and without therapeutic value to the person subjected to the research.

I. Basic Principles

1. Clinical research must conform to the moral and scientific principles that justify medical research, and should be based on laboratory and animal experiments or other scientifically established facts.

2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

II. Clinical Research Combined with Professional Care

1. In the treatment of the sick person the doctor must be free to use a new therapeutic measure if in his judgment it offers hope of saving life, re-establishing health, or alleviating suffering.

If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient has been given a full explanation. In case of legal incapacity consent should also be procured from the legal guardian; in case of physical incapacity the permission of the legal guardian replaces that of the patient.

2. The doctor can combine clinical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that clinical research is justified by its therapeutic value for the patient.

III. Non-therapeutic Clinical Research

1. In the purely scientific application of clinical research carried out on a human being it is the duty of the doctor to remain the protector of the life and health of that person on whom clinical research is being carried out.

2. The nature, the purpose, and the risk of clinical research must be explained to the subject by the doctor.

3a. Clinical research on a human being cannot be undertaken without his free consent, after he has been fully informed; if he is legally incompetent the consent of the legal guardian should be procured.

3b. The subject of clinical research should be in such a mental, physical, and legal state as to be able to exercise fully his power of choice.

3c. Consent should as a rule be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject, even after consent is obtained.

4a. The investigator must respect the right of each individual to safeguard his personal integrity, especially if the subject is in a dependent relationship to the investigator.

4b. At any time during the course of clinical research the subject or his guardian should be free to withdraw permission for research to be continued. The investigator or the investigating team should discontinue the research if in his or their judgment it may, if continued, be harmful to the individual.

1032657

FORM P-4A

MEMORANDUM

TO Dr. James L. Liverman
Dr. William G. Pollard

DATE February 28, 1972

SUBJECT Statement of Compliance - PHS/DHEW

COPIES TO File

This document needs your signatures. It is a General Institutional Assurance for research on human subjects as required by the Public Health Service and the Department of Health, Education, and Welfare. I don't believe that it presents any special problems, and it is not necessary for you to read all of it unless you wish to do so.

Gould A. Andrews, M.D.

pe

Attachment

1032658

GENERAL INSTITUTIONAL ASSURANCE

Statement of Compliance

Oak Ridge Associated Universities and Oak Ridge National Laboratory will comply with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education, and Welfare.

These institutions have jointly established and do maintain a committee competent to review projects and activities that involve human subjects. The committee is assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.
The risks to subjects are outweighed by potential benefits.
The informed consent of subjects will be obtained by methods that are adequate and appropriate.

These institutions will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgement of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interests.

These institutions will encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

These institutions will provide for the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

These institutions will maintain appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

These institutions will periodically reassure themselves through appropriate administrative overview that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with the assurance as accepted by the Department of Health, Education, and Welfare.

0032659

OAK RIDGE ASSOCIATED UNIVERSITIES

Signature William Y. Pollard

Title Executive Director

Date February 28, 1972

OAK RIDGE NATIONAL LABORATORY

Signature Bruce L. Silverman

Title Associate Director for Biomedical and Environmental Science

Date March 2, 1972

Attachment: Implementing Guidelines

federal register

Tuesday
May 12, 1981

Part II

Department of Energy

Privacy Act of 1974; Proposal of New Systems

1032660

DEPARTMENT OF ENERGY

Privacy Act of 1974; Proposal of New Systems

AGENCY: Department of Energy.

ACTION: Proposal of three new systems of records.

SUMMARY: The Department of Energy is proposing three new systems of records subject to the Privacy Act of 1974 (Pub. L. 93-579; 5 U.S.C. 552a(o)].

DATES: Written comments on or before June 8, 1981.

ADDRESSES: Written comments should be directed to the following address: U.S. Department of Energy, Phillip M. Kannan, Attorney, Office of Chief Counsel, P.O. Box E, Oak Ridge, Tennessee 37830 (615) 576-1204.

FOR FURTHER INFORMATION CONTACT: U.S. Department of Energy, Milton Jordan, Director, Division of FOI and Privacy Acts Activities, Forrestal Building, Room 1G-051, Washington, DC 20585, (202) 252-5922.

A. Supplementary Information

I. Report on three New Systems of Records.
II. Comments Procedure.
III. System Notice DOE—The Radiation Accident Registry.
VI. System Notice DOE—The Department of Energy Radiation Study Registry.
V. System Notice DOE—The US-DTPA Registry.

1. *Background:* This Report of New Systems, consisting of three separate parts, is submitted by the Department of Energy as required by the Privacy Act of 1974, 5 U.S.C. 552a(o). The Office of Management and Budget requires a Report on New Systems by a Government agency whenever a new system of records is proposed or certain significant changes occur to previously established systems. The Department of Energy is submitting the Reports on New System required by OMB Circular A-108 concurrently with the publication of this Federal Register notice. At this time, the Department of Energy is proposing to establish three systems of records for which no notice has yet been published. Their proposed designations are as follows:

(a) The Radiation Accident Registry
(b) The Department of Energy Radiation Study Registry
(c) The US-DTPA Registry

2. DOE-*71*, the Radiation Accident Registry: (a) *Purpose:* This system will serve primarily to provide complete clinical and accident histories as basis for clinical and epidemiolcgical studies of the life-time morbidity of individuals accidentally exposed to acute dose of ionizing radiation, to provide data for comparative studies of the efficacies of the methods and regimens used in the diagnosis and therapy of acute radiation-induced injuries, and to serve as a resource of technical and medical data for the eduction of physicians, health physicists and allied health care personnel.

(b) *Authority:* This system is established under the authority vested in the Secretary contained in 5 U.S.C. 301 and Section 644 of the Department of Energy Organization Act, Pub. L. 95-91, to prescribe such procedural and administrative rules as he may deem necessary or appropriate to manage functions vested in him.

(c) Potential consequence on individual privacy, and:

(d) Safeguards against unauthorized access.

The data in the system of records will be available only to scientists and supporting staff. Any reports generated will not identify the individuals to whom the data pertains. Thus, there will be a minimal effect on the privacy of the individuals. There will be no other effect on any other personal or property right of the individuals. Thus, it is the evaluation of the Department that the proposed system will have no detrimental effect on federalism or separation of power.

The records will be maintained in locked file cabinets or on computer storage devices in locked security areas. These areas are not accessible to members of the public. Only scientists approved by the Department of Energy will have access to this information. Reports published based on this information will not identify the individuals. It is the Department's evaluation that the risk of unauthorized disclosure is minimal.

3. DOE-*72*, The Department of Energy Radiation Study Registry:

(a) *Purpose:* This system will provide complete clinical histories as a basis for life-time morbidity studies of civilians in a defined population whose exposure to ionizing radiation at one of DOE's (or its predecessor's) plant sites, laboratories, test stations, or nuclear naval bases was at least 5 REM in any calendar year.

(b) *Authority:* This system is established under the authority vested in the Secretary contained in 5 U.S.C. 301 and Section 644 of the Department of Energy Organization Act, Pub. L. 95-91, to prescribe such procedural and administrative rules as he may deem necessary or appropriate to manage functions vested in him.

(c) Potential consequences on individual privacy.

4. DOE-*73*, The US-DTPA Registry:

(a) *Purpose:* This system will provide complete clinical histories of individuals treated with diethylenetriaminepentaacetic acid (DTPA) in either the calcium or zinc form and administered intravenously, intramuscularly, orally, or by inhalation of the aerosol preparation of the drug. Such histories will be the basis of studies by epidemiological methods to identify any long-term, adverse or side effects of DTPA.

(b) *Authority:* This system is established under the authority vested in the Secretary contained in 5 U.S.C. 301 and Section 644 of the Department of Energy Organization Act, Pub. L. 95-91, to prescribe such procedural and administrative rules as he may deem necessary or appropriate to manage functions vested in him.

B. Comments Pocedure

As provided by Section 3(e)(11) of the Privacy Act of 1974 (5 U.S.C. 552a(e)(11), interested persons are invited to submit written data, views or arguments related to these proposal to: Phillip M. Kannan, Attorney, U.S. Department of Energy, Office of Chief Counsel, P.O. Box E, Oak Ridge, Tennessee 37830, (615) 576-1204.

Comments should be identified on the outside of the envelope and on the documents submitted to the Department of Energy with the designation *"Department of Energy Privacy Act Systems Proposals."* These comments and all other relevant information will be considered by the Department of Energy before the various proposals are adopted in their final form.

Any information or data considered by the person furnishing it to be confidential must be so identified and submitted in writting, one copy only. The Department of Energy reserves the right to determine the confidential status of the information or data and to treat it according to that determination.

If no comments to the contrary are received with respect to a particular proposed system, it is the intent of the Department of Energy to operate any such system as proposed at the expiration of the 60-day advance notice period for informing Congress and the Office of Management and Budget of proposed new systems, as defined in OMB Circular A-108.

The Department of Energy has determined that this document does not contain a proposal requiring preparation of a regulatory analysis under Executive Order 12044.

1032661

(Privacy Act of 1974, Pub. L. 93-579; Department of Energy Organization Act, Pub. L. 95-91; Executive Order 12009, 42 FR 46267; and those authorities vested in the Department's predecessor agencies which are incorporated by reference in Title III of the Department of Energy Organization Act)

In consideration of the foregoing, the measures described above are proposed. Set forth below as Sections III-V of SUPPLEMENTARY INFORMATION, respectively, is a listing of the three Department of Energy Systems as proposed.

Issued in Washington, D.C., April 23, 1981.

William S. Heffelfinger,

Director of Administration.

DOE 71

System name: The Radiation Accident Registry.

Security classification: Unclassified.

System location: Oak Ridge Operations Office, P.O. Box E, Oak Ridge, Tennessee 37830.

Categories of Individuals Covered by the System:

1. Those persons accidentally exposed to acute doses of ionizing radiation as defined by exposure dose criteria agreed to by the Department of Energy and the Nuclear Regulatory Commission by an interagency agreement. The dose criteria established by this agreement include one or more of the following: (a) Greater than or equal to 25 REM (Roentgen Equivalent Man) to the whole body, active blood-forming organs or gonads; (b) greater than or equal to 600 REM to skin of whole body or extremities; (c) greater than or equal to 75 REM to other tissues or organs from an external source; (d) greater than or equal to ½ NCRP maximum permissible organ burden internally; all those medical misadministrations of radioisotopes that result in a dose or organ burden equal to or greater than those given above.

2. Those individuals known to have been involved in an event in which one or more other persons received a dose equal to or in excess of the DOE/NRC criteria but whose personal dose was less than these criteria. The histories of these individuals contribute control population data.

Categories of Records in the System:

1. Official accident reports including reports of those accidents that ahve occurred within the jurisdiction of the Nuclear Regulatory Commission and which have been transferred to the Department of Energy for the Accident Registry according to the Department of Energy/Nuclear Regulatory Commission agreement.

2. Names, addresses, social security numbers or other identifiers, and vital status information such as age, sex, race, etc.

3. Original or copied medical records compiled at the time of the accident. Such records include physician and hospital records, diagnostic and laboratory test reports, radiographs, EKGs, etc., and radiation exposure reports.

4. Original or copies of medical records of illnesses, examinations, including routine follow-up exams, investigations, etc., that have occurred since the radiation exposure.

5. Photographs or facsimiles of radiation-induced injuries.

6. Search and contact information for registrants as yet not identified and/or located.

7. Consent to release information forms completed by registrants.

8. Death certificates (copies).

9. Anecdotal information.

10. Correspondence relating to the accident and/or the individuals involved; originals and copies.

Authority for Maintenance of the System:

5 U.S.C. 301; Department of Energy Organization Act, including authorities incorporated by reference in Title III of the Department of Energy Organization Act; Executive Order 12009.

Routine Uses of Records Maintained in the System, Including Categories of Users and the Purposes of Such Uses:

1. To provide a current record of radiation accidents for use by the Department of Energy, and its contractors and consultants.

2. To identify specific populations for use in epidemiological and clinical studies.

3. To conduct medical surveillance during the lifetime of the registrants.

4. Additional uses 4, 8, 9, 10, as listed in Appendix B to the Department of Energy publication of systems of records, 45 FR 51125, 8/30/79.[1]

Policies and Practices for Storing, Retrieving, Accessing, Retaining, and Disposing of Records in the System:

Storage: Paper records, computer tapes, computer printouts, punched cards, discs, magnetic tape and microfilm.

Retrievability: By name and social security number.

Safeguards: Records are maintained in locked security areas in locked file cabinets. Access is limited to individuals whose official duties require access.

Retention and Disposal:

Records retention and disposal authorities are contained in the DOE Order 1324.1, "Records Disposition." Records within the Department of Energy are destroyed by shredding, burning, or burial in a sanitary landfill, as appropriate.

System Manager(s) and Address:

The Manager of the Oak Ridge Operations Office is the System Manager.

Notification Procedure:

a. Requests by an individual to determine if a system of records contains information about him or her should be directed to the Privacy Act Officer, Department of Energy, P.O. Box E, Oak Ridge, Tennessee 37830 in accordance with the Department of Energy's Privacy Act regulations (10 CFR Part 1008, 45 FR 61576, September 16, 1980).

b. Required identifying information: Name, social security number, and time period.

Record Access Procedures:

a. Requests by an individual for access to a system of records that contains information about him or her should be directed to the Privacy Act Officer, Department of Energy, P.O. Box E, Oak Ridge, Tennessee 37830 in accordance with the Department of Energy's Privacy Act regulations (10 CFR Part 1008, 45 FR 61576, September 16, 1980).

b. Required identifying information: Name, social security number, and time period.

Record Source Categories:

The individual, medical records, physicians, medical institutions, and reports of incident/accident investigations from private and public sources, radiation dosimetry records, security clearance records and employment records.

Systems Exempted from Certain Provisions of the Act: None.

DOE 72

System name: The Department of Energy Radiation Study Registry.

Security classification: Unclassified.

System location: Oak Ridge Operations Office, P.O. Box E, Oak Ridge, Tennessee 37830

[1] These routine uses are reprinted below.

1032662

Categories of Individuals Covered by the System:

Registrants are those present and former employees of contractors of the Department of Energy and its predecessor organizations including the Manhattan District, USAEC, and ERDA, and present and former civilian employees in the Department of Energy Naval Reactor Program who received a whole body exposure of ionizing radiation equal to or in excess of 5 REM in any one calendar year.

Categories of Records in the System:

1. Rosters of names of individuals meeting the above criteria for inclusion in the Registry submitted through the Department of Energy field operation offices from Department of Energy-owned and operated facilities and sites. In addition to names of such individuals, these rosters include social security number or other identifying information, sex, race, date of birth, date and/or place of death, first date of hire, last date of termination, continuity of hire, year in which they received first dose, greater than or equal to 5 REM, actual radiation dose in excess of 5 REM, total career radiation esposure dose.

2. Original or copied lifetime medical records from plant and private physicians and hospitals including routing physical examinations, reports of diagnostic and laboratory tests, radiographs, EKGS, etc., or abstracted portions of such records as are required for the purposes of the study.

3. Search and contact information for registrants who are no longer employed at qualified sites or who are deceased.

4. Death Certificates.

Authority for Maintenance of the System:

5 U.S.C. 301: Department of Energy Organization Act, including authorities incorporated by reference in Title III of the Department of Energy Organization Act; Executive Order 12009.

Routine Uses of Records Maintained in the System, Including Categories of Users and the Purposes of Such Uses:

1. To provide a current record of registrants for use by Department of Energy, and its contractors and consultants.

2. To identify specific populations for use in epidemiological and clinical studies.

3. To conduct medical surveillance during the lifetime of the registrants.

4. Additional uses 4, 8, 9, 10, as listed in Appendix B to the Department of Energy publication of systems of records, 45 FR 51125, 8/30/79. [1]

Policies and Practices for Storing, Retrieving, Accessing, Retaining, and Disposing of Records in the System:

Storage: Paper records, computer tapes, computer printouts, punched cards, dics, magnetic tape and microfilm.

Retrievability: By name and social security number.

Safeguards: Records are maintained in locked security areas in locked file cabinets. Access is limited to individuals whose official duties require access.

Retention and Disposal: Records retention and disposal authorities are contained in the DOE Order 1324.1, "Records Disposition." Records within the Department of Energy are destroyed by shredding, buring, or burial in a sanitary landfill, as appropriate.

System Manager(s) and Address: The Manager of the Oak Ridge Operations Office is the System Manager.

Notification Procedure:

a. Requests by an individual to determine if a system of records contains information about him or her should be directed to the Privacy Act Officer, Department of Energy, P.O. Box E, Oak Ridge, Tennessee 37830 in accordance with the Department of Energy's Privacy Act regulations (10 CFR Part 1008, 45 FR 61578, September 16, 1980).

b. Required identifying information: Name, social security number, and time period.

Record Access Procedures:

a. Requests by an individual for access to a system of records that contains information about him or her should be directed to the Privacy Act Officer, Department of Energy, P.O. Box E, Oak Ridge, Tennessee 37830 in accordance with the Department of Energy's Privacy Act regulations (10 CFR Part 1008, 45 FR 61578, September 16, 1980).

b. Required identifying information: Name, social security number, and time period.

Record Source Categories:

The individual, medical records, physicians, medical institutions, and reports of incident/accident investigations from private and public sources, radiation dosimetry records, security clearance records and employment records [1]

[1] These routine uses are reprinted below.

Systems Exempted from Certain Provisions of the Act: None.

DOE 73

System name: The US-DTPA Registry.

Security classification: Unclassified.

System location: Oak Ridge Operations Office, P.O. Box E, Oak Ridge, Tennessee 37830.

Categories of Individuals Covered by the System:

Registrants are those individuals who, because of real or suspected internal contamination with transuranic elements, have received diethyl-enetriaminepentaacetic acid (DTPA), in the calcium or zinc form during the course of chelation therapy. Administration of the agent DTPA is limited to physicians who are co-investigators with the Department of Energy contractor staff on the Investigative New Drug License of the Food and Drug Administration.

Categories of Records in the System:

1. The records compiled by the physician administering DTPA in the event of an exposure that was known to have or was suspected of having caused transuranic contamination internally requiring chelation therapy with DTPA. These records include a description of the exposure, the results of serial bioassays and investigations conducted to evaluate the level of internal contamination and the efficacy of subsequent chelation by DTPA. The form of DTPA and the route and frequency of administration are recorded together with an untoward effects of the therapy.

2. Names, social security numbers or other identifiers and vital status of treated persons. The last known addresses and the names of the private physicians of individuals who have relocated or who are no longer within the practice of the administering physician(s) are included in the DTPA Registry to facilitate the search and contact of these individuals.

3. Original or copies of medical records of illnesses, examinations, including routine followup examinations, investigations, etc., that have occurred since the initial administration of DTPA.

4. Death certification.

Authority for Maintenance of the System:

5 U.S.C. 301: Department of Energy Organization Act, including authorities incorporated by reference in Title III of the Department of Energy Organization Act; Executive Order 12009.

1032663

Routine Uses of Records Maintained in the System, Including Categories of Users and the Purposes of Such Uses:

1. To provide a current record of individuals treated with DTPA for use by the Department of Energy and its contractors and consultants.

2. To identify by epidemiological methods any long-term untoward effects associated with DTPA therapy.

3. To provide information to FDA in accord with the I.N.D. license and issuances.

4. Additional uses 4, 8, 9, 10, as listed in Appendix B.[1]

Policies and Practices for Storing, Retrieving Accessing, Retaining, and Disposing of Records in the System:

Storage: Paper records, computer tapes, computer printouts, punched cards, discs, magnetic tape and microfilm.

Retrievability: By name and social security number.

Safeguards: Records are maintained in locked security areas in locked file cabinets. Access is limited to individuals whose official duties require access.

Retention and Disposal: Records retention and disposal authorities are contained in the DOE Order 1324.1, "Records Disposition." Records within the Department of Energy are destroyed by shredding, burning, or burial in a sanitary landfill, as appropriate.

System Manager(s) and Address:

The Manager of the Oak Ridge Operations Office is the System Manager.

Notification Procedure:

a. Requests by an individual to determine if a system of records contains information about him or her should be directed to the Privacy Act Officer, Department of Energy, P.O. Box E, Oak Ridge, Tennessee 37830 in accordance with the Department of Energy's Privacy Act regulations (10 CFR Part 1008, 45 FR 61576, September 16, 1980).

b. Required identifying information: Name, social security number, and time period.

Record Access Procedures:

a. Requests by an individual for access to a system of records that contains information about him or her should be directed to the Privacy Act Officer, Department of Energy, P.O. Box E, Oak Ridge, Tennessee 37830 in accordance with the Department of Energy's Privacy Act regulations (10 CFR Part 1008, 45 FR 61576, September 16, 1980).

b. Required identifying information: Name, social security number, and time period.

Contesting Record Procedures:

a. Requests by an individual to correct or amend the content of a record containing information about him or her should be directed to the Privacy Act Officer, Department of Energy, P.O. Box E, Oak Ridge, Tennessee 37830 in accordance with the Department of Energy's Privacy Act regulations (10 CFR Part 1008, 45 FR 61576, September 16, 1980).

Record source Categories:

The individual, medical records, physicians, medical institutions, and reports of incident/accident investigations from private and public sources, radiation dosimetry records, security clearance records and employment records.

Systems Exempted from Certain Provisions of the Act: None.

Appendix B—Additional Routine Uses

The following routine uses apply to and are incorporated by reference into each system of records as stated therein:

1. In the event that a record within this system of records maintained by this agency indicates a violation or potential violation of law, whether civil, criminal or regulatory in nature, and whether arising by general statute or particular program pursuant thereto, the relevant records in the system of records may be referred as a routine use to the appropriate agency, whether Federal, State, local, or foreign, charged with the responsibility of investigating or prosecuting such violation or charged with enforcing or implementing the statute, or rule, regulation or order issued pursuant thereto.

2. A record from this system of records may be disclosed as a routine use to a Federal, State, or local agency maintaining civil, criminal, or other relevant enforcement information or other pertinent information, such as current licenses, if necessary, to obtain information relevant to an agency decision concerning the hiring or retention of an employee, the issuance of a security clearance, the letting of a contract, or the issuance of a license, grant, or other benefit.

3. A record from this system of records may be disclosed, as a routine use, to a Federal agency, in response to its request, in connection with the hiring or retention of an employee, the issuance of a security clearance, the reporting of an investigation of an employee, the letting of a contract, or the issuance of a license, grant, or other benefit by the requesting agency, to the extent that the information is relevant and necessary to the requesting agency's decision on the matter.

4. A record from this system of records may be disclosed, as a routine use (a) to appropriate parties engaged in litigation or in preparation of possible litigation, such as potential witnesses, for the purpose of securing their testimony when necessary; (b) to courts, magistrates or administrative tribunals; (c) to parties and their attorneys for the purpose of proceeding with litigation or settlement of disputes; and (d) to individuals seeking information by using established discovery procedures, whether in connection with civil, criminal, or regulatory proceedings.

5. A record maintained by this agency to carry out its functions which relates to civil and criminal proceedings may be disclosed to the news media in accordance with guidelines contained in Department of Justice regulations 28 CFR 50.2.

6. A record maintained by this agency to carry out its functions may be disclosed to foreign governments in accordance with treaty obligations.

7. A record from this system of records may be disclosed to the Office of Management and Budget in connection with the review of private relief legislation as set forth in OMB Circular No. A-19 at any stage of the legislative coordination and clearance process as set forth in that Circular.

8. A record from this system of records may be disclosed, as a routine use, to DOE contractors in performance of their contracts, and their officers and employees who have a need for the record in the performance of their duties subject to the same limitations applicable to DOE officers and employees under the Privacy Act.

[1] These routine uses are reprinted below.

1032664

9. A record in this system of records may be disclosed, as a routine use, to a member of Congress submitting a

[redacted]

from the member with respect to the subject matter of the record.

10. A record in this system of records which contains medical and/or psychological information may be disclosed, as a routine use, to the physician or mental health professional of any individual submitting a request for access to the record under the Privacy Act of 1974 and DOE's Privacy Act regulations if, in its sole judgment and good faith, DOE believes that disclosure of the medical and/or psychological information directly to the individual who is the subject of the record could have an adverse effect upon that individual, in accordance with the provisions of 5 U.S.C. 552a(f)(3) and applicable DOE regulations.

[FR Doc. 81-14227 Filed 5-11-81; 8:45 am]
BILLING CODE 6450-01-M

OAK RIDGE ASSOCIATED UNIVERSITIES
INCORPORATED
P. O. BOX 117
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8411

March 6, 1972

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants
Department of Health, Education, and Welfare
Public Health Service
National Institutes of Health
Bethesda, Maryland 20014

Dear Doctor Chalkley:

In line with our request to you for a General Institutional Assurance, we are enclosing a Statement of Compliance reflecting the present DHEW policy. This Statement of Compliance, signed by appropriate officials of Oak Ridge Associated Universities and Oak Ridge National Laboratory, has also been reviewed and approved by the Committee on Human Studies that acts for the two institutions.

Thank you very much for your help with this.

Sincerely,

Gould A. Andrews, M.D.
Chairman,
The Medical Division

GAA/pe

Enclosure

1032666

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

MAR 10 1972

1716

Gould A. Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Andrews:

In association with its responsibilities regarding the review and acceptance of assurances on the use of human subjects, this office periodically issues a cumulative list of institutions which have filed acceptable general assurances.

Since many institutions are involved in cooperative activities, the enclosed copy of the "Forty-third Cumulative List. . ." will facilitate determining if cooperating institutions have filed acceptable general assurances and have committees with which you can work.

We are also using this letter to advise you of the current status of your own institution. Our records indicate that:

- ☐ Your revised assurance of compliance with Department of Health, Education, and Welfare policy has been accepted and you have been so notified.
- ☐ Your revised assurance of compliance with DHEW policy has been received and is under review.
- ☐ Your committee structure only has been submitted.
- ☑ You have not submitted a substantive response to previous memoranda requesting compliance with DHEW policy.

The code designations (2)-(9) immediately preceding the institution's name indicate your assurance status as of February 11, 1972. If you note any discrepancy between your understanding of your status and the code listing, please let us know.

The DHEW policy permits us to interpret assurances of compliance with the older Public Health Service policy as temporarily meeting the Departmental requirements. However, institutions not in compliance with DHEW policy as of July 1, 1972, will be deleted from the cumulative list.

Sincerely yours,

D. T. Chalkley, Ph.D.
Special Assistant to the Director
Division of Research Grants

1032667

Enclosure

GENERAL INSTITUTIONAL ASSURANCE

Statement of Compliance

Oak Ridge Associated Universities and Oak Ridge National Laboratory will comply with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education, and Welfare.

These institutions have jointly established and do maintain a committee competent to review projects and activities that involve human subjects. The committee is assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.
The risks to subjects are outweighed by potential benefits.
The informed consent of subjects will be obtained by methods that are adequate and appropriate.

These institutions will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgement of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interests.

These institutions will encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

These institutions will provide for the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

These institutions will maintain appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

These institutions will periodically reassure themselves through appropriate administrative overview that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with the assurance as accepted by the Department of Health, Education, and Welfare.

1032668

OAK RIDGE ASSOCIATED UNIVERSITIES

Signature William G. Pollard

Title Executive Director

Date February 28, 1972

OAK RIDGE NATIONAL LABORATORY

Signature Ernest L. Liverman

Title Associate Director for Biomedical and Environmental Science

Date March 2, 1972

Attachment: Implementing Guidelines

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

March 31, 1972 1716

Gould A. Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

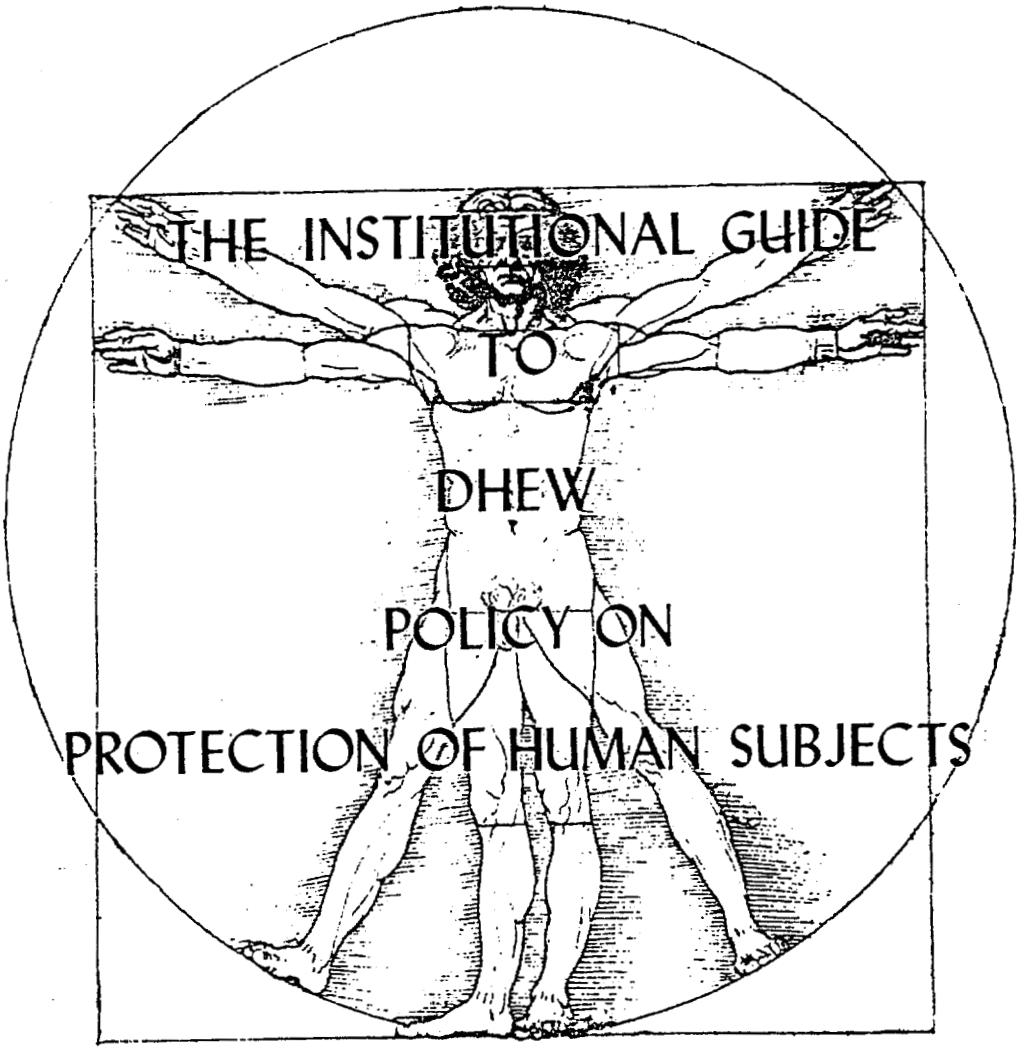
Dear Dr. Andrews:

Thank you for your letter of March 6, 1972, together with your "general" institutional assurance, to comply with DHEW policy on protection of human subjects, We also need a list of your Review Committee by name, position, and other indications of competence such as earned degrees, board certifications, licensures, etc. Upon receiving this list we will be able to complete our review of your assurance.

Sincerely yours,

Mark H. Conner, Ph.D.
Institutional Relations Branch
Division of Research Grants

1032669

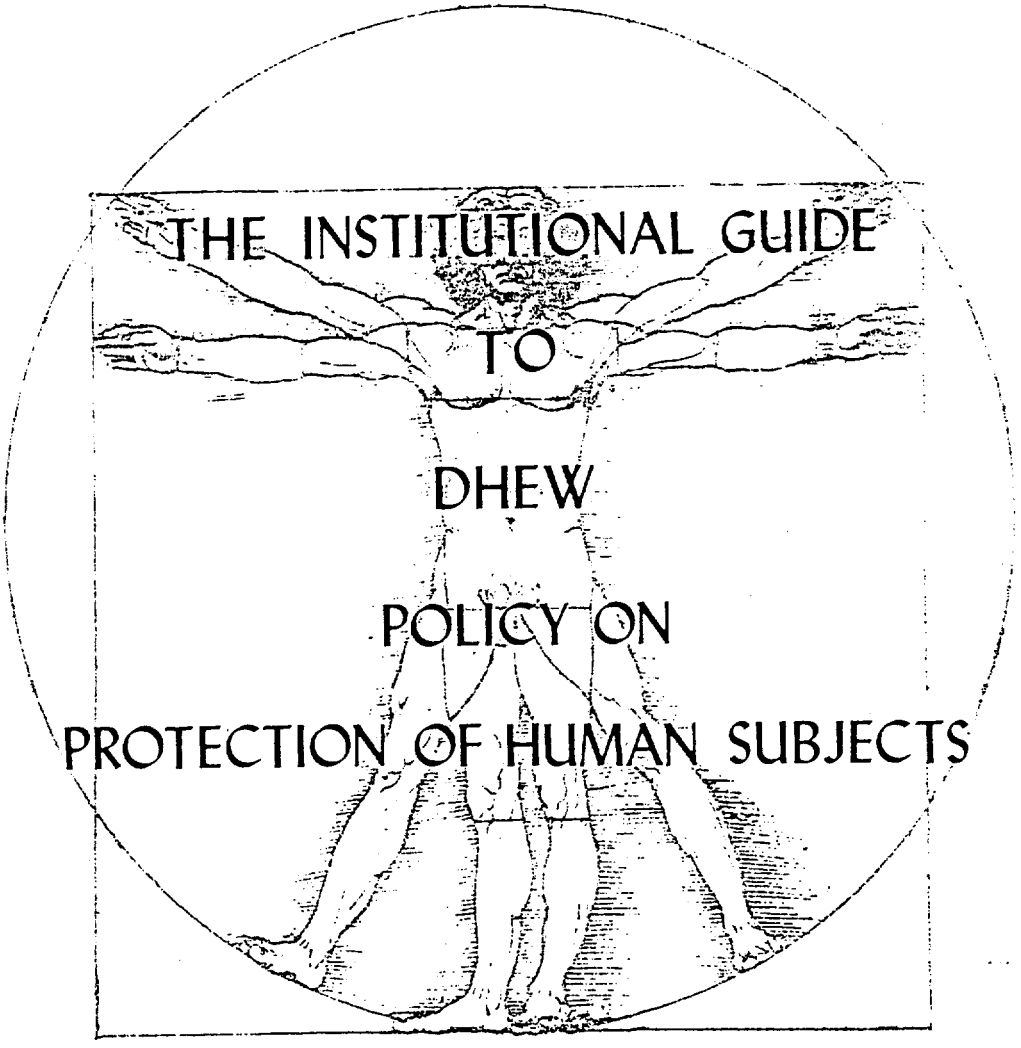


April 5, 1972

Copies to: Members of Human Studies Committee

Medical Division Sr. Staff

1032670



THE INSTITUTIONAL GUIDE TO DHEW POLICY ON PROTECTION OF HUMAN SUBJECTS

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service — National Institutes of Health

1032671

DHEW Publication No. (NIH) 72–102

December 1, 1971

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, D.C. 20402- Price 25 cents

Stock Number 1740 - 0326

1032672

FOREWORD

The Department's basic policy, quoted in the first few paragraphs of this Guide, is simple in concept. However, simplicity in conception is not always easily translated into simplicity in application. Many of the basic terms of the policy, such as subject, risk, and informed consent, are differently understood in the several professions that participate in the varied grant and contract programs supported by the Department. This Guide provides working definitions of the policy's more critical terms, and outlines flexible operating procedures which can be adapted to a variety of grant and contract mechanisms.

A flexible policy is essential. Research, development, and the reduction to practice of new ideas are not carried out in a practical, ethical, or legal vacuum. The public interest obviously would not be served by an inflexible approach to what can or should be done. Ultimately, the decisions required by this policy must depend upon the common sense and sound professional judgment of reasonable men. The Department's policy and the Guide are intended to provide room for the exercise of this judgment.

In its present form, the Guide reflects several years' experience with an earlier Public Health Service policy. It incorporates many comments and suggestions by representatives of grantee and contractor institutions, and by consultants and staff of the operating agencies of the Department. Future experience in the application of the policy in the fields of health, education, and welfare will simultaneously raise questions and suggest changes. Correspondence should be addressed to the Chief, Institutional Relations Section, Division of Research Grants, National Institutes of Health, Bethesda, Md. 20014.

D. T. Chalkley, Ph. D.
Chief, Institutional Relations Section
Division of Research Grants, NIH, DHEW

ng Office

1032673

CONTENTS

	Page
FOREWORD	iii
POLICY: Grants and Contracts	1
APPLICABILITY	1
A. General	1
B. Subject—Definition	1
C. At Risk—Definition	2
D. Types of Risks and Applicability of the Policy	2
E. Established and Accepted Methods	3
F. Necessity to Meet Needs	3
INSTITUTIONAL REVIEW	4
A. Initial Review of Projects	4
1. Committee, Composition and Functions	4
2. Statement of Principles	5
3. Review Process	5
a. Rights and Welfare of Subjects: Identity of Subjects, Confidentiality and Privacy, Legal Rights	5
b. Risk/Benefit Considerations: Benefits to Subjects—Substantial or Negligible, Volunteers, Motivation	6
c. Informed Consent: Basic Elements; Institutional Liability for Negligence, Debriefing	7
B. Continuing Review	8
C. Communication of the Committee's Action, Advice, and Counsel	9
D. Maintenance of an Active and Effective Committee	9
ASSURANCES	9
A. Negotiation of Assurances	9
B. Types of Assurances	10
1. General Assurance	10
2. Special Assurance	10
C. Minimum Requirements for General Assurances	10
1. Statement of Compliance	10
2. Implementing Guidelines	10
a. Statement of Principles	10
b. Committee Membership	10
c. Specific Procedures, Review of Proposals	10
d. Specific Procedures, Advice to and Reports from Project Directors	11
e. Specific Procedures, Institutional Follow-up on Committee Action	11
D. Minimum Requirements for Special Assurance	11

1032674

Page

TIMING AND CERTIFICATION OF INSTITUTIONAL REVIEW ____ 11

A. General Assurances ____ 11
1. Timely Review ____ 11
2. Pending Review ____ 11
3. Completion of Pending Review ____ 12
4. Proposals Lacking Definite Plans ____ 12
5. Proposals Submitted With No Intent of Involving Human Subjects ____ 12
B. Special Assurances ____ 13

COOPERATIVE ACTIVITIES ____ 13

A. Institutions With General Assurances ____ 13
1. Institutional Review Relationships ____ 13
a. Cooperating Institutions With Accepted General Assurances ____ 13
b. Cooperating Institutions With No Accepted General Assurance ____ 14
c. Interinstitutional Joint Reviews ____ 14
B. Institutions With Special Assurances ____ 14

INSTITUTIONAL ADMINISTRATION OF ASSURANCES ____ 14

A. Institutional Responsibility ____ 14
B. Executive Functions ____ 15
C. Assurance Implementation ____ 15
D. Documentation ____ 15
1. General ____ 15
2. Informed Consent ____ 16
a. Written Consent ____ 16
b. Oral Consent "Short" Form ____ 16
c. Modification of Written or Oral Consent Forms ____ 16
3. Reporting to DHEW ____ 16

ENFORCEMENT ____ 17

DEPARTMENTAL REVIEW OF ASSURANCES ____ 17

ATTACHMENT

A EXAMPLE OF A STATEMENT OF COMPLIANCE (PART ONE OF A GENERAL INSTITUTIONAL ASSURANCE) ____ 18
B SPECIAL INSTITUTIONAL ASSURANCE IN CONNECTION WITH SINGLE PROJECTS INVOLVING HUMAN SUBJECTS ____ 19
INSTRUCTIONS FOR PREPARING SPECIAL ASSURANCE ____ 21
C LIST OF CODES OR STATEMENTS OF PRINCIPLES ____ 23

1032675

Page
11
11
11
11
12
12
12
13
13
13
13
13
14
14
14
14
14
15
15
16
16
16
16
16
17
17
18
19
21
23

NOTE

Bold face indicates policy as stated in DHEW Grant Administration Manual Chapter 1-40.

Light face indicates interpretation of DHEW policy.

1032676

POLICY

Safeguarding the rights and welfare of human subjects involved in activities supported by grants or contracts from the Department of Health, Education, and Welfare is the responsibility of the institution which receives or is accountable to the DHEW for the funds awarded for the support of the activity.

In order to provide for the adequate discharge of this institutional responsibility, it is the policy of the Department that no grant or contract for an activity involving human subjects shall be made unless the application for such support has been reviewed and approved by an appropriate institutional committee.

This review shall determine that the rights and welfare of the subjects involved are adequately protected, that the risks to an individual are outweighed by the potential benefits to him or by the importance of the knowledge to be gained, and that informed consent is to be obtained by methods that are adequate and appropriate.

In addition the committee must establish a basis for continuing review of the activity in keeping with these determinations.

The institution must submit to the DHEW, for its review, approval, and official acceptance, an assurance of its compliance with this policy. The institution must also provide with each proposal involving human subjects a certification that it has been or will be reviewed in accordance with the institution's assurance.

No grant or contract involving human subjects at risk will be made to an individual unless he is affiliated with or sponsored by an institution which can and does assume responsibility for the protection of the subjects involved.

Since the welfare of subjects is a matter of concern to the Department of Health, Education, and Welfare as well as to the institution, no grant or contract involving human subjects shall be made unless the proposal for such support has been reviewed and approved by an appropriate professional committee within the responsible component of the Department. As a result of this review, the committee may recommend to the operating agency, and the operating agency may require, the imposition of specific grant or contract terms providing for the protection of human subjects, including requirements for informed consent.

APPLICABILITY

A. *General*

This policy applies to all grants and contracts which support activities in which subjects may be at risk.

B. *Subject*

This term describes any individual who may be at risk as a conse-

1032677

quence of participation as a subject in research, development, demonstration, or other activities supported by DHEW funds.

This may include patients; outpatients; donors of organs, tissues, and services; informants; and normal volunteers, including students who are placed at risk during training in medical, psychological, sociological, educational, and other types of activities supported by DHEW.

Of particular concern are those subjects in groups with limited civil freedom. These include prisoners, residents or clients of institutions for the mentally ill and mentally retarded, and persons subject to military discipline.

The unborn and the dead should be considered subjects to the extent that they have rights which can be exercised by their next of kin or legally authorized representatives.

C. *At Risk*

An individual is considered to be "at risk" if he may be exposed to the possibility of harm—physical, psychological, sociological, or other—as a consequence of any activity which goes beyond the application of those established and accepted methods necessary to meet his needs. The determination of when an individual is at risk is a matter of the application of common sense and sound professional judgment to the circumstances of the activity in question. Responsibility for this determination resides at all levels of institutional and departmental review. Definitive determination will be made by the operating agency.

D. *Types of Risks and Applicability of the Policy*

1. Certain risks are inherent in life itself, at the time and in the places where life runs its course. This policy is not concerned with the ordinary risks of public or private living, or those risks associated with admission to a school or hospital. It is not concerned with the risks inherent in professional practice as long as these do not exceed the bounds of established and accepted procedures, including innovative practices applied in the interest of the individual patient, student or client.

Risk and the applicability of this policy are most obvious in medical and behavioral science research projects involving procedures that may induce a potentially harmful altered physical state or condition. Surgical and biopsy procedures; the removal of organs or tissues for study, reference, transplantation, or banking; the administration of drugs or radiation; the use of indwelling catheters or electrodes; the requirement of strenuous physical exertion; subjection to deceit, public embarrassment, and humiliation are all examples of procedures which require thorough scrutiny by both the Department of Health, Education, and Welfare and institutional committees. In general those projects which involve risk of physical or psychological injury require prior written consent.

2. There is a wide range of medical, social, and behavioral projects and activities in which no immediate physical risk to the subject is involved; e.g., those utilizing personality inventories, interviews, questionnaires, or the use of observation, photographs, taped records, or stored data. However, some of these procedures may involve varying degrees of discomfort, harassment, invasion of privacy, or may constitute a threat to the

1032678

subject's dignity through the imposition of demeaning or dehumanizing conditions.

3. There are also medical and biomedical projects concerned solely with organs, tissues, body fluids, and other materials obtained in the course of the routine performance of medical services such as diagnosis, treatment and care, or at autopsy. The use of these materials obviously involves no element of physical risk to the subject. However, their use for many research, training, and service purposes may present psychological, sociological, or legal risks to the subject or his authorized representatives. In these instances, application of the policy requires review to determine that the circumstances under which the materials were procured were appropriate and that adequate and appropriate consent was, or can be, obtained for the use of these materials for project purposes.

4. Similarly, some studies depend upon stored data or information which was often obtained for quite different purposes. Here, the reviews should also determine whether the use of these materials is within the scope of the original consent, or whether consent can be obtained.

E. *Established and Accepted Methods*

Some methods become established through rigorous standardization procedures prescribed, as in the case of drugs or biologicals, by law or, as in the case of many educational tests, through the aegis of professional societies or nonprofit agencies. Acceptance is a matter of professional response, and determination as to when a method passes from the experimental stage and becomes "established and accepted" is a matter of judgment.

In determining what constitutes an established and accepted method, consideration should be given to both national and local standards of practice. A management procedure may become temporarily established in the routine of a local institution but still fail to win acceptance at the national level. A psychological inventory may be accepted nationally, but still contain questions which are disturbing or offensive to a local population. Surgical procedures which are established and accepted in one part of the country may be considered experimental in another, not due to inherent deficiencies, but because of the lack of proper facilities and trained personnel. Diagnostic procedures which are routine in the United States may pose serious hazards to an undernourished, heavily infected, overseas population.

If doubt exists as to whether the procedures to be employed are established and accepted, the activity should be subject to review and approval by the institutional committee.

F. *Necessity to Meet Needs*

Even if considered established and accepted, the method may place the subject at risk if it is being employed for purposes other than to meet the needs of the subject. Determination by an attending professional that a particular treatment, test, regimen, or curriculum is appropriate for a particular subject to meet his needs limits the attendant risks to those inherent in the delivery of services, or in training.

On the other hand, arbitrary, random, or other assignment of subjects

1032679

to differing treatment or study groups in the interests of a DHEW supported activity, rather than in the strict interests of the subject, introduces the possibility of exposing him to additional risk. Even comparisons of two or more established and accepted methods may potentially involve exposure of at least some of the subjects to additional risks. Any alteration of the choice, scope, or timing of an otherwise established and accepted method, primarily in the interests of a DHEW activity, also raises the issue of additional risk.

If doubt exists as to whether the procedures are intended solely to meet the needs of the subject, the activity should be subject to review and approval by the institutional committee.

INSTITUTIONAL REVIEW

A. *Initial Review of Projects*

1. Review must be carried out by an appropriate institutional committee. The committee may be an existing one, such as a board of trustees, medical staff committee, utilization committee, or research committee, or it may be specially constituted for the purpose of this review. Institutions may utilize subcommittees to represent major administrative or subordinate components in those instances where establishment of a single committee is impracticable or inadvisable. The institution may utilize staff, consultants, or both.

The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of projects and activities commonly conducted by the institution. The committee's membership, maturity, experience, and expertise should be such as to justify respect for its advice and counsel. No member of an institutional committee shall be involved in either the initial or continuing review of an activity in which he has a professional responsibility, except to provide information requested by the committee. In addition to possessing the professional competence to review specific activities, the committee should be able to determine acceptability of the proposal in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes.[1] The committee may therefore need to include persons whose primary concerns lie in these areas rather than in the conduct of research, development, and service programs of the types supported by the DHEW.

If an institution is so small that it cannot appoint a suitable committee from its own staff, it should appoint members from outside the institution.

Committee members shall be identified by name, occupation or position, and by other pertinent indications of experience and competence in areas pertinent to the areas of review such as earned degrees, board certifications, licensures, memberships, etc.

Temporary replacement of a committee member by an alternate of comparable experience and competence is permitted in the event a mem-

[1] In the United States, the regulations of the Food and Drug Administration (21 CFR 130) provide that the committee *must* possess competencies to determine acceptability of the project in these terms in order to review proposals for investigational new drug (IND) studies.

1032680

ber is momentarily unable to fulfill committee responsibility. The DHEW should be notified of any permanent replacement or additions.

2. The institution should adopt a statement of principles that will assist it in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may be an appropriate existing code or declaration or one formulated by the institution itself.[2] It is to be understood that no such principles supersede DHEW policy or applicable law.

3. Review begins with the identification of those projects or activities which involve subjects who may be at risk. In institutions with large grant and contract programs, administrative staff may be delegated the responsibility of separating those projects which do not involve human subjects in any degree; i.e., animal and nonhuman materials studies. However, determinations as to whether any project or activity involves human subjects at risk is a professional responsibility to be discharged through review by the committee, or by subcommittees.

If review determines that the procedures to be applied are to be limited to those considered by the committee to be established, accepted, and necessary to the needs of the subject, review need go no further; and the application should be certified as approved by the committee. Such projects involve human subjects, but these subjects are not considered to be at risk.

If review determines that the procedures to be applied will place the subject at risk, review should be expanded to include the issues of the protection of the subject's rights and welfare, of the relative weight of risks and benefits, and of the provision of adequate and appropriate consent procedures.

Where required by workload considerations or by geographic separation of operating units, subcommittees or mail review may be utilized to provide preliminary review of applications.

Final review of projects involving subjects at risk should be carried out by a quorum of the committee.[3] Such review should determine, through review of reports by subcommittees, or through its own examination of applications or of protocols, or through interviews with those individuals who will have professional responsibility for the proposal project or activity, or through other acceptable procedures that the requirements of the institutional assurance and of DHEW policy have been met, specifically that:

a. The rights and welfare of the subjects are adequately protected.

Institutional committees should carefully examine applications, protocols, or descriptions of work to arrive at an independent determination of possible risks. The committee must be alert to the possibility that investigators, program directors, or contractors may, quite unintentionally, introduce unnecessary or unacceptable hazards, or fail to provide adequate safeguards. This possibility is particularly true if the project crosses disciplinary lines, involves new and untried procedures, or involves established and accepted procedures which are new to the personnel applying them. Committees must also assure

[2] Some of the existing codes or statements of principles concerned with the protection of human subjects in research, investigation, and care are listed in attachment C.

[3] In the United States, the quorum reviewing investigational new drug studies must satisfy requirements of the Food and Drug Administration (21 CFR 130).

1032681

themselves that proper precautions will be taken to deal with emergencies that may develop even in the course of seemingly routine activities.

When appropriate, provision should be made for safeguarding information that could be traced to, or identified with, subjects. The committee may require the project or activity director to take steps to insure the confidentiality and security of data, particularly if it may not always remain under his direct control.

Safeguards include, initially, the careful design of questionnaires, inventories, interview schedules, and other data gathering instruments and procedures to limit the personal information to be acquired to that absolutely essential to the project or activity. Additional safeguards include the encoding or enciphering of names, addresses, serial numbers, and of data transferred to tapes, discs, and printouts. Secure, locked spaces and cabinets may be necessary for handling and storing documents and files. Codes and ciphers should always be kept in secure places, distinctly separate from encoded and enciphered data. The shipment, delivery, and transfer of all data, printouts, and files between offices and institutions may require careful controls. Computer to computer transmission of data may be restricted or forbidden.

Provision should also be made for the destruction of all edited, obsolete or depleted data on punched cards, tapes, discs, and other records. The committee may also determine a future date for destruction of all stored primary data pertaining to a project or activity.

Particularly relevant to the decision of the committees are those rights of the subject that are defined by law. The committee should familiarize itself through consultation with legal counsel with these statutes and common law precedents which may bear on its decisions. The provisions of this policy may not be construed in any manner or sense that would abrogate, supersede, or moderate more restrictive applicable law or precedential legal decisions.

Laws may define what constitutes consent and who may give consent, prescribe or proscribe the performance of certain medical and surgical procedures, protect confidential communications, define negligence, define invasion of privacy, require disclosure of records pursuant to legal process, and limit charitable and governmental immunity (see, e.g., the University of Pittsburgh Law Manual).

b. The risks to an individual are outweighed by the potential benefits to him or by the importance of the knowledge to be gained.

The committee should carefully weigh the known or foreseeable risks to be encountered by subjects, the probable benefits that may accrue to them, and the probable benefits to humanity that may result from the subject's participation in the project or activity. If it seems probable that participation will confer substantial benefits on the subjects, the committee may be justified in permitting them to accept commensurate or lesser risks. If the potential benefits are insubstantial, or are outweighed by risks, the committee may be justified in permitting the subjects to accept these risks in the interests of humanity. The committee should consider the possibility that subjects, or those authorized to represent subjects, may be motivated to accept risks for unsuitable or inadequate reasons. In such instances the consent procedures adopted should incorporate adequate safeguards.

1032682

Compensation to volunteers should never be such as to constitute an undue inducement.

No subject can be expected to understand the issues of risks and benefits as fully as the committee. Its agreement that consent can reasonably be sought for subject participation in a project or activity is of paramount practical importance.

"The informed consent of the subject, while often a legal necessity is a goal toward which we must strive, but hardly ever achieve except in the simplest cases."

(Henry K. Beecher, M.D.)

c. The informed consent of subjects will be obtained by methods that are adequate and appropriate.

Note.—In the United States, adherence to the regulations of the Food and Drug Administration (21 CFR 130) governing consent in projects involving investigational new drugs (IND) is required by law.

Informed consent is the agreement obtained from a subject, or from his authorized representative, to the subject's participation in an activity.

The basic elements of informed consent are:

1. **A fair explanation of the procedures to be followed, including an identification of those which are experimental;**
2. **A description of the attendant discomforts and risks;**
3. **A description of the benefits to be expected;**
4. **A disclosure of appropriate alternative procedures that would be advantageous for the subject;**
5. **An offer to answer any inquiries concerning the procedures;**
6. **An instruction that the subject is free to withdraw his consent and to discontinue participation in the project or activity at any time.**

In addition, the agreement, written or oral, entered into by the subject, should include no exculpatory language through which the subject is made to waive, or to appear to waive, any of his legal rights, or to release the institution or its agents from liability for negligence.[4]

Informed consent must be documented (see Documentation, p. 35).

Consent should be obtained, whenever practicable, from the subjects themselves. When the subject group will include individuals who are not legally or physically capable of giving informed consent, because of age, mental incapacity, or inability to communicate, the review committee should consider the validity of consent by next of kin, legal guardians, or by other qualified third parties representative of the subjects' interests. In such instances, careful consideration should be given by the committee not only to whether these third parties can be presumed to have the necessary depth of interest and concern with the subjects' rights and welfare, but also to whether these third parties will be legally authorized to expose the subjects to the risks involved.

[4] Use of exculpatory clauses in consent documents is considered contrary to public policy. *Tunkl vs. Regents of University of California*, 60 Cal. 2d 92, 32 Cal. Rptr.33, 383 P. 2d 441 (1963), Annot., 6 A.L.R. 3d 693 (1966).

1032683

The review committee will determine if the consent required, whether to be secured before the fact, in writing or orally, or after the fact following debriefing, or whether implicit in voluntary participation in an adequately advertised activity, is appropriate in the light of the risks to the subject, and the circumstances of the project.

The review committee will also determine if the information to be given to the subject, or to qualified third parties, in writing or orally, is a fair explanation of the project or activity, of its possible benefits, and of its attendant hazards.

Where an activity involves therapy, diagnosis, or management, and a professional/patient relationship exists, it is necessary "to recognize that each patient's mental and emotional condition is important . . . and that in discussing the element of risk, a certain amount of discretion must be employed consistent with full disclosure of fact necessary to any informed consent." [5]

Where an activity does not involve therapy, diagnosis, or management, and a professional/subject rather than a professional/patient relationship exists, "the subject is entitled to a full and frank disclosure of all the facts, probabilities, and opinions which a reasonable man might be expected to consider before giving his consent." [6]

When debriefiing procedures are considered as a necessary part of the plan, the committee should ascertain that these will be complete and prompt.

B. *Continuing Review*

This is an essential part of the review process. While procedures for continuing review of ongoing projects and activities should be based in principle on the initial review criteria, they should also be adapted to the size and administrative structure of the institution. Institutions which are small and compact and in which the committee members are in day-to-day contact with professional staff may be able to function effectively with some informality. Institutions which have placed responsibility for review in boards of trustees, utilization committees, and similar groups that meet on frequent schedules may find it possible to have projects re-reviewed during these meetings.

In larger institutions with more complex administrative structures and specially appointed committees, these committees may adopt a variety of continuing review mechanisms. They may involve systematic review of projects at fixed intervals, or at intervals set by the committee commensurate with the project's risk. Thus, a project involving an untried procedure may initially require reconsideration as each subject completes his involvement. A highly routine project may need no more than annual review. Routine diagnostic service procedures, such as biopsy and autopsy, which contribute to research and demonstration activities generally require no more than annual review. Spot checks may be used to supplement scheduled reviews.

Actual review may involve interviews with the responsible staff, or

[5] *Salgo vs. Leland Stanford Jr. University Board of Trustees* (154 C.A. 2nd 560; 317 P. 2d 1701).

[6] *Halushka vs. University of Saskatchewan,* (1965) 53 D.L.R. (2d).

1032684

review of written reports and supporting documents and forms. In any event, such review must be completed at least annually to permit certifications of review on noncompeting continuation applications.

C. *Communication of the Committee's Action, Advice, and Counsel*

If the committee's overall recommendation is favorable, it may simultaneously prescribe restrictions or conditions under which the activity may be conducted, define substantial changes in the research plans which should be brought to its attention, and determine the nature and frequency of interim review procedures to insure continued acceptable conduct of the research.

Favorable recommendations by an institutional committee are, of course, always subject to further appropriate review and rejection by institution officials.

Unfavorable recommendations, restrictions, or conditions cannot be removed except by the committee or by the action of another appropriate review group described in the assurance filed with the Department of Health, Education, and Welfare.

Staff with supervisory responsibility for investigators and program directors whose projects or activities have been disapproved or restricted, and institutional administrative and financial officers should be informed of the committee's recommendations. Responsible professional staff should be informed of the reasons for any adverse actions taken by the institutional committee.

The committee should be prepared at all times to provide advice and counsel to staff developing new projects or activities or contemplating revision of ongoing projects or disapproved proposals.

D. *Maintenance of an Active and Effective Committee*

Institutions should establish policy determining overall committee composition, including provisions for rotation of memberships and appointment of chairmen. Channels of responsibility should be established for implementation of committee recommendations as they may affect the actions of responsible professional staff, grants and contracts officers, business officers, and other responsible staff. Provisions should be made for remedial action in the event of disregard of committee recommendations.

ASSURANCES

A. *Negotiation of Assurances*

An institution applying to the DHEW for a grant or contract involving human subjects must provide written assurance that it will abide by DHEW policy. The assurance shall embody a statement of compliance with DHEW requirements for initial and continuing committee review of the supported activities; a set of implementing guidelines, including identification of the committee, and a description of its review procedures or, in the case of special assurances concerned with single projects or activities, a report of initial findings and pro-

1032685

posed continuing review procedures. Institutions that have not previously filed assurances should request instructions for the preparation of an assurance from the Division of Research Grants, National Institutes of Health.

Negotiation of assurances is the responsibility of the DRG, NIH. Negotiation will be initiated on receipt of a copy of a grant application, a contract proposal, or other documentation identifying the project and the offeror or sponsoring institution.

Assurances will not be accepted from institutions or institutional components which do not have control over the expenditure of DHEW grant or contract funds unless they are an active part of a cooperative project or activity.

An assurance will be accepted only after review and approval by the DRG, NIH.

B. *Types of Assurance*

Assurances may be one of two types:

1. *General assurance.*—A general assurance describes the review and implementation procedures applicable to all DHEW-supported activities within an institution, regardless of the number, location, or types of its components (see attachment A). General assurances will be required from institutions having a significant number of concurrent DHEW projects or activities involving human subjects.

2. *Special assurance.*—A special assurance will, as a rule, describe those review and implementation procedures applicable to a single project or activity (see attachment B). Special assurances may also be approved in modified forms to meet unusual requirements either of the operating agency or of the institution receiving a grant or contract. Special assurances are not to be solicited from institutions which have accepted general assurances on file.

C. *Minimum Requirements for General Assurances*

1. *Statement of compliance.*—A formal statement of compliance with DHEW policy must be executed by an appropriate institutional official.

2. *Implementing guidelines.*—The institution must include as part of its assurance implementing guidelines that specifically provide for:

a. The statement of principles that will assist the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may be an appropriate existing code or declaration or one formulated by the institution itself.

b. A committee or committee structure which will conduct initial and continuing reviews. Committee members shall be identified by name, occupation or position, and by other pertinent indications of experience and competence in areas pertinent to the areas of review such as earned degrees, board certifications, licensures, memberships, etc.

c. The procedures which the institution will follow in carrying out its initial and continuing review of proposals and activities to insure that:

1032686

(1) The rights and welfare of subjects are adequately protected;
(2) The risks to subjects are outweighed by potential benefits;
(3) The informed consent of subjects will be obtained by methods that are adequate and appropriate.

d. The procedures which the committee will follow to provide advice and counsel to project and program directors with regard to the committee's actions as well as the requirement for reporting to the committee any emergent problems or proposed procedural changes.

e. The procedures which the institution will follow to maintain an active and effective committee and to implement its recommendations.

D. *Minimum Requirements for Special Assurance*

An acceptable special assurance covering a single activity consists of a properly completed statement of compliance, similar to that illustrated by attachment B. This assurance shall identify the specific grant or contract involved by its number, if known; by its full title; and by the name of the project or program director, principal investigator, fellow, or other person immediately responsible for the conduct of the activity. The assurance shall be signed by a committee of not fewer than three members and executed by an appropriate institutional official. The committee shall describe in general terms those risks to the subject that it recognizes as inherent in the activity. Consent procedures to be used are to be described. Any consent statement to be signed, heard, or read by the subject or responsible third parties should be attached. The assurance should outline the circumstances under which the director or investigator will be required to inform the committee of proposed changes in the activity, or of emergent problems involving human subjects. The assurance should also indicate whether the director or investigator will be required to submit written reports, appear for interview, or be visited by the committee or committees to provide for continuing review. It should also indicate the intervals at which such reviews will take place.

TIMING AND CERTIFICATION OF INSTITUTIONAL REVIEW

A. *General Assurances*

1. *Timely review.*—All proposals involving human subjects submitted by institutions with accepted general assurances should, whenever possible, be given institutional review and approval prior to submission to the DHEW. The proposal or application should be appropriately marked in the spaces provided on forms, or the following statement should be typed on the lower or right hand margin of the page bearing the name of the institutional official authorized to sign or execute applications or proposals for the institution:
"HUMAN SUBJECTS—REVIEWED AND APPROVED ON ___(date)___."
(This date should be no more than 90 days prior to the submission date, and must not be more than 12 months prior to the proposed starting date.)

2. *Pending review.*—If it will be necessary to delay the review, the

1032687

proposal is to be appropriately marked in the spaces provided on forms, or the following statement is to be typed in the lower or right hand margin of the page bearing the name of the institutional official authorized to sign or execute applications or proposals for the institution:

"HUMAN SUBJECTS—REVIEW PENDING ON ___(date)___."

(This date should be at least one month earlier than the proposed starting date of the project to avoid possible conflict with the award date.)

3. *Completion of pending review.*—Review should be initiated as soon as possible after the submission of the proposal so that final action can be completed prior to the pending review date. If this final action is disapproval, or is approval contingent on substantive changes in the proposal, the operating agency is to be notified promptly by telegram; an immediate confirmatory letter; and, where appropriate, by withdrawal of the application from further consideration by the agency.

4. *Institutional review of proposals lacking definite plans or specifications for the involvement of human subjects.*—Certain types of proposals are submitted with the knowledge that human subjects are to be involved within the project period, but definite plans for this involvement cannot properly be included in the proposal. These include (1) certain training grants where trainee projects remain to be selected, and (2) research, pilot, or developmental studies in which involvement depends upon such things as the completion of instruments, or of prior animal studies, or upon the purification of compounds.

Such proposals should be reviewed and certified in the same manner as more complete proposals. The initial certification indicates institutional approval of the applications as submitted, and commits the institution to later review of the plans when completed. Such later review should be completed prior to the beginning of the budget period during which actual involvement of human subjects is to begin.

5. *Institutional review of proposals not submitted with the intent of involving human subjects.*—If a proposal, at the time it is submitted to the DHEW, does not anticipate involving or intend to involve human subjects, no certification should be submitted. In those instances, however, where funds are awarded in response to the proposal and it later becomes appropriate to use all or parts of these funds for activities which will involve human subjects, such use must be reviewed and approved in accordance with the institutional assurance prior to the use of subjects:

a. Where support is provided by project grants or contracts, review and approval of such changes must be certified to the awarding agency or contracting agency, together with a description of the proposed change in the project plan or contract workscope. Subjects should not be used prior to receipt of approval from agency staff or from the project officer concerned.

b. Where support is provided by a mandatory grant or institutional grant, in which cases the institution determines within broad guidelines the project or activities supported, including the use of human

1032688

subjects (i.e., general research support grants, clinical research center projects), review must be carried out in accordance with the institutional assurance. Certification for individual projects need not be forwarded to the awarding agency.

Whenever the committee is uncertain as to whether a change should or should not be reported, the question should be referred to the operating agency concerned.

All certifications are subject to verfication by DHEW representatives authorized to examine institutional and committee records.

B. *Special Assurances*

When a special assurance is submitted, it provides certification for the initial grant or contract period concerned. No additional documentation is required. If the terms of the grant or contract provide for additional years of support, with annual obligation or funds, the noncompeting renewal application or proposal shall be certified in the manner described in the preceding section.

COOPERATIVE ACTIVITIES

Cooperative activities are those which involve other than the grantee or prime contractor (such as a contractor under a grantee or a subcontractor under a prime contractor). In such instances the grantee or prime contractor may obtain access to all or some of the human subjects involved through the cooperating institution. Regardless of the distances involved and the nature of the cooperative arrangement, the basic DHEW policy applies and the grantee or prime contractor remains responsible for safeguarding the rights and welfare of the subjects. The manner in which this responsibility can be discharged depends on whether the grantee or contractor holds an institutional general assurance or an institutional special assurance.

A. *Institutions with General Assurances*

1. Initial and continuing institutional review may be carried out by one or a combination of procedures:

—By the grantee's or contractor's committee;
—By the committee reviews conducted at both institutions; or
—Through cooperation of appropriate individuals or committees representing the cooperating institution.

The procedures to be followed must be made a matter of record in the institutional files for the grant or contract before funds are released by the grantee or contractor for the cooperative project. There are three relationships that may govern in reference to the cooperating institution:

a. Cooperating institutions with accepted general assurances When the cooperating institution has on file with the DHEW an accepted general assurance, the grantee or contractor may request the cooperator to conduct its own independent review and to report to the grantee's or contractor's committee the cooperating committee's recommendations on those aspects of the activity that concern indi-

1032689

viduals for whom the cooperating institution has responsibility in accordance with its own assurance. The grantee or contractor may, at its discretion, concur with or further restrict the recommendations of the cooperating institution. It is the responsibility of the grantee or contractor to maintain communication with the cooperating institutional committees. The cooperating institution should promptly notify the grantee or contracting institution whenever the cooperating institution finds the conduct of the project or activity within its purview unsatisfactory.

b. Cooperating institution with no accepted general assurance When the cooperating institution does not have an accepted assurance on file with the DHEW, the awarding agency concerned may request the DRG, NIH, to negotiate an assurance.

c. Interinstitutional joint reviews.—The grantee or contracting institution may wish to develop an agreement with cooperating institutions to provide for a review committee with representatives from cooperating institutions. Representatives of cooperating institutions may be appointed as *ad hoc* members of the grantee or contracting institution's existing review committee or, if cooperation is on a frequent or continuing basis as between a medical school and a group of affiliated hospitals, appointments may be made permanent. Under some circumstances component subcommittees may be established within cooperating institutions. All such cooperative arrangements must be accepted by the Department as part of a general assurance, ar as an amendment to a general assurance, or in unusual situations as determined by the DRG, NIH, as a special assurance.

B. *Institutions with Special Assurances*

While responsibility for initial and continuing review necessarily lies with the contractor, the DHEW will also require acceptable assurances from those cooperating institutions having immediate responsibility for subjects.

If the cooperating institution has on file with the DHEW an accepted general assurance, the contractor shall request the cooperator to conduct its own independent review of those aspects of the project or activity which will involve human subjects for which it has immediate responsibility. Such a request shall be in writing and should provide for direct notification of the contractor's committee in the event that the cooperator's committee finds the conduct of the activity unsatisfactory.

If the cooperating institution does not have an accepted general assurance on file with the DHEW, the operating agency concerned must request the DRG, NIH, to negotiate an assurance.

INSTITUTIONAL ADMINISTRATION OF ASSURANCES

A. *Institutional Responsibility*

The grantee or contracting institution's administration is accountable to the Department for effectively carrying out the provisions of the institutional assurance for the protection of human subjects as ac-

1032690

cepted and recognized by the Department. Revisions in the institutional assurance, including the implementing procedures, are to be reported to the Department prior to the date such revisions become effective. Revision without prior notification may result in withdrawal of departmental recognition of the institution's assurance.

B. *Executive Functions*

Specific executive functions to be conducted by the institutional administration include institutional policy formulation, development, promulgation, and continuing indoctrination of personnel. Appropriate administrative assistance and support must be provided for the committee's functions. Implementation of the committee's recommendations through appropriate administrative action and followup is a condition of acceptance of an assurance. Committee approvals and recommendations are, of course, subject to review and to disapproval or further restriction by institutional officials. Committee disapprovals, restrictions, or conditions cannot be rescinded or removed except by action of the committee or another appropriate review group as described and accepted in the assurance filed with the Department.

C. *Assurance Implementation*

Under no circumstances shall proposed activity plans, not approved by the committee, be implemented with Department funds. The principal investigator, program or project director, or other responsible staff must be notified as promptly as possible of committee actions, including any restrictive recommendations made by the institutional committee or the administration. They must also be informed and reminded of their continuing responsibility to bring to the attention of the committee any proposed significant changes in project or activity plans or any emergent problems that will affect human subjects. Where continuing review of projects involves the channels of administrative authority in the institution, notification of committee actions should be sent through these channels. Establishment of mechanisms for consultation and appeal by investigators and subjects may be an important condition of acceptance of an assurance by the Department.

D. *Documentation*

1. *General.*—Development of appropriate documentation and reporting procedures is an essential administrative function. The files must include copies of all documents presented or required for initial and continuing review by the institutional review committee and transmittals on actions, instructions, and conditions resulting from review committee deliberations addressed to the activity director are to be made part of the official institutional files for the supported activity. Committee meeting minutes including records of discussions of substantive issues and their resolution are to be retained by the institution and be made available upon request to representatives of the DHEW.

1032691

2. *Informed consent.*—An institution proposing to place any individual at risk is obligated to obtain and document his informed consent; the terms "*at risk*" and "informed consent" will apply as defined previously.

The actual procedure in obtaining informed consent and the basis for committee determinations that the procedures are adequate and appropriate are to be fully documented. The documentation will follow one of the following three forms:

a. Provision of a written consent document embodying all of the basic elements of informed consent. *This form is to be signed by the subject or his authorized representative.* A sample of the form as approved by the committee is to be retained in its records. Completed forms are to be handled in accordance with institutional practice.

b. Provision of a "short" form written consent document indicating that the basic elements of informed consent have been presented orally to the subject. Written summaries of what is to be said to the patient are to be approved by the committee. *The "short" form is to be signed by the subject or his authorized representative and an auditor-witness to the oral presentation and to the subject's or his authorized representative's signature.* A copy of the approved summary, annotated to show any additions, is to be signed by the persons obtaining the consent on behalf of the institution and by the auditor-witness. Sample copies of the consent form and of the summaries as approved by the committee are to be retained in its records. Completed forms are to be handled in accordance with institutional practice.

c. Modification of either of the above two primary procedures. *All such modifications must be approved by the committee in the minutes signed by the committee chairman.* Granting of permission to use modified procedures imposes additional responsibility upon the review committee and the institution to establish that the risk to any subject is minimum, that use of either of the primary procedures for obtaining informed consent would surely invalidate objectives of considerable immediate importance, and that any reasonable alternative means for attaining these objectives would be less advantageous to the subject.

The committee's reasons for permitting modification or elimination of any of the six basic elements of informed consent, or for altering requirements for a subject's signature, or for signature of an auditor-witness, or for substitution (i.e., debriefing), or other modification of full, complete, written prior consent, must be individually and specifically documented in the minutes and in reports of committee actions to the institutional files. Approval of any such modifications should be regularly reconsidered as a function of continuing review and as required for annual review, with documentation of reaffirmation, revision, or discontinuation as appropriate.

3. *Reporting to DHEW.*—No routine reports to DHEW are required. Significant changes in policy, procedure, or committee structure shall, however, be promptly reported to the DRG, NIH, for review and acceptance. Review of these changes or of institutional and other records of performance under the terms and conditions of DHEW

1032692

policy, may require renegotiation of the assurance or such other action as may be appropriate.

ENFORCEMENT

The DRG, NIH, will follow up reports by reviewers, evaluators, consultants, and staff of the DHEW indicating concern for the welfare of subjects involved in approved and funded grants or contracts, and of subjects potentially involved in activities approved but not funded, and in disapproved proposals. On the basis of these reports and of other sources of information, the DRG, NIH, may, in collaboration with the operating agency concerned, correspond with or visit institutions to discuss correction of any apparent deficiencies in its implementation of the procedures described in its institutional assurance.

If, in the judgment of the Secretary, an institution has failed in a material manner to comply with the terms of this policy with respect to a particular DHEW grant or contract, he may require that it be terminated in the manner provided for in applicable grant or procurement regulations. The institution shall be promptly notified of such finding and of the reason therefor.

If, in the judgment of the Secretary, an institution fails to discharge its responsibilities for the protection of the rights and welfare of the individuals in its care, whether or not DHEW funds are involved, he may question whether the institution and the individuals concerned should remain eligible to receive future DHEW funds for activities involving human subjects. The institution and individuals concerned shall be promptly notified of this finding and of the reasons therefor.

DEPARTMENTAL REVIEW OF ASSURANCES

All assurances submitted for approval are to be forwarded to the DRG, NIH, for review and acceptance on behalf of the Department. Review will be principally concerned with the adequacy of the proposed committee in the light of the probable scope of the applicant institution's activities, and with the appropriateness of the proposed initial and continuing review in the light of the probable risks to be encountered, the types of subject populations involved, and the size and complexity of the institution's administration. Institutions submitting inadequate assurances will be informed of deficiencies. The appropriate operating agency will be kept informed, on request, of the status and acceptance of an assurance.

1032693

ATTACHMENT A

EXAMPLE OF A STATEMENT OF COMPLIANCE PART ONE OF A GENERAL INSTITUTIONAL ASSURANCE

The (name of institution) will comply with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education, and Welfare. In fulfillment of its assurance:

This institution will establish and maintain a committee competent to review projects and activities that involve human subjects. The committee will be assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.
The risks to subjects are outweighed by potential benefits.
The informed consent of subjects will be obtained by methods that are adequate and appropriate.

This institution will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interests.

This institution will encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

This institution will provide for the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

This institution will maintain appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

This institution will periodically reassure itself through appropriate administrative overview that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with its assurance as accepted by the Department of Health, Education, and Welfare.

Official signing for the Institution

Signature _____

Title _____

Date _____

Enclosure: Implementing Guidelines, Part Two of a General Institutional Assurance.

1032694

ATTACHMENT B

EXAMPLE OF A STATEMENT OF COMPLIANCE SPECIAL INSTITUTIONAL ASSURANCE IN CONNECTION WITH SINGLE PROJECTS INVOLVING HUMAN SUBJECTS

(0) The (name of institution) will comply with the policy for the protection of human subjects participating in projects or activities supported by grants and contracts made by the Department of Health, Education, and Welfare. This policy requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. An initial review of the application for a grant or contract identified as _____ submitted by this institution on behalf of _____ indicates that:

(1) In the opinion of this committee the risks to the rights and welfare of the subject in this project or activity are:

The committee states that adequate safeguards against these risks have been provided.

(2) In the opinion of the committee the potential benefits of this activity to the subjects outweigh any probable risks. This opinion is justified by the following reasons:

(3) In the opinion of the committee the following informed consent procedures will be adequate and appropriate. Documentation is attached.

(4) The committee agrees to arrange for a continuing exchange of information and advice between itself and the investigator or director, particularly to deal with proposed changes in project or activity design, or with emergent problems which may alter the investigational situation with regard to the criteria cited above. This exchange will be implemented through:

This institution will provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects.

(5) The signatures, names, and occupations or titles of the members of the committee are listed below.

Signature	Name	Occupation or Title
Signature	Name	Occupation or Title
Signature	Name	Occupation or Title
Signature	Name	Occupation or Title

Date of Committee Approval _____

(Continued page 20)

(6) Official signing for Institution _____

Signature

_____

Name

_____

Title

_____

Address

_____

Institution

_____

_____

Telephone Number

Date _____

(see instructions)

1032696

ATTACHMENT B

INSTRUCTIONS

An acceptable special institutional assurance consists of a properly completed formal statement of compliance with Department of Health, Education, and Welfare policy (see attachment B), signed by a committee of not less than three members and by an official authorized to sign for the institution. The explanatory paragraphs which follow refer to the corresponding section of the attachment.

(0) This should identify the application for a grant, contract, or award by its identifying number, where known, or by its full title. The name should be that of the investigator, program director, fellow, or other individual immediately responsible for the conduct of the work.

(1) The committee should identify in general terms those risks that it recognizes as probable occurrences; i.e., "Aggravation of anxiety status through contact with interviewers," "Preservation of confidentiality of data," "Renal injury subsequent to multiple biopsy," "Possibility of side reactions to drugs," "Possible local hematosis and nerve injury associated with venipuncture."

(2) The committee should identify the benefits to the subject or to mankind in general that will accrue through the subject's participation in the project. This should be followed by a brief discussion, weighing the risks against the benefits.

(3) Consent procedures should be described and the minimum statement to be used should be attached. "Students responding to the attached advertisement will be interviewed." "The project outline will be submitted to the executive council of the PTA." "Individual teachers will be asked to allow an observer in the rooms chosen." "Superintendents of several State mental hospitals will be approached. The attached statement to the next of kin or guardian will be signed by the principal investigator and the superintendent." "The following special consent form will be signed by each subject and his or her spouse or next of kin before acceptance of the subject." "No prior consent will be sought. The following debriefing schedule will be followed within 30 minutes after completion of the test."

(4) This should indicate whether the investigator or director will be required to submit written reports, or to appear for interviews, or will be visited by the committee or committee representatives, and at approximately what intervals these steps will be carried out.

(5) No further explanation is necessary. (The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of the project. The committee may be an existing one, or one especially appointed for the purpose. The institution may utilize staff, consultants, or both. The membership should possess not only broad competence to comprehend the nature of the project, but also other competencies necessary in the judgments as to acceptability of the project or activity in terms of institutional regulations, relevant law, standards of professional practice, and community acceptance. The com-

1032697

mittee's maturity and experience should be such as to justify respect for its advice and counsel.)

(No individual involved in the conduct of the project shall participate in its review, except to provide information to the committee.)

(Committee members should be identified in the assurance by name, positions, earned degrees, board certifications, licensures, memberships, and other indications of experience, competence, and interest.)

The completed assurance should be attached to the application, or returned directly to the office requesting its submission.

1032698

ATTACHMENT C

Codes or statements of principles which are concerned with the protection of human subjects in research, investigation, and care have been issued by:

Organization	Code; adoption date	Reference
World Medical Association 10 Columbus Circle New York, N.Y. 10019 (code available from AMA; see address listed herein)	The Declaration of Helsinki; Recommendations Guiding Doctors in Clinical Research; 1964	J.A.M.A., 197(11):32, Sept. 12, 1966
Nuernberg Military Tribunals: U.S. v. Karl Brandt	Text from which the "Nuernberg Code" is derived.	Trials of War Criminals Before the Nuernberg Military Tribunals, vol. II, pp. 181–82; GPO 1949
American Medical Association 535 North Dearborn Street Chicago, Ill. 60610	AMA Ethical Guidelines for Clinical Investigation; Nov. 30, 1966	←
(British) Medical Research Council 20 Park Crescent London W.1, England	Responsibility in Investigations on Human Subjects; 1964	Report of the Medical Research Council for 1962–1963, (Cmnd. 2382), pp. 21–25
(Canadian) Medical Research Council Montreal Road Ottawa 7, Ontario, Canada	Medical Research Council; Extramural Programme; 1966	←
American Association on Mental Deficiency 20 North Street Willimantic, Conn. 06226	Statement on the Use of Human Subjects for Research; May 1969	American Journal of Mental Deficiency, 74 (1):157, July 1969
American Nurses' Association 10 Columbus Circle New York, N.Y. 10019	The Nurse in Research; ANA Guidelines on Ethical Values; January 1968	←
American Personnel and Guidance Association 1607 New Hampshire Avenue, N.W. Washington, D.C. 20009	American Personnel and Guidance Association; Code of Ethical Standards; no date specified	←
American Psychological Association, Inc. 1200 17th Street, N.W. Washington, D.C. 20036	Ethical Standards of Psychologists; Copyrighted January 1963	American Psychologist, 18 (1):56–60, January 1963
International League of Societies for the Mentally Handicapped 12 Rue Forestiere Brussels 5, Belgium	Declaration of General and Special Rights of the Mentally Retarded; Oct. 24, 1968	←

Organization	Code; adoption date	Reference
National Association of Social Workers 2 Park Avenue New York, N.Y. 10016	NASW Code of Ethics; Oct. 13, 1968	←

☆ U.S. GOVERNMENT PRINTING OFFICE: 1972 O—445-427

1032700

April 3, 1972

Mark H. Conner, Ph.D.
Institutional Relations Branch
Division of Research Grants
HEW
National Institutes of Health
Westwood Building - Room 422
Bethesda, Maryland 20014

Dear Doctor Conner:

We are enclosing a listing of our Committee on Human Studies, with biographical data, as requested in your letter of March 31.

Thank you very much for your consideration of our request for "general" institutional assurance.

Sincerely,

Gould A. Andrews, M.D.
Chairman,
The Medical Division

GAA/pe

Enclosure

1032701

OFFICE MEMORANDUM

Gould Andrews - ORAU

T. A. Lincoln, M.D.

DATE: April 10, 1972

SUBJECT: Institutional Guide To DHEW Policy on Protection of Human Subjects (Dec 1, 1971)

Have you seen this revision on DHEW's Policy on Protection of Human Subjects? I got a copy from Joe Goldstein while attending a meeting of the Internal Emitter Treatment - Working Group. When a revised IND is submitted and accepted, I shall need review by our Human Studies Committee before I can give any more DTPA for employees who have accidental overexposure to P.

Tom

TAL:ph

Encl.

1032702

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

1716

April 25, 1972

Mr. James L. Liverman
Associate Director for
Biomedical and Environmental Sciences
Oak Ridge National Laboratory
Oak Ridge, Tennessee 37830

Dear Mr. Liverman:

We are pleased to inform you that the National Institutes of Health, acting for the entire Department of Health, Education, and Welfare, has reviewed and accepted the general assurance dated March 2, 1972, submitted by the Oak Ridge National Laboratory, as being in essential compliance with the requirements contained in DHEW Grants Administration Manual Chapter 1-40 effective April 15, 1971.

It is necessary that this office be kept informed on a current basis of any changes in policies, procedures, or committee composition relating to this requirement.

We appreciate your cooperation in this matter. We welcome any comments or suggestions you may wish to make with regard to the administration of this policy.

Sincerely yours,

S/

Stephen P. Hatchett, Ph.D.
Director, Division of Research Grants

cc:
Mr. William G. Pollard
Executive Director
Oak Ridge Associated Universities, Inc.
Oak Ridge, Tennessee 37830

Gould A. Andrews, M.D.
Chairman, Medical Division
Oak Ridge Associated Universities, Inc.
Oak Ridge, Tennessee 37830

1032703

GENERAL INSTITUTIONAL ASSURANCE

Statement of Compliance

Oak Ridge Associated Universities and Oak Ridge National Laboratory will comply with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education, and Welfare.

These institutions have jointly established and do maintain a committee competent to review projects and activities that involve human subjects. The committee is assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.
The risks to subjects are outweighed by potential benefits.
The informed consent of subjects will be obtained by methods that are adequate and appropriate.

These institutions will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgement of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interests.

These institutions will encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

These institutions will provide for the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

These institutions will maintain appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

These institutions will periodically reassure themselves through appropriate administrative overview that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with the assurance as accepted by the Department of Health, Education, and Welfare.

1032704

OAK RIDGE ASSOCIATED UNIVERSITIES

Signature William G. Pollard

Title Executive Director

Date February 28, 1972

OAK RIDGE NATIONAL LABORATORY

Signature Orner L. Peterman

Title Associate Director for Biomedical and Environmental Science

Date March 2, 1972

Attachment: Implementing Guidelines

OAK RIDGE NATIONAL LABORATORY
OPERATED BY
UNION CARBIDE CORPORATION
NUCLEAR DIVISION

POST OFFICE BOX X
OAK RIDGE, TENNESSEE 37830

June 2, 1972

Dr. John R. Totter, Director
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington, D. C. 20545

Dear John:

Enclosed is the letter of acceptance of our General Institutional Assurance, Statement of Compliance, by the National Institutes of Health, acting for the Department of Health, Education and Welfare. This Statement is in regard to the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from DHEW.

This is being sent to you in the interest of keeping you informed and up-to-date.

Sincerely yours,

James L. Liverman
ORNL Associate Director for
Biomedical and Environmental
Sciences

JLL:lmm

Enclosures

cc: G. A. Andrews
W. G. Pollard
A. M. Weinberg

1032705

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

July 5, 1972

TO : Officers Responsible for Institutional Implementation of DHEW Policy on Protection of Human Subjects

FROM : Chief, Institutional Relations Branch, Division of Research Grants, NIH, DHEW

SUBJECT: Considerations in the Review of Projects (2)

Human Subject, Definition

In the conversion from the now obsolete Public Health Service policy on the "Protection of the Individual as a Research Subject" to the Department of Health, Education, and Welfare policy on the "Protection of Human Subjects" the definition of "subject" changed from "any human being exposed to any research procedure as a result of the availability of Public Health Service funds. . ."to, ". . .any individual who may be at risk as a consequence of participation as a subject in research, development, demonstration, or other activities supported by DHEW funds."

The DHEW policy further defines the term "at risk" as the exposure of an individual to the possibility of harm--physical, psychological, sociological, or other--as a consequence of any activity which goes beyond the application of those established and accepted methods necessary to meet his needs.

Reasons for making this change in definition of the subject are several. Under the old PHS policy only the National Institutes of Health, the Health Services and Mental Health Administration, the Food and Drug Administration and a few other agencies were initially involved. The traditional "research grant" was the principal mode of support. In broadening the policy to accommodate the several other agencies of the DHEW, including the Office of Education and the Social and Rehabilitation Services, where the "research" grant or contract is not the principal support mechanism, it became necessary to redefine the "subject" to include others whose rights and welfare were also clearly "at risk." An acceptable definition of "research" or the "research subject," to encompass the possibilities for human subject involvement does not appear to be feasible from the experience with the PHS policy.

0032706

It is the intent of this definition of the "subject at risk" to exclude all accepted and established service functions such as the normal relationship of patients to physicians; students to professors; and other clients to professionals in which the patient, student, or client (or his authorized representative) is receiving aid or services intended only to meet his own personal needs. The normal employee--employer relationship in which legitimate services are rendered for salary, wages, or renumeration in keeping with

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

July 5, 1972

TO : Officers Responsible for Institutional Implementation of DHEW Policy on Protection of Human Subjects

FROM : Chief, Institutional Relations Branch, DRG, NIH, DHEW

SUBJECT: Considerations in the Review of Projects (3)

Medicine: Fetal Studies

The attached guidelines have been issued by the Director, NIH. While this constitutes official NIH policy with regard to the review of grants and contracts, and the negotiation of contracts, it does not constitute DHEW policy and is not binding on grantee institutions with respect to projects or activities supported by other components of the DHEW. However, since the guidelines are not inconsistent with overall DHEW policy they are forwarded for your consideration.

"Scientific studies of the human fetus are an integral and necessary part of research concerned with the health of women and children. Because of the unique problems involved and a growing competence and interest in this field, ethically and scientifically acceptable guidelines for the conduct of such investigation must be developed.

1. In all cases, applicable state and/or national laws shall be binding.

2. Guidelines for human investigation used to protect the rights of minors and other helpless subjects are applicable.

3. The study protocol must be reviewed and approved by the appropriate institutional review committee to insure that the rights of the mother and fetus will be fully considered.

   (a) It is the duty of these committees to insure that the investigator shall not be involved in the decision to terminate a pregnancy, the product of which is intended for study within his own research project or authority.

   (b) Continuing review by the institutional committee must be undertaken in approved projects.

4. Informed consent must be obtained from the appropriate party(ies)."

D. T. Chalkley, Ph.D.

1032707

See Headcount –

UNITED STATES
ATOMIC ENERGY COMMISSION
OAK RIDGE OPERATIONS
P.O. BOX E
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8611

OCT 17 1972

Dr. William G. Pollard
Executive Director
Oak Ridge Associated
Universities
Post Office Box 117
Oak Ridge, Tennessee

DATE 10-18-72
COPIES TO Dr Andrews ltr
W Harmon with attach.
WL Rose – Ltr
Howard – file copy and original for transmittal by Sec. 7C.
See P. 18 FF

Dear Dr. Pollard:

RESEARCH INVOLVING USE OF HUMAN SUBJECTS

A letter from Dr. John A. Totter dated May 22, 1970, to Dr. Gould Andrews informed him that the AEC had adopted the policy of the National Institutes of Health with respect to the protection of human subjects used in AEC sponsored research studies, and specified certain administrative procedures to assure that such research is conducted in accordance with the policies outlined in the U. S. Public Health Service booklet entitled "The Institutional Guide to DHEW Policy on Protection of Human Subjects". A copy of this publication is enclosed.

At the time this policy was established, it was requested that all contractors reaffirm their adherence to such policies annually along with their 189's or renewal proposals. This reassurance was omitted from FY 1973 189 submissions from the Medical Division, ORAU.

It will be appreciated if you will forward the enclosed PHS publication to Dr. Gould Andrews along with our request that he reaffirm their adherence to the policies specified. Please send such reassurance to this office at your earliest convenience so that it can be attached to your 189's.

Sincerely,

Joseph A. Lenhard, Director
Research and Technical Support Division

ORR:REB

Enclosure:
PHS Publication

1032708

GENERAL INSTITUTIONAL ASSURANCE

Statement of Compliance

Oak Ridge Associated Universities (ORAU) is in compliance with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education, and Welfare.

ORAU has established and does maintain a committee competent to review projects and activities that involve human subjects. The committee is assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.
The risks to subjects are outweighed by potential benefits.
The informed consent of subjects will be obtained by methods that are adequate and appropriate.

This institution will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgement of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interests.

We encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

The ORAU Research Hospital staff provides facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

The staff also maintains appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

Through appropriate administrative overview ORAU reassures itself that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with the assurance as accepted by the Department of Health, Education, and Welfare.

OAK RIDGE ASSOCIATED UNIVERSITIES

Signature_____
Medical Division Chairman

Signature_____
Executive Director

Date October 25, 1972

1032709

GENERAL INSTITUTIONAL ASSURANCE

Statement of Compliance

Oak Ridge Associated Universities (ORAU) is in compliance with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education, and Welfare.

ORAU has established and does maintain a committee competent to review projects and activities that involve human subjects. The committee is assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.
The risks to subjects are outweighed by potential benefits.
The informed consent of subjects will be obtained by methods that are adequate and appropriate.

This institution will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgement of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interests.

We encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

The ORAU Research Hospital staff provides facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

The staff also maintains appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

Through appropriate administrative overview ORAU reassures itself that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with the assurance as accepted by the Department of Health, Education, and Welfare.

OAK RIDGE ASSOCIATED UNIVERSITIES

Signature _____
Medical Division Chairman

Signature William G. Pollard
Executive Director

Date October 25, 1972

1032710

November 6, 1972

Mr. Joseph A. Lenhard, Director
Research and Technical Support Division
U. S. Atomic Energy Commission
Oak Ridge, Tennessee

Subject: RESEARCH INVOLVING USE OF HUMAN SUBJECTS - YOUR LETTER OF OCTOBER 17, 1972

Dear Mr. Lenhard:

In response to your letter, ORAU's "General Institutional Assurance" has been executed by Dr. Gould Andrews, chairman of our Medical Division, in compliance with the AEC-NIH policy with respect to the protection of human subjects used in AEC sponsored research.

We have established necessary procedures to assure reaffirmation of this policy will be executed annually and will accompany our form 189 budget presentations or renewal proposals. We are enclosing eight copies of the assurance statement dated October 25, 1972. We shall appreciate your attaching copies of the statement to our FY 1973 189 budget submissions.

Sincerely yours,
Original Signed By
PAUL M. ELZA

William G. Pollard
Executive Director

ELZA:nm

Attachments

1032711

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

February 9, 1973

FORTY-SIXTH CUMULATIVE LIST OF INSTITUTIONS IN COMPLIANCE WITH DHEW POLICY ON THE PROTECTION OF HUMAN SUBJECTS

1. UNSOLICITED PROPOSALS - GRANTS

   a. If professional review of the proposal indicates that it involves human subjects at risk in research, development, demonstration or other activities, as defined in DHEW Grants Administration Manual 1-40, check the institution name against the list. If the institution is on the list, check the signature page of the proposal for certification of the date on which the institution's committee on protection of human subjects has completed, or will complete, its review. Then:

   b. If the institution is not on the list, and an award is to be made, a copy of the application should be forwarded to the Institutional Relations Branch, DRG, NIH, Westwood Building, Room 422 for prior negotiation of an institutional assurance and certification of review. Or:

   c. If the institution is on the list, but has not certified its review and approval, this should be requested by the agency intending to make the award, using form HEW 596 or equivalent (See back page of the list. Copies of this form are available from IRB, DRG, NIH). No award should be made prior to receipt of a properly dated certification except as provided for by grants Administration Manual Section 1-40-50 C.2.

   d. If the institution is on the list and has certified its review and approval prior to the proposed starting date of the project, and award can be made as provided for by Grants Administration Manual Section 1-40-50 C.1.

2. AWARD OF A DHEW GRANT OR CONTRACT IN SUPPORT OF A PROJECT INVOLVING HUMAN SUBJECTS TO A NON-ASSURED INSTITUTION, OR TO AN ASSURED INSTITUTION WHICH HAS NOT PROPERLY CERTIFIED ITS REVIEW AND APPROVAL OF THE PROJECT, INDICATES THE OPERATING AGENCY'S DETERMINATION THAT THESE SUBJECTS ARE NOT AT RISK.

1032712

3. CONTRACTS

If an operating agency determines that contract performance will involve risk to human subjects, the request for proposal must include the "Notice to Offerors" required by 41 CFR 3-4.5504(a).

When a sole source has been identified, or selection of a successful bidder is substantially complete, instructions for completion of the contract proposal should embody the certification requirements in 41 CFR 3-4.5504(b). Acceptance of the certification should be governed by the provision of paragraphs 1., b., c., d. above.

4. RESTRICTION CODES preceding institution names indicate the status of the institution's assurance in terms of the new DHEW policy on protection of human subjects:

ABSENCE OF A RESTRICTION CODE indicates that the institution has filed an assurance reflecting committee competence to deal with all probable applications to DHEW, and that negotiation of this assurance is complete.

CODE (2) indicates that the committee has professional competence to review all probable proposals to DHEW except those involving medicine, surgery, or investigational new drug studies.

CODE (3) indicates a medically oriented institution that has yet to insure adequate lay representation on its committee as required by FDA regulations. This code is of concern only to the FDA, and to institutions that must comply with its regulations.

CODE (4) indicates an institution with medical competence, but not in the field of surgery. Most of these institutions are concerned with studies in the field of psychiatry or with the delivery of related services.

CODES (5), and (6) are unassigned.

CODE (7) indicates that the committee has professional competence to review all probable proposals to DHEW except those involving surgery or investigational new drug studies.

CODE (8) indicates that the institution has filed an assurance of compliance with DHEW policy, but that negotiation is not complete and the assurance subject to disapproval.

CODE (9) usually indicates that the institution's assurance does not cover all of it's components, or that type (2), (3), or (4) restrictions apply to one or more components. Please call the Human Subjects Protection Desk (301) 496-7005 for an explanation.

D. T. Chalkley, Ph.D.
Chief, Institutional Relations Branch
Division of Research Grants

1032713

0533	CRAFTS-FARROW STATE HOSPITAL	COLUMBIA
0533	FRIENDSHIP CENTER	COLUMBIA
0533	GEORGETOWN-HORRY MENTAL HEALTH CLINIC	CONWAY
0533	GREENVILLE AREA MENTAL HEALTH CENTER	GREENVILLE
0533	ORANGEBURG AREA MENTAL HEALTH CLINIC	ORANGEBURG
0533	PEE-DEE MENTAL HEALTH CENTER	FLORENCE
0533	SOUTH CAROLINA DEPARTMENT OF MENTAL HEALTH	COLUMBIA
0533	DIV OF ALCOHOL AND DRUG ADDICTION SERVICES	COLUMBIA
0533	DIV OF COMMUNITY MTl HLTH SERVICES SPEC PROJ	COLUMBIA
0533	LONG TERM CARE SERVICES	COLUMBIA
0240	SOUTH CAROLINA, MEDICAL UNIVERSITY OF	CHARLESTON
0533	SOUTH CAROLINA STATE HOSPITAL	COLUMBIA
0533	SOUTH CAROLINA WAR VETERANS HOME	COLUMBIA
0533	SPARTANBURG AREA MENTAL HEALTH CENTER	SPARTANBURG
0533	SUMTER-CLARENDON-KERSHAW MENTAL HEALTH CENTER	SUMTER
0533	TRI-COUNTY MENTAL HEALTH CENTER	BENNETTSVILLE
0533	WILLIAM S HALL PSYCHIATRIC INSTITUTE	COLUMBIA
0533	YORK-CHESTER-LANCASTER MENTAL HEALTH CENTER	ROCK HILL

TENNESSEE

1696	(4)ARLINGTON HOSPITAL AND SCHOOL	ARLINGTON
0490	(8)GEORGE PEABODY COLLEGE FOR TEACHERS	NASHVILLE
0393	MEHARRY MEDICAL COLLEGE	NASHVILLE
1716	OAK RIDGE ASSOCIATED UNIVERSITIES, INC.	OAK RIDGE
1716	OAK RIDGE NATIONAL LABORATORY	OAK RIDGE
0648	ST JUDE CHILDRENS RESEARCH HOSPITAL	MEMPHIS
0170	TENNESSEE, UNIV OF, MEDICAL UNITS	MEMPHIS
0124	TENNESSEE, UNIVERSITY OF - KNOXVILLE	KNOXVILLE
0401	VANDERBILT UNIVERSITY	NASHVILLE
1800	VETERANS ADMINISTRATION HOSPITAL-MEMPHIS	MEMPHIS

TEXAS

0912	(8)ABILENE STATE SCHOOL	ABILENE
0912	(8)AMARILLO STATE CENTER FOR HUMAN DEVELOPMENT	AMARILLO
0912	(8)AUSTIN STATE HOSPITAL	AUSTIN
0912	(8)AUSTIN STATE SCHOOL	AUSTIN
0307	BAYLOR COLLEGE OF MEDICINE	HOUSTON

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0813	(8)BAYLOR UNIVERSITY	WACO
0912	(8)BEAUMONT STATE CENTER FOR HUMAN DEVELOPMENT	BEAUMONT
0912	(8)BIG SPRING STATE HOSPITAL	BIG SPRING
0912	(8)CORPUS CHRISTI STATE SCHOOL	CORPUS CHRISTI
0912	(8)DALLAS STATE ADULT MENTAL HEALTH CLINIC	DALLAS
0912	(8)DENTON STATE SCHOOL	DENTON
0912	(8)FORT WORTH STATE ADULT MENTAL HEALTH CLINIC	FORT WORTH
0912	(8)HARLINGEN STATE ADULT MENTAL HEALTH CLINIC	HARLINGEN
0419	(8)J K & SUSIE L WADLEY RES INST AND BLOOD BANK	DALLAS
0912	(8)KERRVILLE STATE HOSPITAL	KERRVILLE
0912	(8)LUBBOCK STATE SCHOOL	LUBBOCK
0912	(8)LUFKIN STATE SCHOOL	LUFKIN
0912	(8)MEXIA STATE SCHOOL	MEXIA
0912	(8)RICHMOND STATE SCHOOL	RICHMOND
0912	(8)RUSK STATE HOSPITAL	RUSK
0912	(8)SAN ANTONIO STATE ADULT MENTAL HLTH CLINIC	SAN ANTONIO
0912	(8)SAN ANTONIO STATE HOSPITAL	SAN ANTONIO
2344	(2)SOUTHWEST EDUCATIONAL DEVELOPMENT CORPORATION	AUSTIN
2344	(2)SOUTHWEST EDUCATIONAL DEVELOPMENT LABORATORY	AUSTIN
1631	(8)SOUTHWEST RESEARCH INSTITUTE	SAN ANTONIO
0912	(8)TERRELL STATE HOSPITAL	TERRELL
1045	(2)TEXAS A & M UNIV, COLLEGE STATION CAMPUS ONLY	COLLEGE STATION
0912	(8)TEXAS DEPT OF MENTAL HLTH AND MENTAL RETARD	AUSTIN
0590	TEXAS INSTITUTE FOR REHAB AND RESEARCH	HOUSTON
0912	(8)TEXAS RESEARCH INST FOR MENTAL SCIENCES	HOUSTON
1211	(8)TEXAS, UNIV OF, AT ARLINGTON	ARLINGTON
0669	(8)TEXAS, UNIV OF, DENTAL BRANCH	HOUSTON
0113	TEXAS, UNIV OF, M D ANDERSON HOSP AND TUMOR INS	HOUSTON
0123	(8)TEXAS, UNIV OF, MAIN UNIVERSITY	AUSTIN
0107	(8)TEXAS, UNIV OF, MEDICAL BRANCH	GALVESTON
0040	(8)TEXAS, UNIV OF, MEDICAL SCHOOL	SAN ANTONIO
0552	(8)TEXAS, UNIV OF, SOUTHWESTERN MED SCH	DALLAS
0912	(8)TRAVIS STATE SCHOOL	AUSTIN
0912	(8)WICHITA FALLS STATE HOSPITAL	VERNON
0912	(8)WICHITA FALLS STATE HOSPITAL	WICHITA FALLS

UTAH

0933	(8)BRIGHAM YOUNG UNIVERSITY	PROVO
2426	DESERET FOUNDATION FOR MED EDU AND RES	SALT LAKE CITY
0235	UTAH, UNIVERSITY OF	SALT LAKE CITY

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

See page 18

September 6, 1973

FORTY-EIGHTH CUMULATIVE LIST OF INSTITUTIONS IN COMPLIANCE WITH DHEW POLICY ON PROTECTION OF HUMAN SUBJECTS

NOTE: Award of a DHEW grant or contract in support of a project involving human subjects to a non-assured institution, or to an assured institution which has not properly certified its review and approval of the project, indicates the operating agency's determination that these subjects are not at risk.

1. UNSOLICITED PROPOSALS - GRANTS

a. If professional review of the proposal indicates that it involves human subjects at risk in research, development demonstration or other activities, as defined in DHEW Grants Administration Manual Chapter 1-40, check the institution's name against the list. If the institution is on the list, check the signature page of the proposal for certification of the date on which the institution's committee on protection of human subjects has completed, or will complete, its review.

b. If the institution is on the list and has certified its review and approval prior to the proposed starting date of the project, an award can be made as provided for by Grants Administration Manual Section 1-40-50, C.1.

c. If the institution is on the list, but has not certified its review and approval, this should be requested from the institution by the agency intending to make the award, using for HEW 596 or equivalent (See back page of the list. Copies of this form are available from IRB, DRG, NIH.) No award should be made prior to receipt of a properly dated certification except as provided for by Grants Administration Manual Section 1-40-50, C.2.

1032716

d. If the institution is not on the list, and an award is to be made, a copy of the application and summary sheet should be forwarded to the Institutional Relations Branch, DRG, NIH, Westwood Building, Room 303, for prior negotiation of an institutional assurance and certification of review. Occasionally institutions not on the list will certify their review of projects involving human subjects. This should be ignored, and the proposal forwarded to Institutional Relations Branch (IRB) for assurance negotiation.

3. CONTRACTS

If an operating agency determines that contract performance will involve risk to human subjects, the request for proposal must include the "Notice to Offerors" required by 41 CFR 3-4.5504(a).

When a sole source has been identified, or selection of a successful bidder is substantially complete, instructions for completion of the contract proposal should embody the certification requirements in 41 CFR 3-4.5504(b). Acceptance of the certification should be governed by the provision of paragraphs 1., b., c., d. above.

4. RESTRICTION CODES preceding institution names indicate the status of the institution's assurance in terms of the DHEW policy on protection of human subjects:

ABSENCE OF A RESTRICTION CODE indicates that the institution has filed an assurance reflecting committee competence to deal with all probable applications to DHEW.

CODE (2) indicates that the committee has professional competence to review all probable proposals to DHEW except those involving medical, surgical, or investigational new drug studies.

CODE (3) indicates a medically oriented institution that has yet to insure adequate lay representation on its committee as required by FDA reguations. This code is of concern only to the FDA, and to institutions that must comply with its regulations.

CODE (4) indicates an institution with medical competence, but not in the field of surgery. Most of these institutions are concerned with studies in the field of psychiatry or with the delivery of related services.

CODES (5), and (6) are unassigned.

CODE (7) indicates that the committee has professional competence to review all probable proposals to DHEW except those involving surgical or investigational new drug studies.

CODE (8) indicates that the institution has filed an assurance which has not been accepted as fully complying with DHEW policy. Please call the Human Subjects Protection Desk (301) 496-7005 for an explanation.

CODE (9) usually indicates that the institution's assurance does not cover all of it's components, or that type (2), (3), or (4) restrictions apply to one or more components. Please call the Human Subjects Protection Desk (301) 496-7005 for an explanation.

D. T. Chalkley, Ph.D.
Chief, Institutional Relations Branch
Division of Research Grants

1032718

	ALABAMA	
2104	ALABAMA DEPT OF MENTAL HEALTH	MONTGOMERY
2104	ALABAMA DEPT OF MENTAL HEALTH, DIV OF COM SVS	MONTGOMERY
0198	ALABAMA, UNIVERSITY OF, BIRMINGHAM	BIRMINGHAM
0610	ALABAMA, UNIVERSITY OF, TUSCALOOSA	UNIVERSITY
2104	ALBERT P BREWER MENTAL RETARDATION CENTER	MOBILE
2104	BRYCE HOSPITAL	TUSCALOOSA
2104	LURLEEN B. WALLACE MENTAL RETARDATION CENTER	DECATUR
2104	PARTLOW STATE SCHOOL AND HOSPITAL	TUSCALOOSA
2104	SEARCY HOSPITAL	MOUNT VERNON
0055	TUSKEGEE INSTITUTE	TUSKEGEE INST
	ARIZONA	
0799	(2)ARIZONA STATE UNIVERSITY	TEMPE
0504	(4)ARIZONA TRAINING PROGRAM AT COOLIDGE	COOLIDGE
0026	ARIZONA, UNIVERSITY OF	TUCSON
1287	ST JOSEPHS HOSPITAL AND MEDICAL CENTER	PHOENIX
1632	(8)VETERANS ADMINISTRATION HOSPITAL-TUCSON	TUCSON
	ARKANSAS	
0336	ARKANSAS, UNIVERSITY OF, MEDICAL CENTER	LITTLE ROCK
	CALIFORNIA	
0784	(2)AMERICAN INSTITUTES FOR RESEARCH	PALO ALTO
0261	(4)CALIFORNIA DEPT OF PUBLIC HEALTH	BERKELEY
0330	(2)CALIFORNIA DEPT OF YOUTH AUTHORITY	SACRAMENTO
0144	(2)CALIFORNIA INSTITUTE OF TECHNOLOGY	PASADENA
0420	(2)CALIFORNIA STATE UNIV, SAN DIEGO	SAN DIEGO
0278	CALIFORNIA, UNIV OF, BERKELEY	BERKELEY
0195	(4)CALIFORNIA, UNIV OF, DAVIS	DAVIS
0380	CALIFORNIA, UNIV OF, IRVINE	IRVINE
0238	CALIFORNIA, UNIV OF, LOS ANGELES	LOS ANGELES
0193	(4)CALIFORNIA, UNIV OF, RIVERSIDE	RIVERSIDE
0389	CALIFORNIA, UNIV OF, SAN DIEGO	LA JOLLA

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032719

0155		CALIFORNIA, UNIV OF, SAN FRANCISCO	SAN FRANCISCO
0282	(4)	CALIFORNIA, UNIV OF, SANTA BARBARA	SANTA BARBARA
0205	(4)	CALIFORNIA, UNIV OF, SANTA CRUZ	SANTA CRUZ
0028		CAMARILLO STATE HOSPITAL	CAMARILLO
0234		CEDARS SINAI MEDICAL CENTER	LOS ANGELES
0135		CHILDRENS HOSPITAL OF LOS ANGELES	LOS ANGELES
0287		CHILDRENS HOSPITAL OF SAN FRANCISCO	SAN FRANCISCO
0009		CITY OF HOPE NATIONAL MEDICAL CENTER	DUARTE
2259	(2)	FAR WEST LABORATORY FOR EDUCATIONAL RESEARCH AND DEVELOPMENT	BERKELEY
1838		HUNTINGTON INSTITUTE OF APPLIED MEDICAL RES	PASADENA
1838		HUNTINGTON MEMORIAL HOSPITAL	PASADENA
2400		INSTITUTE OF MEDICAL SCIENCES	SAN FRANCISCO
0214		KAISER FOUNDATION RESEARCH INSTITUTE, INCLUDING ITS REGIONAL DIVISIONS IN NORTHERN CALIF, SOUTHERN CALIF, AND OREGON	OAKLAND
0226		LOMA LINDA UNIVERSITY	LA SIERRA
0226		LOMA LINDA UNIVERSITY	LOMA LINDA
0359		L A CO HARBOR GEN HOSP, ATTENDING STAFF ASSN OF	TORRANCE
0213		LOS ANGELES COUNTY-UNIV OF SOUTHERN CALIFORNIA MEDICAL CENTER, PROFESSIONAL STAFF ASSN OF	LOS ANGELES
1288	(8)	MEMORIAL HOSPITAL OF LONG BEACH	LONG BEACH
0367	(2)	MENTAL RESEARCH INSTITUTE	PALO ALTO
0145		MOUNT ZION HOSPITAL AND MEDICAL CENTER	SAN FRANCISCO
0710		PACIFIC STATE HOSPITAL	POMONA
2400		PACIFIC, UNIVERSITY OF THE, SCHOOL OF DENTISTRY	SAN FRANCISCO
0082		PALO ALTO MEDICAL RESEARCH FOUNDATION	PALO ALTO
1838		PASADENA HOSPITAL ASSOCIATION, LTD	PASADENA
2400		PRESBYTERIAN HOSPITAL	SAN FRANCISCO
0067		RANCHOS LOS AMIGOS HOSPITAL AND ITS ATTENDING STAFF ASSOCIATION	DOWNEY
1416	(3)	RAND CORPORATION	SANTA MONICA
1096		SALK INSTITUTE	SAN DIEGO
1175	(3)	SAN DIEGO BIO-MEDICAL RESEARCH INSTITUTE	SAN DIEGO
0420	(2)	SAN DIEGO STATE UNIVERSITY FOUNDATION	SAN DIEGO
0729	(8)	SAN FRANCISCO STATE COLLEGE	SAN FRANCISCO
0729	(8)	SAN FRANCISCO STATE COLLEGE, FREDERIC BURK FOUNDATION FOR EDUCATION	SAN FRANCISCO
0108		SCRIPPS CLINIC AND RESEARCH FOUNDATION	LA JOLLA
0201		SONOMA STATE HOSPITAL	ELDRIDGE
0122		SOUTHERN CALIFORNIA, UNIVERSITY OF	LOS ANGELES
0378	(2)	STANFORD RESEARCH INSTITUTE	MENLO PARK
0011		STANFORD UNIVERSITY	STANFORD

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032720

1796		VETERANS ADMINISTRATION HOSPITAL-SEPULVEDA	SEPULVEDA
1658		VETERANS ADMINISTRATION HOSPITAL-WADSWORTH	LOS ANGELES
1591	(2)	WRIGHT INSTITUTE	BERKELEY

COLORADO

0267		CHILDRENS ASTHMA RESEARCH INSTITUTE AND HOSP	DENVER
0845		CHILDRENS HOSPITAL	DENVER
1144	(4)	COLORADO STATE UNIVERSITY	FORT COLLINS
0455		COLORADO, UNIVERSITY OF	BOULDER
0268		COLORADO, UNIVERSITY OF, MEDICAL CENTER	DENVER
1350	(8)	DENVER DEPARTMENT OF HEALTH AND HOSPITALS	DENVER
1350	(8)	DENVER GENERAL HOSPITAL	DENVER
1350	(8)	DENVER HEALTH RESEARCH FOUNDATION, INC	DENVER
0277	(2)	DENVER, UNIVERSITY OF	DENVER
0068	(4)	NATIONAL JEWISH HOSPITAL	DENVER

CONNECTICUT

0039		CONNECTICUT, UNIVERSITY OF	STORRS
1966		CONNECTICUT, UNIVERSITY OF, HEALTH CENTER	HARTFORD
1533		CONNECTICUT VALLEY HOSPITAL	MIDDLETOWN
0007		INSTITUTE OF LIVING	HARTFORD
0003		JOHN B PIERCE FOUNDATION OF CONNECTICUT	NEW HAVEN
0243		YALE UNIVERSITY	NEW HAVEN

DELAWARE

0148		ALCOHOLISM DETOXIFICATION AND TREATMENT CENTER	WILMINGTON
0148		DELAWARE DIVISION OF MENTAL HEALTH	NEW CASTLE
0148		DELAWARE STATE HOSPITAL	NEW CASTLE
0013		DELAWARE, UNIVERSITY OF	NEWARK
0148		FERNHOOK MENTAL HYGIENE CLINIC	NEW CASTLE
0148		GOVERNOR BACON HEALTH CENTER	DELAWARE CITY
0148		INNER-CITY MENTAL HYGIENE CLINIC	WILMINGTON
0148		KENT COUNTY MENTAL HYGIENE CLINIC	DOVER
0148		NEWARK MENTAL HYGIENE CLINIC	NEWARK

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0148	SOUTHERN NEW CASTLE COUNTY COMMUNITY M H CTR	NEW CASTLE
0148	SUSSEX COUNTY COMMUNITY MENTAL HEALTH CENTER	LEWES
0148	SUSSEX COUNTY MENTAL HYGIENE CLINIC	GEORGETOWN
0148	TERRY CHILDRENS PSYCHIATRIC CENTER	NEW CASTLE
0148	WILMINGTON MENTAL HYGIENE CLINIC	WILMINGTON

DISTRICT OF COLUMBIA

0784	(2) AMERICAN INSTITUTES FOR RESEARCH	WASHINGTON
1674	(2) BUREAU OF SOCIAL SCIENCE RESEARCH	WASHINGTON
0365	(2) CATHOLIC UNIVERSITY OF AMERICA	WASHINGTON
0042	CHILDRENS HOSPITAL OF THE DISTRICT OF COLUMBIA AND ITS RESEARCH FOUNDATION	WASHINGTON
2058	(2) FEDERAL CITY COLLEGE	WASHINGTON
1249	(2) GALLAUDET COLLEGE	WASHINGTON
0294	(2) GEORGE WASHINGTON UNIV. EXCEPT SCHOOL OF MEDICINE	WASHINGTON
0294	GEORGE WASHINGTON UNIV, SCHOOL OF MEDICINE	WASHINGTON
0228	GEORGETOWN UNIVERSITY	WASHINGTON
0178	GORGAS MEMORIAL INSTITUTE	WASHINGTON
0841	HOWARD UNIVERSITY	WASHINGTON
2063	(2) INSTITUTE FOR SERVICES TO EDUCATION	WASHINGTON
1989	NATIONAL ACADEMY OF SCIENCES INCLUDING NATIONAL ACADEMY OF ENGINEERING, INSTITUTE OF MEDICINE AND NATIONAL RESEARCH COUNCIL	WASHINGTON
1036	(2) NATIONAL CHILDRENS CENTER, INC.	WASHINGTON
0180	WASHINGTON HOSPITAL CENTER	WASHINGTON

FLORIDA

2093	(2) FLORIDA ATLANTIC UNIVERSITY	BOCA RATON
0260	FLORIDA STATE DIV OF HEALTH, ALL COMPONENTS	JACKSONVILLE
0119	(2) FLORIDA STATE UNIVERSITY	TALLAHASSEE
0382	FLORIDA, UNIVERSITY OF	GAINESVILLE
0840	MIAMI HEART INSTITUTE	MIAMI BEACH
0301	MIAMI, UNIVERSITY OF	CORAL GABLES
0301	MIAMI, UNIVERSITY OF	MIAMI
2321	PAPANICOLAOU CANCER RESEARCH INSTITUTE	MIAMI
1065	SOUTH FLORIDA, UNIVERSITY OF	ST PETERSBURG
1065	SOUTH FLORIDA, UNIVERSITY OF	TAMPA

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

GEORGIA

0197	(4) BATTEY STATE HOSPITAL	ROME
0197	(4) CENTRAL STATE HOSPITAL	MILLEDGEVILLE
0138	EMORY UNIVERSITY DIV OF BASIC HEALTH SCIENCES	ATLANTA
0622	EMORY UNIVERSITY GRAD SCH OF ARTS AND SCIENCES	ATLANTA
0138	EMORY UNIVERSITY NELL HODGSON WOODRUFF SCHOOL OF NURSING	ATLANTA
0595	EMORY UNIVERSITY SCHOOL OF DENTISTRY	ATLANTA
0138	EMORY UNIVERSITY SCHOOL OF MEDICINE	ATLANTA
0197	(4) GEORGIA DEPT OF HUMAN RESOURCES DIVISIONS OF PHYSICAL HEALTH AND MENTAL HEALTH	ATLANTA
0520	(3) GEORGIA INSTITUTE OF TECHNOLOGY	ATLANTA
0151	GEORGIA, MEDICAL COLLEGE OF	AUGUSTA
0197	(4) GEORGIA MENTAL HEALTH INSTITUTE	ATLANTA
0197	(4) GEORGIA REGIONAL HOSPITAL AT ATLANTA	ATLANTA
0197	(4) GEORGIA REGIONAL HOSPITAL AT AUGUSTA	AUGUSTA
0197	(4) GEORGIA REGIONAL HOSPITAL AT SAVANNAH	SAVANNAH
0197	(4) GEORGIA RETARDATION CENTER	CHAMBLEE
0248	(2) GEORGIA, UNIVERSITY OF	ATHENS
0197	(4) GRACEWOOD STATE SCHOOL AND HOSPITAL	GRACEWOOD
1467	GRADY MEMORIAL HOSPITAL	ATLANTA
0197	(4) NORTHWEST REGIONAL HOSPITAL	ROME
0197	(4) SOUTHWESTERN STATE HOSPITAL	THOMASVILLE
0197	(4) WEST CENTRAL REGIONAL HOSPITAL	COLUMBUS

HAWAII

0104	(4) HAWAII, UNIVERSITY OF	HONOLULU

ILLINOIS

1223	(2) ADOLF MEYER CENTER	DECATUR
0395	AMERICAN DENTAL ASSOCIATION	CHICAGO
0332	(7) ANNA STATE HOSPITAL	ANNA
1626	CHICAGO, UNIV OF, DIV OF BIOLOGICAL SCIENCES AND PRITZKER SCHOOL OF MEDICINE	CHICAGO

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1626	(2) CHICAGO, UNIV OF, DIV OF SOCIAL SCIENCES, CTR FOR HLTH ADM STUDIES, GRAD SCHOOL OF EDU	CHICAGO
1626	(2) CHICAGO, UNIV OF, SCHOOL OF SOCIAL SERVICE ADM	CHICAGO
0182	EVANSTON HOSPITAL	EVANSTON
0430	HEALTH SCIENCES, UNIV OF/CHICAGO MEDICAL SCHOOL	CHICAGO
0053	HEKTOEN INSTITUTE FOR MEDICAL RESEARCH	CHICAGO
1561	(4) ILLINOIS STATE PSYCHIATRIC INSTITUTE	CHICAGO
0345	ILLINOIS, UNIV OF, AT CHICAGO CIRCLE	CHICAGO
0291	ILLINOIS, UNIV OF, MEDICAL CENTER CAMPUS INCLUDING THE CLINICAL SCHOOLS AT PEORIA AND ROCKFORD	CHICAGO
0102	ILLINOIS, UNIV OF, URBANA-CHAMPAIGN CAMPUS	URBANA
1373	(2) LINCOLN STATE SCHOOL	LINCOLN
0095	MICHAEL REESE HOSPITAL AND MEDICAL CENTER	CHICAGO
0430	MOUNT SINAI HOSPITAL MEDICAL CENTER	CHICAGO
0518	(2) NORTHERN ILLINOIS UNIVERSITY	DEKALB
0190	NORTHWESTERN UNIVERSITY	CHICAGO
0190	NORTHWESTERN UNIVERSITY	EVANSTON
1518	PEORIA STATE HOSPITAL	PEORIA
0175	RUSH-PRESBYTERIAN-ST LUKES MEDICAL CENTER	CHICAGO
0309	SOUTHERN ILLINOIS UNIVERSITY	CARBONDALE
1970	(4) WESTERN ILLINOIS UNIVERSITY	MACOMB

	INDIANA	
0314	(2) DEPAUW UNIVERSITY	GREENCASTLE
0945	(7) FORT WAYNE STATE HOSPITAL AND TRAINING CTR	FT WAYNE
0185	INDIANA UNIVERSITY AND INDIANA UNIV FDN	BLOOMINGTON
0185	INDIANA UNIVERSITY AND INDIANA UNIV FDN	INDIANAPOLIS
0185	INDIANA UNIVERSITY-PURDUE UNIVERSITY	INDIANAPOLIS
0185	INDIANA UNIVERSITY REGIONAL CAMPUSES AT FORT WAYNE, GARY, JEFFERSONVILLE, KOKOMO, RICHMOND, AND SOUTH BEND	
1397	INDIANAPOLIS CENTER FOR ADVANCED RESEARCH	INDIANAPOLIS
0883	LARUE D CARTER MEMORIAL HOSPITAL	INDIANAPOLIS
1697	MARION COUNTY ASSN FOR RETARDED CHILDREN, INC	INDIANAPOLIS
1246	METHODIST HOSPITAL OF INDIANA, INC	INDIANAPOLIS
1176	NEW CASTLE STATE HOSPITAL	NEW CASTLE
1119	(7) NOTRE DAME, UNIVERSITY OF	NOTRE DAME
0131	(4) PURDUE UNIVERSITY AND PURDUE RESEARCH FDN	LAFAYETTE

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

	IOWA	
0343	(2) IOWA STATE UNIVERSITY OF SCIENCE AND TECHNOLOGY	AMES
0209	IOWA, UNIVERSITY OF	IOWA CITY
0856	(3) WOODWARD STATE HOSPITAL-SCHOOL	WOODWARD
	KANSAS	
0038	(4) KANSAS STATE UNIVERSITY	MANHATTAN
0157	(4) KANSAS, UNIVERSITY OF	LAWRENCE
0229	KANSAS, UNIVERSITY OF, MEDICAL CENTER	KANSAS CITY
0081	(4) MENNINGER FOUNDATION	TOPEKA
	KENTUCKY	
0223	KENTUCKY, UNIVERSITY OF	LEXINGTON
0223	KENTUCKY, UNIVERSITY OF, RESEARCH FOUNDATION	LEXINGTON
0527	(4) LOUISVILLE, UNIVERSITY OF, EXCEPT SCH OF MED	LOUISVILLE
0527	LOUISVILLE, UNIVERSITY OF, FOUNDATION	LOUISVILLE
0023	LOUISVILLE, UNIVERSITY OF, SCHOOL OF MEDICINE	LOUISVILLE
	LOUISIANA	
0442	(8) ALTON OCHSNER MEDICAL FOUNDATION	NEW ORLEANS
0262	(9) LOUISIANA STATE UNIV AND A & M COLL SYS	BATON ROUGE
0262	(8) LOUISIANA STATE UNIV AND A & M COLL SYS	NEW ORLEANS
2428	(2) LOUISIANA STATE UNIV IN BATON ROUGE	BATON ROUGE
2420	(4) LOUISIANA STATE UNIV IN NEW ORLEANS	NEW ORLEANS
0137	(3) PINECREST STATE SCHOOL	PINEVILLE
0018	TULANE MEDICAL CENTER	NEW ORLEANS
2386	(2) TULANE UNIVERSITY EXCEPT MEDICAL CENTER	NEW ORLEANS

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

MAINE

0513	MAINE MEDICAL CENTER	PORTLAND

MARYLAND

0784	(2) AMERICAN INSTITUTES FOR RESEARCH	SILVER SPRING
0402	BALTIMORE CITY HOSPITALS	BALTIMORE
0895	(4) COLUMBIA UNION COLLEGE, DEPT OF NURSING	TAKOMA PARK
1247	EYE RESEARCH FOUNDATION OF BETHESDA	BETHESDA
0186	(4) FRIENDS MEDICAL SCIENCE RESEARCH CENTER, INC	BALTIMORE
2245	HUNTINGDON RESEARCH CENTER	BALTIMORE
0640	(4) INSTITUTE FOR BEHAVIORAL RESEARCH, INC	SILVER SPRING
0174	JOHNS HOPKINS HOSPITAL	BALTIMORE
0274	JOHNS HOPKINS UNIV SCH OF HYGIENE AND PUB HLTH	BALTIMORE
0174	JOHNS HOPKINS UNIV SCHOOL OF MEDICINE	BALTIMORE
0326	MARYLAND, UNIVERSITY OF, BALTIMORE CAMPUS	BALTIMORE
0296	MARYLAND, UNIVERSITY OF, COLLEGE PARK CAMPUS	COLLEGE PARK
0400	SINAI HOSPITAL OF BALTIMORE, INC	BALTIMORE

MASSACHUSETTS

0286	BETH ISRAEL HOSPITAL OF BOSTON	BOSTON
0554	BOSTON CITY HOSPITAL	BOSTON
0554	BOSTON DEPARTMENT OF HEALTH AND HOSPITALS	BOSTON
0554	BOSTON DEPARTMENT OF COMMUNITY HEALTH	BOSTON
0488	BOSTON HOSPITAL FOR WOMEN	BOSTON
0783	BOSTON STATE HOSPITAL	BOSTON
0322	(2) BOSTON UNIVERSITY, CHARLES RIVER CAMPUS	BOSTON
0550	BOSTON UNIVERSITY MEDICAL CENTER	BOSTON
0550	BOSTON UNIVERSITY, SCHOOL OF GRADUATE DENTISTRY	BOSTON
0550	BOSTON UNIVERSITY, SCHOOL OF MEDICINE	BOSTON
0132	(2) BRANDEIS UNIVERSITY	WALTHAM
2396	(4) CENTER FOR BLOOD RESEARCH	BOSTON
0771	CHILDRENS CANCER RESEARCH FOUNDATION	BOSTON
0406	CHILDRENS HOSPITAL MEDICAL CENTER	BOSTON
0117	(3) CLARK UNIVERSITY	WORCESTER
0098	DANVERS STATE HOSPITAL	HATHORNE
0412	FORSYTH DENTAL CENTER	BOSTON
2042	EUNICE KENNEDY SHRIVER CENTER	WALTHAM

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032726

2238	(3) HARVARD UNIV, FACULTY OF ARTS AND SCIENCES	CAMBRIDGE
2494	(2) HARVARD UNIV, FACULTY OF GRAD SCH OF EDUCATION	CAMBRIDGE
2398	HARVARD UNIV SCHOOL OF PUBLIC HEALTH	BOSTON
0791	JOSLIN DIABETES FOUNDATION, INC.	BOSTON
0087	LAHEY CLINIC FOUNDATION	BOSTON
0449	LEMUEL SHATTUCK HOSPITAL	JAMAICA PLAIN
0554	LONG ISLAND CHRONIC DISEASE HOSPITAL	BOSTON HARBOR
2304	(9) MASSACHUSETTS DEVELOPMENTAL DISABILITIES CNCL	BOSTON
0097	(4) MASSACHUSETTS INSTITUTE OF TECHNOLOGY	CAMBRIDGE
0597	MASSACHUSETTS MENTAL HEALTH CENTER	BOSTON
0597	MASSACHUSETTS MENTAL HEALTH RESEARCH CORP	BOSTON
0147	(2) MASSACHUSETTS, UNIVERSITY OF-AMHERST	AMHERST
0554	MATTAPAN CHRONIC DISEASE HOSPITAL	MATTAPAN
0576	MC LEAN HOSPITAL	BELMONT
0494	NEW ENGLAND DEACONESS HOSPITAL	BOSTON
0133	NEW ENGLAND MEDICAL CENTER HOSPITALS	BOSTON
0297	NORTHEASTERN UNIVERSITY	BOSTON
0429	PETER BENT BRIGHAM HOSPITAL	BOSTON
0410	RETINA FOUNDATION	BOSTON
0404	ROBERT B BRIGHAM HOSPITAL	BOSTON
0854	ST ELIZABETHS HOSPITAL	BOSTON
0351	ST MARGARETS HOSPITAL	BOSTON
0554	TRUSTEES OF HEALTH & HOSPITALS, CITY OF BOSTON	BOSTON
2107	TUFTS-NEW ENGLAND MEDICAL CENTER	BOSTON
2379	TUFTS UNIVERSITY-BOSTON	BOSTON
0266	(2) TUFTS UNIVERSITY-MEDFORD	MEDFORD
0550	UNIVERSITY HOSPITAL, INC	BOSTON
2042	WALTER E FERNALD STATE SCHOOL	WAVERLEY
0085	WORCESTER FOUNDATION FOR EXP BIOLOGY	SHREWSBURY
1284	(4) WORCESTER STATE HOSPITAL	WORCESTER

MICHIGAN

0363	CHILD RESEARCH CENTER OF MICHIGAN	DETROIT
0363	CHILDRENS HOSPITAL OF MICHIGAN	DETROIT
0497	DETROIT, UNIVERSITY OF	DETROIT
0357	EDSEL B FORD INSTITUTE	DETROIT
0357	HENRY FORD HOSPITAL	DETROIT
0615	MICHIGAN DEPT OF PUBLIC HEALTH	LANSING
0384	MICHIGAN STATE UNIVERSITY	EAST LANSING
0295	MICHIGAN, UNIVERSITY OF	ANN ARBOR

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0008	SINAI HOSPITAL OF DETROIT	DETROIT
2483	VETERANS ADMINISTRATION HOSPITAL-ANN ARBOR	ANN ARBOR
0354	WAYNE STATE UNIVERSITY	DETROIT
0720	WESTERN MICHIGAN UNIVERSITY	KALAMAZOO

MINNESOTA

0065	HENNEPIN COUNTY GENERAL HOSPITAL	MINNEAPOLIS
0041	MAYO FOUNDATION	ROCHESTER
0065	MINNEAPOLIS MEDICAL RESEARCH FOUNDATION, INC	MINNEAPOLIS
0463	MINNESOTA, UNIV OF	DULUTH
0463	MINNESOTA, UNIV OF	MINNEAPOLIS
0463	MINNESOTA, UNIV OF	MORRIS
0463	MINNESOTA, UNIV OF	ST PAUL
0463	MINNESOTA, UNIV OF, TECHNICAL COLLEGE	CROOKSTON
0463	MINNESOTA, UNIV OF, TECHNICAL COLLEGE	WASECA

MISSISSIPPI

0561	(2)MISSISSIPPI, UNIVERSITY OF	UNIVERSITY
0366	MISSISSIPPI, UNIVERSITY OF, MEDICAL CENTER	JACKSON

MISSOURI

0298	CANCER RESEARCH CENTER	COLUMBIA
2358	(2)CEMREL, INC	ST ANN
0298	ELLIS FISCHEL STATE CANCER HOSPITAL	COLUMBIA
0424	JEWISH HOSPITAL OF ST LOUIS	ST LOUIS
2365	(2)MID-CONTINENT REGIONAL EDUCATIONAL LABORATORY	KANSAS CITY
0292	(2)MISSOURI, UNIV OF, EXCEPT MEDICAL CENTER	COLUMBIA
0292	MISSOURI, UNIV OF, MEDICAL CENTER INCLUDING MISSOURI INSTITUTE OF PSYCHIATRY	COLUMBIA
0292	MISSOURI, UNIV OF	KANSAS CITY
0292	(2)MISSOURI, UNIV OF	ROLLA
0292	(2)MISSOURI, UNIV OF	ST LOUIS
0292	MISSOURI, UNIV OF, REG MED PROG, ALL CAMPUSES	
0356	ST LOUIS UNIVERSITY	ST LOUIS

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

2056	VETERANS ADMINISTRATION HOSPITAL-KANSAS CITY	KANSAS CITY
2351	WASHINGTON UNIV SCHOOL OF MEDICINE	ST LOUIS

NEBRASKA

1120	CREIGHTON UNIVERSITY	OMAHA
1781	VETERANS ADMINISTRATION HOSPITAL-OMAHA	OMAHA

NEVADA

0762	(2) NEVADA, UNIVERSITY OF, RENO CAMPUS	RENO

NEW HAMPSHIRE

0427	(2) DARTMOUTH COLL FACULTY OF ARTS AND SCIENCES	HANOVER
0227	DARTMOUTH MEDICAL SCHOOL	HANOVER
1006	(4) NEW HAMPSHIRE HOSPITAL	CONCORD
1006	(4) NEW HAMPSHIRE STATE DIVISION OF MENTAL HEALTH	CONCORD

NEW JERSEY

0981	(2) EDUCATIONAL TESTING SERVICE	PRINCETON
0349	NEW JERSEY, COLL OF MEDICINE AND DENTISTRY OF	NEWARK
0349	NEW JERSEY DENTAL SCHOOL	JERSEY CITY
0349	NEW JERSEY MEDICAL SCHOOL	NEWARK
0837	NEWARK BETH ISRAEL MEDICAL CENTER	NEWARK
0570	(2) PRINCETON UNIVERSITY	PRINCETON
0349	RUTGERS MEDICAL SCHOOL	PISCATAWAY
0300	(4) RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY	CAMDEN
0300	(4) RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY	NEW BRUNSWICK
0300	(4) RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY	NEWARK

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032729

		NEW MEXICO	
0141		LOVELACE FOUNDATION FOR MED ED AND RES	ALBUQUERQUE
0472		NEW MEXICO, UNIVERSITY OF	ALBUQUERQUE
0353		NEW MEXICO, UNIVERSITY OF, HEALTH SCIENCES GROUP-SCHOOL OF MEDICINE, COLLEGES OF PHARMACY AND NURSING	ALBUQUERQUE
		NEW YORK	
2129	(4)	AMERICAN HEALTH FOUNDATION	NEW YORK
2116	(2)	BARNARD COLLEGE	NEW YORK
0341		BETH ISRAEL MEDICAL CENTER	NEW YORK
0423		BRONX-LEBANON HOSPITAL CENTER	NEW YORK
1064		BROOKHAVEN NATIONAL LABORATORY MEDICAL DEPARTMENT	UPTON
2368	(2)	CENTER FOR URBAN EDUCATION	NEW YORK
2277	(2)	CHILD WELFARE LEAGUE OF AMERICA	NEW YORK
0381		CHILDRENS HOSPITAL OF BUFFALO	BUFFALO
0437	(2)	COLUMBIA UNIV, EXCEPT HEALTH SCIENCES DIV	NEW YORK
0034		COLUMBIA UNIV HEALTH SCIENCES DIV INCLUDING COLLEGE OF PHYSICIANS AND SURGEONS, SCHOOLS OF PUBLIC HEALTH AND ADMINISTRATIVE MEDICINE, NURSING, AND ORAL AND DENTAL SURGERY	NEW YORK
0373	(2)	COLUMBIA UNIVERSITY TEACHERS COLLEGE	NEW YORK
0526		COMMUNITY BLOOD COUNCIL OF GREATER NEW YORK	NEW YORK
0063	(3)	CORNELL UNIV, EXCEPT MED COLL AND SCH OF NURS	ITHACA
0245		CORNELL UNIV, MEDICAL COLLEGE	NEW YORK
0109		EASTMAN DENTAL CENTER	ROCHESTER
0456		HEALTH RESEARCH, INC, ALBANY DIVISION	ALBANY
0456		HEALTH RESEARCH, INC ROSWELL PARK DIVISION	BUFFALO
0456		HOMER FOLKS TUBERCULOSIS HOSPITAL	ONEONTA
0621		HOSPITAL FOR JOINT DISEASES AND MED CENTER	NEW YORK
0047		HOSPITAL FOR SPECIAL SURGERY	NEW YORK
1005	(4)	JEWISH BOARD OF GUARDIANS	NEW YORK
0368		JEWISH HOSPITAL AND MEDICAL CENTER OF BROOKLYN	BROOKLYN
0369		KINGSBROOK JEWISH MED CTR&ISAAC ALBERT RES INST	NEW YORK
2375		LONG ISLAND JEWISH-HILLSIDE MEDICAL CENTER	NEW HYDE PARK
0397		MAIMONIDES MEDICAL CENTER	BROOKLYN
0086		MARY IMOGENE BASSETT HOSPITAL	COOPERSTOWN
2518		MEADOWBROOK MEDICAL EDUCATION AND RES FDN	EAST MEADOW
0383		MEMORIAL HOSP FOR CANCER AND ALLIED DISEASES	NEW YORK
0059		MONTEFIORE HOSPITAL AND MEDICAL CENTER	NEW YORK

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032730

0139		MOUNT SINAI SCHOOL OF MEDICINE	NEW YORK
2518		NASSAU COUNTY MEDICAL CENTER	EAST MEADOW
0526		NEW YORK BLOOD CENTER	NEW YORK
1370	(4)	NEW YORK CITY DEPARTMENT OF HEALTH	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF, BRONX COMMUNITY COLL	BRONX
0765	(2)	NEW YORK, CITY UNIV OF, BROOKLYN COLLEGE	BROOKLYN
0765	(2)	NEW YORK, CITY UNIV OF, CITY COLLEGE	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF GRAD SCH AND UNIV CTR	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF, HERBERT H LEHMAN COLL	BRONX
0765	(2)	NEW YORK, CITY UNIV OF, HOSTOS COMMUNITY COLL	BRONX
0765	(2)	NEW YORK, CITY UNIV OF, HUNTER COLLEGE	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF, JOHN JAY COLLEGE OF CRIMINAL JUSTICE	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF, KINGSBOROUGH CMTY COLL	BROOKLYN
0765	(2)	NEW YORK, CITY UNIV OF, LAGUARDIA CMTY COLL	LONG ISLAND
0765	(2)	NEW YORK, CITY UNIV OF, MANHATTAN CMTY COLL	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF, NEW YORK CITY CMTY COLL	BROOKLYN
0765	(2)	NEW YORK, CITY UNIV OF, QUEENS COLLEGE	FLUSHING
0765	(2)	NEW YORK, CITY UNIV OF, QUEENSBOROUGH CMTY COLL	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF, RESEARCH FOUNDATION	NEW YORK
0765	(2)	NEW YORK, CITY UNIV OF, RICHMOND COLLEGE	STATEN ISLAND
0765	(2)	NEW YORK, CITY UNIV OF, STATEN ISLAND CMTY COLL	STATEN ISLAND
0765	(2)	NEW YORK, CITY UNIV OF, YORK COLLEGE	JAMAICA
0456		NEW YORK DEPARTMENT OF HEALTH	ALBANY
0624	(9)	NEW YORK DEPARTMENT OF MENTAL HYGIENE	ALBANY
0208		NEW YORK MEDICAL COLLEGE-FLOWER AND FIFTH AVENUE HOSPITALS INCLUDING METROPOLITAN HOSPITAL AND BIRD S. COLER MEMORIAL HOSPITAL	NEW YORK
0456		NEW YORK STATE REHABILITATION HOSPITAL	WEST HAVERSTRAW
0374	(2)	NEW YORK, STATE UNIV OF, AT ALBANY	ALBANY
0508	(3)	NEW YORK, STATE UNIV OF, AT BINGHAMTON	BINGHAMTON
0163		NEW YORK, STATE UNIV OF, AT BUFFALO	BUFFALO
0596		NEW YORK, STATE UNIV OF, AT STONY BROOK	STONY BROOK
0474	(7)	NEW YORK, STATE UNIV OF, COLLEGE AT BROCKPORT	BROCKPORT
0506		NEW YORK, STATE UNIV OF, COLLEGE AT BUFFALO	BUFFALO
0259	(4)	NEW YORK, STATE UNIV OF, COLLEGE AT CORTLAND	CORTLAND
0457		NEW YORK, STATE UNIV OF, COLLEGE OF ARTS AND SCIENCES AT GENESEO	GENESEO
0386	(2)	NEW YORK, STATE UNIV OF, COLLEGE AT OSWEGO	OSWEGO
0220		NEW YORK, STATE UNIV OF, COLLEGE OF FORESTRY	SYRACUSE

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0305		NEW YORK, STATE UNIV OF, DOWNSTATE MED CTR	BROOKLYN
0127		NEW YORK, STATE UNIV OF, UPSTATE MED CTR	SYRACUSE
0390	(2)	NEW YORK UNIVERSITY, EXCLUSIVE OF THE MED CTR	NEW YORK
0405		NEW YORK UNIVERSITY MEDICAL CENTER	NEW YORK
0788		NORTH SHORE HOSPITAL	MANHASSET
0615	(2)	POLYTECHNIC INSTITUTE OF BROOKLYN	BROOKLYN
2247		PUBLIC HEALTH RESEARCH INSTITUTE	NEW YORK
1001		RENSSELAER POLYTECHNIC INSTITUTE	TROY
0624	(9)	RESEARCH FOUNDATION FOR MENTAL HYGIENE	ALBANY
0172		ROCHESTER, UNIVERSITY OF	ROCHESTER
0230		ROCKEFELLER UNIVERSITY	NEW YORK
2036	(4)	ROCKLAND COUNTY HEALTH AND SOCIAL SERVICES COMP	POMONA
0491		ROOSEVELT HOSPITAL	NEW YORK
0456		ROSWELL PARK MEMORIAL INSTITUTE	BUFFALO
0536		SLOAN-KETTERING INSTITUTE FOR CANCER RES	NEW YORK
0076		ST LUKES HOSPITAL CENTER	NEW YORK
0376		ST VINCENTS HOSP AND MED CTR OF N Y	NEW YORK
0280	(2)	SYRACUSE UNIVERSITY	SYRACUSE
2438		TRUDEAU INSTITUTE	SARANAC LAKE
0621		RESEARCH INSTITUTE FOR SKELETOMUSCULAR DISEASES	NEW YORK
0217		UNION UNIVERSITY, ALBANY MEDICAL COLLEGE	ALBANY
1740		VETERANS ADMINISTRATION HOSPITAL-BRONX	NEW YORK
2045		VETERANS ADMINISTRATION HOSPITAL-NORTHPORT	NORTHPORT
0002		YESHIVA UNIV, ALBERT EINSTEIN COLL OF MED	BRONX

NORTH CAROLINA

0699		CHARLOTTE MEMORIAL HOSPITAL	CHARLOTTE
0191		DUKE UNIVERSITY	DURHAM
2382	(2)	NATIONAL LABORATORY FOR HIGHER EDUCATION	DURHAM
2242	(2)	NORTH CAROLINA A & T STATE UNIVERSITY	GREENSBORO
0285	(2)	NORTH CAROLINA STATE UNIVERSITY AT RALEIGH	RALEIGH
0177		NORTH CAROLINA, UNIVERSITY OF, AT CHAPEL HILL	CHAPEL HILL
0242		WAKE FOREST UNIVERSITY, BOWMAN GRAY SCH OF MED	WINSTON-SALEM
1087	(2)	WAKE FOREST UNIVERSITY, EXCEPT SCH OF MEDICINE	WINSTON-SALEM
0078	(2)	WESTERN CAROLINA CENTER	MORGANTON

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032732

0362	WILLS EYE HOSPITAL AND RESEARCH INSTITUTE	PHILADELPHIA
0054	WISTAR INSTITUTE	PHILADELPHIA

RHODE ISLAND

0467	BROWN UNIVERSITY	PROVIDENCE
0318	RHODE ISLAND HOSPITAL	PROVIDENCE

SOUTH CAROLINA

0533	AIKEN-BARNWELL MENTAL HEALTH CENTER	AIKEN
0533	ANDERSON-OCONEE-PICKENS MENTAL HEALTH CTR	ANDERSON
0533	BECKMAN CENTER FOR MENTAL HEALTH SERVICES	GREENWOOD
0533	CHARLESTON AREA MENTAL HEALTH CENTER	CHARLESTON
0533	COASTAL EMPIRE MENTAL HEALTH CENTER	BEAUFORT
0533	COLUMBIA AREA MENTAL HEALTH CENTER	COLUMBIA
0533	CRAFTS-FARROW STATE HOSPITAL	COLUMBIA
0533	FRIENDSHIP CENTER	COLUMBIA
0533	GEORGETOWN-HORRY MENTAL HEALTH CLINIC	CONWAY
0533	GREENVILLE AREA MENTAL HEALTH CENTER	GREENVILLE
0533	ORANGEBURG AREA MENTAL HEALTH CLINIC	ORANGEBURG
0533	PEE-DEE MENTAL HEALTH CENTER	FLORENCE
0533	SOUTH CAROLINA DEPARTMENT OF MENTAL HEALTH	COLUMBIA
0533	DIV OF ALCOHOL AND DRUG ADDICTION SERVICES	COLUMBIA
0533	DIV OF COMMUNITY MT1 HLTH SERVICES SPEC PROJ	COLUMBIA
0533	LONG TERM CARE SERVICES	COLUMBIA
0240	SOUTH CAROLINA, MEDICAL UNIVERSITY OF	CHARLESTON
0533	SOUTH CAROLINA STATE HOSPITAL	COLUMBIA
0629	(4) SOUTH CAROLINA, UNIVERSITY OF	COLUMBIA
0533	SOUTH CAROLINA WAR VETERANS HOME	COLUMBIA
0533	SPARTANBURG AREA MENTAL HEALTH CENTER	SPARTANBURG
0533	SUMTER-CLARENDON-KERSHAW MENTAL HEALTH CENTER	SUMTER
0533	TRI-COUNTY MENTAL HEALTH CENTER	BENNETTSVILLE
0533	WILLIAM S HALL PSYCHIATRIC INSTITUTE	COLUMBIA
0533	YORK-CHESTER-LANCASTER MENTAL HEALTH CENTER	ROCK HILL

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032733

TENNESSEE

1696	(4)	ARLINGTON HOSPITAL AND SCHOOL	ARLINGTON
0393		MEHARRY MEDICAL COLLEGE	NASHVILLE
1716		OAK RIDGE ASSOCIATED UNIVERSITIES, INC.	OAK RIDGE
1716		OAK RIDGE NATIONAL LABORATORY	OAK RIDGE
0648		ST JUDE CHILDRENS RESEARCH HOSPITAL	MEMPHIS
0170		TENNESSEE, UNIV OF, MEDICAL UNITS	MEMPHIS
0124		TENNESSEE, UNIVERSITY OF - KNOXVILLE	KNOXVILLE
0401		VANDERBILT UNIVERSITY	NASHVILLE
1800		VETERANS ADMINISTRATION HOSPITAL-MEMPHIS	MEMPHIS

TEXAS

0307		BAYLOR COLLEGE OF MEDICINE	HOUSTON
0813	(2)	BAYLOR UNIVERSITY	WACO
2344	(2)	SOUTHWEST EDUCATIONAL DEVELOPMENT CORPORATION	AUSTIN
2344	(2)	SOUTHWEST EDUCATIONAL DEVELOPMENT LABORATORY	AUSTIN
1045	(2)	TEXAS A & M UNIV, COLLEGE STATION CAMPUS ONLY	COLLEGE STATION
0590		TEXAS INSTITUTE FOR REHAB AND RESEARCH	HOUSTON
1121	(7)	TEXAS, UNIV OF, AT ARLINGTON	ARLINGTON
0123	(9)	TEXAS, UNIV OF, AT AUSTIN	AUSTIN
0669		TEXAS, UNIV OF, AT HOUSTON DENTAL BRANCH	HOUSTON
0113		TEXAS, UNIV OF, M D ANDERSON HOSP AND TUMOR INS	HOUSTON
0107		TEXAS, UNIV OF, MEDICAL BRANCH AT GALVESTON	GALVESTON
0040	(8)	TEXAS, UNIV OF, MEDICAL SCHOOL	SAN ANTONIO

UTAH

0933	(2)	BRIGHAM YOUNG UNIVERSITY	PROVO
2426		DESERET FOUNDATION FOR MED EDU AND RES	SALT LAKE CITY
0235		UTAH, UNIVERSITY OF	SALT LAKE CITY

VERMONT

0194		VERMONT, UNIVERSITY OF	BURLINGTON
2335		VETERANS ADM CENTER-WHITE RIVER JUNCTION	WHITE RIVER JCT

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

	VIRGINIA	
2275	(9) HUMAN RESOURCES RESEARCH ORGANIZATION	ALEXANDRIA
0634	LYNCHBURG TRAINING SCHOOL AND HOSPITAL	MADISON HEIGHTS
0239	VIRGINIA COMMONWEALTH UNIVERSITY, MEDICAL COLLEGE OF VIRGINIA, HEALTH SCIENCES DIV	RICHMOND
0306	VIRGINIA, UNIVERSITY OF	CHARLOTTESVILLE
0575	(2) WILLIAM AND MARY, COLLEGE OF	WILLIAMSBURG
	WASHINGTON	
0522	CHILDRENS ORTHOPEDIC HOSPITAL AND MED CTR	SEATTLE
0029	PACIFIC NORTHWEST RESEARCH FOUNDATION	SEATTLE
0900	VIRGINIA MASON RESEARCH CENTER INCLUDING MASON CLINIC AND VIRGINIA MASON HOSPITAL	SEATTLE
1717	WASHINGTON DEPT OF SOCIAL AND HEALTH SERVICES	OLYMPIA
0105	(3) WASHINGTON STATE UNIVERSITY	PULLMAN
0299	WASHINGTON, UNIVERSITY OF	SEATTLE
	WEST VIRGINIA	
2376	(2) APPALACHIA EDUCATIONAL LABORATORY, INC	CHARLESTON
0431	WEST VIRGINIA UNIVERSITY	MORGANTOWN
	WISCONSIN	
0315	CENTRAL WISCONSIN COLONY AND TRAINING SCH	MADISON
2132	(2) LAWRENCE UNIVERSITY	APPLETON
0387	MARQUETTE UNIVERSITY	MILWAUKEE
0763	MENDOTA STATE HOSPITAL	MENDOTA
0503	(4) SOUTHERN WISCONSIN COLONY AND TRAINING SCH	UNION GROVE
0077	WISCONSIN, MEDICAL COLLEGE OF	MILWAUKEE
0319	WISCONSIN, UNIVERSITY OF, MADISON CAMPUS	MADISON
2106	(2) WISCONSIN, UNIVERSITY OF, PARKSIDE	KENOSHA

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032735

	SWITZERLAND	
1137	WORLD HEALTH ORGANIZATION	GENEVA
	UNITED KINGDOM	
1080	LONDON, UNIV OF, INSTITUTE OF NEUROLOGY	LONDON

TOTAL INSTITUTIONS COVERED BY ACCEPTABLE GENERAL ASSURANCES 561

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6) UNASSIGNED
(7) NO SURGICAL OR IND STUDIES
(8) STATUS UNDETERMINED (CALL 301-496-7005 FOR CURRENT INFORMATION)
(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032736

Form Approved
OMB No. 68-R1143

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS CERTIFICATION

IDENTIFICATION NUMBER (If known)

☐ Contract ☐ New
☐ Grant ☐ Renewal
☐ Fellowship ☐ Continuation

STATEMENT OF POLICY: Safeguarding the rights and welfare of human subjects involved in activities supported by grants or contracts from the DHEW is the responsibility of the institution which receives or is accountable to the DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of the Department that no grant or contract for an activity involving human subjects shall be made unless the application for such support has been reviewed and approved by an appropriate institutional committee. (Reference: "Institutional Guide to DHEW Policy on the Protection of Human Subjects.")

1. TITLE OF PROPOSAL

2. PROJECT DIRECTOR/PROGRAM DIRECTOR/FELLOW

POSITION TITLE

3. INSTITUTIONAL COMPONENT OR DEPARTMENT

4. CHECK ONE OF THE FOLLOWING STATEMENTS AS APPLICABLE:

☐ A. This application does not propose any activities that would invo[lve] ngs who might be considered subjects, human material, or persona[l] y or secondary sources.

☐ B. This is to CERTIFY that this application which d[oes] human subjects has been reviewed and approved the date of_____ in accor[dance] institutional assurance on file with [DHEW]. certification is invalid if revie[wed] year.)

☐ C. This is to CERTIFY th[at] is pending review [by] policy and th[at] does not [involve] office [of] [DHEW] [committee] [ap]proved, the agency [will] [no]tify immediately by telephone, [and] [con]firm the revised or planned date of

☐ D. T[his] [application] no[t] [involve] [human] [sub]jects. This institution does not on [file] [with] the DHEW. I understand that information for [which] [it] [is] [to] be received should the application become eligible

FOR COPIES CALL (301) 496-7005 OR WRITE TO THE INSTITUTIONAL RELATIONS BRANCH

5. SIGNATURE OF INSTITUTIONAL OFFICIAL AUTHORIZED TO SIGN PROPOSALS | DATE

6. TITLE | TELEPHONE NO. (Code, No., Extension)

7. NAME AND ADDRESS OF INSTITUTION (Street, City, State, zip code)

NOTE TO AGENCY: This form should NOT be included with application forms that have provision for human subject certification. It may be used to request certification, or correction of certification.

HEW 596 (Formerly NIH 1611)
8-72

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO THE AGENCY REQUESTING ITS COMPLETION

10327137

GENERAL INSTITUTIONAL ASSURANCE

Statement of Compliance

Oak Ridge Associated Universities (ORAU) is in compliance with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education, and Welfare.

ORAU has established and does maintain a committee competent to review projects and activities that involve human subjects. The committee is assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.
The risks to subjects are outweighed by potential benefits.
The informed consent of subjects will be obtained by methods that are adequate and appropriate.

This institution will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgement of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interests.

We encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

The ORAU Research Hospital staff provides facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

The staff also maintains appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

Through appropriate administrative overview ORAU reassures itself that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with the assurance as accepted by the Department of Health, Education, and Welfare.

OAK RIDGE ASSOCIATED UNIVERSITIES

Signature _____
Medical Division Chairman

Signature William G. Pollard
Executive Director

Date October 25, 1972

1032138

November 6, 1972

Mr. Joseph A. Lenhard, Director
Research and Technical Support Division
U. S. Atomic Energy Commission
Oak Ridge, Tennessee

Subject: RESEARCH INVOLVING USE OF HUMAN SUBJECTS - YOUR LETTER OF OCTOBER 17, 1972

Dear Mr. Lenhard:

In response to your letter, ORAU's "General Institutional Assurance" has been executed by Dr. Gould Andrews, chairman of our Medical Division, in compliance with the AEC-NIH policy with respect to the protection of human subjects used in AEC sponsored research.

We have established necessary procedures to assure reaffirmation of this policy will be executed annually and will accompany our form 189 budget presentations or renewal proposals. We are enclosing eight copies of the assurance statement dated October 25, 1972. We shall appreciate your attaching copies of the statement to our FY 1973 189 budget submissions.

Sincerely yours,
Original Signed By
PAUL M. ELZA

William G. Pollard
Executive Director

ELZA:nm

Attachments

1032739

2/27/74

This mailing includes the following enclosures:
Minutes of December 11 meeting
Review of Active Research Projects
Memo dated February 18
Dr. Ricks' rewritten proposal
Consent form for Dr. Ricks' proposal
Improved consent form for Dr. Goswitz's proposal
February 27 memo with Dr. Tyndall's new proposal which requires action

To the Committee on Human Studies

A. B. Brill
C. L. Edwards
M. E. Koons
R. D. Lange
T. A. Lincoln
B. M. Nelson
J. B. Storer

The minutes on our meeting of December 11, 1973 are being sent out rather belatedly. Included are the following requested items:

1) A rewritten version of Dr. Ricks' proposal entitled, "Feasibility of Measuring Cognitive and Psychomotor Functions after Total-Body Irradiation in Man."

2) A consent form for the above proposal.

3) An improved consent form for Dr. Goswitz's proposal entitled, "Effect of Splenectomy and Total-Body Irradiation on Onset of Blast Crisis and Survival in Chronic Granulocytic Leukemia."

(Dr. Nelson's proposal, "Fate of Labeled Mononuclear Blood Cells in Tissues, Especially in Lymph Nodes, Spleen, and Marrow," was rewritten slightly without change in substance and is not included.)

I would appreciate a note for the record indicating that you have received this material and calling attention to any aspect that is unsatisfactory.

Dr. Ketchel has supplied some answers to the incidental questions raised about his proposal, "Female Reaction to Sperm Histocompatibility Antigens." The project is being considered for funding by NIH. The human studies are dependent on positive results in preliminary animal work, and the human experiments are not yet completely planned. The population of subjects would probably be obtained from the Planned Parenthood group in Oak Ridge; Dr. Ketchel is a Board Member of this organization. For the tests for histocompatibility antigens, the control sera used would be from other couples in the study. For the blocking antibody studies, control sera would need to come from males or from females who had never been exposed to semen.

1032740

UNITED STATES
ATOMIC ENERGY COMMISSION
OAK RIDGE OPERATIONS
P.O. BOX E
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8611

June 4, 1974

DATE 6-10-74 am
COPIES TO Bergen
Martin
Landall

Jim - Please collect comments and draft response to meet required date
E

Dr. William G. Pollard
Executive Director
Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee

Dear Dr. Pollard:

ANNUAL HEALTH PROTECTION AND ENVIRONMENTAL MANAGEMENT APPRAISAL OF ORAU - 1974

The annual appraisal of the health protection and environmental management programs was conducted during the week of March 11, 1974, by members of the ORO Safety and Environmental Control Division. The findings have been discussed with members of your staff.

Enclosed are six copies of the formal report of the appraisal. You may proceed with implementation of the recommendations unless there are sound reasons why they are not warranted. In any event, your comments with regard to the conduct of the appraisal, the general content of the report, and the detailed plans for implementing or otherwise handling the recommendations are requested by June 26, 1974.

The cooperation extended by members of your staff during the appraisal is appreciated. We are pleased to report the continued safe operation of ORAU as indicated by this appraisal.

Sincerely,

Joseph A. Lenhard

Joseph A. Lenhard, Director
Research and Technical Support Division

OSH:RDS

Enclosure:
Appraisal Report (6 cys)

cc w/encl:
J. H. Hill
D. A. Horsewood
W. H. Travis

1032741

USAEC-ORO

HEALTH PROTECTION APPRAISAL

OAK RIDGE ASSOCIATED UNIVERSITIES

MARCH 1974

by

R. D. SMITH
R. W. POE
J. T. DUFOUR
R. O. EDDINS

1032742

I. Purpose and Scope

The annual health protection and environmental pollution appraisal was conducted during March 11-15, 1974. This appraisal was conducted by Messrs. R. D. Smith, R. W. Poe, J. T. Dufour of the Health Protection Branch, and R. O. Eddins of the Environmental Protection Branch, Safety and Environmental Control Division. The areas covered by this appraisal include health physics, industrial hygiene, environmental pollution, pesticides, and with special emphasis being placed this year on medical research.

II. Summary

The health physics and industrial hygiene programs of ORAU are considered to be very good. The Medical Division program in the area of human experimentation is undergoing some reorganization and has the earmarks of developing into a well organized program capable of fulfilling DHEW guidelines concerning the participant's safety. Two recommendations in the area of documentation and a suggestion in the findings should aid in this reorganization. Although pesticide use at ORAU is minimal, there are certain minimum health protection requirements applicable for their use, and a 1973 appraisal recommendation concerning these requirements had not been implemented at the time of the 1974 appraisal. This was pointed out during the critique and ORAU management assured the reviewers this recommendation would receive timely attention. In the area of environmental protection, ORAU is conforming to all applicable state and federal emission criteria.

III. Recommendations

A. Recommendations of the 1973 Appraisal

It was recommended that:

1. The responsibilities of the Radiation and Chemical Safety Officer and the General Safety Officer be formally documented in enough detail to eliminate

1032743

any jurisdictional discrepancies, and eliminate the dual responsibility concept now utilized in some areas in favor of a singly responsible officer.

An internal memorandum was prepared delineating each safety officer's responsibilities. An industrial hygiene safety manual was prepared which fully defines the program responsibilities and standards. This recommendation is considered implemented.

2. A respiratory protection program be established in accordance with ANSI Z88.2-1969 and, further that one individual be given the responsibility for coordination of all facets of the program.

   The R&CSO has been given this responsibility, and the program is considered to be in compliance with ANSI Z88.2-1969. This recommendation is considered to be implemented.

3. Training procedures be developed covering the proper use of pesticides, health hazards, and the necessary protective equipment to be used by employees, and that records of training and retraining be maintained.

   This recommendation has not been implemented and is repeated in this report.

4. The dose information form used by the Medical Division for ordering radioisotopes for patients be initiated in writing by the requesting physician.

A radioisotope order form has been developed which the physician initiates in writing, and the form has check off points at each major step up to and including administration. These forms are maintained in the patient's medical folder and in a master file. This recommendation is considered implemented.

B. Recommendations of the 1974 Appraisal

It is recommended that:

1. The Human Studies Committee document its procedure(s) used to assure the adequate implementation of its recommendations and/or limitations and conditions placed upon research proposals. (Section IV.C.3.)

2. Research proposals for studies involving human subjects include not only an evaluation of the physical harm but also an opinion of the psychological, and sociological harm associated with the proposed research. (Section IV.C.3.)

3. Training procedures be developed covering the proper use of pesticides, health hazards, and the necessary protective equipment to be used by employees, and that records of training and retraining be maintained (a repeated recommendation from the 1973 appraisal). (Section IV.F.2.)

IV. Findings

A. Organization

The ORAU health physics, industrial hygiene, and environmental protection programs are operated by the Radiation and Chemical Safety Officer, two technicians, and a half-time secretary. Collectively, their 3-1/2 man year effort is distributed approximtely

1.75 for health physics, 0.75 for industrial hygiene, 0.5 for environmental pollution, and 0.5 for miscellaneous special projects, teaching, and committee work.

B. Health Physics

The health physics program was found to be in good shape and run in a professional manner. A review of the records and tour of most ORAU facilities support this finding. Radiation exposures continue to remain quite low with a maximum exposure of about 470 mRem and an average of about 92 mRem. ORAU changes film badges on a quarterly basis and due to the minimum sensitivity of the film (20 mRem) all zeros are recorded as 20 mRem. Therefore, the minimum recorded exposure of ORAU employees is 80 mRem/year.

About five employees are monitored for neutron exposure. During the changeout of a 4 mg ^{252}Cf source for an 18.8 mg ^{252}Cf source, two employees received the only neutron exposure recorded for ORAU. The maximum was 150 mRem.

Internal exposures are determined through applicable Carbon-14 breath analysis, tritium bioassay analysis, and whole body counting. The results of all these techniques indicate no significant internal exposure among ORAU employees.

Course participants are monitored for internal and external radiation exposure when necessary. These exposures are comparable to those received by ORAU employees.

1032746

C. ORAU Medical Division

1. Patient Safety Program

The emphasis of this year's health protection appraisal was on programs in the Medical Division designed to protect human subjects from possible hazards in medical research with experimental drugs and procedures. These programs were reviewed using the "Institutional Guide to Department of Health, Education, and Welfare Policy on Protection of Human Subjects" as a guide. The Medical Division has two established committees, with separate responsibilities, to review research proposals and to ensure that adequate precautions will be taken in all medical research at ORAU. First, the Medical Radionuclide Committee must approve all medical radionuclide used at ORAU. Secondly, the Human Studies Committee must review and approve research proposals primarily to ensure that the benefit outweighs the risk, which includes an assessment of the hazards, precautions, and the information to be presented to the patient to gain informed consent.

2. Medical Radionuclide Committee

Since the last appraisal the Committee for Use of Radioisotopes in Humans has been renamed the Medical Radionuclide Committee and is also operating under a revised charter. This committee is charged with the responsibility, as defined by its charter, to ensure that the administration of radionuclides to humans at ORAU is adequately controlled and to ensure the safety of each person administered a radionuclide. To

aid the committee in carrying out this responsibility, researchers are required to submit a research proposal with sufficient information for the committee to make a determination on the safety of the radionuclide for its intended use. Proposals must be submitted not only for radionuclides used in experimental procedures but also those used in well established procedures which have been approved by the FDA and the AEC. The committee assigns a dose range to each radionuclide it considers safe for a given procedure, within which the researcher must operate. To go beyond this range, the research must again receive committee approval.

One significant change in the revised committee's charter is the deletion of ORAU policy guidelines defining the maximum radiation dose to human subjects not receiving medical benefit from their participation in medical research programs. These radiation dose guidelines limited the maximum dose to these persons to occupational exposure limits. It is the understanding of the chairman of this committee that considerations of maximum doses are now done solely by the Committee on Human Studies. The Committee on Human Studies documented guidelines, however, have not yet been revised to include any dose guidelines. Thus, it is suggested that guidelines representing ORAU policy be incorporated in the Committee on Human Studies guidelines.

3. Committee on Human Studies

A review of the minutes of the Committee on Human Studies (CHS) meetings pointed up documentation deficiencies in the handling of committee recommendations. These minutes

represent the records of actions taken by the committee. In cases where the CHS made recommendations and/or placed conditions on research proposals, their records did not always indicate what decision had been made by the committee as to the adequacy of the implementation. In most cases it is not readily apparent what action was taken with regard to the recommendation, except the committee may have given approval for continuation of the research. It is felt by the reviewers that formal procedures stating steps to be followed in gaining approval for recommendation implementation is a necessary part of the CHS operating guidelines, and further that the committee's records reflect the actions taken by the committee. Thus, it is recommended that the CHS formally document procedures used to assure the adequate implementation of its recommendations and/or conditions placed upon research proposals.

One of the primary functions of the CHS is to make an assessment of the risk versus benefit of all research proposals at ORAU. Inherent in this assessment is the obligation to make sure that adequate steps are taken to minimize the risk, if possible. In this respect, this committee is doing a commendable job. There is, however, a responsibility on the researcher to identify the possible risk to human subject associated with the research he proposes. In reviewing several research proposals, it became apparent that only the physical risks to patient were being presented in the proposal for assessment by the committee. The reviewers were informed that many times the committee has had questions with regard to psychological

hazard, and on occasions patients have been restricted from some research, by the researcher, for psychological reasons. While it appears that a valid effort is being made to minimize psychological risk of some research, the proper documentation has not been kept. Thus, it is recommended that research proposals and the minutes of committee meetings for studies involving human subjects include not only an evaluation of the physical harm but also an opinion on the possible psychological and sociological harm associated with the proposed research.

4. ORAU Radiopharmaceutical Procedure

As a result of a misadministration of a radionuclide to two Oak Ridge Hospital patients last year, ORAU was requested to formalize a procedure dealing with the administration of radionuclides. The draft of this procedure was discussed during the appraisal. The definition of misadministration and the action to be taken was the only exception taken by the reviewers. As a result of the discussion, ORAU agreed to modify the procedure to require an internal investigation of any administration of a radionuclide which differed by ± 20% of the prescribed amount and not approved by the attending physician before administration. Additionally, any administration of a radionuclide exceeding the maximum amount approved by the ORAU Medical Radionuclide Committee will require notification of the AEC.

The procedure additionally assigns the Chief Clinician the responsibility of advising the patient or a responsible relative of a misadministration, if in the doctor's opinion,

it could cause a demonstrably adverse effect on the patient, and if so advising would not be contrary to the patient or relative's best interest.

D. Industrial Hygiene

During the appraisal, extensive discussions held with the R&CSO indicated that problem areas at ORAU have been dealt with in an effective manner. The major IH problem is the control of toxic chemicals as used in research and daily activities at ORAU. Other major areas of concern are shops, (dust from wood, metal, paints, lead) animal handling (infections, allergies to dander, use of ether, and the associated biohazards). Many of these areas have resulted in specific programs as described below. Others like carcinogens, precipitated by the Emergency Temporary Standard issued in May 1973, have been handled in a way which can be endorsed by the reviewers. The only carcinogen still being used at ORAU is benzidine. Its use is the subject of a safety bulletin which includes practices consistent with ORO interpretations of the permanent carcinogen standard. Other carcinogens found on site have been disposed of in an acceptable manner. Another area of discussion was the ORAU pesticide program. This subject will be covered in detail in Section IV.F.E. of this report.

1. Trouble Shooting

A considerable amount of time is devoted to checking out new operations, investigating incidents, complying with requests for information from the AEC, making requested inspections, etc. These activities are an essential part of an active IH program, and have been performed effectively during the past year.

2. Toxic Chemical Labeling

An effective program for labeling of both large and small quantities of toxic chemicals has been initiated. The R&CSO staff actively survey areas to assure that labels are being applied and that employees are aware of the program and its purpose. The continuing effectiveness of this program will be assessed in future appraisals.

As an integral part of the toxic chemical labeling and control program, the R&CSO receives copies of all relevant purchase orders for chemicals, compressed gases, insecticides, pesticides, herbicides, germicides, paint thinner, degreasers, solvents and cleaners, housekeeping chemicals, etc. They are also in the process of requesting the same for ultra-violet sources, lasers, and microwave sources. This information assists in both the early implementation of required controls, and in some cases the suggested substitution of a less hazardous item.

3. Noise

The only major noise source at ORAU is the emergency generator which has been monitored at 113dB. A sign has been posted and earmuffs are required during operation. The effectiveness of this administrative control is being evaluated by the R&CSO.

4. Hood Surveys

Laboratory hoods are checked for maintenance of designed flow rates every six months. Appreciable decrements in performance are investigated and repaired.

1032752

5. Ultra-Violet

There are a considerable number of sources at ORAU; most are used for sterilization. R&CSO is evaluating any potential hazard associated with these devices. At this time only the units at the Marmoset Facility warrant concern. In the near future signs will be posted and the appropriate instructions issued to affected employees.

6. Industrial Hygiene Manual

During the past year, R&CSO has prepared and issued and Industrial Hygiene Manual. This document which includes policies, standards, responsibilities, and procedures is considered by the reviewers to be an excellent description of the ORAU industrial hygiene program.

7. Manuals and Safety Bulletins

R&CSO periodically issues documents on safety, film badges, radiation safety, radiation warning signs, respirator protection program, laboratory safety, perchloric acid safety and benzidine. This is regarded as an effective means of communicating safety information to new employees and to inform and reemphasize safety practices to veteran employees.

8. Respirators

The R&CSO has been assigned the responsibility of administering ORAU's respiratory protection program. ORAU's written procedure further delegates the responsibility of employee training and equipment maintenance

to division chairman and department heads. Respirator usage at ORAU is minimal, and most respirators are for emergency use and training. A number of respirators have been purchased which considerably increases the protection capabilities of this program. The application of pesticides, etc., by Technical Services, is the only function routinely requiring the use of a respirator. Additional training in regard to the proper care and storage of this equipment appears necessary for the routine users in Technical Services (see Section IV.F.2.). ORAU's compliance with ANSI Z88.2-1969 is considered adequate for their needs.

E. Facilities

Tours of ORAU facilities included the hospital, Tyrone Road Laboratory, Special Training Division, Museum and the associated shops, and the Lipid Lab. These tours were interesting and informative and afforded the opportunity to assess the effectiveness of ORAU health protection programs in its most practical field applications. The reviewers were satisfied that a safe and healthful working environment is being maintained by the R&CSO in cooperation with supervisors and employees.

F. Environmental Management

1. General

ORAU continues to have minimal impact on the local air quality since natural gas is utilized for heating at all its facilities. Liquid radioactive effluents continue

1032754

to be very small from the Medical Division. ORAU conducts no incineration or open burning of waste. All non-contaminated dry trash is disposed of in the Oak Ridge municipal landfill and has only minor impact.

2. Pesticides

ORAU has modified its pesticide program in that a contract pest control company now performs all termite treatment in addition to indoor treatment. The R&CSO should review the contract to ensure that the pesticide used is registered for the intended use and complies with all legal and environmental requirements. The R&CSO presently performs this review on pesticides purchase requests and this would just be an extension of this task. In addition, the pesticide contractor shall be licensed and furnish ORAU with the following information on the pesticide used:

a. trade name and chemical name,
b. EPA registration number, and
c. complete analysis

The lockers utilized for pesticide storage are to be labeled. Respirators and solvents are not to be stored in the lockers as was observed during this appraisal. All unlabeled containers (bottles, coffee cans, etc.) are to be discarded and are not to be stored in the lockers. The dieldrin on hand is to be disposed of since this pesticide has been banned by EPA.

The General Safety Officer should (1) initiate periodical pesticide training, (2) document such training, and (3) formalize instructions in a document to include safety precautions, the proper use and care of safety equipment, hazards associated with the chemicals used, symptoms of overexposure, and first aid. The latter was a recommendation from the 1973 appraisal and was not implemented. Upon completion of the document in Item 3 above, it is requested that a copy be timely provided to the S&EC Division for review.

Reviewers:

R. D. Smith
Health Physicist

R. W. Poe
Health Physicist

J. T. Dufour
Industrial Hygienist

R. O. Eddins
Safety Engineer

1032756

IMPORTANT NOTICE

Research Projects Involving Human Subjects

The purpose of this notice is to provide clarification of Item 7. Research Involving Human Subjects on page 3 and the second sentence in Section C on page 9 of the Instruction Sheet (Rev. 2-73) for Form NIH 398. DHEW regulations define "subject at risk" as "any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service."

DHEW is concerned with the protection of the rights and welfare of human subjects in all research, development, and related activities. The Department's regulations (45 C.F.R., Part 46) are concerned with protection of rights to privacy, the need for informed consent, protection of confidentiality of data, and protection against physical, psychological, sociological, or legal risks. The need for protection of rights and welfare and protection against risks to the individual is not limited to activities involving children and adults but also includes the fetus, the abortus and the dead. The uses of organs, tissues, body fluids, or graphic, written or recorded information, while they present no physical risks to the subjects, may create medico-legal risks, or expose the subject to public embarrassment or humiliation through break of confidentiality and invasion of privacy. The major focus of a project (for example, on a medical procedure) is not the sole determinant of the need for protections. The safeguarding and confidentiality of medical records and other forms of data collected on individuals and groups and the use of such data either by the investigator conducting the original research, concurrent use of the data by other investigators, or use of the data at a later time are considered within the scope of concern of this policy.

While safeguarding the rights and welfare of subjects at risk is primarily the responsibility of the organization conducting grant activities, the responsibility for determining the adequacy of proposed procedures is shared by organizational review committees and DHEW staff and advisory committees. Therefore, if the proposal involves human subjects, the principal investigator shall, under the heading HUMAN SUBJECTS at the end of the Methods of Procedure section of the application:

1) Describe the requirements for a subject population and explain the rationale for using in this population special groups such as prisoners, children, the mentally disabled or groups whose ability to give voluntary informed consent may be in question.

1032757

2) Describe and assess any potential risks—physical, psychological, social, legal or other—and assess the likelihood and seriousness of such risks. If methods of research create potential risks, describe other methods, if any, that were considered and why they will not be used.

3) Describe consent procedures to be followed, including how and where informed consent will be obtained.

4) Describe procedures (including confidentiality safeguards) for protecting against or minimizing potential risks and an assessment of their likely effectiveness.

5) Assess the potential benefits to be gained by the individual subject, as well as benefits which may accrue to society in general as a result of the planned work.

6) Analyze the risk-benefit ratio.

The statements are subject to review, approval, and modification by your local organizational review committee. To insure timely completion of this review, your application and any additional materials requested by the committee should be submitted for local review well in advance of Public Health Service deadlines. If this review is not completed in advance of the deadline, it will be your responsibility to see that any modifications of the Methods of Procedure or HUMAN SUBJECTS section as a result of the review are forwarded to the PHS. These should be sent directly to the Division of Research Grants, NIH, Bethesda, Maryland 20014, and should be identified by principal investigator's name, project title, and name of organization precisely as entered on the receipt of application card returned with the original application.

The regulations concerned with the protection of human subjects effective July 1, 1974, require that organizational review and approval be completed and certified prior to submission of proposals to DHEW. However, by separate notice, the DHEW will provide that for a period of one year from the effective date of these regulations, organizations may submit certifications no later than 30 days following the deadline for which the proposal was submitted, or, if no deadline is specified, 30 days following the submission of the proposal. If a certification is not received within the 30 days, as provided above, the application will be administratively withdrawn by the Division of Research Grants and returned to the applicant institution.

After July 1, 1975, organizational review and approval must be completed and certified prior to submission of proposals to DHEW.

August 1, 1974

Rec 21 Aug 74

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

See page 18

August 1, 1974

FORTY-NINTH CUMULATIVE LIST OF ORGANIZATIONS AND INSTITUTIONS IN COMPLIANCE WITH DHEW POLICY AND REGULATIONS ON PROTECTION OF HUMAN SUBJECTS

NOTE: The DHEW policy on protection of human subjects was codified on July 1, 1974, in the Code of Federal Regulations (45 CFR 46). Copies of these regulations can be obtained from the Institutional Relations Branch, DRG, NIH. On July 12, 1974, the President signed P.L. 93-348, including amendments to the Act, similar in purpose to DHEW policy and regulations. DHEW will shortly amend the regulations to conform in detail to the Act.

1. UNSOLICITED PROPOSALS - GRANTS OR CONTRACTS INVOLVING HUMAN SUBJECTS

a. If DHEW professional review of the proposal indicates that it does not involve human subjects at risk in research, development, or related activities as defined in 45 CFR 46, these regulations do not apply and the application can be processed without further regard to this list.

b. If DHEW professional review of the proposal indicates that it involves human subjects at risk, check the institution's name against the list, and:

(i) If it is not on the list, a copy of the proposal should be promptly forwarded to the IRB, DRG, NIH, for negotiation of a special assurance and implementation of the regulations.

Page 18 — (ii) If it is on the list, check the face or signature page of the proposal for the certification date on which the institution's review committee or board on protection of human subjects has completed or will complete its review.

--If the application was submitted for a deadline on or before July 1, 1974, the certification date may be prior to the submission date or "pending" at some time prior to the starting date. If the date is "pending" the institution should be instructed to complete its review as soon as possible and to certify completion of such review on HEW Form 596 or equivalent. DHEW processing of the application must not be completed until this certification is received.

1032759

--If the application was submitted for a deadline after July 1, 1974, the certification date must be prior to the submission date or else certification of such review on HEW Form 596 or equivalent must be received within 30 days after the deadline. (If the proposal was not submitted for a deadline, as in the case of certain small grant and other special programs, the certification must follow the proposal within the 30 days after the submission date.)

2. SOLICITED PROPOSALS - CONTRACTS OR GRANTS INVOLVING HUMAN SUBJECTS

Draft requests for proposals (RFPs, RFCs, or RFAs) should be reviewed to determine whether performance will involve human subjects at risk. If these will be involved, the RFP should include the "Notice to Offerors" required by 41 CFR 3-4.5504(a).

Sole source responses to RFPs should be considered to be submitted as of the closing date of the RFP and should then be handled as in 1.b. above.

Competitive responses to RFPs should be considered to be submitted as of the date of submission of the best and final offer, following establishment of the zone of consideration or source selection, and should then be treated as in 1.b. above.

3. RESTRICTION CODES preceding institution names indicate the status of the institution's assurance in terms of DHEW policy and regulations on protection of human subjects. If it is proposed to award a grant or contract involving research falling within the restricted area, it will be necessary to get in touch with the IRB to arrange renegotiation of the grantee or contractor assurance or implementation.

ABSENCE OF A RESTRICTION CODE indicates that the institution has filed an assurance and implementation reflecting committee competence to deal with all probable applications to DHEW.

CODE (2) indicates that the committee has professional competence to review all probable proposals to DHEW except those involving medical, surgical, or investigational new drug studies.

CODE (3) indicates a medically oriented institution that is not qualified to review activities involving investigational new drugs (INDs).

CODE (4) indicates an institution with medical competence, but not in the field of surgery. Most of these institutions are concerned with studies in the field of psychiatry or with the delivery of related services.

CODES (5), and (6) are unassigned.

1032760

CODE (7) indicates that the committee has professional competence to review all probable proposals to DHEW except those involving surgical or investigational new drug studies.

CODE (8) is currently unassigned.

CODE (9) usually indicates that the institution's assurance and implementation does not cover all of its components, or that type (2), (3), or (4) restrictions apply to one or more components. Please call the Human Subjects Protection Desk (301) 496-7005 for an explanation.

D. T. Chalkley

D. T. Chalkley, Ph.D.
Chief, Institutional Relations Branch
Division of Research Grants

1032761

0332	(7)ANNA STATE HOSPITAL	ANNA
1626	CHICAGO, UNIV OF, DIV OF BIOLOGICAL SCIENCES AND PRITZKER SCHOOL OF MEDICINE	CHICAGO
1626	(2)CHICAGO, UNIV OF, DIV OF SOCIAL SCIENCES, CTR FOR HLTH ADM STUDIES, GRAD SCHOOL OF EDU	CHICAGO
1626	(2)CHICAGO, UNIV OF, SCHOOL OF SOCIAL SERVICE ADM	CHICAGO
0182	EVANSTON HOSPITAL	EVANSTON
0430	HEALTH SCIENCES, UNIV OF/CHICAGO MEDICAL SCHOOL	CHICAGO
0053	HEKTOEN INSTITUTE FOR MEDICAL RESEARCH	CHICAGO
1561	(4)ILLINOIS STATE PSYCHIATRIC INSTITUTE	CHICAGO
0345	ILLINOIS, UNIV OF, AT CHICAGO CIRCLE	CHICAGO
0291	ILLINOIS, UNIV OF, MEDICAL CENTER CAMPUS INCLUDING THE CLINICAL SCHOOLS AT PEORIA AND ROCKFORD	CHICAGO
0102	ILLINOIS, UNIV OF, URBANA-CHAMPAIGN CAMPUS	URBANA
1373	(2)LINCOLN STATE SCHOOL	LINCOLN
0095	MICHAEL REESE HOSPITAL AND MEDICAL CENTER	CHICAGO
0518	(2)NORTHERN ILLINOIS UNIVERSITY	DEKALB
0190	NORTHWESTERN UNIVERSITY	CHICAGO
0190	NORTHWESTERN UNIVERSITY	EVANSTON
0175	RUSH-PRESBYTERIAN-ST LUKES MEDICAL CENTER	CHICAGO
0309	SOUTHERN ILLINOIS UNIVERSITY	CARBONDALE
2606	(2)SOUTHERN ILLINOIS UNIVERSITY	EDWARDSVILLE
1970	(4)WESTERN ILLINOIS UNIVERSITY	MACOMB

INDIANA

0314	(2)DEPAUW UNIVERSITY	GREENCASTLE
0945	(7)FORT WAYNE STATE HOSPITAL AND TRAINING CTR	FT WAYNE
0185	INDIANA UNIVERSITY AND INDIANA UNIV FDN	BLOOMINGTON
0185	INDIANA UNIVERSITY AND INDIANA UNIV FDN	INDIANAPOLIS
0185	INDIANA UNIVERSITY-PURDUE UNIVERSITY	INDIANAPOLIS
0185	INDIANA UNIVERSITY REGIONAL CAMPUSES AT FORT WAYNE, GARY, JEFFERSONVILLE, KOKOMO, RICHMOND, AND SOUTH BEND	
1397	INDIANAPOLIS CENTER FOR ADVANCED RESEARCH	INDIANAPOLIS
0883	LARUE D CARTER MEMORIAL HOSPITAL	INDIANAPOLIS
1697	MARION COUNTY ASSN FOR RETARDED CHILDREN, INC	INDIANAPOLIS
1246	METHODIST HOSPITAL OF INDIANA, INC	INDIANAPOLIS
1176	NEW CASTLE STATE HOSPITAL	NEW CASTLE

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1119	(7)NOTRE DAME, UNIVERSITY OF	NOTRE DAME
0131	(4)PURDUE UNIVERSITY AND PURDUE RESEARCH FDN	LAFAYETTE
	IOWA	
0343	(2)IOWA STATE UNIVERSITY OF SCIENCE AND TECHNOLOGY	AMES
0209	IOWA, UNIVERSITY OF	IOWA CITY
0856	(3)WOODWARD STATE HOSPITAL-SCHOOL	WOODWARD
	KANSAS	
0038	(4)KANSAS STATE UNIVERSITY	MANHATTAN
0157	(4)KANSAS, UNIVERSITY OF	LAWRENCE
0229	KANSAS, UNIVERSITY OF, MEDICAL CENTER	KANSAS CITY
0081	(4)MENNINGER FOUNDATION	TOPEKA
	KENTUCKY	
0223	KENTUCKY, UNIV OF, INCLUDING RESEARCH FDN	LEXINGTON
0527	(4)LOUISVILLE, UNIVERSITY OF, EXCEPT SCH OF MED	LOUISVILLE
0527	LOUISVILLE, UNIVERSITY OF, FOUNDATION	LOUISVILLE
0023	LOUISVILLE, UNIVERSITY OF, SCHOOL OF MEDICINE	LOUISVILLE
	LOUISIANA	
0262	(9)LOUISIANA STATE UNIV AND A & M COLL SYS	BATON ROUGE
2428	(2)LOUISIANA STATE UNIV IN BATON ROUGE	BATON ROUGE
2420	(4)UNIVERSITY OF NEW ORLEANS, LAKE FRONT	NEW ORLEANS
2485	LOUISIANA STATE UNIVERSITY MEDICAL CENTER	NEW ORLEANS
0137	(3)PINECREST STATE SCHOOL	PINEVILLE
0018	TULANE MEDICAL CENTER	NEW ORLEANS
2386	(2)TULANE UNIVERSITY EXCEPT MEDICAL CENTER	NEW ORLEANS

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032763

0357	EDSEL B FORD INSTITUTE	DETROIT
0357	HENRY FORD HOSPITAL	DETROIT
0615	MICHIGAN DEPT OF PUBLIC HEALTH	LANSING
0384	MICHIGAN STATE UNIVERSITY	EAST LANSING
0295	MICHIGAN, UNIVERSITY OF	ANN ARBOR
0008	SINAI HOSPITAL OF DETROIT	DETROIT
2483	VETERANS ADMINISTRATION HOSPITAL-ANN ARBOR	ANN ARBOR
0354	WAYNE STATE UNIVERSITY	DETROIT
0720	WESTERN MICHIGAN UNIVERSITY	KALAMAZOO

MINNESOTA

0065	HENNEPIN COUNTY GENERAL HOSPITAL	MINNEAPOLIS
0041	MAYO FOUNDATION	ROCHESTER
0065	MINNEAPOLIS MEDICAL RESEARCH FOUNDATION, INC	MINNEAPOLIS
0463	MINNESOTA, UNIVERSITY OF	AUSTIN
0463	MINNESOTA, UNIV OF	DULUTH
0463	MINNESOTA, UNIV OF	MINNEAPOLIS
0463	MINNESOTA, UNIV OF	MORRIS
0463	MINNESOTA, UNIV OF	ST PAUL
0463	MINNESOTA, UNIV OF, TECHNICAL COLLEGE	CROOKSTON
0463	MINNESOTA, UNIV OF, TECHNICAL COLLEGE	WASECA

MISSISSIPPI

0561	(2)MISSISSIPPI, UNIVERSITY OF	UNIVERSITY
0366	MISSISSIPPI, UNIVERSITY OF, MEDICAL CENTER	JACKSON

MISSOURI

0298	CANCER RESEARCH CENTER	COLUMBIA
2358	(2)CEMREL, INC	ST ANN
0298	ELLIS FISCHEL STATE CANCER HOSPITAL	COLUMBIA
0424	JEWISH HOSPITAL OF ST LOUIS	ST LOUIS
2365	(2)MID-CONTINENT REGIONAL EDUCATIONAL LABORATORY	KANSAS CITY
0292	(2)MISSOURI, UNIV OF, EXCEPT MEDICAL CENTER	COLUMBIA
0292	MISSOURI, UNIV OF, MEDICAL CENTER INCLUDING	COLUMBIA

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032764

	MISSOURI INSTITUTE OF PSYCHIATRY	
0292	MISSOURI, UNIV OF	KANSAS CITY
0292	(2)MISSOURI, UNIV OF	ROLLA
0292	(2)MISSOURI, UNIV OF	ST LOUIS
0292	MISSOURI, UNIV OF, REG MED PROG, ALL CAMPUSES	
0356	ST LOUIS UNIVERSITY	ST LOUIS
2056	VETERANS ADMINISTRATION HOSPITAL-KANSAS CITY	KANSAS CITY
0279	WASHINGTON UNIVERSITY	ST. LOUIS
2351	WASHINGTON UNIV SCHOOL OF MEDICINE	ST LOUIS
	NEBRASKA	
1120	CREIGHTON UNIVERSITY	OMAHA
1781	VETERANS ADMINISTRATION HOSPITAL-OMAHA	OMAHA
	NEVADA	
0762	(2)NEVADA, UNIVERSITY OF, RENO CAMPUS	RENO
	NEW HAMPSHIRE	
0427	(2)DARTMOUTH COLL FACULTY OF ARTS AND SCIENCES	HANOVER
0227	DARTMOUTH MEDICAL SCHOOL	HANOVER
1006	(4)NEW HAMPSHIRE HOSPITAL	CONCORD
1006	(4)NEW HAMPSHIRE STATE DIVISION OF MENTAL HEALTH	CONCORD
	NEW JERSEY	
0981	(2)EDUCATIONAL TESTING SERVICE	PRINCETON
0349	NEW JERSEY, COLL OF MEDICINE AND DENTISTRY OF	NEWARK
0349	NEW JERSEY DENTAL SCHOOL	JERSEY CITY
0349	NEW JERSEY MEDICAL SCHOOL	NEWARK
0837	NEWARK BETH ISRAEL MEDICAL CENTER	NEWARK
0570	(2)PRINCETON UNIVERSITY	PRINCETON
0349	RUTGERS MEDICAL SCHOOL	PISCATAWAY

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0300	(4)RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY	CAMDEN
0300	(4)RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY	NEW BRUNSWICK
0300	(4)RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY	NEWARK

NEW MEXICO

0141	LOVELACE FOUNDATION FOR MED ED AND RES	ALBUQUERQUE
0472	NEW MEXICO, UNIVERSITY OF	ALBUQUERQUE
0353	NEW MEXICO, UNIVERSITY OF, HEALTH SCIENCES GROUP-SCHOOL OF MEDICINE, COLLEGES OF PHARMACY AND NURSING	ALBUQUERQUE

NEW YORK

2129	(4)AMERICAN HEALTH FOUNDATION	NEW YORK
2116	(2)BARNARD COLLEGE	NEW YORK
0341	BETH ISRAEL MEDICAL CENTER	NEW YORK
0423	BRONX-LEBANON HOSPITAL CENTER	NEW YORK
1064	BROOKHAVEN NATIONAL LABORATORY MEDICAL DEPARTMENT	UPTON
2368	(2)CENTER FOR URBAN EDUCATION	NEW YORK
2277	(2)CHILD WELFARE LEAGUE OF AMERICA	NEW YORK
0381	CHILDRENS HOSPITAL OF BUFFALO	BUFFALO
0437	(2)COLUMBIA UNIV, EXCEPT HEALTH SCIENCES DIV	NEW YORK
0034	COLUMBIA UNIV HEALTH SCIENCES DIV INCLUDING COLLEGE OF PHYSICIANS AND SURGEONS, SCHOOLS OF PUBLIC HEALTH AND ADMINISTRATIVE MEDICINE, NURSING, AND ORAL AND DENTAL SURGERY	NEW YORK
0373	(2)COLUMBIA UNIVERSITY TEACHERS COLLEGE	NEW YORK
0526	COMMUNITY BLOOD COUNCIL OF GREATER NEW YORK	NEW YORK
0063	(3)CORNELL UNIV, EXCEPT MED COLL AND SCH OF NURS	ITHACA
0245	CORNELL UNIV, MEDICAL COLLEGE	NEW YORK
0109	EASTMAN DENTAL CENTER	ROCHESTER
0456	HEALTH RESEARCH, INC, ALBANY DIVISION	ALBANY
0456	HEALTH RESEARCH, INC ROSWELL PARK DIVISION	BUFFALO
0456	HOMER FOLKS TUBERCULOSIS HOSPITAL	ONEONTA
0621	HOSPITAL FOR JOINT DISEASES AND MED CENTER	NEW YORK
0047	HOSPITAL FOR SPECIAL SURGERY	NEW YORK
1005	(4)JEWISH BOARD OF GUARDIANS	NEW YORK
0368	JEWISH HOSPITAL AND MEDICAL CENTER OF BROOKLYN	BROOKLYN

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0369	KINGSBROOK JEWISH MED CTR & ISAAC ALBERT RES INST	NEW YORK
2375	LONG ISLAND JEWISH-HILLSIDE MEDICAL CENTER	NEW HYDE PARK
0397	MAIMONIDES MEDICAL CENTER	BROOKLYN
0086	MARY IMOGENE BASSETT HOSPITAL	COOPERSTOWN
2518	MEADOWBROOK MEDICAL EDUCATION AND RES FDN	EAST MEADOW
0383	MEMORIAL HOSP FOR CANCER AND ALLIED DISEASES	NEW YORK
0059	MONTEFIORE HOSPITAL AND MEDICAL CENTER	NEW YORK
0139	MOUNT SINAI SCHOOL OF MEDICINE	NEW YORK
2518	NASSAU COUNTY MEDICAL CENTER	EAST MEADOW
0173	(2)NEW SCHOOL FOR SOCIAL RESEARCH	NEW YORK
0526	NEW YORK BLOOD CENTER	NEW YORK
1370	(4)NEW YORK CITY DEPARTMENT OF HEALTH	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF, BRONX COMMUNITY COLL	BRONX
0765	(2)NEW YORK, CITY UNIV OF, BROOKLYN COLLEGE	BROOKLYN
0765	(2)NEW YORK, CITY UNIV OF, CITY COLLEGE	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF GRAD SCH AND UNIV CTR	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF, HERBERT H LEHMAN COLL	BRONX
0765	(2)NEW YORK, CITY UNIV OF, HOSTOS COMMUNITY COLL	BRONX
0765	(2)NEW YORK, CITY UNIV OF, HUNTER COLLEGE	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF, JOHN JAY COLLEGE OF CRIMINAL JUSTICE	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF, KINGSBOROUGH CMTY COLL	BROOKLYN
0765	(2)NEW YORK, CITY UNIV OF, LAGUARDIA CMTY COLL	LONG ISLAND
0765	(2)NEW YORK, CITY UNIV OF, MANHATTAN CMTY COLL	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF, NEW YORK CITY CMTY COLL	BROOKLYN
0765	(2)NEW YORK, CITY UNIV OF, QUEENS COLLEGE	FLUSHING
0765	(2)NEW YORK, CITY UNIV OF, QUEENSBOROUGH CMTY COLL	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF, RESEARCH FOUNDATION	NEW YORK
0765	(2)NEW YORK, CITY UNIV OF, RICHMOND COLLEGE	STATEN ISLAND
0765	(2)NEW YORK, CITY UNIV OF, STATEN ISLAND CMTY COLL	STATEN ISLAND
0765	(2)NEW YORK, CITY UNIV OF, YORK COLLEGE	JAMAICA
0456	NEW YORK DEPARTMENT OF HEALTH	ALBANY
0624	(9)NEW YORK DEPARTMENT OF MENTAL HYGIENE	ALBANY
0208	NEW YORK MEDICAL COLLEGE-FLOWER AND FIFTH AVENUE HOSPITALS INCLUDING METROPOLITAN HOSPITAL AND BIRD S. COLER MEMORIAL HOSPITAL	NEW YORK
0456	NEW YORK STATE REHABILITATION HOSPITAL	WEST HAVERSTRAW
0374	(2)NEW YORK, STATE UNIV OF, AT ALBANY	ALBANY
0508	(3)NEW YORK, STATE UNIV OF, AT BINGHAMTON	BINGHAMTON
0163	NEW YORK, STATE UNIV OF, AT BUFFALO	BUFFALO
0596	NEW YORK, STATE UNIV OF, AT STONY BROOK	STONY BROOK

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0474	(7)NEW YORK, STATE UNIV OF, COLLEGE AT BROCKPORT	BROCKPORT
0506	NEW YORK, STATE UNIV OF, COLLEGE AT BUFFALO	BUFFALO
0259	(4)NEW YORK, STATE UNIV OF, COLLEGE AT CORTLAND	CORTLAND
0457	NEW YORK, STATE UNIV OF, COLLEGE OF ARTS AND SCIENCES AT GENESEO	GENESEO
0386	(2)NEW YORK, STATE UNIV OF, COLLEGE AT OSWEGO	OSWEGO
0220	NEW YORK, STATE UNIV OF, COLLEGE OF FORESTRY	SYRACUSE
0305	NEW YORK, STATE UNIV OF, DOWNSTATE MED CTR	BROOKLYN
0127	NEW YORK, STATE UNIV OF, UPSTATE MED CTR	SYRACUSE
0390	(2)NEW YORK UNIVERSITY, EXCLUSIVE OF THE MED CTR	NEW YORK
0405	NEW YORK UNIVERSITY MEDICAL CENTER	NEW YORK
0788	NORTH SHORE HOSPITAL	MANHASSET
0612	(2)POLYTECHNIC INSTITUTE OF NEW YORK	BROOKLYN
2247	PUBLIC HEALTH RESEARCH INSTITUTE	NEW YORK
1001	RENSSELAER POLYTECHNIC INSTITUTE	TROY
0624	(9)RESEARCH FOUNDATION FOR MENTAL HYGIENE	ALBANY
0172	ROCHESTER, UNIVERSITY OF	ROCHESTER
0230	ROCKEFELLER UNIVERSITY	NEW YORK
2036	(4)ROCKLAND COUNTY HEALTH AND SOCIAL SERVICES COMP	POMONA
0491	ROOSEVELT HOSPITAL	NEW YORK
0456	ROSWELL PARK MEMORIAL INSTITUTE	BUFFALO
0536	SLOAN-KETTERING INSTITUTE FOR CANCER RES	NEW YORK
0076	ST LUKES HOSPITAL CENTER	NEW YORK
0376	ST VINCENTS HOSP AND MED CTR OF N Y	NEW YORK
0280	(2)SYRACUSE UNIVERSITY	SYRACUSE
2438	TRUDEAU INSTITUTE	SARANAC LAKE
0621	RESEARCH INSTITUTE FOR SKELETOMUSCULAR DISEASES	NEW YORK
0217	UNION UNIVERSITY, ALBANY MEDICAL COLLEGE	ALBANY
1740	VETERANS ADMINISTRATION HOSPITAL-BRONX	NEW YORK
2045	VETERANS ADMINISTRATION HOSPITAL-NORTHPORT	NORTHPORT
0002	YESHIVA UNIV, ALBERT EINSTEIN COLL OF MED	BRONX

NORTH CAROLINA

0699	CHARLOTTE MEMORIAL HOSPITAL	CHARLOTTE
0191	DUKE UNIVERSITY	DURHAM
2382	(2)NATIONAL LABORATORY FOR HIGHER EDUCATION	DURHAM
2242	(2)NORTH CAROLINA A & T STATE UNIVERSITY	GREENSBORO
0285	(2)NORTH CAROLINA STATE UNIVERSITY AT RALEIGH	RALEIGH
0177	NORTH CAROLINA, UNIVERSITY OF, AT CHAPEL HILL	CHAPEL HILL
0242	WAKE FOREST UNIVERSITY, BOWMAN GRAY SCH OF MED	WINSTON-SALEM

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1087	(2)WAKE FOREST UNIVERSITY, EXCEPT SCH OF MEDICINE	WINSTON-SALEM
0078	(2)WESTERN CAROLINA CENTER	MORGANTON

OHIO

0485	(2)AKRON, UNIVERSITY OF	AKRON
0544	(2)BOWLING GREEN STATE UNIVERSITY	BOWLING GREEN
1167	CASE WESTERN RESERVE UNIVERSITY	CLEVELAND
0088	CHILDRENS HOSPITAL & RESEARCH FOUNDATION	CINCINNATI
0249	CHILDRENS HOSPITAL RESEARCH FOUNDATION	COLUMBUS
0667	CINCINNATI, UNIV OF, EXCEPT MEDICAL CENTER	CINCINNATI
0337	CINCINNATI, UNIV OF, MEDICAL CENTER	CINCINNATI
0502	CLEVELAND CLINIC FDN & EDUCATIONAL FDN	CLEVELAND
0171	(4)CLEVELAND PSYCHIATRIC INSTITUTE	CLEVELAND
1004	FAIRHILL MENTAL HEALTH CENTER	CLEVELAND
0160	FELS RESEARCH INSTITUTE	YELLOW SPRINGS
1936	JEWISH HOSPITAL ASSN INCLUDING THE HOSPITAL, CHILDRENS PSYCHIATRIC CTR, SCH OF NURSING, AND MAY INSTITUTE FOR MEDICAL RESEARCH	CINCINNATI
0542	KENT STATE UNIVERSITY	KENT
0269	MOUNT SINAI HOSPITAL OF CLEVELAND	CLEVELAND
1724	OHIO, MEDICAL COLLEGE OF, AT TOLEDO	TOLEDO
0121	OHIO STATE UNIV & RESEARCH FOUNDATION	COLUMBUS
0662	ST LUKES HOSPITAL	CLEVELAND
0626	ST VINCENT CHARITY HOSPITAL	CLEVELAND
0350	UNIVERSITY HOSPITALS OF CLEVELAND	CLEVELAND

OKLAHOMA

0327	OKLAHOMA MEDICAL RESEARCH FOUNDATION	OKLAHOMA CITY
2402	(2)OKLAHOMA, UNIV OF	NORMAN
0241	OKLAHOMA, UNIV OF, HEALTH SCIENCES CENTER	OKLAHOMA CITY

OREGON

0134	GOOD SAMARITAN HOSPITAL AND MEDICAL CENTER	PORTLAND
0214	KAISER FOUNDATION RESEARCH INSTITUTE	PORTLAND

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0043	MEDICAL RESEARCH FOUNDATION OF OREGON	PORTLAND
2399	(2)NORTHWEST REGIONAL EDUCATIONAL LABORATORY	PORTLAND
0505	(2)OREGON RESEARCH INSTITUTE	EUGENE
0111	(7)OREGON STATE UNIVERSITY	CORVALLIS
0048	OREGON, UNIV OF, DENTAL SCHOOL	PORTLAND
0288	(2)OREGON, UNIV OF, GRADUATE SCHOOL	EUGENE
0281	OREGON, UNIV OF, MEDICAL SCHOOL	PORTLAND

PENNSYLVANIA

0125	ALBERT EINSTEIN MEDICAL CENTER	PHILADELPHIA
0952	ALLEGHENY GENERAL HOSPITAL	PITTSBURGH
0784	(2)AMERICAN INSTITUTES FOR RESEARCH	PITTSBURGH
0338	ARTHUR P. NOYES RESEARCH FOUNDATION, INC	NORRISTOWN
0444	BRYN MAWR HOSPITAL	BRYN MAWR
0444	BRYN MAWR HOSPITAL, JOHN S SHARPE RES FDN OF	BRYN MAWR
0436	(2)BUCKNELL UNIVERSITY	LEWISBURG
1218	(2)CARNEGIE-MELLON UNIVERSITY	PITTSBURGH
2566	CHILDRENS HEART HOSPITAL OF PHILADELPHIA	PHILADELPHIA
0129	CHILDRENS HOSPITAL OF PHILADELPHIA	PHILADELPHIA
0360	CHILDRENS HOSPITAL OF PITTSBURGH	PITTSBURGH
1556	FRANKLIN INSTITUTE	PHILADELPHIA
0475	HAHNEMANN MEDICAL COLLEGE AND HOSPITAL	PHILADELPHIA
0045	INSTITUTE FOR CANCER RESEARCH	PHILADELPHIA
0273	LANKENAU HOSPITAL	PHILADELPHIA
0189	MAGEE-WOMENS HOSPITAL	PITTSBURGH
2121	(2)MARYWOOD COLLEGE	SCRANTON
0338	NORRISTOWN STATE HOSPITAL	NORRISTOWN
0333	PENNSYLVANIA HOSPITAL	PHILADELPHIA
0222	PENNSYLVANIA, MEDICAL COLLEGE OF	PHILADELPHIA
0573	(4)PENNSYLVANIA STATE UNIVERSITY & CMNWLTH CAMPS	UNIVERSITY PARK
1668	PENNSYLVANIA STATE UNIVERSITY MILTON S HERSHEY MEDICAL CENTER	HERSHEY
0012	PENNSYLVANIA, UNIVERSITY OF	PHILADELPHIA
1531	PHILADELPHIA DEPARTMENT OF PUBLIC HEALTH	PHILADELPHIA
0044	PHILADELPHIA GENERAL HOSPITAL	PHILADELPHIA
0344	PHILADELPHIA PSYCHIATRIC CENTER	PHILADELPHIA
0881	PHILADELPHIA STATE HOSPITAL	PHILADELPHIA
1532	(4)PITTSBURGH CHILD GUIDANCE CENTER	PITTSBURGH
0418	PITTSBURGH, UNIVERSITY OF	PITTSBURGH
2200	PRESBYTERIAN-UNIVERSITY HOSPITAL	PITTSBURGH

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032770

0465	PRESBYTERIAN-UNIV OF PENNSYLVANIA MED CTR	PHILADELPHIA
2264	(2)RESEARCH FOR BETTER SCHOOLS, INC.	PHILADELPHIA
0795	ST JOSEPH HOSPITAL RESEARCH INSTITUTE	LANCASTER
0334	TEMPLE UNIVERSITY	PHILADELPHIA
0049	THOMAS JEFFERSON UNIVERSITY, ALL COMPONENTS	PHILADELPHIA
0952	WILLIAM H SINGER MEMORIAL RESEARCH INSTITUTE OF ALLEGHENY GENERAL HOSPITAL	PITTSBURGH
0362	WILLS EYE HOSPITAL AND RESEARCH INSTITUTE	PHILADELPHIA
0054	WISTAR INSTITUTE	PHILADELPHIA

RHODE ISLAND

0467	BROWN UNIVERSITY	PROVIDENCE
0318	RHODE ISLAND HOSPITAL	PROVIDENCE
2212	ROGER WILLIAMS GENERAL HOSPITAL	PROVIDENCE

SOUTH CAROLINA

0533	AIKEN-BARNWELL MENTAL HEALTH CENTER	AIKEN
0533	ANDERSON-OCONEE-PICKENS MENTAL HEALTH CTR	ANDERSON
0533	BECKMAN CENTER FOR MENTAL HEALTH SERVICES	GREENWOOD
0533	CHARLESTON AREA MENTAL HEALTH CENTER	CHARLESTON
0533	COASTAL EMPIRE MENTAL HEALTH CENTER	BEAUFORT
0533	COLUMBIA AREA MENTAL HEALTH CENTER	COLUMBIA
0533	CRAFTS-FARROW STATE HOSPITAL	COLUMBIA
0533	FRIENDSHIP CENTER	COLUMBIA
0533	GEORGETOWN-HORRY MENTAL HEALTH CLINIC	CONWAY
0533	GREENVILLE AREA MENTAL HEALTH CENTER	GREENVILLE
0533	ORANGEBURG AREA MENTAL HEALTH CLINIC	ORANGEBURG
0533	PEE-DEE MENTAL HEALTH CENTER	FLORENCE
0533	SOUTH CAROLINA DEPARTMENT OF MENTAL HEALTH	COLUMBIA
0533	DIV OF ALCOHOL AND DRUG ADDICTION SERVICES	COLUMBIA
0533	DIV OF COMMUNITY MTI HLTH SERVICES SPEC PROJ	COLUMBIA
0533	LONG-TERM CARE SERVICES	COLUMBIA
0240	SOUTH CAROLINA, MEDICAL UNIVERSITY OF	CHARLESTON
0533	SOUTH CAROLINA STATE HOSPITAL	COLUMBIA
0629	(4)SOUTH CAROLINA, UNIVERSITY OF	COLUMBIA
0533	SOUTH CAROLINA WAR VETERANS HOME	COLUMBIA
0533	SPARTANBURG AREA MENTAL HEALTH CENTER	SPARTANBURG

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

0533	SUMTER-CLARENDON-KERSHAW MENTAL HEALTH CENTER	SUMTER
0533	TRI-COUNTY MENTAL HEALTH CENTER	BENNETTSVILLE
0533	WILLIAM S HALL PSYCHIATRIC INSTITUTE	COLUMBIA
0533	YORK-CHESTER-LANCASTER MENTAL HEALTH CENTER	ROCK HILL

TENNESSEE

1696	(4)ARLINGTON HOSPITAL AND SCHOOL	ARLINGTON
0393	MEHARRY MEDICAL COLLEGE	NASHVILLE
1716	OAK RIDGE ASSOCIATED UNIVERSITIES, INC.	OAK RIDGE
1716	OAK RIDGE NATIONAL LABORATORY	OAK RIDGE
0648	ST JUDE CHILDRENS RESEARCH HOSPITAL	MEMPHIS
0170	TENNESSEE, UNIV OF, MEDICAL UNITS	MEMPHIS
0124	TENNESSEE, UNIVERSITY OF - KNOXVILLE	KNOXVILLE
0401	VANDERBILT UNIVERSITY	NASHVILLE
1800	VETERANS ADMINISTRATION HOSPITAL-MEMPHIS	MEMPHIS

TEXAS

0307	BAYLOR COLLEGE OF MEDICINE	HOUSTON
0813	(2)BAYLOR UNIVERSITY	WACO
1843	BEXAR COUNTY HOSPITAL DISTRICT	SAN ANTONIO
2344	(2)SOUTHWEST EDUCATIONAL DEVELOPMENT CORPORATION	AUSTIN
2344	(2)SOUTHWEST EDUCATIONAL DEVELOPMENT LABORATORY	AUSTIN
1045	(2)TEXAS A & M UNIV, COLLEGE STATION CAMPUS ONLY	COLLEGE STATION
0590	TEXAS INSTITUTE FOR REHAB AND RESEARCH	HOUSTON
1121	(7)TEXAS, UNIV OF, AT ARLINGTON	ARLINGTON
0123	(9)TEXAS, UNIV OF, AT AUSTIN	AUSTIN
0669	TEXAS, UNIV OF, AT HOUSTON DENTAL BRANCH	HOUSTON
2615	TEXAS, UNIV OF, HEALTH SCIENCE CTR AT DALLAS INCLUDING SW MED SCH, GRAD SCH OF BIOMEDICAL SCIENCES, AND SCH OF ALLIED HEALTH SCIENCES	DALLAS
2255	TEXAS, UNIV. OF, HEALTH SCIENCE CTR-SAN ANTONIO INCLUDING MED SCH, DENTAL SCH, AND GRAD SCH OF BIOMEDICAL SCIENCES	SAN ANTONIO
0113	TEXAS, UNIV OF, M D ANDERSON HOSP AND TUMOR INS	HOUSTON
0107	TEXAS, UNIV OF, MEDICAL BRANCH AT GALVESTON	GALVESTON

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

1032772

	UTAH	
0933	(2)BRIGHAM YOUNG UNIVERSITY	PROVO
2426	DESERET FOUNDATION FOR MED EDU AND RES	SALT LAKE CITY
0235	UTAH, UNIVERSITY OF	SALT LAKE CITY
	VERMONT	
0194	VERMONT, UNIVERSITY OF	BURLINGTON
2335	VETERANS ADM CENTER-WHITE RIVER JUNCTION	WHITE RIVER JCT
	VIRGINIA	
2275	(9)HUMAN RESOURCES RESEARCH ORGANIZATION	ALEXANDRIA
0634	LYNCHBURG TRAINING SCHOOL AND HOSPITAL	MADISON HEIGHTS
0239	VIRGINIA COMMONWEALTH UNIVERSITY, MEDICAL COLLEGE OF VIRGINIA, HEALTH SCIENCES DIV	RICHMOND
0306	VIRGINIA, UNIVERSITY OF	CHARLOTTESVILLE
0575	(2)WILLIAM AND MARY, COLLEGE OF	WILLIAMSBURG
	WASHINGTON	
0522	CHILDRENS ORTHOPEDIC HOSPITAL AND MED CTR	SEATTLE
2627	FRED HUTCHINSON CANCER RESEARCH CENTER	SEATTLE
0029	PACIFIC NORTHWEST RESEARCH FOUNDATION	SEATTLE
0900	VIRGINIA MASON RESEARCH CENTER INCLUDING MASON CLINIC AND VIRGINIA MASON HOSPITAL	SEATTLE
1717	WASHINGTON DEPT OF SOCIAL AND HEALTH SERVICES	OLYMPIA
0105	(3)WASHINGTON STATE UNIVERSITY	PULLMAN
0299	WASHINGTON, UNIVERSITY OF	SEATTLE
	WEST VIRGINIA	
2376	(2)APPALACHIA EDUCATIONAL LABORATORY, INC	CHARLESTON
0431	WEST VIRGINIA UNIVERSITY	MORGANTOWN

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

	WISCONSIN	
0315	CENTRAL WISCONSIN COLONY AND TRAINING SCH	MADISON
2132	(2)LAWRENCE UNIVERSITY	APPLETON
0387	MARQUETTE UNIVERSITY	MILWAUKEE
0763	MENDOTA STATE HOSPITAL	MENDOTA
0503	(4)SOUTHERN WISCONSIN COLONY AND TRAINING SCH	UNION GROVE
0077	WISCONSIN, MEDICAL COLLEGE OF	MILWAUKEE
0319	WISCONSIN, UNIVERSITY OF, MADISON CAMPUS	MADISON
2106	(2)WISCONSIN, UNIVERSITY OF, PARKSIDE	KENOSHA
0256	PUERTO RICO, UNIV OF, MEDICAL SCIENCES CAMPUS	SAN JUAN
1188	LEONARD WOOD MEMORIAL (AMERICAN LEPROSY FDN), PHILIPPINE DIVISION OF	CEBU
	SWITZERLAND	
1137	WORLD HEALTH ORGANIZATION	GENEVA
	UNITED KINGDOM	
1080	LONDON, UNIV OF, INSTITUTE OF NEUROLOGY	LONDON

TOTAL INSTITUTIONS WITH ACCEPTABLE GENERAL ASSURANCES 569

RESTRICTION CODE
(2) NO MEDICAL, SURGICAL OR IND STUDIES
(3) NO IND STUDIES
(4) NO SURGICAL STUDIES
(5-6)UNASSIGNED
(7) NO SURGICAL OR IND STUDIES

(9) COMPLEX RESTRICTION (CALL 301-496-7005 FOR DETAILS)

Form Approved
OMB No. 68-R1143

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

IDENTIFICATION NUMBER (If known)

PROTECTION OF HUMAN SUBJECTS CERTIFICATION

☐ Contract ☐ New
☐ Grant ☐ Renewal
☐ Fellowship ☐ Continuation

STATEMENT OF POLICY: Safeguarding the rights and welfare of human subjects involved in activities supported by grants or contracts from the DHEW is the responsibility of the institution which receives or is accountable to the DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of the Department that no grant or contract for an activity involving human subjects shall be made unless the application for such support has been reviewed and approved by an appropriate institutional committee. (Reference: "Institutional Guide to DHEW Policy on the Protection of Human Subjects.")

1. TITLE OF PROPOSAL

2. PROJECT DIRECTOR/PROGRAM DIRECTOR/FELLOW

POSITION TITLE

3. INSTITUTIONAL COMPONENT OR DEPARTMENT

4. CHECK ONE OF THE FOLLOWING STATEMENTS AS APPLICABLE:

☐ A. This application does not propose any activities that would invo[illegible] ngs who might be considered subjects, human material, or personal[illegible] y or secondary sources.

☐ B. This is to CERTIFY that this application which d[illegible] human subjects has been reviewed and approved the date of_____ in accor[illegible] institutional assurance on file with [illegible] certification is invalid if revie[illegible] year.)

☐ C. This is to CERTIFY th[illegible] is pending review [illegible] policy and the [illegible] does not [illegible] office [illegible] [illegible]jects [illegible].n the DHEW [illegible] committee [illegible].ied, the agency [illegible]tely by telephone, [illegible]d or planned date of

☐ D. T[illegible] [illegible]jects. This institution does not no[illegible] the DHEW. I understand that information on [illegible] [illegible]eived should the application become eligible for [illegible]

FOR COPIES CALL (301) 496-7005 OR WRITE TO THE INSTITUTIONAL RELATIONS BRANCH

5. SIGNATURE OF INSTITUTIONAL OFFICIAL AUTHORIZED TO SIGN PROPOSALS | DATE

6. TITLE | TELEPHONE NO. (Code, No., Extension)

7. NAME AND ADDRESS OF INSTITUTION (Street, City, State, zip code)

NOTE TO AGENCY: This form should NOT be included with application forms that have provision for human subject certification. It may be used to request certification, or correction of certification.

HEW 596 (Formerly NIH 1611)
8-72

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO THE AGENCY REQUESTING ITS COMPLETION

0032116

UNITED STATES GOVERNMENT

2-Way Memo

Finalized
JWR 10/11/74

DATE OF MESSAGE	9/6/74
DATE OF REPLY	10/11/74

INSTRUCTIONS
Use routing symbols whenever possible.
SENDER:
Forward original and one copy. Conserve space.
RECEIVER:
Reply below the message, keep one copy, return one copy.

Object: FIRST INTERIM AUDIT REPORT ON EXAMINATION OF PATIENT SELECTION CRITERIA AT OAK RIDGE ASSOCIATED UNIVERSITIES, CONTRACT NO. AT(40-1)-GEN-33, FISCAL YEAR 1974, ASSIGNMENT NO. 4-02-1

From: J. W. Rose, Jr., Assistant Treasurer
Oak Ridge Associated Universities

5027—101

FOLD — FOLD

USE BRIEF, INFORMAL LANGUAGE

Attached are two copies of the subject audit report for your review, comment, and return. Please let us have your comments by September 30, 1974.

HAH/jd

Report with management comments handed to Mr Sam Kalfes of A.C.C. at OAK Admin. Bldg. to deliver to Mr Mark Lee at A.C.C. on 10-11-74 -

JWR 10/11/74

To: M. A. Lee, Chief
Audit Branch

REC'D. MEDICAL DIVISION 10 Oct 74

1032776 — 2. TO BE RETURNED TO ORIGINATOR

OPTIONAL FORM 27
OCTOBER 1962
GSA GEN. REG. NO. 27

FIRST INTERIM AUDIT REPORT
ON EXAMINATION OF PATIENT SELECTION CRITERIA
AT OAK RIDGE ASSOCIATED UNIVERSITIES
CONTRACT NO. AT(40-1)-GEN-33
FISCAL YEAR 1974

ASSIGNMENT NO.: 4-02-1
DATE:

1032777

ASSIGNMENT NO.: 4-02-1
DATE:

TO : Manager of Operations, ORO

THROUGH: Director of Finance, ORO

FROM : Chief, Audit Branch, Finance Division, ORO

SUBJECT: FIRST INTERIM AUDIT REPORT ON EXAMINATION OF PATIENT SELECTION CRITERIA AT OAK RIDGE ASSOCIATED UNIVERSITIES, CONTRACT NO. AT(40-1)-GEN-33, FISCAL YEAR 1974

SYMBOL : AFA:HAH/EAP

I. Purpose and Scope

The purpose of this audit was to examine the criteria and procedures used to select patients at the Oak Ridge Associated Universities (ORAU) Medical Division and to review and evaluate the controls which assure the establishment, maintenance, use and evaluation of the criteria.

II. Background

ORAU operates a hospital to perform research in selected areas of nuclear medicine. Because the type of patient is important to the outcome of the particular research being performed, patients must be selected who are compatible with research objectives. Selection criteria are made up of such items as type of disease, the patient's age, and previous treatments which the patient may or may not have undergone. Patient selection criteria are formulated and set forth in proposed research documents called protocols detailing the medical procedures proposed to accomplish research program objectives. Any medical procedure, other than regular patient care and generally accepted therapy, must be authorized by an approved research protocol.

Protocols and criteria contained therein developed by the Medical Division staff are approved by the Chief of Clinical Services and the Medical Division Chairman, as a part of the objectives of the research program. Protocols are then submitted to a Committee on Human Studies for further review and approval. The committee is composed of medical doctors from ORAU, ORNL, and other medical research institutions and one lawyer from UCCND. Protocol objectives are evaluated by the committee on the basis of their scientific merit and weighed against risks to which patients are exposed.

Weekly consultations are held in which the management of all patients is reviewed by the clinical staff and the Medical Division Chairman. At these consultations, the medical history of new in-patients is also reviewed thus providing a review of the compatibility of probable diagnosis with selection criteria.

1032778

Medical research information is acquired from the observations of in-patients. Information is also obtained from other patients called out-patients who are treated on a regular basis in an out-patient clinic. Out-patients may be former in-patients, potential in-patients, or patients with a disease that is related to one of the ongoing programs.

III. Summary of Findings

ORAU's practices generally conform to existing policies and procedures. There are instances in which improved controls and procedures appear to be warranted. The results of our examination and other comments are summarized below. References to detailed comments in Section IV of this report are shown parenthetically.

A. Selection Criteria

In two instances research protocol did not contain any written patient selection criteria (See IV.A.2.). We recommend that written patient selection criteria be included specifically in all research protocols or other documents related to the program for which patients are required.

Management Comments:

page=2=

The work on thyroid cancer started in 1950 and has in recent years consisted mainly of follow-up data collection. The use of surgery and radioiodine is now so widely accepted that it does not seem necessary to describe it in a research protocol.

A large gallium 67 program is described and documented (No. 9 in the book). The other ^{67}Ga study (No. 14 ~~was~~ was a very limited trial, ~~was a very limited~~, and a special study concerned with subcutaneous absorption. It has been completed and deactivated.

B. Selection Criteria Approval

1. Patient selection criteria formulated and approved by the Medical Division are reviewed by ORAU's Committee on Human Studies. This committee was established to conform to DHEW policies which the AEC has adopted.

1032779

The Chairman of ORAU's Medical Division serves as Chairman of the Committee on Human Studies, and the Chief of Clinical Services at times is listed as an active committee member. We believe that since both of these individuals have an active role in administering ORAU medical research programs, there is the appearance of a conflict of interest when, as committee members, they approve the use of humans in ORAU program (See IV B.2.a.). We recommend that ORAU review the composition of the Committee on Human Studies and change the status of the Chairman of the Medical Division and the Chief of Clinical Services to ex-officio members of the committee to relieve the appearance of a conflict of interest and comply with DHEW policy.

~~B-1-(page-3).~~

Dr. Edwards has been an exofficio member and when not listed as such, this was in error. Our committee requires unanimous approval of projects and the chairman does not vote. A special effort is made to prevent any influencing of the committee by any member who might have an interest in a project. It appears necessary that an ORAU staff member be in a position to activate meetings of the committee and be sure that reports are prepared. We are examining other mechanisms for meeting these questions.

2. Records of committee meetings [illegible] or no indication of committee deliberations and decisions concerning the review of patient selection criteria and particular research project applications (See IV.B.2.b.). We recommend that ORAU improve the documentation of the committee's meetings by recording in more detail the committee's discussion and decision concerning a particular research project application.

Management Comments:

~~page-3~~

2. The deliberations are reported in some detail when there is extensive discussion. In some instances the proposals are so non-controversial that little discussion occurs.

1032780

C. Patient Selection

We were unable to determine the criteria under which several persons were accepted as patients. A relative of a former staff member was assigned a patient number although no patient chart or other record of medical treatment could be found to indicate the probable diagnosis and protocol under which the patient was admitted. (See IV.C.2.a.).

One in-patient and one out-patient had a probable diagnosis which did not seem to meet any existing criteria for selection. The Medical Division maintains that the latter patients, in areas of related interests, were admitted for teaching purposes (See IV.C.2.b.). We recommend that only patients meeting established written criteria be admitted or accepted as patients, and that appropriate records be maintained which justify the admission. If the study of patients outside the specific areas of research interest is needed for continue physician competency and growth, any cases selected on this basis should be openly recorded and documented as such. We further recommend that ORAU define their physicians' related areas of interest, establish appropriate patient selection criteria for these areas, and also seek AEC concurrence for the level of effort to be expended.

Management Comments:

C. Only a very minute portion of the Medical Division's effort has been devoted to patients not directly in planned programs. The rare exceptions involve scientific and humanitarian considerations which we are not able to circumscribe in bureaucratic language.

D. Patients From Consultation and Contractual Services

ORAU physicians furnish free consultations to physicians who have patients in the Oak Ridge Hospital of the Methodist Church (ORHMC). These consultations are separate from services in nuclear medicine performed under a contract between ORAU and ORHMC. Sometimes ORAU laboratory analysis of human material is involved. In addition, the Chief of Clinical Services consults regularly in Knoxville and with referring physicians in other nearby communities. (See IV.D.2.b.).

1032781

The practice of medicine by ORAU physicians with respect to non-ORAU patients, that is activities in which the AEC may have no interest or knowledge, may possibly expose the physicians, ORAU and ultimately AEC to claims from patients or families.

We recommend that ORAU carefully examine all activities of staff physicians to determine the potential for such claims and liabilities to ORAU and to the AEC, and that AEC endorsement be obtained of those related interests which are of benefit to the AEC programs and of the level of effort to be expended in relationship to the degree of identified risk.

Management Comments:

D. We have been repeatedly encouraged to broaden the relationships of the Division and to avoid the criticism that we are isolated. We have been encouraged by AEC to become involved in the East Tennessee Cancer Research Center and have done so. Such contacts made possible the referral of patients for our research programs. The Chairman of the Division is aware of the level of these activities and considers them authorized functions under the Commission's program.

IV. Detailed Comments

A. Selection Criteria

1. Audit Coverage

The existence of patient selection criteria was identified Because criteria are generally contained in research protocols, we examined all protocols and related records. The relation of criteria to program objectives was reviewe together with the conversion of criteria to the kind and type of patient required.

2. Comment

No written patient selection criteria was found for those patients accepted for treatment under protocol number 5, "Use of Radioiodine in Surgical Removal of Thyroid Cancer, and protocol number 14, "Tracer Study with ^{67}Ga."

1032782

B. Selection Criteria Approval

1. Audit Coverage

We reviewed the procedures for the establishment, review and update of patient selection criteria. We also determined how criteria were communicated to those selecting patients and how the adequacy of criteria was evaluated.

2. Comment

a. There is a potential conflict of interest because two of the ORAU medical doctors on the Committee on Human Studies have an active role in administering ORAU medical programs. The chairman of ORAU's Medical Division serves as the Chairman of the Committee on Human Studies. The Chief of Clinical Services is listed at times as an active committee member and at other times as an ex-officio member. DHEW policy for committees reviewing use of humans in research, which AEC has adopted, states that committee members will be excluded from reviews of projects in which they have an active role or a conflict of interest. A conflict of interest may appear to exist if it appears that the Chairman of the Medical Division and the Chief of Clinical Services participate in decisions to approve the use of humans in ORAU research programs for which they have helped to formulate the medical procedure to be followed and under which they may actively participate in selecting and treating patients.

b. ORAU's committee records, which detail the review and approval of patient selection criteria, consist of meeting minutes, review and action forms, and project applications. At times committee minutes and review and action forms contained little or no indication of committee deliberations on a particular project. A significant number of review and action forms were unsigned by the designated committee members leaving some doubt as to their status as an official record.

C. Patient Selection

1. Audit Coverage

The procedures for selecting patients were examined to determine the assignment of responsibility for patient selection, the controls to assure adherence to selection criteria and to determine if selection criteria had been converted into the kinds and types of information needed about patients to permit an evaluation of their possible

1032783

acceptance. The possible impact on objectives of not having or failure to follow criteria was also considered. A representative sample of patient numbers was chosen for detailed review with the Chief of Clinical Services of probable diagnosis and applicable protocols.

2. Comments

a. In one instance, a patient number (2128) had been assigned to the wife of a physician who was employed by ORAU at the time as a clinician. No patient chart or other record of medical treatment was found. We were unable to determine if the patient met any selection criteria existing at the time.

b. Although hyperthyroidism was not a medical condition under study, one in-patient (Patient Number 2585) and one out-patient (Patient Number 2467) were accepted for treatment with only this diagnosis. The Division chairman stated that they have admitted some patients with hyperthyroidism for "teaching purposes," to obtain scans and illustrative material for physician's courses and as broadening experience for resident physicians.

D. Patients From Consultation and Contractual Services

1. Audit Coverage

The sample of patient numbers referred to previously (IV.C.1), revealed that some human materials were received for analysis from outside ORAU for which patient numbers were assigned. This led to an examination of contractual relations between ORAU and the Oak Ridge Hospital of the Methodist Church (ORHMC) under which some ORHMC patients also became ORAU patients. The subject of consultations between ORAU physicians and physicians at ORHMC and surrounding communities was also reviewed.

2. Comments

a. A contract between ORAU and the ORHMC by which ORAU provided certain services in nuclear medicine for a fee, expired in August 1971, and had not been renewed, although services continued to be rendered. ORAU became aware of this lapse in 1973 and has since reinstated the contract.

1032784

b. ORAU physicians consult with physicians who have patients in the ORHMC separate from the above contract. On occasion, human material from these patients is analyzed in ORAU Medical Division laboratories. ORAU patient numbers are assigned. No fees appear to be involved. In addition, the Chief of Clinical Services consults regularly in Knoxville, and from time to time with referring physicians in other nearby communities, although no formal recognition of these activities nor their extent has been made by AEC. It seems that these activities may expose ORAU, its physicians, and ultimately AEC to claims and liabilities. The benefit to AEC programs and AEC knowledge of and agreement to these activities is not well established in the documentation available to us.

c. We were unable to determine if ORAU insurance would afford any measure of protection under the circumstances described above.

M. A. Lee
Chief, Audit Branch

Harrel/Piercy:kmp

1032785

Oak Ridge Associated Universities
Incorporated
P.O. Box 117 - Oak Ridge, Tennessee 37830
Telephone 615 483-8411

October 18, 1974

Howard —

Mr. Joseph A. Lenhard, Director
Research and Technical Support Division
U. S. Atomic Energy Commission
Oak Ridge, Tennessee 37830

Subject: FIRST INTERIM AUDIT REPORT - PATIENT SELECTION CRITERIA - ORAU, FY 74 - MANAGEMENT COMMENT

Dear Mr. Lenhard:

The subject audit report, designated Assignment No. 4-02-1, was hand carried to ORAU in draft for management review and comment.

The audit was performed in a comprehensive and careful manner. Many of the findings could prove of real value in the management of this activity. They have been reviewed by our staff physicians, and notes have been made for future reference.

Detailed comment does not appear pertinent at this time, inasmuch as clinical in-patient operations by ORAU have been in the process of termination for several weeks. Because of this, it is not now anticipated that patient selection criteria for admittance of patients to hospital care will be required in the future.

ORAU Medical Division Programs are under review, and new or revised programs have not yet been authorized. Should future programs require patient selection criteria, our Medical Division will give careful attention to the findings and recommendations of the audit report.

It is our view that further comment at this time would not be relevant to present operations. Should you need additional information regarding past practices, we would be pleased to respond.

Sincerely yours,

PHILIP L. JOHNSON

Philip L. Johnson
Executive Director

PME:kb

bc: Dr. Andrews
Mr. Rose

Copy to Mr. [illegible]

0132786

UNITED STATES
ATOMIC ENERGY COMMISSION
OAK RIDGE OPERATIONS
P.O. BOX E
OAK RIDGE, TENNESSEE 37830

AREA CODE 615
TELEPHONE 483-8611

DEC 11

December 9, 1974

DATE

COPIES TO Andrews — Edwards

Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

Gentlemen:

AUDIT REPORT 4-02-1, ORAU, PATIENT SELECTION CRITERIA

Attached are two copies of the subject audit report for your use and retention.

In view of the fact that clinical operations have been terminated, and on the basis of your response to the draft report stating that careful attention would be given to the findings and recommendations should future programs require use of patient selection criteria, we do not believe any further action is required at this time. We have closed the audit report.

Sincerely,

for Joseph A. Lenhard, Director
Research & Tech. Support Division

Enclosure:
As stated above

1032787

FORM P-4

MEMORANDUM

TO: Dr. Andrews DATE: December 16, 1974

SUBJECT: AUDIT REPORT - PATIENT SELECTION CRITERIA

COPIES TO: File and Dr. Edwards (without attachment)

The attached audit report re outpatient selection and our Committee on Human Use provides certain comments and suggestions that merit consideration even though our clinical volume has been greatly reduced. By reassigning the chairmanship of the committee, and assigning Chief of Clinical Services as an ex officio member, I believe the primary improvement will be implemented.

If there are clear mistakes in any of the patient cases references, a memo documenting the facts would be appreciated. No response to ORO is indicated.

Philip L. Johnson
Executive Director

PLJ:ahp

Attachment

1032788

INTERIM GUIDELINES FOR THE IMPLEMENTATION OF THE MORATORIUM OF FETAL RESEARCH CONDUCTED OR SUPPORTED BY THE DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

On July 12, 1974, the National Research Act, Public Law 93-348, was enacted including the following provision:

> "Section 213. Until the (National Advisory) Commission (for the Protection of Human Subjects of Biomedical and Behavioral Research) has made its recommendations to the Secretary . . . the Secretary may not conduct or support research in the United States or abroad on a living human fetus, before or after the induced abortion of such fetus, unless such research is done for the purpose of assuring the survival of such fetus."

On August 27, 1974, the Secretary published in the Federal Register (39 FR 30962) a notice publicizing this moratorium. Simultaneously he required grantees and contractors of the Department conducting fetal research to advise awarding agencies how they propose to comply with the moratorium. The Institutional Relations Branch, NIH (since renamed "Office for Protection from Research Risks"), was designated as the focal point for interpretation of the terms of the moratorium. An advisory group was established under the chairmanship of the Deputy Director for Science, NIH, to assist this Office in reaching its decision. The advisory group has adopted the interim guidelines listed below.

Institutions seeking formal opinions from NIH as to the acceptability of a particular research project under the interim guidelines should address

1032789

the Chief, Office for Protection from Research Risks, NIH, Bethesda, Maryland 20014. The project must have the prior approval of the appropriate Institutional Review Board as described on the institution's assurance of compliance with Department of Health, Education, and Welfare policy and regulations. The letter requesting the opinion must be signed by the Chairman of that institution's Review Board or other authorized institutional official.

1. Applicability. These guidelines are applicable to all research activities involving the pregnant woman, the living fetus, the living abortus, conducted directly by the Department or supported by the Department under grant or contract or other mechanisms.

2. Definitions.

(a) "Fetus" means the product of conception, exclusive of extra-fetal membranes and fluid, from the time of implantation to the time of delivery or abortion.

(b) "Abortus" means a fetus after it is expelled or extracted whole, prior to viability, whether spontaneously or as a result of medical or surgical intervention. The term does not apply to the extra fetal membranes or the placenta, fetal material which is macerated at the time of expulsion or extraction, or to the cells, tissues, or organs excised from a dead fetus.

(c) "Viability" means the ability of the fetus, after either spontaneous or induced delivery or abortion, to survive (given the benefit of available medical therapy) to the point of independently maintaining

heart beat and respiration. If the fetus has this ability, it is a viable, immature, premature, or mature infant. For the purposes of these guidelines, any fetus which meets one or more of the following criteria must be considered to be at least a viable immature infant and not an abortus: body weight of 500 grams or more, crown-rump length in excess of 21 cm., estimated age of 24 weeks following the last normal menstrual period.

(d) "Pregnancy" means the period of time from medical confirmation of conception until delivery or abortion.

(e) "Life" means the presence of those vital signs which are characteristic of that particular stage of development. The fetus is presumed to be living from the medical confirmation of conception until at such later time fetal life can be objectively established by the presence of positive signs, such as fetal heartbeat, circulation, and related vital signs such as respiration.

(f) "Death" means the absence of life, as evidenced by the cessation of heartbeat, circulation, and related vital signs such as respiration.

(g) "Organization" means any public or private institution or agency (including Federal, State, and local Government agencies).

3. Research Involving the Pregnant Woman. No research shall be conducted involving the pregnant woman unless (1) it is expected to be of direct therapeutic benefit to her particular fetus or increase its chances of survival; or (2) the use of the research procedure, modality, device, or material can reasonably be expected to have no adverse effect on the fetus.

4. Research on the Living Fetus. No research shall be conducted on the living fetus unless it is expected to be of direct therapeutic benefit to that particular fetus or to increase its chances of survival.

5. Research on the Living Abortus. No research shall be conducted on a living abortus except where the purpose of the activity is to explore new methods which may enable that particular abortus to become viable.

6. Research on the Dead Fetus or Dead Abortus. Research involving a dead fetus or dead abortus is not restricted but shall be conducted in accordance with any applicable State or local laws, particularly those governing autopsy and permission therefor.

7. Research Involving the Dead Fetus or Dead Abortus as an Organ or Tissue Source. Research involving the dead fetus or abortus as an organ or tissue source is not restricted but shall be conducted in accordance with any applicable State or local laws, particularly those governing anatomical gifts.

8. Use of Research Procedures to Meet Health Needs of the Mother. No provision of these guidelines is to be interpreted as prohibiting the use of a procedure, modality, device, or material when, in the opinion of the attending physician, such use is necessary to meet the health needs of a particular pregnant woman.

9. Award of Contracts. No contract shall be awarded with a workscope incorporating research prohibited under these guidelines.

10. No grant shall be awarded to support research prohibited under these guidelines. Where an award is made in response to an application which includes both prohibited and nonprohibited research, the award shall include the following clause:

> "Acceptance of this award constitutes the agreement of the grantee on the part of itself and of any named principal investigator, that no parts of the funds awarded shall be used to support any research on a living human fetus, as prohibited by Section 213 of Public Law 93-348, specifically that research described (identify by grant application page and paragraph)."

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Office of the Secretary

[45 CFR Part 46]

PROTECTION OF HUMAN SUBJECTS

Correction of Preamble to Proposed Policy

In the August 23, 1974 issue of the FEDERAL REGISTER (39 FR 30548), the Department of Health, Education, and Welfare published a notice of proposed rulemaking governing research, development, and related activities, supported by the Department, involving the fetus, abortus, pregnant women, in vitro fertilization, prisoners, and the institutionalized mentally disabled.

After publication the following errors were noted in the preamble to the proposed rulemaking:

(1) The initial three paragraphs of Section C on page 30650 fail to indicate that, because of the Department's concern about the ethical issues surrounding in vitro fertilization (whether or not implantation is contemplated), the proposed rulemaking would require that all activities involving in vitro fertilization be reviewed by the Ethical Advisory Board prior to funding. In order to make clear this concern these paragraphs have been revised to read as follows:

• • • • •

C. A number of respondents recommended that the policy governing in vitro fertilization be strengthened, on the one hand, or liberalized, on the other. The Department has considered these recommendations, and concluded that while it is necessary to impose certain restraints, it is contrary to the interests of society to set permanent restrictions on research which are based on the successes and limitations of current technology. Therefore, the Department would expect the Ethical Advisory Board, which must review all applications involving in vitro fertilization (whether or not implantation is contemplated) to weigh, with respect to specific proposals, the state of the art, legal issues, community standards, and the availability of guidelines to govern each research situation. In sum, if there is a possibility that the conceptus might be sustained in vitro beyond the earliest stages of development, the Ethical Advisory Board is to consider this possibility, and determine what guidelines should govern decisions affecting that fetus, if the research is to be permitted. If, on the other hand, implantation is attempted and achieved, then regulations governing the fetus in utero shall apply.

• • • • •

(2) Several sentences were inadvertently omitted from the first and second paragraphs of the discussion of "Viability of the Fetus" in the first column on page 30651. These sentences are now inserted and as revised, the paragraphs read as follows:

2. "Viability of the Fetus." Some respondents suggested specific criteria such as birth weight, crown-rump length, or gestational age, similar to those used in England, such criteria to be reviewed and reissued periodically by the Department. It was emphasized that the use of such objective criteria might simplify problems involved in determining what types of research might be permissible. Some respondents urged that presence of fetal heartbeat be definitive (whether or not there is respiration) while others urged that identifiable cortical activity be specified as an alternative sign of viability. Others objected strenuously to any distinction as to the nature of fetal life, holding that the physician's obligation should be the same to any fetus regardless of weight, size, or age of gestation.

The Department, having reviewed these comments, concludes that the distinction between a viable and a nonviable fetus is both valid and meaningful. At the same time, the Department does not believe that the use of weight, size, gestational age and/or cortical activity is a valid substitute for the judgment of a physician, particularly in view of the wide variation in the facilities and arts available to him both in this country and abroad. The Department further concludes that the issue of viability is a function of technological advance [see § 46.303(e) of the regulations], and therefore must be decided with reference to the medical realities of the present time, while reserving the right to redefine the parameters as conditions warrant."

• • • • •

(3) Section H on page 30651 incorrectly implies that, under the proposed rulemaking, fetuses for which abortion is contemplated may be placed at greater risk than fetuses in general. In fact, however, as is stated already in section F on page 30651, the proposed rulemaking bans the undertaking of research, development, or related activities involving the fetus prior to the commencement of the abortion procedure, at which point the question of risk to the fetus is no longer an issue. Such activities which are permitted under the regulations would be reviewed by the Ethical Advisory Board prior to funding. Section H should therefore be deleted and section I on the same page relettered section H.

Dated: October 21, 1974.

CASPAR W. WEINBERGER,
Secretary.

[FR Doc.74-24994 Filed 10-24-74;8:45 am]

RECD. MEDICAL DIVISION 15 NOV 74

1032794

Sare -

See p. 18

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

June 1, 1975

50TH CUMULATIVE LIST OF ORGANIZATIONS AND INSTITUTIONS IN COMPLIANCE WITH DHEW POLICY AND REGULATIONS ON PROTECTION OF HUMAN SUBJECTS

NOTE: TECHNICAL AMENDMENTS to the DHEW regulations on protection of human subjects (45 CFR 46) appeared in the Federal Register on March 13, 1975. These bring the regulations into line with provisions of the National Research Act. Copies of the amended regulations can be obtained from the Office for Protection from Research Risks, OD, NIH, Bethesda, Maryland 20014.

NOTE: SUBMISSION OF CERTIFICATIONS - The May 20, 1975 Federal Register includes a notice concerning submission of assurances and certifications as requested by the technical amendments. Sections 46.11 and 46.12 of the amendments authorize the Secretary to permit institutions to delay review and approval of applications or proposals by their Institutional Review Boards until after the applications or proposals have been submitted to DHEW. The notice is for the purpose of permitting such delay to a limited extent.

Whenever possible, such review and approval should occur prior to submission of the application or proposal and a certification to that effect should be included in or with the application or proposal itself, preferably on form HEW 596 (Rev. 2/75). Under no circumstances will the review of an application by DHEW be completed until certification is received. The point at which review will be deferred or terminated is left to the operating agency involved.

Institutions having on file with DHEW an approved general assurance must submit certification within 30 days of the receipt of a written request therefor; and in any event these institutions must submit such certification within 90 days after the deadline for which the application or proposal was submitted or, if no deadline is specified, within 90 days following the submission date of the application or proposal.

Institutions not having on file an approved general assurance must submit in or with the application or proposal for activities covered by 45 CFR Part 46, a special assurance. Requirements for such a special assurance can be satisfied by proper completion of form HEW 596 (Rev. 2/75); boxes 1, 2, 3, 4A, 7, and 8.

1032795

Institutions having submitted such a special assurance must submit the required documentation and additional assurances of compliance, and certification of review and approval of the application or proposal by its Institutional Review Board, within 30 days of the receipt of a written request for the submission of such additional assurances and certification.

NOTE: CHANGE IN LISTING - The left hand column of the "List" identifies each institution that has a general assurance by its DHEW assurance number. These numbers should be inserted in the first blank in paragraph 4B of form HEW 596 (Rev. 2/75) when certifying review and approval of applications and proposals.

1. UNSOLICITED PROPOSALS - GRANTS OR CONTRACTS INVOLVING HUMAN SUBJECTS

a. If DHEW operating agency professional review of the proposal, including review of any accompanying form HEW 596 (Rev. 2/75) or equivalent, submitted by the institution indicates that it does not involve human subjects (box 3A of HEW 596), as defined in 45 CFR 46, these regulations do not apply and the application can be processed without further regard to this list.

b. If DHEW operating agency professional review, including review of any accompanying form HEW 596 (Rev. 2/75) or equivalent, submitted by the institution indicates that it does involve human subjects (box 3B of HEW 596) the next step is to determine whether the institution has checked either box 4A or 4B.

- If 4A is checked, this means that the applicant institution has given special assurance relating to the specific proposal submitted but further documentation and certification of review are still necessary. The operating agency (not applicant institution) must forward a copy of the proposal to OPRR, OD, NIH, Westwood Building, Room 303, Bethesda, Maryland, 20014, for further negotiation and certification of review.

- If 4B is checked by an institution having an approved general assurance on file, the paragraph should include a DHEW assurance "G" number (such as "G2104"), matching the number given in this list, and a meeting date. The meeting date should be prior to submission but must be no more than 90 days following a deadline or submission date. The operating agency concerned may define "deadline" and "submission" dates to fit administrative requirements.

2. SOLICITED PROPOSALS - GRANTS OR CONTRACTS INVOLVING HUMAN SUBJECTS

Draft requests for proposals (RFPs or RFAs) should be reviewed to determine whether performance will involve human subjects at risk. If these will be involved, the RFP should include the "Notice to Offerors" required by 41 CFR 3-4.5504(a). Offerings and proposals submitted in response to the RFP should be handled as in 1.b. above.

Operating agencies may define "submission date" to fit administrative requirements. It is suggested that sole source responses to RFPs should be considered to be submitted as of the closing date of the RFP and should then be handled as in 1.b. above.

Competitive responses to RFPs should be considered to be submitted as of the date of submission of the best and final offer, following establishing of the zone of consideration or source selection, and should then be treated as in 1.b. above.

3. RESTRICTION CODES preceding institution names indicate the status of the institution's assurance in terms of DHEW policy and regulations on protection of human subjects. If it is proposed to award a grant or contract involving research falling within the restricted area, it will be necessary to get in touch with the IRB to arrange renegotiation of the grantee or contractor assurance or implementation.

ABSENCE OF A RESTRICTION CODE indicates that the institution has filed an assurance and implementation reflecting committee competence to deal with all probable applications to DHEW.

CODE (2) indicates that the committee has professional competence to review all probable proposals to DHEW except those involving medical, surgical, or investigational new drug studies.

CODE (3) indicates a medically oriented institution that is not qualified to review activities involving investigational new drugs (INDs).

CODE (4) indicates an institution with medical competence, but not in the field of surgery. Most of these institutions are concerned with studies in the field of psychiatry or with the delivery of related services.

CODES (5) and (6) are unassigned.

CODE (7) indicates that the committee has professional competence to review all probable proposals to DHEW except those involving surgical or investigational new drug studies.

CODE (8) indicates status undetermined

CODE (9) complex restriction usually indicates that the institution's assurance and implementation does not cover all of its components, or that type (2), (3), or (4) restrictions apply to one or more components.

4. QUESTIONS with regard to specific aspects of the operation may be addressed to:

   a) Status of Special and General Assurance Certification - Mrs. Florence R. Ober or responsible professional. (301) 496-7005

   b) General Assurances, Policy - Dr. R. C. Backus (301) 496-7006

   c) Special Assurances, Policy - Dr. Joseph R. Marches (301) 496-7005

   d) Contract Problems, General - Dr. Roy Kinard (301) 496-7006

5. FORMS

Bulk orders for additional copies of HEW 596 should be addressed to Chief, Office Services Section, DRG, NIH, Westwood Building, Room A-17, Bethesda, Maryland 20014.

Single copies of HEW 596 can be obtained from OPRR or by duplicating the back pages of this listing.

D. T. Chalkley

D. T. Chalkley, Ph.D.
Director, Office for Protection
from Research Risks
Office of the Director
National Institutes of Health

1032798

General Assurance Number		
	ALABAMA	
G2104	Alabama Dept of Mental Health	Montgomery
G2104	Alabama Dept of Mental Health, Div of Com Svs	Montgomery
G0198	Alabama, University of, Birmingham	Birmingham
G0610	Alabama, University of, Tuscaloosa	University
G2104	Albert P. Brewer Mental Retardation Center	Mobile
G2381	(2)Auburn University	Auburn
G2104	Bryce Hospital	Tuscaloosa
G2104	Lurleen B. Wallace Mental Retardation Center	Decatur
G2104	Partlow State School and Hospital	Tuscaloosa
G2104	Searcy Hospital	Mount Vernon
G0055	Tuskegee Institute	Tuskegee
	ARIZONA	
G0799	(2)Arizona State University	Tempe
G0504	(4)Arizona Training Program at Coolidge	Coolidge
G0026	Arizona, University of	Tucson
G1287	St. Josephs Hospital and Medical Center	Phoenix
	ARKANSAS	
G0336	Arkansas, University of, Medical Center	Little Rock
	CALIFORNIA	
G0784	(2)American Institutes for Research	Palo Alto
G0261	(4)California Dept of Public Health	Berkeley
G0330	(2)California Dept of Youth Authority	Sacramento
G0144	(2)California Institute of Technology	Pasadena
G0420	(2)California State Univ, San Diego	San Diego
G0278	California, Univ of, Berkeley	Berkeley
G0195	(4)California, Univ of, Davis	Davis
G0380	California, Univ of, Irvine	Irvine
G0238	California, Univ of, Los Angeles	Los Angeles
G0193	(4)California, Univ of, Riverside	Riverside
G0389	California, Univ of, San Diego	La Jolla

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0155	California, Univ of, San Francisco	San Francisco
G0282	(4)California, Univ of, Santa Barbara	Santa Barbara
G0205	(2)California, Univ of, Santa Cruz	Santa Cruz
G0028	Camarillo State Hospital	Camarillo
G0234	Cedars Sinai Medical Center	Los Angeles
G2564	Charles R. Drew Postgraduate Medical School	Los Angeles
G0135	Childrens Hospital of Los Angeles	Los Angeles
G0287	Childrens Hospital of San Francisco	San Francisco
G0009	City of Hope National Medical Center	Duarte
G2259	(2)Far West Laboratory for Educational Research and Development	San Francisco
G1838	Huntington Institute of Applied Medical Research	Pasadena
G1838	Huntington Memorial Hospital	Pasadena
G2400	Institute of Medical Sciences	San Francisco
G2367	John Wesley County Hosp Attending Staff Assn	Los Angeles
G0214	Kaiser Foundation Research Institute Including Its Regional Divisions in North Calif, Southern Calif, and Oregon	Oakland
G0226	Loma Linda University	La Sierra
G0226	Loma Linda University	Loma Linda
G0359	L A Co Harbor Gen Hosp, Attending Staff Assn of	Torrance
G0213	L A Co Hosp-Univ of So Calif Med Ctr, Professional Staff Assn of	Los Angeles
G2564	Martin Luther King, Jr. Gen Hosp and Its Staff Assn Fdn	Los Angeles
G0367	(2)Mental Research Institute	Palo Alto
G0145	Mount Zion Hospital and Medical Center	San Francisco
G0710	Pacific State Hospital	Pomona
G2400	Pacific, University of the, School of Dentistry	San Francisco
G0082	Palo Alto Medical Research Foundation	Palo Alto
G1838	Pasadena Hospital Association, Ltd	Pasadena
G2400	Presbyterian Hospital	San Francisco
G0067	Rancho Los Amigos Hospital and Its Professional Staff Assocation	Downey
G1416	(3)Rand Corporation	Santa Monica
G1096	Salk Institute	San Diego
G0420	(2)San Diego State University Foundation	San Diego
G0108	Scripps Clinic and Research Foundation	La Jolla

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0201	Sonoma State Hospital	Eldridge
G0122	Southern California, University of	Los Angeles
G0378	Stanford Research Institute	Menlo Park
G0011	Stanford University	Stanford
G1796	Veterans Administration Hospital-Sepulveda	Sepulveda
G1658	Veterans Administration Hospital-Wadsworth	Los Angeles
G1591	(2)Wright Institute	Berkeley
	COLORADO	
G0845	Childrens Hospital	Denver
G2823	Colorado Regional Cancer Center, Inc	Denver
G1144	(4)Colorado State University	Fort Collins
G0455	Colorado, University of	Boulder
G0268	Colorado, University of, Medical Center	Denver
G0277	(2)Denver, University of	Denver
G0267	National Asthma Center, All Components	Denver
G0068	(4)National Jewish Hospital	Denver
	CONNECTICUT	
G0039	Connecticut, University of	Storrs
G1966	Connecticut, University of, Health Center	Hartford
G1533	Connecticut Valley Hospital	Middletown
G0007	Institute of Living	Hartford
G0003	John B. Pierce Foundation of Connecticut	New Haven
G0243	Yale University	New Haven
	DELAWARE	
G0148	Alcoholism Detoxification and Treatment Center	Wilmington
G0148	Delaware Division of Mental Health	New Castle
G0148	Delaware State Hospital	New Castle
G0013	(2)Delaware, University of	Newark
G0148	Fernhook Mental Hygiene Clinic	New Castle
G0148	Governor Bacon Health Center	Delaware City
G0148	Inner-City Mental Hygiene Clinic	Wilmington

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

1032801

General Assurance Number		
G0148	Kent County Mental Hygiene Clinic	Dover
G0148	Newark Mental Hygiene Clinic	Newark
G0148	Southern New Castle County Community M H Ctr	New Castle
G0148	Sussex County Community Mental Health Center	Lewes
G0148	Sussex County Mental Hygiene Clinic	Georgetown
G0148	Terry Childrens Psychiatric Center	New Castle
G0148	Wilmington Mental Hygiene Clinic	Wilmington
	DISTRICT OF COLUMBIA	
G0784	(2)American Institutes for Research	Washington
G1674	(2)Bureau of Social Science Research	Washington
G0365	(2)Catholic University of America	Washington
G0042	Childrens Hospital of the District of Columbia and Its Research Foundation	Washington
G2058	(2)Federal City College	Washington
G1249	(2)Gallaudet College	Washington
G0294	(2)George Washington Univ Except School of Medicine	Washington
G0294	George Washington Univ, School of Medicine	Washington
G0228	Georgetown University	Washington
G0178	Gorgas Memorial Institute	Washington
G0841	Howard University	Washington
G2063	(2)Institute for Services to Education	Washington
G1188	Leonard Wood Memorial (American Leprosy Fdn), Philippine Division of	Washington
G1989	National Academy of Sciences Including National Academy of Engineering, Institute of Medicine and National Research Council	Washington
G1036	(2)National Childrens Center, Inc	Washington
G0180	Washington Hospital Center	Washington
	FLORIDA	
G2093	(2)Florida Atlantic University	Boca Raton
G0260	Florida State Div of Health, All Components	Jacksonville
G0119	(2)Florida State University	Tallahassee

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

1032802

General Assurance Number		
G0382	Florida, University of	Gainesville
G0840	Miami Heart Institute	Miami Beach
G0301	Miami, University of	Coral Gables
G0301	Miami, University of	Miami
G0275	Mt. Sinai Med Ctr of Greater Miami	Miami Beach
G2321	Papanicolaou Cancer Research Institute	Miami
G1065	South Florida, University of	St. Petersburg
G1065	South Florida, University of	Tampa
	GEORGIA	
G0138	Emory University Div of Basic Health Sciences	Atlanta
G0622	Emory University Grad Sch of Arts and Sciences	Atlanta
G0138	Emory University Nell Hodgson Woodruff School of Nursing	Atlanta
G0595	Emory University School of Dentistry	Atlanta
G0138	Emory University School of Medicine	Atlanta
G0197	(2)Georgia Dept of Human Resources, All Units	Atlanta
G0520	(3)Georgia Institute of Technology	Atlanta
G0151	Georgia, Medical College of	Augusta
G0248	(2)Georgia, University of	Athens
G1467	Grady Memorial Hospital	Atlanta
	HAWAII	
G0104	(4)Hawaii, University of	Honolulu
	IDAHO	
G1869	Mountain States Tumor Institute	Boise
	ILLINOIS	
G1223	(2)Adolf Meyer Center	Decatur
G0395	American Dental Association	Chicago
G0332	(7)Anna State Hospital	Anna

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

1032803

General Assurance Number		
G1626	Chicago, Univ of, Div of Biological Sciences and Pritzker School of Medicine	Chicago
G1626	(2)Chicago, Univ of, Div of Social Sciences, Ctr for Hlth Adm Studies, Grad School of Education	Chicago
G1626	(2)Chicago, Univ of, School of Social Service Adm	Chicago
G0114	Children's Memorial Hospital	Chicago
G0182	Evanston Hospital	Evanston
G0430	Health Sciences, Univ of/Chicago Medical School	Chicago
G0053	Hektoen Institute for Medical Research	Chicago
G1561	(4)Illinois State Psychiatric Institute	Chicago
G0345	Illinois, Univ of, at Chicago Circle	Chicago
G0291	Illinois, Univ of, Medical Center Campus Including the Clinical Schools at Peoria and Rockford	Chicago
G0102	Illinois, Univ of, Urbana-Champaign Campus	Urbana
G1373	(2)Lincoln State School	Lincoln
G0095	Michael Reese Hospital and Medical Center	Chicago
G0518	(2)Northern Illinois University	DeKalb
G0190	Northwestern University	Chicago
G0190	Northwestern University	Evanston
G0175	Rush-Presbyterian-St. Lukes Medical Center	Chicago
G0309	Southern Illinois University	Carbondale
G2606	(2)Southern Illinois University	Edwardsville
G1970	(4)Western Illinois University	Macomb
	INDIANA	
G0314	(2)Depauw University	Greencastle
G0945	(7)Fort Wayne State Hospital and Training Ctr	Ft. Wayne .
G0185	Indiana University and Indiana Univ Fdn	Bloomington
G0185	Indiana University and Indiana Univ Fdn	Indianapolis
G0185	Indiana University-Purdue University	Indianapolis
G0185	Indiana University Regional Campuses at Fort Wayne, Gary, Jeffersonville, Kokomo, Richmond, and South Bend	

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G1397	Indianapolis Center for Advanced Research	Indianapolis
G0883	Larue D. Carter Memorial Hospital	Indianapolis
G1697	Marion County Assn for Retarded Children, Inc	Indianapolis
G1246	Methodist Hospital of Indiana, Inc	Indianapolis
G1176	New Castle State Hospital	New Castle
G1119	(7)Notre Dame, University of	Notre Dame
G0131	(4)Purdue University and Purdue Research Fdn	Lafayette
	IOWA	
G0343	(2)Iowa State University of Science and Technology	Ames
G0209	Iowa, University of	Iowa City
G0856	(3)Woodward State Hospital-School	Woodward
	KANSAS	
G0038	(4)Kansas State University	Manhattan
G0157	(4)Kansas, University of	Lawrence
G0229	Kansas, University of, Medical Center	Kansas City
G0081	(4)Menninger Foundation	Topeka
	KENTUCKY	
G0223	Kentucky, Univ of, Including Research Fdn	Lexington
G0527	(4)Louisville, University of, Except Sch of Med	Louisville
G0527	Louisville, University of, Foundation	Louisville
G0023	Louisville, University of, School of Medicine	Louisville
	LOUISIANA	
G0262	(9)Louisiana State Univ and A & M Coll Sys	Baton Rouge
G2428	(2)Louisiana State Univ in Baton Rouge	Baton Rouge
G2485	Louisiana State University Medical Center	New Orleans
G2420	(4)New Orleans, University of, Lake Front	New Orleans
G0137	(3)Pinecrest State School	Pineville

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0018	Tulane Medical Center	New Orleans
G2386	(2)Tulane University Except Medical Center	New Orleans
	MAINE	
G0513	Maine Medical Center	Portland
	MARYLAND	
G0784	(2)American Institutes for Research	Silver Spring
G0402	Baltimore City Hospitals	Baltimore
G0895	(4)Columbia Union College, Dept of Nursing	Takoma Park
G1247	Eye Research Foundation of Bethesda	Bethesda
G0186	(4)Friends Medical Science Research Center, Inc	Baltimore
G2245	(9)Huntingdon Research Center	Brooklandville
G0640	(4)Institute for Behavioral Research, Inc	Silver Spring
G0174	Johns Hopkins Hospital	Baltimore
G0274	Johns Hopkins Univ Sch of Hygiene and Pub Hlth	Baltimore
G0174	Johns Hopkins Univ School of Medicine	Baltimore
G0326	Maryland, University of, Baltimore Campus	Baltimore
G0296	Maryland, University of, College Park Campus	College Park
G0400	Sinai Hospital of Baltimore, Inc	Baltimore
	MASSACHUSETTS	
G0286	Beth Israel Hospital of Boston	Boston
G0554	Boston City Hospital	Boston
G0554	Boston Department of Health and Hospitals	Boston
G0554	Boston Department of Community Health	Boston
G0488	Boston Hospital for Women	Boston
G0783	Boston State Hospital	Boston
G0322	(2)Boston University, Charles River Campus	Boston
G0550	Boston University Medical Center	Boston
G0550	Boston University, School of Graduate Dentistry	Boston
G0550	Boston University, School of Medicine	Boston

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0132	(2)Brandeis University	Waltham
G2396	(4)Center for Blood Research	Boston
G0406	Childrens Hospital Medical Center	Boston
G0117	(3)Clark University	Worcester
G0098	Danvers State Hospital	Hathorne
G2042	Eunice Kennedy Shriver Center	Waltham
G0410	Eye Research Institute of Retina Foundation	Boston
G0412	Forsyth Dental Center	Boston
G2397	Harvard Medical School and School of Dental Med	Boston
G2238	(3)Harvard Univ, Faculty of Arts and Sciences	Cambridge
G2494	(2)Harvard Univ, Faculty of Grad Sch of Education	Cambridge
G2398	Harvard Univ, School of Public Health	Boston
G2573	Harvard University, University Health Services	Cambridge
G0791	Joslin Diabetes Foundation, Inc	Boston
G0087	Lahey Clinic Foundation	Boston
G0449	Lemuel Shattuck Hospital	Jamaica Plain
G0554	Long Island Chronic Disease Hospital	Boston Harbor
G2304	(9)Massachusetts Developmental Disabilities Cncl	Boston
G0212	Massachusetts Eye and Ear Infirmary	Boston
G0167	Massachusetts General Hospital	Boston
G0097	(4)Massachusetts Institute of Technology	Cambridge
G0597	Massachusetts Mental Health Center	Boston
G0597	Massachusetts Mental Health Research Corp	Boston
G0147	(2)Massachusetts, University of - Amherst	Amherst
G0554	Mattapan Chronic Disease Hospital	Mattapan
G0576	McLean Hospital	Belmont
G0494	New England Deaconess Hospital	Boston
G0133	New England Medical Center Hospitals	Boston
G0297	Northeastern University	Boston
G1316	(4)Paul A. Dever State School	Taunton
G0429	Peter Bent Brigham Hospital	Boston
G2515	(7)Research Institute for Educational Problems	Cambridge
G0404	Robert B. Brigham Hospital	Boston
G0854	St. Elizabeths Hospital	Boston
G0351	St. Margarets Hospital	Boston

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0771	Sidney Farber Cancer Center	Boston
G0554	Trustees of Health & Hospitals, City of Boston	Boston
G2107	Tufts-New England Medical Center	Boston
G2379	Tufts University - Boston	Boston
G0266	(2)Tufts University - Medford	Medford
G0550	University Hospital, Inc	Boston
G2042	Walter E. Fernald State School	Waverley
G0085	Worcester Foundation for Exp Biology	Shrewsbury
G1284	(4)Worcester State Hospital	Worcester
	MICHIGAN	
G0363	Child Research Center of Michigan	Detroit
G0363	Childrens Hospital of Michigan	Detroit
G0497	Detroit, University of	Detroit
G0357	Edsel B. Ford Institute	Detroit
G0357	Henry Ford Hospital	Detroit
G0656	Michigan Cancer Foundation	Detroit
G0615	Michigan Dept of Public Health	Lansing
G0384	Michigan State University	East Lansing
G0295	Michigan, University of	Ann Arbor
G0008	Sinai Hospital of Detroit	Detroit
G2483	Veterans Administration Hospital-Ann Arbor	Ann Arbor
G0354	Wayne State University	Detroit
G0720	Western Michigan University	Kalamazoo
	MINNESOTA	
G0065	Hennepin County General Hospital	Minneapolis
G0041	Mayo Foundation	Rochester
G0065	Minneapolis Medical Research Foundation, Inc	Minneapolis
G0463	Minnesota, University of	Austin
G0463	Minnesota, University of	Duluth
G0463	Minnesota, University of	Minneapolis
G0463	Minnesota, University of	Morris
G0463	Minnesota, University of	St. Paul
G0463	Minnesota, University of, Technical College	Crookston
G0463	Minnesota, University of, Technical College	Waseca

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
	MISSISSIPPI	
G0561	(2)Mississippi, University of	University
G0366	Mississippi, University of, Medical Center	Jackson
	MISSOURI	
G2791	(7)American Nurses' Assoc, Inc	Kansas City
G0298	Cancer Research Center	Columbia
G2358	(2)Cemrel, Inc	St. Ann
G0298	Ellis Fischel State Cancer Hospital	Columbia
G0424	Jewish Hospital of St. Louis	St. Louis
G2365	(2)Mid-Continent Regional Educational Laboratory	Kansas City
G0292	(2)Missouri, Univ of, Except Medical Center	Columbia
G0292	Missouri, Univ of, Medical Center Including Missouri Institute of Psychiatry	Columbia
G0292	Missouri, University of	Kansas City
G0292	(2)Missouri, University of	Rolla
G0292	(2)Missouri, University of	St. Louis
G0292	Missouri, University of, Reg Med Prog, All Campuses	
G0356	St. Louis University	St. Louis
G2056	Veterans Administration Hospital-Kansas City	Kansas City
G0279	Washington University	St. Louis
G2351	Washington University School of Medicine	St. Louis
	NEBRASKA	
G1120	Creighton University	Omaha
G0407	Nebraska, University of, Including SUN	Lincoln
G0407	Nebraska, Univ of, Including the Medical Ctr	Omaha
G1781	Veterans Administration Hospital-Omaha	Omaha
	NEVADA	
G0762	(2)Nevada, University of, Reno Campus	Reno
	NEW HAMPSHIRE	
G0427	(2)Dartmouth Coll Faculty of Arts and Sciences	Hanover
G0227	Dartmouth Medical School	Hanover
G1006	(4)New Hampshire Hospital	Concord
G1006	(4)New Hampshire State Division of Mental Health	Concord

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
	NEW JERSEY	
G0981	(2)Educational Testing Service	Princeton
G0349	New Jersey, Coll of Medicine and Dentistry of	Newark
G0349	New Jersey Dental School	Jersey City
G0349	New Jersey Medical School	Newark
G0837	Newark Beth Israel Medical Center	Newark
G0570	(2)Princeton University	Princeton
G0349	Rutgers Medical School	Piscataway
G0300	(4)Rutgers, The State University of New Jersey	Camden
G0300	(4)Rutgers, The State University of New Jersey	New Brunswick
G0300	(4)Rutgers, The State University of New Jersey	Newark
	NEW MEXICO	
G0141	Lovelace Foundation for Med Educ and Res	Albuquerque
G0472	New Mexico, University of	Albuquerque
G0353	New Mexico, University of, Health Sciences Group-School of Medicine, Colleges of Pharmacy and Nursing	Albuquerque
	NEW YORK	
G0217	Albany Medical College of Union University	Albany
G2129	(4)American Health Foundation	New York
G2116	(2)Barnard College	New York
G0341	Beth Israel Medical Center	New York
G0423	Bronx-Lebanon Hospital Center	New York
G1064	Brookhaven National Laboratory Medical Department	Upton
G2368	(2)Center for Urban Education	New York
G2277	(2)Child Welfare League of America	New York
G0381	Childrens Hospital of Buffalo	Buffalo
G0437	(2)Columbia Univ, Except Health Sciences Div	New York
G0034	Columbia Univ Health Sciences Div Including College of Physicians and Surgeons, Schools of Public Health and Administrative Medicine, Nursing, and Oral and Dental Surgery	New York
G0373	(2)Columbia University Teachers College	New York
G0526	Community Blood Council of Greater New York	New York
G0063	(3)Cornell Univ, Except Med Coll and Sch of Nursing	Ithaca

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0245	Cornell University, Medical College	New York
G0109	Eastman Dental Center	Rochester
G0456	Health Research, Inc, Albany Division	Albany
G0456	Health Research, Inc, Roswell Park Division	Buffalo
G0456	Helen Hayes Hospital	West Haverstraw
G0456	Homer Folks Tuberculosis Hospital	Oneonta
G0621	Hospital for Joint Diseases and Medical Center	New York
G0047	Hospital for Special Surgery	New York
G1005	(4)Jewish Board of Guardians	New York
G0368	Jewish Hospital and Medical Center of Brooklyn	Brooklyn
G0369	Kingsbrook Jewish Med Ctr & Isaac Albert Res Inst	New York
G2375	Long Island Jewish-Hillside Medical Center	New Hyde Park
G0397	Maimonides Medical Center	Brooklyn
G0086	Mary Imogene Bassett Hospital	Cooperstown
G2518	Meadowbrook Medical Education and Res Fdn	East Meadow
G0383	Memorial Hosp for Cancer and Allied Diseases	New York
G0059	Montefiore Hospital and Medical Center	New York
G0139	Mount Sinai School of Medicine	New York
G2518	Nassau County Medical Center	East Meadow
G0173	(2)New School for Social Research	New York
G0526	New York Blood Center	New York
G1370	(4)New York City Department of Health	New York
G0765	(2)New York, City University of	New York
G0765	(2)New York, City Univ of, Bronx Community College	Bronx
G0765	(2)New York, City Univ of, Brooklyn College	Brooklyn
G0765	(2)New York, City Univ of, City College	New York
G0765	(2)New York, City Univ of, Grad Sch and Univ Ctr	New York
G0765	(2)New York, City Univ of, Herbert H. Lehman College	Bronx
G0765	(2)New York, City Univ of, Hostos Community College	Bronx.
G0765	(2)New York, City Univ of, Hunter College	New York
G0765	(2)New York, City Univ of, John Jay College of Criminal Justice	New York
G0765	(2)New York, City Univ of, Kingsborough Cmty Coll	Brooklyn
G0765	(2)New York, City Univ of, Laguardia Cmty Coll	Long Island
G0765	(2)New York, City Univ of, Manhattan Cmty Coll	New York
G0765	(2)New York, City Univ of, New York City Cmty Coll	Brooklyn

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0765	(2)New York, City Univ of, Queens College	Flushing
G0765	(2)New York, City Univ of, Queensborough Cmty Coll	New York
G0765	(2)New York, City Univ of, Research Foundation	New York
G0765	(2)New York, City Univ of, Richmond College	Staten Island
G0765	(2)New York, City Univ of, Staten Island Cmty Coll	Staten Island
G0765	(2)New York, City Univ of, York College	Jamaica
G0456	New York Department of Health	Albany
G0624	(9)New York Department of Mental Hygiene	Albany
G0208	New York Medical College-Flower and Fifth Avenue Hospitals Including Metropolitan Hospital and Bird S. Coler Memorial Hospital	New York
G0374	(2)New York, State Univ of, at Albany	Albany
G0508	(3)New York, State Univ of, at Binghamton	Binghamton
G0163	New York, State Univ of, at Buffalo	Buffalo
G0596	New York, State Univ of, at Stony Brook	Stony Brook
G0474	(7)New York, State Univ of, College at Brockport	Brockport
G0506	New York, State Univ of, College at Buffalo	Buffalo
G0259	(4)New York, State Univ of, College at Cortland	Cortland
G0457	New York, State Univ of, College of Arts and Sciences at Geneseo	Geneseo
G0386	(2)New York, State Univ of, College at Oswego	Oswego
G0220	New York, State Univ of, College of Forestry	Syracuse
G0305	New York, State Univ of, Downstate Med Ctr	Brooklyn
G0127	New York, State Univ of, Upstate Med Ctr	Syracuse
G0390	(2)New York University, Exclusive of the Med Ctr	New York
G0405	New York University Medical Center	New York
G0788	North Shore Hospital	Manhasset
G2247	Public Health Research Institute	New York
G1001	Rensselaer Polytechnic Institute	Troy
G0624	(9)Research Foundation for Mental Hygiene	Albany
G0172	Rochester, University of	Rochester
G0230	Rockefeller University	New York
G2036	(4)Rockland County Health and Social Services Comp	Pomona
G0491	Roosevelt Hospital	New York
G0456	Roswell Park Memorial Institute	Buffalo

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0536	Sloan-Kettering Institute for Cancer Research	New York
G0076	St. Lukes Hospital Center	New York
G0376	St. Vincents Hosp and Med Ctr of NY	New York
G0280	(2)Syracuse University	Syracuse
G2438	Trudeau Institute	Saranac Lake
G0621	Research Institute for Skeletomuscular Diseases	New York
G1740	Veterans Administration Hospital-Bronx	New York
G2045	Veterans Administration Hospital-Northport	Northport
G0002	Yeshiva Univ, Albert Einstein Coll of Med	Bronx
	NORTH CAROLINA	
G0699	Charlotte Memorial Hospital	Charlotte
G0191	Duke University	Durham
G2382	(2)National Laboratory for Higher Education	Durham
G2242	(2)North Carolina A & T State University	Greensboro
G0285	(2)North Carolina State University at Raleigh	Raleigh
G0177	North Carolina, University of, at Chapel Hill	Chapel Hill
G0242	Wake Forest University, Bowman Gray Sch of Med	Winston-Salem
G1087	(2)Wake Forest University, Except Sch of Medicine	Winston-Salem
G0078	(2)Western Carolina Center	Morganton
	OHIO	
G0485	(2)Akron, University of	Akron
G0544	(2)Bowling Green State University	Bowling Green
G1167	Case Western Reserve University	Cleveland
G0088	Childrens Hospital & Research Foundation	Cincinnati
G0249	Childrens Hospital Research Foundation	Columbus
G0667	Cincinnati, Univ of, Except Medical Center	Cincinnati
G0337	Cincinnati, Univ of, Medical Center	Cincinnati
G0502	Cleveland Clinic Fdn & Educational Fdn	Cleveland
G0171	(4)Cleveland Psychiatric Institute	Cleveland
G1004	Fairhill Mental Health Center	Cleveland
G0160	Fels Research Institute	Yellow Springs
G1936	Jewish Hospital Assn Including the Hospital, Childrens Psychiatric Ctr, Sch of Nursing, and May Institute for Medical Research	Cincinnati

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G0542	Kent State University	Kent
G0269	Mount Sinai Hospital of Cleveland	Cleveland
G1724	Ohio, Medical College of, at Toledo	Toledo
G0121	Ohio State Universty and Research Foundation	Columbus
G0662	St. Lukes Hospital	Cleveland
G0626	St. Vincent Charity Hospital	Cleveland
G0350	University Hospitals of Cleveland	Cleveland
	OKLAHOMA	
G0327	Oklahoma Medical Research Foundation	Oklahoma City
G2402	(2)Oklahoma, University of	Norman
G0241	Oklahoma, University of, Health Sciences Center	Oklahoma City
	OREGON	
G0134	Good Samaritan Hospital and Medical Center	Portland
G0214	Kaiser Foundation Research Institute	Portland
G0043	Medical Research Foundation of Oregon	Portland
G2399	(2)Northwest Regional Educational Laboratory	Portland
G0505	(2)Oregon Research Institute	Eugene
G0111	(7)Oregon State University	Corvallis
G0288	(2)Oregon, University of, Graduate School	Eugene
G0281	Oregon, University of, Health Sciences Center, Including Medical School & Dental School	Portland
	PENNSYLVANIA	
G0125	Albert Einstein Medical Center	Philadelphia
G0952	Allegheny General Hospital	Pittsburgh
G0784	(2)American Institutes for Research	Pittsburgh
G0338	Arthur P. Noyes Research Foundation, Inc	Norristown
G0444	Bryn Mawr Hospital	Bryn Mawr
G0444	Bryn Mawr Hospital, John S. Sharpe Res Fdn of	Bryn Mawr
G0436	(2)Bucknell University	Lewisburg
G1218	(2)Carnegie-Mellon University	Pittsburgh

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined.
(9) Complex Restriction (Call 301-496-7005)

General Assurance Number		
G2566	Childrens Heart Hospital of Philadelphia	Philadelphia
G0129	Childrens Hospital of Philadelphia	Philadelphia
G0360	Childrens Hospital of Pittsburgh	Pittsburgh
G1556	Franklin Institute	Philadelphia
G0475	Hahnemann Medical College and Hospital	Philadelphia
G0045	Institute for Cancer Research	Philadelphia
G0273	Lankenau Hospital	Philadelphia
G0189	Magee-Womens Hospital	Pittsburgh
G2121	(2)Marywood College	Scranton
G0057	Montefiore Hospital	Pittsburgh
G0338	Norristown State Hospital	Norristown
G0333	Pennsylvania Hospital	Philadelphia
G0222	Pennsylvania, Medical College of	Philadelphia
G0573	(4)Pennsylvania State University & Cmnwlth Camps	University Park
G1668	Pennsylvania State University Milton S. Hershey Medical Center	Hershey
G0012	Pennsylvania, University of	Philadelphia
G1531	Philadelphia Department of Public Health	Philadelphia
G0044	Philadelphia General Hospital	Philadelphia
G0344	Philadelphia Psychiatric Center	Philadelphia
G0881	Philadelphia State Hospital	Philadelphia
G1532	(4)Pittsburgh Child Guidance Center	Pittsburgh
G0418	Pittsburgh, University of	Pittsburgh
G2200	Presbyterian-University Hospital	Pittsburgh
G0465	Presbyterian-Univ of Pennsylvania Med Ctr	Philadelphia
G2264	(2)Research for Better Schools, Inc	Philadelphia
G0795	St. Joseph Hospital Research Institute	Lancaster
G0334	Temple University	Philadelphia
G0049	Thomas Jefferson University, All Components	Philadelphia
G0952	William H. Singer Memorial Research Institute of Allegheny General Hospital	Pittsburgh
G0362	Wills Eye Hospital and Research Institute	Philadelphia
G0054	Wistar Institute	Philadelphia

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

1032815

General Assurance Number		
	RHODE ISLAND	
G0467	Brown University	Providence
G0318	Rhode Island Hospital	Providence
G2212	Roger Williams General Hospital	Providence
	SOUTH CAROLINA	
G2621	Clemson University	Clemson
G0533	South Carolina Department of Mental Health	Columbia
G0240	South Carolina, Medical University of	Charleston
G0629	(4)South Carolina, University of	Columbia
	TENNESSEE	
G1696	(4)Arlington Hospital and School	Arlington
G0393	Meharry Medical College	Nashville
G1716	Oak Ridge Associated Universities, Inc	Oak Ridge
G1716	Oak Ridge National Laboratory	Oak Ridge
G0648	St. Jude Childrens Research Hospital	Memphis
G0170	Tennessee, Univ of, Medical Units	Memphis
G0124	Tennessee, University of - Knoxville	Knoxville
G0401	Vanderbilt University	Nashville
G1800	Veterans Administration Hospital-Memphis	Memphis
	TEXAS	
G0307	Baylor College of Medicine	Houston
G0813	(2)Baylor University	Waco
G1843	Bexar County Hospital District	San Antonio
G2344	(2)Southwest Educational Development Corporation	Austin
G2344	(2)Southwest Educational Development Laboratory	Austin
G1045	(2)Texas A & M Univ, College Station Campus Only	College Station
G0590	Texas Institute for Rehabilitation and Research	Houston
G1121	(7)Texas, University of, at Arlington	Arlington
G0123	(9)Texas, University of, at Austin	Austin
G2615	Texas, Univ of, Health Science Ctr at Dallas Including SW Med Sch, Grad Sch of Biomedical Sciences, and Sch of Allied Health Sciences	Dallas

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

General Assurance Number		
G2760	Texas, Univ of, Health Science Ctr at Houston	Houston
G2255	Texas, Univ of, Health Science Ctr - San Antonio Including Med Sch, Dental Sch, and Grad Sch of Biomedical Sciences	San Antonio
G0113	Texas, Univ of, M D Anderson Hosp and Tumor Inst	Houston
G0107	Texas, Univ of, Medical Branch at Galveston	Galveston
	UTAH	
G0933	(2)Brigham Young University	Provo
G2426	Deseret Foundation for Med Educ and Res	Salt Lake City
G0235	Utah, University of	Salt Lake City
	VERMONT	
G0194	Vermont, University of	Burlington
G2335	Veterans Adm Center - White River Junction	White River Jct.
	VIRGINIA	
G2275	(2)Human Resources Research Organization	Alexandria
G0634	Lynchburg Training School and Hospital	Madison Heights
G0239	Virginia Commonwealth University, Medical College of Virginia, Health Sciences Div	Richmond
G0306	Virginia, University of	Charlottesville
G0575	(2)William and Mary, College of	Williamsburg
	WASHINGTON	
G0522	Childrens Orthopedic Hospital and Med Ctr	Seattle
G2627	Fred Hutchinson Cancer Research Center	Seattle
G0029	Pacific Northwest Research Foundation	Seattle
G0900	Virginia Mason Research Center Including Mason Clinic and Virginia Mason Hospital	Seattle
G1717	Washington Dept of Social and Health Services	Olympia
G0105	(3)Washington State University	Pullman
G0299	Washington, University of	Seattle

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005)

1032817

General Assurance Number		
	WEST VIRGINIA	
G2376	(2)Appalachia Educational Laboratory, Inc	Charleston
G0431	West Virginia University	Morgantown
	WISCONSIN	
G0315	Central Wisconsin Colony and Training School	Madison
G2132	(2)Lawrence University	Appleton
G0387	Marquette University	Milwaukee
G0763	Mendota State Hospital	Mendota
G0503	(4)Southern Wisconsin Colony and Training School	Union Grove
G0077	Wisconsin, Medical College of	Milwaukee
G0319	Wisconsin, University of, Madison Campus	Madison
G2106	(2)Wisconsin, University of, Parkside	Kenosha
G0256	Puerto Rico, Univ of, Medical Sciences Campus	San Juan
G1188	Leonard Wood Memorial (American Leprosy Fdn), Philippine Division of	Cebu
	SWITZERLAND	
G1137	World Health Organization	Geneva
	UNITED KINGDOM	
G1080	London, Univ of, Institute of Neurology	London

TOTAL INSTITUTIONS WITH ACCEPTABLE GENERAL ASSURANCES 549

RESTRICTION CODE
(2) No Medical, Surgical or IND Studies
(3) No IND Studies
(4) No Surgical Studies
(5-6)Unassigned
(7) No Surgical or IND Studies
(8) Status Undetermined
(9) Complex Restriction (Call 301-496-7005 For Details)

1032818

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☒ RENEWAL ☐ CONTINUATION

APPLICATION IDENTIFICATION NUMBER (If known)

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of Public Law 93-348, as implemented by Part 46 of Title 45 of the Code of Federal Regulations, as amended, 45 CFR 46. Administration of the DHEW policy and regulation is the responsibility of the Office of Protection from Research Risks, National Institutes of Health, Bethesda, Maryland 20014.

1. TITLE OF PROPOSAL OR ACTIVITY

2. PRINCIPAL INVESTIGATOR/ACTIVITY DIRECTOR/FELLOW

3. DECLARATION THAT HUMAN SUBJECTS EITHER WOULD OR WOULD NOT BE INVOLVED

☐ A. NO INDIVIDUALS WHO MIGHT BE CONSIDERED HUMAN SUBJECTS, INCLUDING THOSE FROM WHOM ORGANS, TISSUES, FLUIDS, OR OTHER MATERIALS WOULD BE DERIVED, OR WHO COULD BE IDENTIFIED BY PERSONAL DATA, WOULD BE INVOLVED IN THE PROPOSED ACTIVITY. (IF NO HUMAN SUBJECTS WOULD BE INVOLVED, CHECK THIS BOX AND PROCEED TO ITEM 7. PROPOSALS DETERMINED BY THE AGENCY TO INVOLVE HUMAN SUBJECTS WILL BE RETURNED.)

☐ B. HUMAN SUBJECTS WOULD BE INVOLVED IN THE PROPOSED ACTIVITY AS EITHER: ☐ NONE OF THE FOLLOWING, OR INCLUDING: ☐ MINORS, ☐ FETUSES, ☐ ABORTUSES, ☐ PREGNANT WOMEN, ☐ PRISONERS, ☐ MENTALLY RETARDED, ☐ MENTALLY DISABLED. UNDER SECTION 6, COOPERATING INSTITUTIONS, ON REVERSE OF THIS FORM, GIVE NAME OF INSTITUTION AND NAME AND ADDRESS OF OFFICIAL(S) AUTHORIZING ACCESS TO ANY SUBJECTS IN FACILITIES NOT UNDER DIRECT CONTROL OF THE APPLICANT OR OFFERING INSTITUTION.

4. DECLARATION OF ASSURANCE/CERTIFICATION OF REVIEW

☐ A. This institution has not previously filed an assurance and assurance implementing procedures for the protection of human subjects with the DHEW that applies to this application or activity. Assurance is hereby given that this institution will comply with requirements of DHEW Regulation 45 CFR 46, that it has established an Institutional Review Board for the protection of human subjects and, when requested, will submit to DHEW documentation and certification of such reviews and procedures as may be required for implementation of this assurance for the proposed project or activity.

☐ B. This institution has an approved general assurance (DHEW Assurance Number _____), or an active special assurance for this ongoing activity, on file with DHEW. The signer CERTIFIES that all activities in this application proposing to involve human subjects have been reviewed and approved by this institution's Institutional Review Board in a convened meeting on the date of _____ in accordance with the requirements of the Code of Federal Regulations on Protection of Human Subjects (45 CFR 46). This certification includes, when applicable, requirements for certifying FDA status for each investigational new drug to be used (see reverse side of this form).

THE INSTITUTIONAL REVIEW BOARD HAS DETERMINED, AND THE INSTITUTIONAL OFFICIAL SIGNING BELOW CONCURS THAT:

Either ☐ Human Subjects Will Not Be At Risk; Or ☐ Human Subjects Will Be At Risk.

5. AND 6. SEE REVERSE SIDE

7. NAME AND ADDRESS OF INSTITUTION

8. TITLE OF INSTITUTIONAL OFFICIAL	TELEPHONE NUMBER
SIGNATURE OF INSTITUTIONAL OFFICIAL	DATE

HEW 596 (Rev. 2/75) ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO REQUESTING AGENCY

(FACE)

1032819

5. INVESTIGATIONAL NEW DRUGS - ADDITIONAL CERTIFICATION REQUIREMENT

Section 46.17 of Title 45 of the Code of Federal Regulations states, "Where an organization is required to prepare or to submit certification. . . and the proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 130.3(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received."

INVESTIGATIONAL NEW DRUG CERTIFICATION

TO CERTIFY COMPLIANCE WITH FDA REQUIREMENTS FOR PROPOSED USE OF INVESTIGATIONAL NEW DRUGS IN ADDITION TO CERTIFICATION OF INSTITUTIONAL REVIEW BOARD APPROVAL, THE FOLLOWING REPORT FORMAT SHOULD BE USED FOR EACH IND (Attach additional IND certifications as necessary):

- IND FORMS FILED: ☐ FDA 1571 ☐ FDA 1572 ☐ FDA 1573
- NAME OF IND AND SPONSOR _____
- DATE OF 30-DAY EXPIRATION OR FDA WAIVER (Future date requires followup report to agency) _____
- FDA RESTRICTION _____
- SIGNATURE OF INVESTIGATOR _____ DATE _____

6. COOPERATING INSTITUTIONS' - ADDITIONAL REPORTING REQUIREMENT

Section 46.16 of Title 45 of the Code of Federal Regulations imposes special requirements on the conduct of studies or activities in which the grantee or prime contractor obtains access to all or some of the subjects through cooperating institutions not under its control. In order that the DHEW be fully informed, the following report is requested when applicable:

USE FOLLOWING REPORT FORMAT FOR EACH INSTITUTION OTHER THAN GRANTEE OR CONTRACTING INSTITUTION WITH RESPONSIBILITY FOR HUMAN SUBJECTS PARTICIPATING IN THIS ACTIVITY: (ATTACH ADDITIONAL REPORT SHEETS AS NECESSARY)

INSTITUTIONAL AUTHORIZATION FOR ACCESS TO SUBJECTS

- SUBJECTS: STATUS (WARDS, RESIDENTS, EMPLOYEES, PATIENTS, ETC.) _____

NUMBER _____ AGE RANGE _____

NAME OF OFFICIAL (please print) _____

TITLE _____ TELEPHONE _____

NAME AND ADDRESS OF COOPERATING INSTITUTION _____

- OFFICIAL SIGNATURE _____

NOTES: (e.g., report of modification in proposal as submitted to agency affecting human subjects involvement)

1032820

Sent 20 Feb 75
To all on committee
(except Dr Nelson)

February 4, 1975

Mr. J. A. Lenhard, Director
Research and Technical Support Division
Energy Research and Development Administration
Oak Ridge, Tennessee 37830

Subject: AUDIT REPORT 4-02-1, PATIENT SELECTION CRITERIA

Dear Mr. Lenhard:

Please find enclosed minutes of an ORAU Committee on Human Studies which convened in Oak Ridge on January 25, 1975. To the extent that portions of an AEC audit concerned with patient selection criteria were discussed at this meeting, you and Dr. Bibb will find these comments of interest.

Sincerely yours,

Original Signed By
PHILIP L. JOHNSON

Philip L. Johnson
Executive Director

PLJ:ahp

Enclosure

bc: Dr. Andrews

1032821

File with Human Research Committee

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

March 6, 1975

TO : Institutional Officers Responsible for Implementation of DHEW Policy and Regulations on Protection of Human Subjects

FROM : Director, Office for Protection from Research Risks
Office of the Director, NIH, DHEW

SUBJECT: Interim Guidelines for Fetal Research

These guidelines are enclosed. They are contained in a policy document implementing a provision of the National Research Act, Public Law 93-348. The provision is quoted in the first paragraph of the guidelines. Note that the burden of the law rests on the Secretary as he conducts research or supports research through grants, contracts, and other types of research agreements. These guidelines will remain in effect until withdrawn, altered, or until superseded by final (not proposed) regulations promulgated by the Secretary.

Since practically all of the inquiries reaching this office have been concerned with research involving only the dead fetus or abortus, your attention is called to the definition of death at 2(f) and the provisions at 6 and 7 concerning the dead fetus or abortus.

It is particularly critical that any institution proposing such research review with counsel the applicable laws including those governing the reporting of births, the reporting of deaths, preserving the sanctity of sepulchre, and autopsy.

It should be noted that in no state does permission to autopsy carry with it any automatic authority to retain organs or tissues except as further provided in medical examiner or other statutes.

Where research is to be conducted, consent should be obtained consistent with the terms of the Uniform Anatomical Gift Act as passed by the state in which fetal or abortal death occurs. This Act specifies who may consent and the terms of that consent.

D. T. Chalkley, Ph.D.

Enclosure

1032822

Signed
FORM

rt No.	Patient	Date	[redacted]	[redacted]
2789		3/24/75	ORAU	Hubner
2790		4/7/75	HNL	"
2791		4/8/75	HNL	Lindrew
2792		4/22/75	ORAU	C&E
2795		4/28/75	HNL	Hubner
2796		4/30/75	"	Lindrew
2797		5/1/75	"	"
2798		5/5/75	"	"
2799		5/6/75	"	"
2800		5/6/75	"	Hubner
2801		5/7/75	"	"
2802		5/7/75	"	"
2006		5/12/75	"	"
2808		5/13/75	"	Edwards
2814		5/20/75	"	Lindrew
2815		5/20/75	"	Hubner
2812		5/19/75	"	"
2813		"	"	"
		3-20-75	ORAU	HUBNER

1032823

Dr. Hubner

Oak Ridge Associated Universities

Incorporated

P.O. Box 117 - Oak Ridge, Tennessee 37830

Telephone 615 483-8411

June 10, 1975

Robert D. Lange, M.D.
Assistant Director
University of Tennessee
Memorial Research Center and Hospital
1924 Alcoa Highway
Knoxville, Tennessee 37920

Dear Bob:

Dr. Bill Nelson's recent resignation, February 28, 1975, and Dr. C. Lowell Edwards' resignation, effective June 13, 1975, create vacancies on the Committee on Human Studies of ORAU and OR-HNL. Also, as Acting Chairman of the Medical and Health Sciences Division, ORAU, I have recently been made aware of the report of the AEC-ORO Audit Report entitled "Patient Selection Criteria," and the need for our Division to comply with the recommendations of this audit as best we can. The time, therefore, seems appropriate for me to communicate with you about these matters.

I asked Dr. Nelson to continue to serve on the Committee but he felt he had to refuse because of the pressures of his new position at Baptist Hospital, Dr. Andrews is willing to continue to act as Secretary for you and the Committee. I would like to suggest that Dr. Karl Hubner be approved as Dr. Edwards' replacement and that I replace Dr. Nelson as pathologist, but that I be the only ex officio or nonvoting member, since I am nominally "in charge" of all the research being proposed from this Division.

The minutes of your meeting 25 January 1975 express the strong disagreement of the Committee with "Conflict of Interest" opinion of the AEC-ORO auditors. This disagreement is in accord with several statements on page 4 of The Institutional Guide to DHEW Policy on Protection of Human Subjects. The gist of these statements is that the members of such a committee can be chosen from the parent institution if there are sufficient staff members to serve. Or, in other words, there is nothing wrong with having your own staff on the Committee. In fact, a Human Use Committee can even consist of the members of some other existing committee of the staff, etc. It also states that Committee members who are involved in a proposed project should not be involved in its initial or continuing reviews. This is an accepted practice that we have always followed, so I do not see that we have any problem at all in this area, and we have no need for permanent "ex officio" members other than perhaps for me.

1032824

The problem of our need, according to ORO-ERDA, to evaluate our research proposals for possible social or psychological risk is more difficult to resolve. The guideline pamphlet is confused here because of its attempt at brevity. I cannot conceive of our ever proposing a project that could produce social or psychological risk for the human subject because we do not do social or behavioral studies. We do need to avoid the use of identifiable photographs of faces and personal information (for example, on sexuality, etc.) which we always do, but we have never had a medical project that utilized personality inventories, interviews, questionnaires, or the use of taped recordings, which could conceivably cause social or psychologic damage to the subject. It seems, however, easier to just modify our form's format so that it reads that the Committee considered whether social and psychologic risks are inherent in the project under review. Maybe this will require a box for you, the Chairman, to check off.

While our practice has always been to return proposals that require restrictions to the proposer for modification to meet any constraints suggested by the Committee, strict compliance with the HEW guide here seems to require our having to have an approval form that lists these restrictions. I do not personally approve of the use of such a form because it allows a restriction to be stated without the investigator having to physically as well as mentally revise his proposal before his proposal can be approved. I have asked Andy, however, to prepare such a form, and it is enclosed for your Committee's consideration.

I am not sure that these suggestions will achieve the necessary level of ERDA compliance that we need, but I am sure they would be considered a healthy first-step. After we accomplish these, they will re-evaluate our progress. The indisputable fact is that we do not want anyone to ever have any cause for believing that we are not protecting our human subjects in all the ways that HEW proscribes and then some.

Yours sincerely,

C. C. Lushbaugh, M.D.
Acting Chairman, Medical
and Health Sciences
Division

CCL:fb

Attachment

cc: Members of Human Studies Committee
Administrative Office
Medical Radionuclide Committee
Mr. Jim Berger (for Hurtubise)

1032825

Ident. No._____

COMMITTEE ON HUMAN STUDIES
of
Oak Ridge Associated Universities
and
Holifield National Laboratory

To Investigators

Your proposed research entitled_____

_____

_____

___/___ Has been approved as submitted

_____ Has been approved with the following limitations or instructions

_____

_____

_____

_____

_____ Has been disapproved because_____

_____

_____

_____
Robert D. Lange, M. D., Chairman
Committee on Human Studies

Please sign one copy and return to me.

1032826

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

July 21, 1975

Gould A. Andrews, M.D.
Chairman, Committee on Human Studies
Chairman, The Medical Division
Oak Ridge Associated Universities
Oak Ridge, Tennessee 37830

Dear Doctor Andrews:

Since your name was given as Chairman in 1972 and no committee updating has ever been submitted, it is very possible that you have been replaced. If so, would you please forward this letter to your successor.

Following Council meetings last March, one application from your institution came to our attention. Even though the project was disapproved on the basis of scientific merit, we would like to mention some general issues which it raises. The project is identified as follows:

1 R01 CA 17580-01 "Esterases and Oncogenesis," Dr. Richard L. Tyndall.

We are aware that there was correspondence between Dr. Tyndall and Dr. MacNamee prior to initial review and between Dr. Tyndall and Dr. Domanski following Council review. Dr. Domanski, however, did not mention the consent form or pursue the matter of whether or not this project or others like it would require committee review, were they to be awarded.

Item 7 of the application was checked to indicate that human subjects were not involved and Dr. Tyndall explained taking this position by stating that the plasmas will have been collected for diagnostic purposes and, moreover, that a "general release form" is signed by a patient when accepted.

In explaining types of risks and applicability of the Department of Health, Education, and Welfare regulations, it is stated that there are medical and biomedical projects concerned solely with organs, tissues, body fluids, or other materials obtained in the course of the routine performance of medical services, such as diagnosis, treatment and care, or at autopsy. The use of these materials obviously involves no element of physical risk to the subject. However, their use for many research, training, and service purposes may present psychological, sociological, or legal risks to the subject or his authorized representatives. In these instances, application of the policy requires review to determine that the circumstances under which the materials were procured were appropriate and that adequate consent was, or can be, obtained for the use of these materials for project purposes. Hence, it is up to the committee to determine whether or not

1032827

the subjects will be at risk resultant of their serum or bone marrow being used for research purposes. We have had numerous problems stemming from the use of 10 ml or smaller blood samples where the information obtained had medico-legal significance, potentially affected the individual's employability or insurability, or reflected on his status in society. Such problems are not always obvious, hence our insistence on committee review.

We also feel compelled, as did the reviewers, to comment on the consent form. This appears to be an extremely inadequate document for the purpose. It is urged that you review the "Hospital Law Manual" which your administrator should have, particularly Consents, Section 3, which discusses the distinction between admission and special consent forms. While the Manual does not cite any Tennessee cases, it discusses Louisiana and Missouri cases in some detail.

The leading Tennessee case on consent is Ball vs. Mallinckrodt Chemical Works (381 S.W. 2d 563, Tenn. 1964): "It is also the duty of a physician or surgeon to disclose to the (patient) facts which are necessary to form the basis of an intelligent consent. Where the consequences are serious and substantially certain to occur, it is (his) duty to disclose such facts to the patient." A mere reservation of the "...right to a full explanation..." does not meet a "...duty to describe..." or "...duty to disclose..." requirement. While this might get by for serum samples, we would not advise its use for anything more serious. Certainly it does not meet the informed consent requirements for DHEW supported projects. I would call your attention to the following sections of the enclosed DHEW regulations, 46.3 Definitions (c) and 46.10 Documentation of informed consent. In regard to the last sentence in your Patient Admittance Agreement, please note section 46.9 Obligation to obtain informed consent; prohibition of exculpatory clauses.

For an explanation of the responsibility of this office relative to this letter, please refer to the enclosed flyer.

Sincerely yours,

Katherine Duncan

Katherine Duncan, M.D.
Office for Protection
from Research Risks
Office of the Director

Enclosures (2)

1032828

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

April 8, 1975

To : Responsible Institutional Officials
and Investigators

From : Office for Protection from Research Risks (OPRR)
Office of the Director, NIH

Subject: Administration of the DHEW Regulations
for the Protection of Human Subjects

As is stated in Part 46 of Title 45 of the Code of Federal Regulations, safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity.

However, it is also stated that notwithstanding any prior review, approval, and certification by the institution, all applications or proposals involving human subjects at risk submitted to DHEW shall be evaluated by the Secretary for compliance through such officers and employees of the Department and such experts or consultants engaged for this purpose as he determines to be appropriate. Hence, initial review groups, advisory councils, and staff of awarding agencies, in addition to evaluating the scientific merit of proposals, also evaluate the adequacy of the provisions for safeguarding the rights and welfare of the subjects.

The OPRR has been delegated the responsibility for the administration of the DHEW policy for the protection of human subjects. In addition to negotiating general and special assurances, our office is charged with maintaining liaison with the institutions and monitoring their compliance with the policy.

In carrying out these assigned duties, our office conveys to the Institutional Review Board responsible for the review of all such projects any concerns expressed by initial review groups and concurred with by advisory councils, relative to the involvement of human subjects, regardless of whether the final recommendation was for approval or disapproval. A staff member of the awarding agency may have included these concerns in a letter to the investigator, or in some instances to an institutional official also. After attempting to determine that there has been no communication to an official, our office then assumes the responsibility for writing. However, letters from this office may for various reasons be subject to a delay of approximately 6 months. We address ourselves only

1032829

to the expressed human subject concerns, and not to the scientific aspects of the proposal; that type of information is provided by staff of the awarding agency only to the principal investigator, either upon his request or if the reviewing groups have recommended communication.

We would like to emphasize that comments conveyed in the attached letter represent those of the reviewers, "such experts or consultants engaged for this purpose" by the Secretary, not those of this office; that they are for the information of the Institutional Review Board; and that they are not intended to direct the institutions' or the investigators' research aims.

Katherine Duncan

Katherine Duncan, M.D.

FORM P-4

MEMORANDUM

TO Dr. Lushbaugh DATE July 10, 1975

SUBJECT Human Studies Committee

COPIES TO

I have retyped the Assurance of Compliance, which I would like for you to check over.

I believe we need to do something about Addendum III, since the membership has changed considerably since the CVs on original members were sent to DHEW.

Frances

I think we need to send the assurance to Chet Richmond for his signature, now with a note telling him that Dr. Johnson won't return from vacation until 7/28. His Secretary said to send with it a copy of the last one signed by Severinghaus (Point out mel Koon to Richmond also get out the C.V.'s on the members and we'll update the membership list and the C.V.'s while waiting for Richmond's signature

1032831

UNION CARBIDE

INTERNAL CORRESPONDENCE

NUCLEAR DIVISION

POST OFFICE BOX X, OAK RIDGE, TENNESSEE 37830

To (Name) Melvin E. Koons
Division
Location 9704-2

Date July 16, 1975

Originating Dept.

Answering letter date

Copy to

Subject ORAU/ORNL Human Use Committee

Dr. Lushbaugh, Oak Ridge Associated Universities, just sent me the attached "Human Use Committee Assurance of Compliance" forms for signature. As the result of a subsequent phone conversation, he suggested I send the material to you for assistance.

I have the following problem: The proposed format refers to "this institute" whereas the previous form referred to "these institutions." This change, according to Lushbaugh, was to comply with the new guidance. The Committee represents both institutions and we would prefer to keep it as such and not have two committees, if possible. Could you reword the agreement or let Lushbaugh know what needs to be done? Could both letterheads be used or is this, in your opinion, really important? Also, is it proper for me to sign the agreement for ORNL (Liverman did in 1972) or does UCCND now require someone else to do so?

Please note the 31 July deadline for completion of action. I appreciate your assistance in this matter.

C. R. Richmond

Chester R. Richmond

CRR:br

Attachments

cc: C. C. Lushbaugh ✓

Frances - now we can contact Mel Koons about our other questions. What were they?

1032832

FORM P-4

MEMORANDUM

TO File DATE July 17, 1975

SUBJECT Committee on Human Studies

COPIES TO

I talked with Chet Richmond today about the Assurance of Compliance requested by NIH by July 31. He tried to pull my leg about our use of the phrase "this institution" instead of "these institutions." Apparently he was thinking of the institutions "ORNL" and "ORAU" while I was thinking of the one "Committee" as the "institution." I suggested that this problem be resolved and meet, at the same time, NIH's request that this assurance be sent in on official letterhead paper, by both ORAU and ORNL filing a letter of assurance signed by both ORAU and ORNL and indicate somehow that there is only one Committee. Since Mel Koons is on this Committee it would seem like an easy job for him.

C. C. Lushbaugh

1032833

Mr. Mel Koons

July 23, 1975

ORAU/ORNL Committee on Human Studies

File

Enclosed are copies of some materials we received recently from DHEW, along with my most recent letter to Dr. Lange, Chairman of the ORAU/ORNL Committee on Human Studies. This letter and these materials may be of aid in regard to Dr. Richmond's July 16 request to you for assistance. We (the Committee and I) also need your legal counsel about "legally effective" and "legally authorized representative," on page 2 of DHEW's instructions, paragraphs marked "Mr. Koons." Our use of the phrase "This Institution" instead of "These Institutions" in the Assurance I sent to Dr. Richmond resulted from my copying the suggested format of Addendum I enclosed, and I feel "these" is more correct in our case. DHEW's request for the Institutional Assurance being "on the institution's letterhead" however confabulates me further since ORNL and ORAU do not have a joint one. How do we get around this request?

C. C. Lushbaugh, M. D.

Enclosures

Copy of May 22 Memo from Chalkley (7 pages)
Addendum I
assurance of Compliance This to These
Dr. Lushbaugh's letter to Lange, July 22.

1032834

Dr. Hubner / RLH

federal register

FRIDAY, JULY 25, 1975

WASHINGTON, D.C.

Volume 40 ■ Number 144

PART II

THE NATIONAL ARCHIVES OF THE UNITED STATES * 1934 *

AUG 1975 RECEIVED Serial Records Branch

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

■

RADIOACTIVE DRUGS AND RADIOACTIVE BIOLOGICAL PRODUCTS

1032835

Title 21—Food and Drugs

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

[Docket No. 75N-0067]

RADIOACTIVE NEW DRUGS AND RADIOACTIVE BIOLOGICS

Termination of Exemptions

In a notice of proposed rule making published in the FEDERAL REGISTER of July 29, 1974 (39 FR 27538), the Commissioner of Food and Drugs proposed to terminate the present exemption for radioactive new drugs (including radioactive biological products) for investigational use from new drug requirements and classify, by use, radioactive drugs either as "new drugs" or as generally recognized as safe and effective for their intended use and therefore not "new drugs" when used under the conditions specified. Interested persons were invited to submit comments on the proposal by September 27, 1974.

The Commissioner of Food and Drugs is terminating the present exemption for radioactive drugs, including radioactive biological products, from the investigational new drug requirements of the Federal Food, Drug, and Cosmetic Act. The Food and Drug Administration (FDA) is establishing regulations to assure that after August 25, 1975 all radioactive drugs, except those for certain research uses, introduced into interstate commerce are subject to a "Notice of Claimed Investigational Exemption for a New Drug" (IND), an approved new drug application (NDA), or a biological product license. In addition, the FDA is establishing regulations setting forth specific conditions under which radioactive drugs for certain research uses, other than clinical trials to determine safety and effectiveness, are not subject to the new drug requirements of the act.

The Commissioner, for the purpose of an orderly development of regulations relating to the establishment of procedures for codifying old drug monographs for prescription drugs which are generally recognized as safe and effective and not misbranded, has redesignated proposed new 21 CFR Part 370 as 21 CFR Part 361 and limited it to drugs used in research. All future old drug monographs for such drugs will be incorporated into Part 361.

The U.S. Nuclear Regulatory Commission (NRC), a new agency created by Pub. L. 93-433 and Executive Order 11834, assumed the licensing and related regulatory responsibilities of the former Atomic Energy Commission (AEC) on January 19, 1975. To conform to this organizational change, all references to the AEC in this regulation and in the preamble have been changed to the NRC. In the quotation from and discussion of comments received from members of the public on this proposed regulation, references to the AEC have been changed to the NRC even though the comments from the public were made prior to the organizational change.

Elsewhere in this issue of the FEDERAL REGISTER the Commissioner is issuing an order effecting a transfer of responsibility for radioactive biological products from the Bureau of Biologics to the Bureau of Drugs.

Comments on the proposal were received from 21 different sources; namely, hospitals, universities, professional organizations, trade associations, manufacturers, Agreement States (i.e., States which, under formal agreement with the NRC, are authorized to license, under Federal law, persons engaged in the possession, use, or transfer of reactor-produced radionuclides in their respective states), and State health departments.

The major areas of concern as expressed by the comments were the composition of the Radioactive Drug Research Committee (proposed as the Radiation Safety Committee), the use of State advisory committees, radiation dosimetry, procedures for providing the summary of information on radioactive drugs for investigational use and the "Report on Research Use of Radioactive Drug" to the NRC and appropriate Agreement States, limitation on pharmacological dose for research not under an IND, and the applicability of the proposed regulation to radiopharmacies. Eight comments supported the proposal in principle but offered suggestions for modification, clarification, and addition to some areas. The principal comments received and the Commission's conclusions are as follows:

DEFINITION OF A RADIOACTIVE DRUG

1. One comment pointed out that in § 312.1 the additional information to be supplied in new items 6.d, 10.a, and 16 of Form FD-1571 is required only if the investigational drug is a "radioactive drug" but the term "radioactive drug" is not defined in the proposed regulation.

The Commissioner has determined that a "radioactive drug" is any substance defined as a drug in section 201 (g) (1) of the Federal Food, Drug, and Cosmetic Act which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any nonradioactive reagent kit or nuclide generator which is intended to be used in the preparation of any such substance. The term "radioactive drug" includes a "radioactive biological product" as defined in 21 CFR 600.3(ee). This definition does not include drugs such as carbon-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides. Section 310.3 has been amended to include this definition in paragraph (n).

IND REQUIREMENTS FOR RADIOACTIVE NEW DRUGS

2. Several comments suggested that the Summary of Information as required by § 312.1 be forwarded directly by the manufacturer to the NRC or Agreement States rather than by the Food and Drug Administration. Such a procedure would enhance the manufacturer's efforts to protect the confidentiality of any proprietary information contained in the summary, would free the FDA from further administrative workload, and would eliminate the possibility of administrative delays in forwarding the necessary information to the NRC or Agreement States. Comments also pointed out that the proposed regulation does not provide a procedure for notifying the NRC and Agreement State authorities that the FDA has approved an NDA or issued a biological product license.

This proposed regulation was not intended to preclude the sponsor from forwarding the Summary of Information directly to the NRC or Agreement States. The proposal was merely a service which FDA would provide to IND sponsors and to the Federal and State licensing agencies to expedite the processing of licensing applications. The Summary of Information serves no regulatory purpose for the FDA. Failure of the IND sponsor to submit the Summary of Information, or to authorize its release to licensing agencies, would not alter the status of the IND.

The Commissioner had intended that the release of the Summary of Information to Federal and State licensing bodies would not waive any confidentiality to which the sponsor of the IND would be entitled under the FDA Public Information regulations (21 CFR Part 4; 21 CFR 312.4; and 21 CFR 314.14). Under these regulations, FDA records which are normally exempt from disclosure (e.g., existence and contents of an IND) may be disclosed, without requiring disclosure to the public at large, to a department or agency that has concurrent jurisdiction over the matter and separate legal authority to obtain the specific information involved, 21 CFR 4.84. The NRC (and through it, the Agreement States) would satisfy these criteria. The regulations require, however, that such disclosure "be pursuant to an agreement that the record shall not be further disclosed by the other department or agency except with the written permission of the Food and Drug Administration." The NRC has informed the FDA that it would not agree to this restriction and would not assure any confidential treatment for the Summary of Information.

The Commissioner believes that, under these circumstances, retaining the Summary of Information would not be justified because the administrative problems which would arise are too numerous. First, separate agreements would be required for each of the 25 Agreement States; besides the practical difficulties involved, the legality of these agreements would be in doubt, since the Agreement States derive authority from the NRC. Secondly, each IND submission with a Summary of Information would have to be examined to determine in which states the IND drug might be used: those with agreements for confidentiality would be notified, but those without, and those under NRC jurisdiction, would not be notified. In short, providing this service would become very complicated. One alternative, to provide that an explicit waiver of confidentiality be signed by the IND sponsor if he chose to submit the Summary of Information, seemed unlikely to generate a significant num-

1032836

ber of cases in which FDA could disclose the Summary of Information. It might also confuse sponsors and lead to erroneous or unintended waivers.

Therefore the Commissioner has deleted item 16 from the proposed amendments to IND Form FD-1571 and item 6.i and item 4.i from the proposed amendments to Forms FD-1572 and FD-1573, respectively. The Commissioner advises that he remains quite willing to adopt a procedure for providing information regarding IND's directly to Federal and State agencies if and when all such agencies agree not to disclose any confidential information so provided without the written permission of the FDA.

The Commissioner advises that the FDA has notified Agreement States and the NRC of all existing approved NDA's and biological product licenses for radioactive drugs and radioactive biological products. Procedures have been established to continue to notify the NRC and all Agreement States of all new approvals of NDA's for radioactive drugs and radioactive biological products. These procedures do not, however, preclude an applicant from notifying the NRC or an Agreement State of an NDA approval.

3. One comment suggested that § 312.1 should include concise and complete details for an acceptable protocol and pointed out that such areas as dosimetry, expected or documented clearance rates, and rationale of diagnosis or therapy were not contained in the new proposed rules.

The Commissioner is of the opinion that the present IND regulations (§ 312.1) and Form FD-1571 with the additions set forth in the proposal, are adequate as requirements for the development of a protocol for producing well-controlled clinical data on radioactive drugs. Each protocol for an IND study for a radioactive drug wil be evaluated individually. In § 312.1, item 10.a of Form FD-1571 requires that the protocol include studies which will obtain sufficient data for dosimetry calculations and that these studies should evaluate the excretion, whole body retention, and organ distribution of the radioactive material. The FDA is currently preparing guidelines for research protocols on radioactive drugs; the Radioactive Pharmaceuticals Advisory Committee is assisting in this and, as drafts are developed, they will be discussed in open sessions of that advisory committee. When adopted, these guidelines will be available from the Agency.

4. One comment questioned whether it was necessary to amend or otherwise alter an existing IND for a nonradioactive investigational new drug if the drug is "tagged" with a radioactive element in accordance with the limitations set forth in proposed §370.100. The comment also expressed the opinion that, if an investigational drug is "tagged" and administered at or near a pharmacologic dose, the new information required in items 6.d and 10.a of Form FD-1571 should be submitted as an amendment to the existing IND and a new IND should not be required.

The Commissioner concludes that it is not necessary to amend an existing IND for a nonradioactive investigational new drug if the drug is "tagged" with a radionuclide in accordance with the limitations set forth in § 361.1 (proposed § 370.100), and the specific research study is within the purposes set forth by that section. The results of the research study using the "tagged" compound must, however, be submitted to the existing IND. If pharmacological data are not sufficient to permit compliance with the requirements of § 361.1, it would of course be necessary to submit a new IND or, preferably, to amend the existing IND for the nonradioactive investigational new drug to conduct a study on the drug "tagged" with a radionuclide, even though the radioactivity limits set forth in § 361.1 are met. To amend an IND in this way, the information required in items 6.d and 10.a of Form FD-1571 must be submitted.

5. One comment suggested that, to assist the Federal and State regulatory agencies in fulfilling their responsibility for licensing the use of radioactive materials, the Summary of Information required in Form FD-1571 should be expanded to include: information describing the plan of investigation in sufficient detail to permit a critical evaluation of the methods and controls to be used; an indication as to whether any complementary drug or radionuclide administration is planned or contemplated in conjunction with the study; an indication of the expected fate of the radiopharmaceutical administered; if for therapeutic purposes, an indication of the expected effects; and calculations of the radiation doses delivered to the whole body and to the critical organ(s).

As stated in paragraph 2 above, the Commissioner has deleted item 16 (Summary of Information) from the amendments to IND Form FD-1571. Information needed by the NRC and Agreement States for licensing purposes must be obtained from the IND sponsors.

6. One comment suggested that, although radiopharmaceuticals are relatively simple organic compounds with little or no toxicological/pharmaceutical activity and may not require chronic toxicity studies, the regulations should require semichronic toxicity studies in anticipation that radiopharmaceuticals may, in the near future, be considerably more complex.

The Commissioner recognizes that an IND for radioactive drugs may in some cases require chronic or subacute toxicity studies. The preamble to the proposed regulations only noted that chronic toxicity studies may not be required for some radioactive drugs. The requirements for any IND will depend on the specific nature of the drug and its proposed uses.

7. One comment argued that the proposed regulations failed to distinguish between "hot" (radioactive) and "cold" (nonradioactive) pharmaceuticals and between diagnostic and therapeutic agents by applying to radioactive pharmaceuticals the same clearance procedures applicable to nonradioactive pharmaceuticals. The comment further suggested that a definitive statement was needed recognizing the difference between these two types of pharmaceuticals, as well as clear guidelines setting forth a workable format from which manufacturers can fashion their studies to comply with investigational new drug as well as new drug application requirements. These guidelines should be specifically tailored to reflect realistically the unique problems in the field of radiopharmaceuticals.

The Commissioner realizes that IND requirements for radioactive drugs will differ in various ways from those involving nonradioactive drugs, and this is clearly stated in the preamble to the proposed regulations. This situation is not unique, however, since requirements for one nonradioactive drug may differ sharply from those for a different nonradioactive drug. The requirements of § 312.1 are general requirements and are regularly adapted as appropriate for specific drugs. The FDA is currently in the process of drafting guidelines for conducting clinical trials involving radioactive drugs.

NDA Requirements for Radioactive New Drugs Generally

8. One comment questioned whether or not a mechanism had been established for filing abbreviated new drug applications for diagnostic radiopharmaceuticals.

The Commissioner advises that no mechanism has been established yet for submitting an abbreviated new drug application for a radioactive drug. The Commissioner recognizes, however, that the amount of clinical data necessary to approve an NDA varies among radioactive drugs, depending on several factors. Applicants are invited to meet with representatives of the FDA, Bureau of Drugs, Division of Oncology and Radiopharmaceutical Drug Products, to discuss the amount of data needed prior to submission of an NDA.

9. One comment suggested that there be a mechanism whereby previous work performed under an IND or an NDA could be referenced for a radiopharmaceutical for which a new use is being developed, provided the previous work is applicable to the new use.

The Commissioner advises that previous unpublished studies relating to a radioactive drug for which a new use is being developed may be incorporated by reference from one IND or NDA file into another only if the sponsor of the previous IND or applicant of the previous NDA authorizes the new sponsor or applicant to use these data.

NDA Requirements for Certain Radioactive New Drugs

10. One comment indicated that, at the outset of the preamble to the proposal, a statement is made that "any radiopharmaceutical which is not a 'new drug,' i.e., when used under the conditions specified, will require neither an IND nor an NDA, but will require certain documentation to establish that the drug is in fact being

1032837

used under the conditions set forth in the regulation." The proposed rules then go on to set dates for the filing of an NDA for all radioactive pharmaceuticals with well-established medical uses. The comment requested clarification as to how those pharmaceuticals listed in § 310.503 (f) (1) relate to those referred to above.

The Commissioner advises that § 310.503(f) (1) lists a group of new drugs, reactor-produced radionuclides and their chemical forms, which the FDA and the NRC have determined have well-established medical uses. In view of the extent of experience with drugs containing these radionuclides, the FDA and the NRC have concluded that they should not be distributed under investigational use labeling when they are actually intended for use in medical practice. Such drug products have not been used to a material extent or for a material time and are not yet regarded as generally recognized as safe and effective for their labeled indications. However, it may reasonably be expected that adequate evidence of safety and effectiveness can be submitted by manufacturers and distributors for use of these drugs as recommended in appropriate labeling. In order to continue shipping in interstate commerce drugs containing these radionuclides, manufacturers and distributors must submit an NDA, IND, or application for a biological product license, on or before August 25, 1975. An IND will not, however, permit continued commercial marketing of these drugs.

On the other hand, § 361.1 (proposed as § 370.100) specifies conditions under which radioactive drugs are generally recognized as safe and effective and therefore are not new drugs. Such drugs do not require an NDA, biological product license, or IND. The statement quoted in the comment referred to the fact that, for these drugs, reports will be required (in the form of annual or special reports from the Radioactive Drug Research Committee (see paragraph 29)) to assure FDA that use of the drug remains within the conditions under which the drug is generally recognized as safe and effective.

11. One comment questioned whether the December 31, 1974 deadline for submission of NDA's applies only to those radioactive drugs listed in "§ 130(c) of the November 13, 1971 FEDERAL REGISTER" and in the table included in § 310.503(f) (1) of the July 29, 1974 proposal.

The Commissioner assumes that the comment meant to refer to "§ 130.49(c) in the FEDERAL REGISTER of November 3, 1971" instead of "§ 130(c) in the FEDERAL REGISTER of November 13, 1971." The December 31, 1974 deadline set forth in the July 29, 1974 proposal for submission of an NDA, IND, or application for a biological product license applies only to drug products, including biological products, which contain any of the radionuclides listed in § 310.503(f) (1) in the "Chemical form" listed and for the indications listed. This deadline has now been extended to August 25, 1975. The purpose of this deadline is to allow manufacturers and distributors who are currently marketing drug products containing any of the radionuclides listed in § 310.503(f) (1) time to submit to the FDA information necessary for continued marketing of these products. This deadline is not applicable to drug products, including biological products, containing any of the radionuclides listed in § 310.503(c) (formerly § 130.49(c)). Manufacturers and distributors were given until March 3, 1972 to submit an NDA, IND, or application for a biological product license to continue distribution of those products for any of the indications listed.

12. One comment pointed out that the November 1971 regulations allowed the submission of a new drug application for an existing product without requiring the prior submission of either clinical data or an investigational new drug application and questioned whether such a policy was still in effect.

The Commissioner advises that this policy is applicable to those radioactive drugs listed in § 310.503(f) (1). These are products which the FDA and the NRC consider to have well-established medical uses. The Commissioner has concluded that manufacturers and distributors of these drugs may reasonably be expected to be able to submit adequate evidence of safety and effectiveness for use as recommended in appropriate labeling without conducting additional clinical studies to obtain such data. The policy is the same as that announced in the November 3, 1971 order for similar radioactive drugs.

13. One comment stated that this proposal "would create a new structure, on a temporary basis, to regulate a relatively small number of drugs." The comment further stated that "it may be more effective to require immediate submission of an IND and to permit the drug's continued use in interstate commerce for a shorter period under the same circumstances as it had been thereto used."

The Commissioner assumes that the comment is in reference to § 310.503 which lists a group of new drugs, reactor-produced radionuclides and their chemical forms, which the FDA and the NRC determined have well-established medical uses. No new structure is proposed to deal with these drugs. In view of the extent of experience with the radionuclides listed in § 310.503(f) (1), the FDA and NRC concluded that they should not be distributed under investigational use labeling when they are actually intended for use in medical practice, and that manufacturers and distributors may reasonably be expected to submit adequate evidence of safety and effectiveness for use as recommended in appropriate labeling. To continue shipping drugs containing these radionuclides in interstate commerce an NDA, IND, or application for a biological product license, must be submitted. An IND will not, however, permit continued commercial marketing of these drugs.

14. One comment requested clarification as to what effect, if any, the revision of § 310.503 would have on lists of "well-established uses" which many Agreement States have developed but which do not totally agree with those of the NRC. Another comment proposed the addition of Indium-113m to the list in § 310.503(f) (1).

The Commissioner has determined that only those radioactive drugs listed under § 310.503 shall be considered by the FDA to have well-established uses in medical practice. In the preamble to the proposal, the Commissioner invited any person who believed that other radioactive drugs are widely used in medical practice and should be added to this list to submit comments and data proposing and justifying the addition of such drugs. The request for addition of the isotope Indium-113m to the well-established list was submitted. The data submitted in support of the request (which is on display in the Hearing Clerk's office) have been reviewed, the Radioactive Pharmaceuticals Advisory Committee consulted, and the request approved. Section 310.503(f) (1) has been modified accordingly.

15. A comment requested that the regulations for radioactive new drugs include provisions to clarify the requirements regarding reactor-produced by-product materials when such products are processed and shipped in bulk to other manufacturers for reprocessing into finished drug forms.

The Commissioner advises that bulk byproduct materials intended for processing, repacking or use in the manufacture of another drug shall be processed, shipped, and labeled in compliance with 21 CFR 201.122 (formerly 21 CFR 1.106 (1)).

NUCLEAR PHARMACY ISSUE

16. One comment questioned whether the FDA had jurisdiction over radioactive drugs, in the investigational stage or for well-established medical uses, that are prepared by the using physician and qualified associate staff rather than procured from a commercial pharmaceutical concern. The comment further stated that the provision of nuclear medicine services and the continued development of techniques, methods and products would be severely inhibited by requiring an IND or NDA under such circumstances, particularly in the larger clinical and research centers where much of the innovative and developmental advances evolve. Another comment questioned whether the proposed regulation was applicable to those so-called "regional radiopharmacies" which manufacture their own radioactive drugs including the non-radioactive components.

Elsewhere in this issue of the FEDERAL REGISTER, the Commissioner is issuing a notice regarding the Food and Drug Administration's policy on the "nuclear pharmacy" issue.

REQUIREMENTS FOR RESEARCH USES OF RADIOACTIVE DRUGS GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED

A. SCOPE OF DETERMINATION

17. One comment stated that in medical institutions operating under an NRC Broad Medical License new radiopharmaceuticals are sometimes developed in-

1032838

ternally and subjected to clinical trials to establish diagnostic or therapeutic efficacy. The comment questioned whether it is necessary for these institutions to submit an IND even though in the developmental and testing phase the drug is not shipped in interstate commerce. The comment further questioned whether such clinical trials relating to diagnostic efficacy were covered by proposed § 370.100 and whether it would be necessary to file reports on investigators of this type approved by a radioisotopes committee under a Broad License, either annually or immediately. If such clinical trials are not covered by proposed § 370.100, would the dose restrictions specified under that section apply?

The Commissioner advises that the FDA has jurisdiction over all drugs, including radioactive drugs, shipped in or introduced into interstate commerce whether prepared by a medical institution, physician, or a commercial drug manufacturer. "Shipment in interstate commerce" is determined not only by the interstate shipment of the final dosage form of the drug product, but also by the interstate shipment of the components of the drug product, as well as other factors. Therefore, where a determination is made that interstate commerce is involved (also see paragraph 15 of this preamble), an IND must be submitted before the drug product may be used in clinical trials.

As stated in the preamble to the proposal, the Commissioner has concluded that the provisions of § 361.1 (proposed § 370.100) are not applicable to clinical trials intended to determine the safety and/or effectiveness of a radioactive drug. Section 361.1 only applies to research "intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a radioactively labeled drug or regarding human physiology, pathophysiology, or biochemistry but not intended for immediate therapeutic, diagnostic, or similar purposes." Clinical trials using new radioactive drugs are subject to the requirements of an IND as set forth in § 312.1. Section 361.1 of this regulation has been clarified to reflect this. The dose restrictions set forth in § 361.1 do not apply to clinical trials conducted under § 312.1.

18. One comment expressed confusion in interpreting the scope of the exemption provided by proposed § 370.100 as it relates to the development of new radioactive diagnostic agents. The comment further stated that it was not clear why the particular agent being studied cannot be used specifically for diagnostic purposes if the criteria for exemption under proposed § 370.100 are met (i.e., radiation safety, pharmacological inactivity, and Radioactive Drug Research Committee approval).

Section 361.1 (proposed § 370.100) provides for the use of tracer amounts of radionuclides, attached to various compounds, in research studies to obtain basic information on drug metabolism, specific physiologic or pathophysiologic processes in humans, and the kinetics, distribution, and localization of the various "tagged" compounds. Certain studies included in this category may be essential parts of the development of a new diagnostic agent (for example, studies conducted to determine where the radioactive drug is localized or the extent to which it is concentrated in certain organs or tissues). Such studies fall within the scope of § 361.1 if other requirements of that section are met. These studies must be distinguished from studies intended to evaluate the safety and effectiveness of a radioactive drug as a diagnostic agent. In this case the drug is used, not as a research tool, but as a new diagnostic agent for which safety and effectiveness must be proven; therefore, there is no basis for concluding that it is generally recognized as safe and effective as a diagnostic agent. The radioactive diagnostic agent, therefore, must be studied under an IND.

B. LIMITS ON PHARMACOLOGICAL DOSE

19. Several comments were received regarding the requirements under the proposed § 370.100 that the pharmacological dose shall be known not to cause any clinically detectable pharmacological effect in human beings. One comment expressed the thought that such a limit on the pharmacological dose was unrealistic and unnecessary and would place severe and unnecessary restrictions upon research in such vital areas as human drug metabolism. The comment further noted that, since doses known not to cause any clinically detectable pharmacological effect are often substantially below the therapeutic dose, radioactive studies conducted with such minute doses would not be representative of the pharmacokinetics of the drug studied at the therapeutic dose. Further, it was stated that such studies would not furnish enough labeled metabolites to conduct metabolite studies. Another comment suggested that the exemption from IND requirements should include the tagging of a drug at a dose level having a pharmacologic effect if that dose level is safe and effective, as evidenced by an approved NDA.

In the preamble to the proposed regulation, the Commissioner made it clear that for radioactive drugs to be considered not new drugs for certain uses it was necessary to conclude that they were generally recognized as safe for such uses. The Commissioner suggested that such a conclusion could certainly be reached, with regard to the pharmacological safety of the drug, if the drug was known not to produce clinically detectable pharmacological effects on the basis of data from studies in human beings. If such data are not available, even the smallest amount of that drug must be assumed to produce pharmacological activity. Once pharmacological activity is known or assumed to occur, pharmacological safety cannot be presumed and other evidence of general recognition of safety is necessary. Without this evidence, the drug is considered to be a new drug, and any research with it must meet the requirements of § 312.1, including the submission of an IND.

The fact that a drug is approved for certain specific uses means that it is considered safe and effective for these uses. It is not considered safe and effective for other uses or for non-therapeutic uses. The Commissioner recognized that the proposed standard for demonstrating general recognition of safety (i.e., the absence of pharmacological activity) was a strict standard and interested persons were invited to submit comments on the appropriateness of the proposed standard. While proposing this standard, the Commissioner also invited comments on an alternative test; namely, that the amount of radioactive drug administered not exceed a dose of 10 percent of the lowest single dose recommended by the drug's labeling, or in the absence of approved labeling, 10 percent of the lowest single dose recommended by recognized medical texts, with the exact dosage being reviewed by a peer committee for safety. Although comments objected to the proposed standard and, in some cases, suggested alternatives, no comments were received which provided reasons for considering any standard, other than the absence of clinically detectable pharmacological activity, as demonstrating general recognition of safety. While the Commissioner may at some future time reconsider this issue, he has concluded that, at present, for the purpose of this regulation, general recognition of pharmacological safety can be considered to exist only when the drug has no clinically detectable pharmacological effect in human beings.

It should be stressed that it is not anticipated that there will necessarily have been a formal dose-response study that defines the lower threshold dose for a clinically detectable pharmacological effect. For example, if the circulating blood levels or excretion rate of an endogenously produced substance is well known, it may be possible for the Radioactive Drug Research Committee (see paragraph 29) to conclude that some small fraction of these levels or rates (e.g., administration over a given interval of a low percentage of the amount of a substance that is produced endogenously during the same interval) represents an amount without detectable pharmacological effect. Or, if large amounts of a substance such as an amino acid or sugar are regularly consumed as foodstuffs, it may be possible for the Radioactive Drug Research Committee to conclude that a small amount of it (e.g., a small percentage of the amount usually consumed during a meal), at least by the oral route, would be without detectable pharmacological activity.

The Commissioner is aware that pharmacokinetic studies or studies requiring isolation of metabolites may require larger amounts of a drug. Such studies may either be conducted under an IND or in persons already receiving the nonradioactive drug for a therapeutic purpose.

20. One comment suggested modification of proposed § 370.100(b)(2) to allow, under well-defined conditions, the administration of the radio-labeled ver-

1032839

sion of a pharmacological agent when this pharmacological agent is administered to the patient in pharmacological doses as part of a therapeutic treatment and to assess the effectiveness of that particular therapy. The comment suggested adding the statement "If a drug is used under protocol for therapeutic purposes, then a minimal dose of the radio-labeled isomer of this drug can be added to help evaluate the radiopharmacokinetics of this drug."

The Commissioner advises that this regulation in no way restricts the use of a nonradioactive drug, i.e., under an IND, NDA, or old drug status, whether or not the radioactively labeled version of this drug is administered at the same time to evaluate the pharmacokinetics of the drug. For such a study to be permitted under § 361.1, the conditions of that section must be met, except that in this case the limitation on pharmacological dose will be such that the aggregate amount of the drug administered (nonradioactive drug and tagged compound) shall be known to remain an appropriate dose for the use for which the nonradioactive drug is being given. The regulation has been clarified to reflect this. The Commissioner also advises that if the nonradioactive drug has an IND, the results of any research studies using the radioactively labeled version of the drug and performed under § 361.1 must be included as part of the required IND reports.

21. One comment stated that the fundamental information to determine what "traditional pharmacology based judgment" means needed amplification and the term "no response" was not clear.

In paragraph D.1 of the preamble to the proposal, the Commissioner stated that "when radioactive drugs are administered in amounts which have been demonstrated not to produce clinically detectable pharmacologic activity in human beings, such drugs are and must be generally recognized as safe from the viewpoint of traditional pharmacology." In this context "traditional pharmacology" was intended only to distinguish hazards related to the toxic effects of the drugs (traditional pharmacology/toxicology) from those related to hazards of radiation. The term "clinically detectable pharmacologic activity" in human beings has been discussed above. Neither the term "no response" nor "traditional pharmacology" are used in the regulation; therefore no change is needed.

C. LIMITS ON RADIATION DOSE

22. One comment indicated that the intent of proposed § 370.100(b)(3) was not clearly stated in the preamble but presumed that the radiation limits are stated so that it will not be necessary to file an IND for research projects which do not lead to diagnostic tests.

The Commissioner advises that the intent of § 361.1 (proposed § 370.100) is to identify a class of drugs that are not new drugs because they are generally recognized as safe and effective under specific circumstances. One of those circumstances is that the radiation dose to subjects does not exceed certain limits. The identification of this drug class as not new drugs has the effect of making it unnecessary to submit an IND before using them.

23. One comment questioned whether it was necessary that there be a radiation dose limit included among the conditions under which the use of radioactive drugs for research is considered safe and effective. The comment stated that "if a local committee is deemed to have the judgment to assess and approve varied lesser dose procedures, need they be limited in regard to the far less frequent situations of a particularly important research study that might necessitate a larger organ dose?" The comment suggested that it might be preferable to offer the option to the local committee of referring to an FDA-sponsored "supercommittee" research proposals which, because of larger dosage or other unusual considerations, the local committee would prefer to have acted upon by a higher authority.

The Commissioner disagrees with the suggestion of the comment. When a pharmacologically inactive amount of a radioactive drug is used, the issue of safety for use in human subjects is entirely related to the amount of radiation administered. Because any exposure to radiation is presumed to have an attendant risk (due to a lack of evidence showing any absolutely safe level of exposure), it is obvious that no radiation exposure can be justified or considered generally recognized as safe as a research tool if the study in which it is used is of poor quality or is not likely to provide useful information. The Commissioner has concluded that the Radioactive Drug Research Committee (see paragraph 29) can assure the quality of studies and the minimization of the radiation dose. Nevertheless, despite this conclusion, the Commissioner has no basis for concluding that all doses of a radioactive drug, even if used for research purposes and monitored by a properly functioning committee, are generally recognized as safe for the intended use. He has therefore concluded that a limit on radiation dose is necessary to make a determination of general recognition of safety for research uses. As discussed below (in paragraph 24), the Commissioner has concluded that the basic occupational radiation protection criteria established by the NRC under 10 CFR 20.101 and 20.102, even though they were not intended to be criteria related in any way to subjects in clinical research, provide a reasonable basis for the determination that a radioactive drug, when administered in amounts such that the pharmacological and radiation dose from such drug is within the limits of § 361.1(b), and under the cognizance of an FDA-approved committee, is generally recognized as safe. It should be emphasized that this limit for purposes of establishing general recognition of safety in no way represents a conclusion that such radiation doses do not represent some element of risk to the individual nor that larger doses are necessarily unsafe. It is further emphasized that setting a limit on radiation dose for purposes of § 361.1 does not alter the requirement that the radiation dose, even though it is within the limit, should be the smallest amount needed to carry out the study. It is only concluded that, within the context of the benefit to be obtained from the research study, that such radiation doses are generally recognized as safe. Radioactive drugs which deliver larger doses are considered to represent new drugs and to require an IND or approved NDA.

24. One comment questioned whether it was appropriate to use the occupational permissible exposure criteria as a limit upon the approval authority of the proposed Radiation Safety Committee (under proposed § 370.100(b)(3)) since such limits were developed for a specific purpose and should not be extended to research use of radiation in human volunteer subjects.

As stated in the preamble to the proposal, the Commissioner fully agrees with the National Council on Radiation Protection and Measurements who, in discussing radiation dose to research subjects, noted that "each proposed human research application must be judged on its merit after review by competent peers, and that dose-limiting recommendations for radiation workers or the public do not apply to the individual to be irradiated." The Commissioner concludes that § 361.1 of this regulation embodies this recommendation and requires that each study be approved by competent peers (the Radioactive Drug Research Committee) and that the radiation dose be kept as low as practicable. The radiation dose criteria in § 361.1(b)(3) are for the purpose of stating that such research studies are generally recognized as safe and not to set a specific dose limit for research subjects.

The Commissioner referred, in the preamble to the proposal, to various studies and published literature which reflect a consensus which permitted the establishment of exposure levels acceptable from the standpoint of radiation safety. The NRC criteria, set forth in 10 CFR 20.101 and 20.102, accord with this consensus.

The NRC requirements take into account both the risk to the public health of larger doses of radiation for a particular group of persons and the risk to the individuals involved. Investigational subjects, like radiation workers, represent a limited segment of the total population; the public health implications of doses of radiation to research subjects appear no different from those resulting from exposure of radiation workers and the risks are equally acceptable to society. Considerations of risk to the individual also appear reasonably similar for both groups. An informed potential research subject is able to make a decision regarding participation in a study because he will, in effect, be deciding whether or not he is willing to participate in the study and assume a risk in the same sense as does a radiation worker. Although the benefits to the individual are quite different, in one case the opportunity to earn a livelihood, in the other the opportunity to participate in a scientific study, each situation in-

1032840

volves a decision to take a specified risk for a specified purpose. The Commissioner concludes that these doses represent a minimal risk to the individual and are appropriate criteria for a general recognition of safety where there are societal benefits from research studies.

25. One comment expressed the opinion that use of the occupational radiation exposure limitation (as an upper limit for exposure of research subjects in studies covered by proposed § 370.100) is too high in comparison with the intended scope of the studies.

The Commissioner notes that it is probable that many studies under § 361.1 (proposed as § 370.100) can be carried out using smaller doses of radiation than would be permitted under the limits on radiation dose. As noted earlier, it is the responsibility of the Radioactive Drug Research Committee (see paragraph 29) to assure that the smallest dose that can be used without jeopardizing the study is used. The Commissioner believes that doses up to the limits set forth in § 361.1 and used under conditions specified in that section can be considered generally recognized as safe and effective and constitute a reasonable limit for research studies conducted under this section. The Food and Drug Administration will continually evaluate the use of radioactive drugs under § 361.1 through the review of the required annual reports submitted by the Radioactive Drug Research Committee. The present criteria for establishing a radiation dose limit will be reconsidered if justified by this evaluation.

26. Several comments questioned the particular radiation dose limits selected. One comment suggested that it would be preferable to state any limitation as a maximum organ dose in any one year with the further qualification that in the event of a very long effective half-life situation, the total dose over the life expectancy of the concerned subject would not exceed some considered value. Another comment stated that it was not clear how the yearly cumulative total for whole body exposure for adults and the yearly total for critical organs were derived.

The Commissioner has reconsidered the proposed maximum radiation doses in light of the comments above and further intra-agency discussion. As originally proposed, maximum yearly doses were given. To provide adequate protection for subjects in special circumstances where long half-life radionuclides are used, the wording has been changed so that there will be both an annual limit on dose received and a limit on the total dose commitment resulting from studies conducted in a single year. Thus, the regulation has been modified to include both the "annual dose" and "total dose commitment" from a study or studies conducted within a single year. In addition, maximum whole body dose and the dose to critical organs (active blood-forming organs, lens of the eye, and gonads) have been made identical. The proposed notice specified limitations for "critical" organs that should have been applied to other organs. This has been corrected in the final order. As modified, the total dose commitment to any research subject, from a single study or cumulatively from a number of studies within a single year may not exceed the total commitment value of 5 rems for exposure to the whole body and critical organs (active blood-forming organs, lens of the eye, and gonads) or 15 rems for exposure to other organs. The designation of whole body, critical organs, and other organs within the various dose categories has been modified in the regulation to conform to terminology used by the NRC.

It is further recognized that significant radioactive contaminants or impurities in a radioactive drug may affect the results of a study or alter the validity of the dose calculations; therefore, any contribution to dose due to significant radioactive contaminants or impurities shall be included in calculating the total radiation dose and dose commitment. In addition, in determining maximum permissible dose limitations, the possibility of followup studies shall be considered for inclusion in the dose calculations. Section 361.1(b)(3) (proposed as § 370.100(b)(3)) has been revised accordingly.

27. One comment raised a question regarding the relationship between exposure history and the radiation limitations. The comment stated that the repeated reference to occupational exposure limitations in proposed § 370.100 (b)(3) and (d)(1) appear to sanction a quarterly occupational exposure of 3 rems. The comment further stated that this level of exposure is allowed in Agreement State and NRC regulations only with a properly completed exposure history and that there is no provision for an exposure history in the proposed regulation. The comment did not object to the 3 rems limit but to the use of such phrases in the proposed § 370.100 as "occupational exposure limitations" and "absorbed dose * * * permissible for occupationally exposed personnel."

The Commissioner believes that the limitations on radiation dose have been clarified in the final order. With the addition of an annual dose, an indication of a quarterly radiation dose is unnecessary. It is thus clear that, with a total annual dose of 5 rems for whole body and critical organs, 3 rems cannot be administered in each quarter.

"Exposure history," as required under NRC and Agreement State regulations, refers to previous occupational exposure. The Commissioner is of the opinion that very few research subjects will have been radiation workers and therefore they will not have an "exposure history." The Commissioner advises that, in revising paragraph (b)(3) and (d)(1) of § 361.1 of the regulation, the phrases "occupational exposure limitations" and "absorbed dose * * * permissible for occupationally exposed personnel" have been deleted.

28. One comment expressed concern that some research programs may also involve radiation doses from radiographic or fluoroscopic procedures such that the total subject dose may exceed the occupational permissible dose limits. The comment further stated that the x-ray dose may or may not be totally or partly of direct diagnostic benefit to the concerned subject or may or may not be part of medical care that the subject would receive if not volunteering for the study. The comment requested clarification as to whether any limitations on radiation dose to the subject that may be set under proposed § 370.100(b)(3) are applicable only to the dose attributable to the radionuclide procedure or only to the dose attributable to the research aspect of the subject's radiation experience during the period of concern, or to some other dose calculation. The comment expressed the opinion that it is not practicable to attempt to set regulatory limits based on the total radiation experience associated with a research use of radioactivity, because of the many considerations involved in assessing the value-risk ratio of an individual research proposal.

The Commissioner advises that the radiation dose limitations under § 361.1 (b)(3) (proposed § 370.100(b)(3)) are the total doses attributable to the research study including the radioactive drug and any doses from x-ray procedures which are considered and integral part of the research study, i.e., would not have occurred but for the study. An x-ray procedure which would have occurred whether or not the patient was part of the research study should not be included in determining the doses attributable to the research study. The Commissioner considers the determination of whether or not a given x-ray procedure is a part of the patient's medical care, as opposed to part of the research procedure, to be one which the Radioactive Drug Research Committee (see paragraph 29) can readily make.

D. RADIOACTIVE DRUG RESEARCH COMMITTEE

29. Comment was received from the Nuclear Regulatory Commission (NRC) requesting that the term Radiation Safety Committee as used in § 361.1 be changed to Radioisotope Research Committee or any other appropriate name. The NRC stated that the term Radiation Safety Committee is used by many hospitals and academic institutions for the committee that reviews the institution's overall program for use of radioactive materials and radiation producing machines, especially from the standpoint of radiation protection which is frequently called health physics.

The Commissioner has therefore concluded that, to distinguish between this committee and the committee required for approval of research uses of radioactive drugs under § 361.1 of this regulation, the term "Radiation Safety Committee" as used in § 361.1 shall be changed to "Radioactive Drug Research Committee." The regulation has been modified accordingly. In stating the following comments and their discussion, the revised committee name is used.

30. One comment recommended that the field of pharmacology be included as a discipline to be considered for repre-

1032841

sentation on a Radioactive Drug Research Committee under the proposed § 370.100(c)(1). Other comments expressed the feeling that a pharmacologist should be a required member of such committee. Comments also differed as to whether a radiopharmacist should be included in the membership of the Radioactive Drug Research Committee. Some comments indicated that there may be some misunderstanding as to who the required members of a Radioactive Drug Research Committee are.

The Commissioner concludes that the composition of the Radioactive Drug Research Committee as set forth in § 361.1(c)(1) is adequate. As stated in the proposed regulation, approval of a Radioactive Drug Research Committee shall be based upon an assessment of the qualifications of the members of the committee and the assurance that all of the necessary fields of expertise are covered. Certification in a particular discipline is not necessary. For example, one of the required members of the Committee shall be a person qualified to formulate radioactive drugs. This person need not necessarily be a radiopharmacists; he may be a physician or other qualified individual. The Commissioner also sees no reason to specify additional disciplines as required members because § 361.1(c)(1) states that the addition of consultants in other pertinent medical disciplines is encouraged. Expertise in any needed area can thus be obtained. The Commissioner advises that the only three required fields of specialization of a Radioactive Drug Research Committee are (1) a physician recognized as a specialist in nuclear medicine, (2) a person qualified by training and experience to formulate radioactive drugs, and (3) a person with special competence in radiation safety and radiation dosimetry. The remaining members shall be selected from individuals qualified in varied disciplines pertinent to the field of nuclear medicine (e.g., radiology, internal medicine, clinical pathology, hematology, endocrinology, radiation therapy, radiation physics, radiation biophysics, health physics, and radiopharmacy). Section 361.1(c)(1) has been rewritten to indicate more explicitly the required members.

31. One comment pointed out that the proposed § 370.100(c) gave no guidance regarding notification of changes in the membership of the Radioactive Drug Research Committee (e.g., because of relocation, retirement, or death of members) and the effect of such changes upon FDA approval of the Committee. The comment suggested that such changes be reported and documented in the annual report and that approval or disapproval of the revised Committee be determined by the FDA following receipt of the annual report.

The Commissioner has studied the comment and concludes that all changes in the membership of the Radioactive Drug Research Committee and selection of new members shall be communicated to the FDA as early as possible so that the FDA may review the qualifications of the new member(s) and the composition of the Committee and be assured that the Committee continues to include all of the necessary fields of expertise. Section 361.1(c)(4) (proposed § 370.100(c)(4)) has been revised to provide for this procedure. The Commissioner advises that once a Radioactive Drug Research Committee is approved, it continues in such status until the approval is withdrawn by the FDA. Individual changes in membership may therefore be implemented without FDA approval; FDA disapproval of a new member would take the form of withdrawal of approval of the Committee.

32. One comment expressed concern over the proliferation of duplicative committees deriving their authority from various Federal and State regulatory agencies. It recommended that FDA limit, at least initially, those committees which it approves pursuant to proposed § 370.100(c)(4) to those already established medical advisory committees of radioactive material licensing agencies and the radiation safety committees of broad medical licensees of the NRC. Another comment expressed concern that the FDA might not approve a Radioactive Drug Research Committee which has been approved as a Broad License Committee by an Agreement State or the NRC, or vice versa, and suggested that there be some criteria for mutual acceptance of a Radioactive Drug Research Committee. The comment further questioned whether the regulation would allow the Medical Committee of a State Radiation Advisory Board to review and approve research programs for small user licensees.

The Commissioner has determined that, to conclude that a radioactive drug is generally recognized as safe and effective when used for certain research studies, it is necessary to establish criteria for use of the drug which include a monitoring of that use by a Radioactive Drug Research Committee. The standards for the composition and functioning of the Radioactive Drug Research Committee are a fundamental element in the Commissioner's determination. The Commissioner cannot assume that the requirements for advisory or review committees of other Federal or State regulatory agencies will assure a committee that meets FDA criteria for a Radioactive Drug Research Committee. Therefore the FDA cannot, without an independent determination, approve a Committee that has been approved by another Agency. However, any established committee, such as the Medical Committee of a State Radiation Advisory Board, may, if constituted in accordance with § 361.1(c)(1), apply to the FDA for approval as a Radioactive Drug Research Committee.

33. One comment questioned the need for each Radioactive Drug Research Committee to meet at least quarterly, as provided in proposed § 370.100(c)(2), because the quantity of business to be considered by the Committee may not justify such frequent meetings.

The Commissioner concurs in part and has concluded that the Radioactive Drug Research Committee shall meet at least once each quarter in which a research activity has been authorized or conducted. No more than 90 days should pass between the start of the research and the monitoring of the study's progress by the Committee. More frequent meetings may be held at the discretion of the Committee.

The Commissioner has also determined that to provide reasonable assurance that the expertise available within the committee will be utilized in committee deliberations, it is necessary to indicate the number of members needed to constitute a quorum. He has concluded that more than 50 percent of the membership of the Committee must be present to constitute a quorum and that there must be appropriate representation of the required fields of specialization. Section 361.1(c)(2) (proposed as § 370.100(c)(2)) has been revised accordingly.

34. One comment expressed the opinion that more efficient use of the concept of a Radioactive Drug Research Committee as a "watchdog body" in cases of experimental use of radioactive drugs should be to expand its function to cover both new and not new radioactive drugs.

The Commissioner advises that review of investigations of new radioactive drugs submitted pursuant to § 312.1 is clearly a regulatory function of the Food and Drug Administration and cannot be delegated to a Radioactive Drug Research Committee. Institutional review is also required for investigational new drugs under an IND where the clinical studies are conducted on institutionalized subjects or are conducted by an individual affiliated with an institution which agrees to assume responsibility for the study. The Radioactive Drug Research Committee would not fulfill this requirement because its composition lacks lay membership. The FDA would, however, look favorably upon a Radioactive Drug Research Committee serving as a subcommittee of an Institutional Review Committee when the Investigational new drug is a radioactive drug. The Commissioner advises that this regulation does not in any way prohibit an institution from involving its Radioactive Drug Research Committee in other policy matters, including use of radioactive new drugs, if it so chooses.

35. One comment suggested that, because of the inherent time delays involved in obtaining protocol review and approval from a Radioactive Drug Research Committee as envisioned by the regulations, and because of the relatively short shelf life of many of the tagged drugs utilized, the regulations include a maximum time limit within which the Committee would have to approve or reject a proposed protocol.

The Commissioner concludes that regulation of the time required for approval or rejection by a Radioactive Drug Research Committee of a proposed protocol must be left to the institution or State or Federal agency with which the Committee is associated. The Commissioner cannot predict the workload of each Radioactive Drug Research Com-

1032842

mittee; therefore, it is not feasible for the FDA to establish a time frame for review and approval or rejection of a proposed protocol. The FDA believes, however, that since the Radioactive Drug Research Committee is composed of persons familiar with the unique problems of research with radioactive drugs, committee review will be responsive to the needs of individual researchers. The Commissioner further assumes that ordinarily approval of a protocol will be sought before the tagged drug is obtained; therefore, the shelf life of the tagged drug will not be germane.

36. Several comments suggested that the "Report on Research Use of Radioactive Drug" which each Radioactive Drug Research Committee is required to submit annually under proposed § 370.100(c)(3) for each study conducted during the preceding year be made available to Agreement States or other licensing agencies for future licensing actions without forfeiting the nondisclosure provisions which apply to proprietary information. Another comment suggested that FDA consider establishing some mechanism of advising its approved Radioactive Drug Research Committees of any studies which have been approved under proposed § 370.100 by any other approved Radioactive Drug Research Committee.

The Commissioner advises that contents of the "Report on Research Use of Radioactive Drug" are available for public disclosure unless confidentiality is requested by the investigator and it is adequately shown by the investigator that the report constitutes a trade secret or confidential commercial information as defined in 21 CFR 4.61. A trade secret, as defined in 21 CFR 4.61, may consist of any formula, pattern, device, or compilation of information which is used in one's business and which gives him an opportunity to obtain an advantage over competitors who do not know or use it. Commercial information that is privileged or confidential means valuable data or information which is used in one's business and is of a type customarily held in strict confidence or regarded as privileged and not disclosed to any member of the public by the person to whom it belongs. Data and information submitted or divulged to the Food and Drug Administration which fall within the definitions of a trade secret or confidential commercial information are not available for public disclosure.

The note under "Report on Research Use of Radioactive Drug" set forth in proposed § 370.100(c)(3), stated that the name of the investigator would not be disclosed publicly. Under the new regulation promulgated under the Freedom of Information Act, such information may be publicly disclosed. Section 361.1(c)(3) (proposed § 370.100(c)(3)) has been revised accordingly.

Therefore, information from this report which is available for public disclosure is also available to Agreement States or other licensing agencies and all Radioactive Drug Research Committees and will be disclosed in accordance with procedures set forth in 21 CFR Part 4. The Commissioner has concluded that it is impractical, because of resource limitations, to provide these reports to Agreement States and other licensing agencies and to other FDA Radioactive Drug Research Committees on a continuing basis. A specific request will be required under the public information regulations (21 CFR Part 4).

37. One comment recommended that the age of all research subjects, not just minors, be included in the "Report on Research Use of Radioactive Drug" set forth in proposed § 370.100(c)(3). Another comment suggested that the number of adults and children be specified separately on each report.

While such data are not necessary to monitor compliance, the Commissioner concludes that data such as the age and sex of all research subjects would be useful in evaluating the total risk to the public health and to individuals. Further, the Commissioner notes that this data would be useful to the FDA in studies of the radiation dose to the public from all radioactive drugs. Accordingly, § 361.1(c)(3) of the regulation has been modified to require the "Report on Research Use of Radioactive Drug" to include the dose to each research subject by age and sex.

38. One comment objected to the requirement of reporting immediately when more than 30 research subjects were involved in a research project under proposed § 370.100 since the individual risks to a human subject receiving radioactive materials are independent of the number of subjects. Another comment felt that annual reporting by the Radioactive Drug Research Committee and their function as a peer review group were sufficient and therefore objected to immediate reporting as stated above or when the research subject is under 18 years of age.

The Commissioner wishes to be certain that the requirements of § 361.1 (proposed § 370.100) are being interpreted and followed in a satisfactory manner. Relatively large research studies, such as those resulting in the exposure of more than 30 research subjects, represent a category of study in which it may be particularly appropriate to examine whether the need for the number of subjects chosen is documented, the radiation dose is well justified, and the distinction between research protocols and clinical trials is observed. Similarly, any study involving radiation exposure to research subjects less than 18 years of age may need special attention to examine the basis for carrying out the study in that age group and assure that the protocol is adequate for the safety of such subjects. The Commissioner emphasizes that the early notification of FDA under these circumstances in no way implies that such studies are unacceptable or inappropriate or that these studies require preclearance by the FDA. Notification is entirely for FDA's internal monitoring of this new regulation.

39. One comment suggested that Item 5 of the "Report of Research Use of Radioactive Drug" be revised to read as follows:

5. Radiation Absorbed Dose:
a. Radionuclide identification.
b. Administered activity dose—child, adult (max.).
c. Maximum number of activity doses per patient.
d. Estimated absorbed dose per single procedure—whole body, gonad and critical organ.

The Commissioner has reviewed the terminology in item 5 and is of the opinion that the requirements should be stated in more specific terms. He has therefore revised these parts of the "Report of Research Use of Radioactive Drug" to read as follows:

5. Name of the radionuclide(s) used, including any present as significant contaminants or impurities.
6. Radiation absorbed dose. Give the methods by which radiation dose commitment was estimated, such as by calculation, by in vivo measurements, by uptake excretion, or by other methods. For each subject, provide:
a. Age, sex.
b. Amount of each radionuclide administered.
c. Estimated absorbed dose per single administration of radioactive drug, expressed as whole body, active blood-forming organs, lens of the eye, gonads, and other organ dose.
d. If more than one administration of a radioactive drug per subject, cumulative radiation dose and dose commitment, expressed as whole body, active blood-forming organs, lens of the eye, gonads, and other organ doses from the administered radionuclides.

E. OTHER CONDITIONS

40. Three comments expressed the opinion that proposed § 370.100(d)(1) should require the radioassay of the pharmaceutical prior to administration and one comment suggested that the use of a dose calibrator be required. One comment assumed that a dose calibrator would be required.

Although proposed § 370.100 implies that the radioactive drug will be assayed prior to use, this is not stated explicitly. The Commissioner therefore concurs with this part of the comment, concluding that radioassay of some kind is necessary prior to use of the radioactive drug. Specific designation of a dose calibrator is inappropriate, however, since other assay methods would be acceptable. Section 361.1(d)(1) (proposed § 370.100(d)(1)) is therefore amended to require radioassay of the radioactive drug prior to its use.

The Commissioner advises that § 361.1(d)(1) has also been amended to state more specifically the requirements which the Radioactive Drug Research Committee must consider to assure that the radiation dose to research subjects is as low as practicable to perform the study and to meet the criteria set forth in § 361.1(b)(3). To help achieve this assurance, two additional requirements have been added to this paragraph; namely, that the radioactive drug chosen for the study has that combination of half-life, types of radiation, radiation

1032843

energy, metabolism, chemical properties, etc., which results in the lowest dose to the whole body or specific organs with which it is possible to obtain the necessary information and that the investigator utilize adequate and appropriate instrumentation for the detection and measurement of the specific radionuclide.

41. One comment stated that proposed § 370.100(d)(5) appeared to prohibit research studies involving metabolism during pregnancy and felt that the acceptability of performing a specific study on pregnant females should be the decision of the FDA-approved Radioactive Drug Research Committee.

Both the International Commission on Radiological Protection (ICRP) and the National Council on Radiation Protection and Measurements (NCRP) have expressed concern over the possible adverse effects on the human embryo and fetus from radiation exposure to pregnant women. The Commissioner has determined that, because of the potential risk to an embryo or fetus, the use of a radioactive drug during pregnancy cannot be generally recognized as safe; therefore, such studies cannot be conducted under § 361.1. This limitation in no way reflects, however, any prejudgment as to whether such a study may be conducted under an IND. The Commissioner emphasizes that the radiation dose limits, pharmacological dose limits, Radioactive Drug Research Committee requirements, and all other requirements of § 361.1 relate only to a specific group of radioactive drugs for certain research uses. There is no intent that any of these limits represent actual or de facto limits for studies conducted under an IND. Therefore, research studies in pregnant women may be permitted where the sponsor submits an IND and complies with the requirements of § 312.1.

42. One comment requested clarification of proposed § 370.100(d)(7) as to whether the statement in "No study involving * * *, no matter how small the amount of radioactivity, shall be permitted * * *." would require Radioactive Drug Research Committee approval for the use of any compound containing naturally occurring radioisotopes such as potassium which contains 0.012 percent K-40.

The Commissioner advises that § 361.1 (proposed § 370.100) pertains only to compounds to which tracer quantities of certain radionuclides have been deliberately attached and not to an element, such as potassium, which contains trace amounts of radioisotopes in its natural state. Section 361.1(d)(7) has been modified to reflect this.

43. One comment questioned the meaning of the word "active" as used in the term "active ingredient," relative to information required on the label by section 502(e) of the act and proposed § 370.100(f) and expressed the feeling that all ingredients in an injectable preparation should be specified and listed under proposed § 370.100(f) and a determination made later on whether they are "active" or not.

The Commissioner advises that the definition of "active ingredient" in 21 CFR 210.3(d)(5) (formerly 21 CFR 133.1(d)(5) prior to recodification published in the FEDERAL REGISTER of March 27, 1975 (40 FR 13998)) is applicable to § 361.1(f)(4) of these regulations. Active ingredient is defined as "any component which is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term shall include those components which may undergo chemical change in the manufacture of the drug and be present in the finished drug product in a modified form intended to furnish the specified activity or effect." The Commissioner agrees that radioactive drug products intended for parenteral administration under § 361.1 should be labeled to identify all inactive ingredients in the same way as other drug products for parenteral administration under § 201.100(b)(5)(iii) (formerly § 1.106(b)(2)(v)(c)) and has modified § 361.1(f) correspondingly. All other label requirements imposed by section 502 (b) and (e) of the act which were stated in the preamble to the proposal have also been listed under § 361.1(f).

The Commissioner also advises that the proposal (in the preamble and proposed § 370.100(f)) indicated label and labeling requirements for radioactive materials. Such requirements are specific label requirements as imposed by section 502 (b) and (e) of the act and certain other requirements and are to appear on the label of the immediate container and shielded container unless otherwise specified. The wording in the final order has been revised to reflect this.

44. One comment suggested revising paragraph (f) of proposed § 370.100 to read: "A radioactive drug prepared, packaged, distributed and primarily intended for use in accordance with the requirements of this section shall be exempt from section 502(f)(1) of the act and section 1.106 of this chapter if the packaging, label and labeling are in compliance with Federal, State, and local law regarding radioactive materials and if the packaging, label and labeling required for radioactive materials by the Nuclear Regulatory Commission and by State and local radiological health authorities bear the following: * * *." The comment further proposed the addition of a new paragraph (f)(6) to read "whether the drug is for investigational use only;" and a new paragraph (f)(7) to read "The expiration date, special storage conditions, pyrogenicity, specific concentration and addition of bacteriostatic agents" and addition of a new sentence reading "In the event that the immediate container of any radioactive drug is too small to contain the information set forth in paragraph seven (7) above, the information shall be furnished in the product's accompanying label."

The Commissioner concludes that the initial wording of § 361.1(f) (proposed § 370.100(f)) is preferable to the suggested alternative. The requirements by the FDA for labeling may be in addition to the requirements of the NRC, other Federal authorities, or State and local radiological health authorities. Paragraph (f) of proposed 370.100 was therefore written to allow the NRC or the State and local health authorities to decide whether they wanted a distinct radioactive warning on the label, apart from other labeling. The suggested alternative does not provide for this.

The suggested paragraph (f)(6) is not applicable since these are not investigational drugs, as that term is normally used (i.e., a drug under an IND), although these drugs are used for research. The statement described in § 361.1(f)(2) is proper for radioactive drugs for research use under this section.

With regard to the suggested paragraph (f)(7), the name and quantity of all bacteriostatic agents and other inactive ingredient(s) are required by 21 CFR 201.100(b)(5)(iii) (formerly 21 CFR 1.106(b)(2)(v)(c)) if a drug product is for parenteral use. Section 361.1(f) (proposed 370.100(f)) has been modified to include this requirement. Section 502(h) of the act requires that drugs liable to deterioration shall bear a statement of such precaution as necessary for the protection of the public health. The Commissioner concludes that, because of the special nature of radioactive drugs, i.e., radioactive decay, the label for such drugs shall contain an expiration date. If special storage conditions are necessary to maintain the drug product's stability for its anticipated shelf life, manufacturers are responsible for providing such information in the labeling. If a radioactive drug is recognized in an official compendium, it shall be labeled as prescribed by such compendium.

Current good manufacturing practices require that the manufacturer assure that the drug finished dosage form has the identity, strength, quality, and purity stated in the labeling. For radioactive drugs for parenteral use, manufacturers must therefore have evidence that the methods of manufacture and sterilization employed are adequate to ensure that each final product is sterile and pyrogen free. It is the responsibility of the Radioactive Drug Research Committee to determine that radioactive materials for parenteral use under § 361.1 are prepared in sterile and pyrogen-free form.

The Commissioner has also concluded that the specific concentration for each radioactive drug should be expressed on the label. Section 361.1(f) (proposed § 370.100(f)) has been revised to require that the label include the total quantity of radioactivity in the drug product's immediate container and the amount of radioactivity per unit volume or unit mass at a designated referenced time. Section 361.1(f) has also been revised to require that the label bear the route of administration if the drug is for other than oral use, as is required for all prescription drugs under 21 CFR 201.100. Information which may be placed on the label of the shielded container only if

1032844

the immediate container label is too small to accommodate all of the necessary information is also specified.

MISCELLANEOUS

45. One comment suggested changing paragraph (b) of proposed § 370.100 to read: "The conditions under which use of any radioactive drug for research, which has been, are now or will be regulated by the Food and Drug Administration or which is introduced into interstate commerce, as safe and effective are:". The comment also suggested adding a new paragraph (d) to proposed § 370.100 to state "These regulations will not act to exempt any drug covered by this part from any other provision of law or regulation applicable thereto."

The Commissioner has concluded that the suggested changes to proposed § 370.100 are unnecessary. This regulation in no way implies that other provisions of law or regulation are not applicable. In fact, the regulation clearly alludes to the licensing requirements of the NRC. This regulation will apply to all radioactive drugs that are generally recognized as safe and effective until future developments, experience, or knowledge necessitates revision.

46. One comment stated that there were no recommendations in the proposed regulations pertaining to the proper disposal of isotopes.

The Commissioner advises that the NRC and Agreement States control radiation safety during the manufacture, use, and disposal of radioactive drugs.

47. One comment asked if a separate office within the FDA had been assigned responsibility solely for radiopharmaceuticals.

The Commissioner advises that for all radioactive drug products, including radioactive biological products, review of a "Notice of Claimed Investigational Exemption for a New Drug," amendments to such notice, a new drug application, amendments and supplements to such application, and approving and monitoring the activities of the Radioactive Drug Research Committee shall be the responsibility of the Radiopharmaceutical Group, Division of Oncology and Radiopharmaceutical Drug Products, (HFD-150), Bureau of Drugs, 5600 Fishers Lane, Rockville, MD 20852. Elsewhere in this issue of the FEDERAL REGISTER, the Commissioner is issuing an order transferring responsibility for radioactive biological products from the Bureau of Biologics to the Bureau of Drugs to consolidate processing of all radioactive drug matters in one office.

48. One comment indicated that proposed § 370.100(f) permits the label and labeling of "tagged" compounds to contain information required by the NRC or State authorities, but this is not mentioned regarding those radioactive drugs covered under topics A, B, and C of the preamble to the proposal.

The Commissioner has determined that all radioactive drugs, including those which require the submission of an NDA, IND, or an application for a biological product license, as discussed under topics A, B, and C of the preamble to the July 29, 1974 proposal, are permitted to have on their label and labeling information required by the NRC and State and local radiation control authorities, if all of the FDA labeling requirements of section 502 of the act and 21 CFR 201.100 (formerly 21 CFR 1.106(b)) are met.

49. One comment expressed concern as to the effect these regulations will exert on existing competition within the radiopharmaceutical industry during the transition from regulation by the NRC to regulation by the FDA. Further, the comment expressed concern regarding the cost of the transition and any competitive disadvantage or restrictions imposed during this transition period. The comment emphasized that it is essential that nothing in these regulations create a competitive advantage for one manufacturer over another.

The Commissioner sees no basis for the concern expressed by the comment.

50. Two comments pointed out a typographical error in the paragraph heading for proposed § 1.105(p). The word "radiocative" should read "radioactive."

The typographical error as noted in the comment has been corrected. In addition, proposed § 1.105(p) has been recodified as § 201.129 in the final regulation in accordance with the recodification of § 1.106 into Part 201, published in the FEDERAL REGISTER of March 27, 1975 (40 FR 13386).

EFFECTIVE DATES

51. One comment requested that the December 31, 1974 and July 1, 1975 deadlines as set forth in the proposal be extended by the FDA on a drug-by-drug and manufacturer-by-manufacturer basis to provide adequate time to comply with the final regulations, following any any modification resulting from comments submitted.

The proposal identified effective dates for specific changes to implement FDA regulations regarding radioactive new drugs. Due to the length of time needed to review the comments and prepare the final regulation, the Commissioner has found it necessary to extend these proposed effective dates as follows: (1) the December 31, 1974 date for submission of an NDA, IND, or an application for a biological product license for each drug containing those radionuclides listed under § 310.503(f)(1) and for submission of the information for an investigational new drug as required by § 310.503(g) is extended to August 25, 1975; (2) the October 1, 1974 date referred to in § 310.503(g) is extended to July 25, 1975; (3) the January 1, 1975 date referred to in § 310.503 (f) (4) and (5) and (h) is extended to after August 25, 1975; (4) the effective date for deleting the "Note" that appears at the end of § 312.1 is extended to after August 25, 1975; and (5) the July 1, 1975 date referred to in § 310.503 (d)(3), (f)(5), and (g) is extended to February 20, 1976. The regulations have been revised accordingly. The Commissioner concludes that there has been adequate discussion and notice of these requirements, and that the time periods established should not result in a hardship to any manufacturer.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 505, 701 (a), 52 Stat. 1052–1053, as amended, 1055 (21 U.S.C. 355, 371(a)), the Public Health Service Act (sec. 351, 58 Stat. 702, as amended (42 U.S.C. 262)), authority delegated to the Commissioner (21 CFR 2.120), and in cooperation with the Nuclear Regulatory Commission, Title 21 of the Code of Federal Regulations is amended as follows:

PART 201—LABELING

1. In Subpart D a new § 201.129 is added to read as follows:

§ 201.129 Drugs and devices; exemption for radioactive drugs for research use.

A radioactive drug intended for administration to human research subjects during the course of a research project intended to obtain basic research information regarding metabolism (including kinetics, distribution, and localization) of a radioactively labeled drug or regarding human physiology, pathophysiology, or biochemistry (but not intended for immediate therapeutic, diagnostic, or similar purposes), under the conditions set forth in § 361.1 of this chapter, shall be exempt from section 502(f)(1) of the act if the packaging, label, and labeling are in compliance with § 361.1(d) of this chapter.

PART 310—NEW DRUGS

2. In § 310.3 add a new paragraph (n) to read as follows:

§ 310.3 Definitions and interpretations.

* * * * *

(n) The term "radioactive drug" means any substance defined as a drug in section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any nonradioactive reagent kit or nuclide generator which is intended to be used in the preparation of any such substance but does not include drugs such as carbon-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides. The term "radioactive drug" includes a "radioactive biological product" as defined in § 600.3(ee) of this chapter.

3. In § 310.503 revise paragraph (d) and add new paragraphs (f), (g), and (h), to read as follows:

§ 310.503 Requirements regarding certain radioactive drugs.

* * * * *

(d) (1) In view of the extent of experience with the isotopes listed in paragraph (c) of this section, the Nuclear Regulatory Commission and the Food and Drug Administration conclude that such isotopes should not be distributed under investigational-use labeling when

1032845

they are actually intended for use in medical practice.

(2) The exemption referred to in paragraph (a) of this section, as applied any drug or biologic containing any the isotopes listed in paragraph (c) of this section, in the "chemical form" and intended for the uses stated, is terminated on March 3, 1972, except as provided in paragraph (d)(3) of this section.

(3) The exemption referred to in paragraph (a) of this section, as applied to any drug or biologic containing any of the isotopes listed in paragraph (c) of this section, in the "chemical form" and intended for the uses stated, for which drug a new drug application or a "Notice of Claimed Investigational Exemption for a New Drug" was submitted prior to March 3, 1972, or for which biologic an application for product license or "Notice of Claimed Investigational Exemption for a New Drug" was submitted prior to March 3, 1972, is terminated either upon issuance of a nonapprovable notice for the new drug application or application for product license or termination of the "Notice of Claimed Investigational Exemption for a New Drug," or on February 20, 1976, whichever occurs first.

* * * * *

(f) (1) Based on its experience in regulating investigational radioactive pharmaceuticals, the Nuclear Regulatory Commission has compiled a list of reactor-produced isotopes for which it considers that applicants may reasonably e expected to submit adequate evidence safety and effectiveness for use as recommended in appropriate labeling; such use may include, among others, the uses in this tabulation:

Isotope	Chemical form	Use
Fluorine 18.	Fluoride	Bone imaging.
Indium-113m.	Diethylenetriamine pentaacetic acid (DTPA).	Brain imaging; kidney imaging.
Do	Chloride	Placenta imaging; blood pool imaging.
Technetium 99m.	Human serum albumin microspheres.	Lung imaging.
Do	Diethylenetriamine pentaacetic acid (Sn).	Kidney imaging; kidney function studies.
Do	do	Brain imaging.
Do	Polyphosphates	Bone imaging.
Do	Technetated aggregated albumin (human).	Lung imaging.
Do	Disodium etidronate.	Bone imaging.

(2) In view of the extent of experience with the isotopes listed in paragraph (f)(1) of this section, the Nuclear Regulatory Commission and the Food and Drug Administration conclude that they should not be distributed under investigational-use labeling when they are actually intended for use in medical practice.

(3) Any manufacturer or distributor interested in continuing to ship in interstate commerce drugs containing the isotopes listed in paragraph (f)(1) of this section for any of the indications listed, shall submit, on or before August 25, 1975 to the Bureau of Drugs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852, a new drug application or a "Notice of Claimed Investigational Exemption for a New Drug" for each such drug for which the manufacturer or distributor does not have an approved new drug application pursuant to section 505(b) of the act. If the drug is a biologic, a "Notice of Claimed Investigation Exemption for a New Drug" or an application for a license under section 351 of the Public Health Service Act shall be submitted to the Bureau of Biologics, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20014, in lieu of any submission to the Bureau of Drugs.

(4) The exemption referred to in paragraph (a) of this section, as applied to any drug or biologic containing any of the isotopes listed in paragraph (f)(1) of this section, in the "chemical form" and intended for the uses stated, is terminated August 25, 1975 except as provided in paragraph (f)(5) of this section.

(5) The exemption referred to in paragraph (a) of this section, as applied to any drug or biologic containing any of the isotopes listed in paragraph (f)(1) of this section in the "chemical form" and intended for the uses stated, for which drug a new drug application or a "Notice of Claimed Investigational Exemption for a New Drug" was submitted to the Bureau of Drugs on or before August 25, 1975 or for which biologic an application for product license or "Notice of Claimed Investigational Exemption for a New Drug" was submitted to the Bureau of Biologics on or before August 25, 1975 is terminated either upon issuance of a nonapprovable notice for the new drug application or application for product license or termination of the "Notice of Claimed Investigational Exemption for a New Drug," or on February 20, 1976 whichever occurs first.

(g) The exemption referred to in paragraph (a) of this section, as applied to any drug intended solely for investigational use as part of a research project, which use had been approved on or before July 25, 1975 in accordance with 10 CFR 35.11 (or equivalent regulation of an Agreement State) is terminated on February 20, 1976 if the manufacturer of such drug or the sponsor of the investigation of such drug submits on or before August 25, 1975 to the Food and Drug Administration, Bureau of Drugs, HFD-150, 5600 Fishers Lane, Rockville, MD 20852, the following information:

(1) The research project title;

(2) A brief description of the purpose of the project;

(3) The name of the investigator responsible;

(4) The name and license number of the institution holding the specific license under 10 CFR 35.11 (or equivalent regulation of an Agreement State);

(5) The name and maximum amount per subject of the radionuclide used;

(6) The number of subjects involved; and

(7) The date on which the administration of the radioactive drugs is expected to be completed.

(h) The exemption referred to in paragraph (a), as applied to any drug not referred to in paragraphs (d), (f), and (g) of this section, is terminated after August 25, 1975.

PART 312—NEW DRUGS FOR INVESTIGATIONAL USE

4. In § 312.1, amend paragraph (a)(2) in Form FD-1571 by adding a new item 6.d and two new sentences to item 10.a and delete in its entirety, effective August 25, 1975, the "Note" regarding an order of the Commissioner of Food and Drugs published in the FEDERAL REGISTER on January 8, 1963 (28 FR 183), as it appears at the end of § 312.1, to read as follows:

§ 312.1 Conditions for exemption of new drugs for investigational use.

(a) * * *

(2) * * *

Form FD-1571

* * * * *

6. * * *

d. If the drug is a radioactive drug, sufficient data must be available from animal studies or previous human studies to allow a reasonable calculation of radiation absorbed dose upon administration to a human being.

* * * * *

10. * * *

a. * * *

If a drug is a radioactive drug, the clinical pharmacology phase must include studies which will obtain sufficient data for dosimetry calculations. These studies should evaluate the excretion, whole body retention, and organ distribution of the radioactive material.

* * * * *

PART 361—PRESCRIPTION DRUGS FOR HUMAN USE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED: DRUGS USED IN RESEARCH

5. Add a new Part 361, consisting at this time of one section, to read as follows:

AUTHORITY: Federal Food, Drug, and Cosmetic Act, Sec. 505, 701(a), 52 Stat. 1052-1053, as amended, 1055 (21 U.S.C. 355, 371(a)); Public Health Service Act, Sec. 351, 58 Stat. 702, as amended (42 U.S.C. 262).

§ 361.1 Radioactive drugs for certain research uses.

(a) Radioactive drugs (as defined in § 310.3(n) of this chapter) are generally recognized as safe and effective when administered, under the conditions set forth in paragraph (b) of this section, to human research subjects during the course of a research project intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a radioactively labeled drug or regarding human physiology, pathophysiology, or biochemistry, but not intended for immediate therapeutic, diagnostic, or similar purposes or to determine the safety and effectiveness of the drug in humans for such purposes (i.e., to carry out a clinical trial). Certain basic research studies,

1032846

e.g., studies to determine whether a drug localizes in a particular organ or fluid space and to describe the kinetics of that localization, may have eventual therapeutic or diagnostic implications, but the initial studies are considered to be basic research within the meaning of this section.

(b) The conditions under which use of radioactive drugs for research are considered safe and effective are:

(1) *Approval by Radioactive Drug Research Committee.* A Radioactive Drug Research Committee, composed and approved by the Food and Drug Administration in accordance with paragraph (c) of this section, has determined, in accordance with the standards set forth in paragraph (d) of this section, that:

(i) The pharmacological dose is within the limits set forth in paragraph (b)(2) of this section;

(ii) The radiation dose is within the limits set forth in paragraph (b)(3) of this section;

(iii) The radiation exposure is justified by the quality of the study being undertaken and the importance of the information it seeks to obtain;

(iv) The study meets the other requirements set forth in paragraph (d) of this section regarding qualifications of the investigator, proper licensure for handling radioactive materials, selection and consent of research subjects, quality of radioactive drugs used, research protocol design, reporting of adverse reactions, and approval by an appropriate Institutional Review Committee; and

(v) The use of the radioactive drug in human subjects has the approval of the Radioactive Drug Research Committee.

(2) *Limit on pharmacological dose.* The amount of active ingredient or combination of active ingredients to be administered shall be known not to cause any clinically detectable pharmacological effect in human beings. If the same active ingredients (exclusive of the radionuclide) are to be administered simultaneously, e.g., under a "Notice of Claimed Investigational Exemption for a New Drug" or for a therapeutic use in accordance with labeling for a drug approved under Part 314 of this chapter, the total amount of active ingredients including the radionuclide shall be known not to exceed the dose limitations applicable to the separate administration of the active ingredients excluding the radionuclide.

(3) *Limit on radiation dose.* The amount of radioactive material to be administered shall be such that the subject receives the smallest radiation dose with which it is practical to perform the study without jeopardizing the benefits to be obtained from the study.

(i) Under no circumstances may the radiation dose to an adult research subject from a single study or cumulatively from a number of studies conducted within 1 year be generally recognized as safe if such dose exceeds the following:

Whole body, active blood-forming organs, lens of the eye, and gonads:

	Rems
Single dose	3
Annual and total dose commitment	5
Other organs:	
Single dose	5
Annual and total dose commitment	15

(ii) For a research subject under 18 years of age at his last birthday, the radiation dose shall not exceed 10 percent of that set forth in paragraph (b)(3)(i) of this section.

(iii) All radioactive material included in the drug either as essential material or as a significant contaminant or impurity shall be included when determining the total radiation doses and dose commitments. Radiation doses from x-ray procedures that are part of the research study (i.e., would not have occurred but for the study) shall also be included. The possibility of followup studies shall be considered for inclusion in the dose calculations.

(iv) Numerical definitions of dose shall be based on an absorbed fraction method of radiation absorbed dose calculation, such as the system set forth by the Medical Internal Radiation Dose Committee of the Society of Nuclear Medicine, or the system set forth by the International Commission on Radiological Protection.

(c) A Radioactive Drug Research Committee, in order to comply with paragraph (b)(1) of this section, shall be composed, shall function, and shall obtain and maintain approval of the Food and Drug Administration in conformity with the following:

(1) *Membership.* A Radioactive Drug Research Committee shall consist of at least five individuals. Each committee shall include the following three individuals: (1) A physician recognized as a specialist in nuclear medicine, (2) a person qualified by training and experience to formulate radioactive drugs, and (3) a person with special competence in radiation safety and radiation dosimetry. The remainder of the committee shall consist of individuals qualified in various disciplines pertinent to the field of nuclear medicine (e.g., radiology, internal medicine, clinical pathology, hematology, endocrinology, radiation therapy, radiation physics, radiation biophysics, health physics, and radiopharmacy). Membership shall be sufficiently diverse to permit expert review of the technical and scientific aspects of proposals submitted to the committee. The addition of consultants in other pertinent medical disciplines is encouraged. A Radioactive Drug Research Committee shall be either associated with a medical institution operated for care of patients and with sufficient scientific expertise to allow for selection of committee members from its faculty, or with a committee established by a State authority to provide advice on radiation health matters. Joint committees involving more than one medical institution which have been established in order to achieve a high level and diversity of experience will be acceptable. The Director of the Bureau of Drugs may modify any of the foregoing requirements in a particular situation where alternative factors provide substantially the same composition and association.

(2) *Function.* Each Radioactive Drug Research Committee shall select a chairman, who shall sign all applications, minutes, and reports of the committee. Each committee shall meet at least once each quarter in which research activity has been authorized or conducted. A quorum consisting of more than 50 percent of the membership must be present with appropriate representation of the required fields of specialization. Minutes shall be kept and shall include the numerical results of votes on protocols involving use in human subjects. No member shall vote on a protocol in which he is an investigator.

(3) *Reports.* Each Radioactive Drug Research Committee shall submit an annual report on or before January 31 of each year to the Food and Drug Administration, Bureau of Drugs, HFD–150, 5600 Fishers Lane, Rockville, MD 20852. The annual report shall include the names and qualifications of the members of, and of any consultants used by, the Radioactive Drug Research Committee, and, for each study conducted during the preceding year, a summary of information presented in the following format:

REPORT ON RESEARCH USE OF RADIOACTIVE DRUG

1. Title of the research project.
2. Brief description of the purpose of the research project.
3. Name of the investigator responsible.
4. Pharmacological dose:
   a. Active ingredients.
   b. Maximum amount administered per subject.
5. Name of the radionuclide(s) used, including any present as significant contaminants or impurities.
6. Radiation absorbed dose. Give the methods by which radiation dose commitment was estimated, such as by calculation, by in vivo measurements, by uptake excretion, or by other methods. For each subject; provide:
   a. Age, sex.
   b. Amount of each radionuclide administered.
   c. Estimated absorbed dose per single administration of radioactive drug, expressed as whole body, active blood-forming organs, lens of the eye, gonads, and other organ dose.
   d. If more than one administration of a radioactive drug per subject, cumulative radiation dose and dose commitment, expressed as whole body, active blood-forming organs, lens of the eye, gonads, and other organ doses from the administered radionuclides.
7. A claim of confidentiality, if any.

NOTE: Contents of this report are available for public disclosure unless confidentiality is requested by the investigator and it is adequately shown by the investigator that the report constitutes a trade secret or confidential commercial information as defined in 21 CFR 4.61.

_____
Investigator

_____
Chairman, Radiation Safety Committee

1032847

At any time a proposal is approved which involves exposure either of more than 30 research subjects, or of any research subject under 18 years of age, the committee shall immediately submit to the Food and Drug Administration a special summary of information in the format shown in this paragraph. Contents of these reports are available for public disclosure, unless confidentiality is requested by the investigator and it is adequately shown by the investigator that the report constitutes a trade secret or confidential commercial information as defined in § 4.61 of this chapter.

(4) *Approval.* Each Radioactive Drug Research Committee shall be specifically approved by the Bureau of Drugs of the Food and Drug Administration. Applications shall be submitted to the Food and Drug Administration, Bureau of Drugs, HFD–150, 5600 Fishers Lane, Rockville, MD 20852, and shall contain the names and qualifications of the members of the committee, and a statement that the committee agrees to comply with the requirements set forth in this section. Approval shall be based upon an assessment of the qualifications of the members of the committee, and the assurance that all necessary fields of expertise are covered. Approval of a committee may be withdrawn at any time for failure of the committee to comply with any of the requirements of this section. Approval of a committee shall remain effective unless and until the FDA withdraws such approval. Changes in membership and applications for new members shall be submitted to the Food and Drug Administration as soon as, or before, vacancies occur on the committee.

(5) *Monitoring.* The Food and Drug Administration shall conduct periodic reviews of approved committees. Monitoring of the activities of the committee shall be conducted through review of its annual report, through review of minutes and full protocols for certain studies, and through on-site inspections.

(d) In making the determinations required in paragraph (b)(1) of this section, a Radiation Safety Committee shall consider the following requirements and assure that each is met:

(1) *Radiation dose to subjects.* To assure that the radiation dose to research subjects is as low as practicable to perform the study and meet the criteria of § 361.1(b)(3), the Radioactive Drug Research Committee shall require that:

(i) The investigator provide absorbed dose calculations based on biologic distribution data available from published literature or from other valid studies.

(ii) The investigator provide for an acceptable method of radioassay of the radioactive drug prior to its use to assure that the dose calculations actually reflect the administered dose.

(iii) The radioactive drug chosen for the study has that combination of half-life, types of radiations, radiation energy, metabolism, chemical properties, etc., which results in the lowest dose to the whole body or specific organs with which it is possible to obtain the necessary information.

(iv) The investigator utilize adequate and appropriate instrumentation for the detection and measurement of the specific radionuclide.

(2) *Pharmacological dosage.* To determine that the amount of active ingredients to be administered does not exceed the limitations set forth in paragraph (b)(2) of this section, the committee shall require that the investigator provide pharmacological dose calculations based on data available from published literature or from other valid human studies.

(3) *Qualifications of investigators.* Each investigator shall be qualified by training and experience to conduct the proposed research studies.

(4) *License to handle radioactive materials.* The responsible investigator or institutions shall, in the case of reactor-produced isotopes, be licensed by the Nuclear Regulatory Commission or Agreement State to possess and use the specific radionuclides for research use or be a listed investigator under a broad license, or in the case of non-reactor-produced isotopes, be licensed by other appropriate State or local authorities, when required by State or local law, to possess and use the specific radionuclides for research use.

(5) *Human research subjects.* Each investigator shall select appropriate human subjects and shall obtain the consent of such human beings or their representatives in accordance with § 310.102 of this chapter. The research subjects shall be at least 18 years of age and legally competent. Exceptions are permitted only in those special situations when it can be demonstrated to the committee that the study presents a unique opportunity to gain information not presently available and requires the use of research subjects less than 18 years of age and is without significant risk to the subject. Studies involving minors shall be supported with review by qualified pediatric consultants to the Radioactive Drug Research Committee. Each female research subject of child-bearing potential shall state in writing that she is not pregnant, or, on the basis of a pregnancy test, be confirmed as not pregnant before she may participate in any study.

(6) *Quality of radioactive drug.* The radioactive drug used in the research study shall meet appropriate chemical, pharmaceutical, radiochemical, and radionuclidic standards of identity, strength, quality, and purity as needed for safety and be of such uniform and reproducible quality as to give significance to the research study conducted. The Radioactive Drug Research Committee shall determine that radioactive materials for parenteral use are prepared in sterile and pyrogen-free form.

(7) *Research protocol.* No matter how small the amount of radioactivity, no study involving administration of a radioactive drug, as defined in § 310.3(n) of this chapter, to research subjects under this section, shall be permitted unless the Radioactive Drug Research Committee concludes, in its judgment, that scientific knowledge and benefit is likely to result from that study. Therefore, the protocol shall be based upon a sound rationale derived from appropriate animal studies or published literature and shall be of sound design such that information of scientific value may result. The radiation dose shall be both sufficient and no greater than necessary to obtain valid measurement. The projected number of subjects shall be sufficient but no greater than necessary for the purpose of the study. The number of subjects shall also reflect the fact that the study is intended to obtain basic research information referred to in paragraph (a) of this section and not intended for immediate therapeutic, diagnostic or similar purposes or to determine the safety and effectiveness of the drug in humans for such purposes (i.e., to carry out a clinical trial).

(8) *Adverse reactions.* The investigator shall immediately report to the Radioactive Drug Research Committee all adverse effects associated with the use of the radioactive drug in the research study. All adverse reactions probably attributable to the use of the radioactive drug in the research study shall be immediately reported by the Radioactive Drug Research Committee to the Food and Drug Administration, Bureau of Drugs, HFD–150, 5600 Fishers Lane, Rockville, MD 20852.

(9) *Approval by Institutional Review Committee.* The investigator shall obtain the review and approval of an Institutional Review Committee which conforms to the requirements of 45 CFR Part 46.

(e) The results of any research conducted pursuant to this section as part of the evaluation of a drug pursuant to § 312.1 of this chapter shall be included in the submissions required under § 312.1 of this chapter.

(f) A radioactive drug prepared, packaged, distributed, and primarily intended for use in accordance with the requirements of this section shall be exempt from section 502(f)(1) of the act and §§ 201.5 and 201.100 of this chapter if the packaging, label, and labeling are in compliance with Federal, State, and local law regarding radioactive materials and if the label of the immediate container and shielded container, if any, either separate from or as part of any label and labeling required for radioactive materials by the Nuclear Regulatory Commission or by State or local radiological health authorities bear the following:

(1) The statement "Caution: Federal law prohibits dispensing without prescription";

(2) The statement "To be administered in compliance with the requirements of Federal regulations regarding radioactive drugs for research use (21 CFR 361.1)";

(3) The established name of the drug, if any;

(4) The established name and quantity of each active ingredient;

(5) The name and half-life of the radionuclide, total quantity of radioactivity in the drug product's immediate con-

1032848

tainer, and amount of radioactivity per unit volume or unit mass at a designated referenced time;

(6) The route of administration, if it is for other than oral use;

(7) The net quantity of contents;

(8) An identifying lot or control number from which it is possible to determine the complete manufacturing history of the package of the drug;

(9) The name and address of the manufacturer, packer, or distributor;

(10) The expiration date, if any;

(11) If the drug is intended for parenteral use, a statement as to whether the contents are sterile;

(12) If the drug is for other than oral use, the names of all inactive ingredients, except that:

(i) Trace amounts of harmless substances added solely for individual product identification need not be named.

(ii) If the drug is intended for parenteral use, the quantity or proportion of all inactive ingredients, except that ingredients added to adjust pH or to make the drug isotonic may be declared by name and a statement of their effect; if the vehicle is water for injection, it need not be named. *Provided, however,* That in the case of containers too small or otherwise unable to accommodate a label with sufficient space to bear all such information, the information required by paragraph (f) (1) and (12) of this section may be placed on the shielded container only.

Effective date. This regulation shall become effective on July 25, 1975. This date is necessary because of the various effective dates set forth for specific changes relating to the transitional regulation of radioactive new drugs from the Nuclear Regulatory Commission to the Food and Drug Administration, and the need for this regulation to be in force as soon as possible so that there will be regulatory control over the safety and effectiveness of all radioactive drugs.

(Secs. 505, 701(a), 52 Stat. 1052-1053, as amended, 1055 (21 U.S.C. 355, 371(a)); the Public Health Service Act (sec. 351, 58 Stat. 702, as amended (42 U.S.C. 262))

Dated: July 18, 1975.

A. M. SCHMIDT,
Commissioner of Food and Drugs.

[FR Doc.75-19316 Filed 7-24-75;8:45 am]

[Docket No. 75N-0068]

RADIOACTIVE BIOLOGICAL PRODUCTS

Reassignment of Responsibility

By this regulation, the Commissioner of Food and Drugs is reassigning responsibility within the Food and Drug Administration for regulating radioactive biological products from the Bureau of Biologics to the Bureau of Drugs. As a result of this reassignment, manufacturers of radioactive biological products will be required to comply with the requirements for drugs (including submitting new drug applications and periodic reports) for such products in lieu of the requirements for biological products (including submitting establishment and product license applications). All future correspondence and submissions regarding radioactive biological products shall be directed to the Bureau of Drugs. This order becomes effective August 25, 1975.

The Division of Biologics Standards (DBS) was transferred from the National Institutes of Health to the Food and Drug Administration (FDA) and renamed the Bureau of Biologics (notice of which was published in the FEDERAL REGISTER of June 29, 1972 (37 FR 12865)). As the first step in effecting an orderly transfer, the DBS was appended to the FDA as a Bureau without any realignment of overlapping or related functions that had developed between DBS and FDA based on historical, statutory, and organizational distinctions.

Since the transfer of DBS to FDA, the Commissioner has reviewed those activities that historically have been conducted by DBS and the Bureau of Biologics under section 351 of the Public Health Service Act as well as those conducted by the FDA, principally the Bureau of Drugs, under the Federal Food, Drug, and Cosmetic Act. He concludes that there is a need for some reassignment of activities regarding radioactive drugs between the Bureau of Biologics and the Bureau of Drugs to provide uniformity in processing and a focal point for action within FDA for this category of products.

The Bureau of Biologics currently exercises primary control over those radioactive drugs which contain a biological product in addition to a radionuclide; such products have been subject to licensure under section 351 of the Public Health Service Act. The Bureau of Drugs regulates all other radioactive drugs.

Radioactive biological products, however, in addition to being subject to section 351 of the Public Health Service Act, are also "drugs" and "new drugs" as those terms are defined in section 201 (g) and (p), respectively, of the Federal Food, Drug, and Cosmetic Act and are therefore subject to the drug provisions of the Federal Food, Drug, and Cosmetic Act, including the new drug provisions. Recognizing this dual jurisdiction over biological products, the Department of Health, Education, and Welfare decided many years ago (prior to the transfer of DBS to FDA) that to market a biological product a manufacturer should not be required to submit both a license application under section 351 of the Public Health Service Act and a new drug application under section 505 of the Federal Food, Drug, and Cosmetic Act. To require such dual submissions would have resulted in unnecessary duplication of effort, both by the manufacturer and by the Department. Instead, to avoid such duplication, only license applications under section 351 of the Public Health Service Act would be required. The new drug regulations (21 CFR 310.4) were amended to state that a new drug would not be deemed subject to the new drug provisions of the Federal Food, Drug, and Cosmetic Act if it is a drug licensed as a biological product under the Public Health Service Act.

The Commissioner now concludes that, since radioactive drugs, including radioactive biological products, are drugs in which the radioactive component is of primary interest, all radioactive drugs should be regulated through only one Bureau to achieve uniformity of treatment through a single contact point. The Commissioner further concludes that the Bureau of Drugs should be responsible for all radioactive drugs because of its existing organizational structure and staffing. The Bureau of Biologics will provide the Bureau of Drugs needed expertise with respect to the biological component of radioactive biological products and will test all samples of such products that are submitted in support of new drug applications.

As a result of this decision to transfer responsibility for radioactive biological products from the Bureau of Biologics to the Bureau of Drugs, all future applications and submissions for radioactive drugs, including radioactive biological products, shall be in the format and follow the procedures prescribed in 21 CFR Part 314. For radioactive biological products, the new drug application prescribed in 21 CFR 314.1 will be deemed to constitute the establishment and product license applications required for biological products; approval of the new drug application shall be in lieu of issuing a product and an establishment license. The requirement to submit new drug applications is not expected to impose any hardship on manufacturers of radioactive biologicals. The evidence required to establish safety and effectiveness are essentially the same for both biological products and new drugs. These are firms now holding biological product licenses for radioactive biological products, and all of them also manufacture other products requiring new drug applications. The impact on the regulated industry should, therefore, not be significant. The Commissioner advises that, if any person is preparing a biological product license application, he should submit it within 30 days in order to have it processed in that form.

In addition, compliance with the provisions of 21 CFR Part 314 shall be deemed to constitute compliance with the provisions of Subchapter F, the biological product regulations, unless the Commissioner makes a determination that a particular regulation in Subchapter F shall be applicable to radioactive drugs containing a biological product. Application of a Subchapter F regulation will only be made when the Commissioner concludes that it is necessary to assure the safety or effectiveness of the product, is not duplicative of the requirements in Part 314, and is to assure the same degree of regulatory control currently exercised over such products. The Commissioner has reviewed the provisions of Subchapter F and concludes at this time that the provisions of § 610.2 Requests for samples and protocols; official release shall remain applicable to radioactive drugs containing

1032849

a biological product. Appropriate changes have been made to this section to reflect that the Director of the Bureau of Drugs may use this section for radioactive drugs containing a biological product when it is deemed necessary for the safety, purity, or potency of the product.

To effect the transfer of responsibility, amendments must be made in 21 CFR Parts 310, 312, 314, 600, 601, and 610. In Part 310, § 310.4 provides the exemption, previously discussed, that a licensed biological product need not also be subject to an approved new drug application; that section is amended to exclude radioactive biological products from this exemption. In Part 312, § 312.1(g) currently provides that a "Notice of Claimed Investigational Exemption for a New Drug" (IND) for a biological product be submitted to the Bureau of Biologics; this section is amended to provide that an IND for a radioactive biological product be submitted to the Bureau of Drugs. In Part 314, § 314.110(a)(7) provides that a new drug application will be refused for filing if the drug is subject to licensing under the Public Health Service Act; this section is amended to permit filing of a new drug application for a radioactive biological product. Part 600 is amended in § 600.3 to include a definition of a radioactive biological product, which is defined as a biological product labeled with a radionuclide or a biological product intended solely to be labeled with a radionuclide. (Elsewhere in this issue of the FEDERAL REGISTER, the Commissioner is issuing a final regulation on radioactive drugs which includes a definition of "radioactive drug" in Part 310; this definition cross-references the new definition in Part 600.) In Part 601, § 601.2 currently outlines the procedures for filing applications for establishment and product licenses or biologics; this section is amended to provide that radioactive biological products shall be covered by new drug applications and not by biological product licenses. Part 610 is amended as discussed above.

These changes are prospective in nature. Every biological product licensed prior to July 1, 1972, is currently under review for safety, effectiveness, and appropriate labeling, as described in 21 CFR 601.25. The product license for such a radioactive biological product, together with portions of the establishment license relevant to the requirements for a new drug application, now constitutes an approved new drug application under section 505 of the Federal Food, Drug, and Cosmetic Act. Any such products, even through new subject to new drug applications, will remain subject to the biological product review, because they were licensed as biological products before July 1, 1972. Those products which are found to be unsafe, or ineffective, or misbranded will be subject to regulatory action. Those which are determined to be safe, effective and not misbranded may continue to be marketed; in addition, the conditions under which an identical, similar or related product may be introduced to the market (i.e., full new drug application, abbreviated new drug applications, or other conditions) will be determined at that time.

A new drug application does not have to be submitted for any radioactive biological product licensed after July 1, 1972, and before the effective date of this order. The product license for such a radioactive biological product, together with portions of the establishment license relevant to the requirements for a new drug application, now constitutes an approved new drug application under section 505 of the Federal Food, Drug, and Cosmetic Act.

Any radioactive biological product for which a license application is pending on the effective date of this order will be processed and approved or disapproved as submitted. Again, no new drug application need be submitted for these products. If the product is found acceptable for licensure, it will be approved as a new drug application in lieu of issuance of a product license.

Future changes in all approved radioactive biological products will be subject to supplemental new drug applications (21 CFR 314.8) rather than amendments to the license. Likewise, all radioactive biological products are subject to the records and reports requirements of 21 CFR 310.300 after the effective date of this section.

Every current "Notice of Claimed Investigational Exemption for a New Drug" for a radioactive biological product will be transferred to the Bureau of Drugs. Any amendments of or supplements to any such notice, and all progress reports regarding such notice, shall be filed in the future with the Bureau of Drugs. Any new "Notice of Claimed Investigational Exemption for a New Drug" for a radioactive biological product shall be submitted directly to the Bureau of Drugs.

For all radioactive biological products, including any subject to pending application for licensure on the effective date of this order, all correspondence, "Notices of Claimed Investigational Exemption for a New Drugs," and original and supplemental new drug applications shall be submitted to the Division of Oncology and Radiopharmaceutical Drug Products (HFD-150), Bureau of Drugs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852. All samples of radioactive biological products submitted in support of a new drug application shall, when notified by the Bureau of Drugs, be sent directly to the Bureau of Biologics, Food and Drug Administration, Bldg. 29A, 8800 Rockville Pike, Bethesda, MD 20014.

The Commissioner notes that the labeling standards under Part 610, Subpart G, of Subchapter F will no longer apply to radioactive biological products; instead, the requirements of 21 CFR Part 201 of Subchapter C will be applicable. In particular, this means that the manufacturer's license number appearing on the container and package labels (21 CFR 610.60(a)(2) and 610.61(b)) is no longer required. To permit an orderly and economical transition regarding labels and labeling of marketed products, the Commissioner will delay the effective date on which marketed radioactive biological products must comply with the requirements of Part 201 until the date on which new labels and/or labeling is printed by the manufacturer of such product, or July 26, 1976, whichever occurs first.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 505, 701(a), 52 Stat. 1052-1053 as amended, 1055 (21 U.S.C. 355, 371(a)), the Public Health Service Act (sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262)), and under authority delegated to the Commissioner (21 CFR 2.120), Chapter I of Title 21 of the Code of Federal Regulations is amended as follows:

PART 310—NEW DRUGS

1. In Subpart A by revising § 310.4 to read as follows:

§ 310.4 Biologics; products subject to license control.

(a) Except for radioactive biological products intended for human use, a new drug shall not be deemed to be subject to section 505 of the act if it is a drug licensed under the Public Health Service Act of July 1, 1944 (58 Stat. 682, as amended (42 U.S.C. 201 et seq.)) or under the animal virus, serum, and toxin law of March 4, 1913 (37 Stat. 832 (21 U.S.C. 151 et seq.)).

(b) A radioactive biological product (as defined in § 600.3(ee) of this chapter) intended for human use is subject to section 505 of the act. Any license for such a radioactive biological product which is issued under the Public Health Service Act of July 1, 1944 (58 Stat. 682, as amended (42 U.S.C. 201 et seq.)) and which has not been revoked or suspended as of August 25, 1975 shall constitute an approved new drug application in effect under the same terms and conditions as set forth in such license and such portions of the establishment license relating to such product, which include data and information required under Part 314 of this chapter for a new drug application. Any such radioactive biological product for which licensure under the Public Health Service Act is pending on August 25, 1975 shall, upon determination that it is acceptable for licensure, be approved as a new drug application in lieu of issuance of a biological product license.

PART 312—NEW DRUGS FOR INVESTIGATIONAL USE

2. In § 312.1 by revising paragraph (g) to read as follows:

§ 312.1 Conditions for exemption for new drugs for investigational use.

* * * * *

(g) A "Notice of Claimed Investigational Exemption for a New Drug" which pertains to a product subject to the licensing provisions of the Public Health Service Act of July 1, 1944 (58 Stat. 682, as amended (42 U.S.C. 201 et seq.)) shall

1032850

be submitted initially to the Director, Bureau of Biologics, 8800 Rockville Pike, Bethesda, MD 20014. Radioactive biological products for human use are not deemed to be subject to the licensing provisions of the Public Health Service Act (see § 310.4 of this chapter) and a "Notice of Claimed Investigational Exemption for a New Drug" which pertains to radioactive biological products shall be submitted to the Division of Oncology and Radiopharmaceutical Drug Products, Bureau of Drugs, 5600 Fishers Lane, Rockville, MD 20852. Amendments of or supplements to such notice, and progress reports, consultations, or other communications with regard to the investigation shall be directed to the same office to which the original notice was sent. A sponsor for a "Notice of Claimed Investigational Exemption for a New Drug" submitted to the Bureau of Biologics shall substitute in reading this section "Bureau of Biologics" for "Bureau of Drugs" wherever it appears.

* * * * *

PART 314—NEW DRUG APPLICATIONS

3. In § 314.110 by revising paragraph (a) (7) to read as follows:

§ 314.110 Reasons for refusing to file applications.

(a) * * *

(7) The new drug is a drug, other than a radioactive biological product (as defined in § 600.3(ee) of this chapter) intended for human use, subject to licensing under the Public Health Service Act of July 1, 1944 (58 Stat. 682, as amended (42 U.S.C. 201 et seq.)).

* * * * *

PART 600—GENERAL PROVISIONS

4. In § 600.3 by adding a new paragraph (ee) to read as follows:

§ 600.3 Definitions.

* * * * *

(ee) "Radioactive biological product" means a biological product which is labeled with a radionuclide or intended solely to be labeled with a radionuclide.

PART 601—LICENSING

5. In § 601.2 by redesignating the present text as paragraph (a) *General* and adding at the end a new sentence and by adding a new paragraph (b). As revised, § 601.2 reads as follows:

§ 601.2 Applications for establishment and product licenses; procedures for filing.

(a) *General.* To obtain a license for any establishment or product, the manufacturer shall make application to the Director, Bureau of Biologics, on forms prescribed for such purpose, and in the case of an application for a product license, shall submit data derived from laboratory and clinical studies which demonstrate that the manufactured product meets prescribed standards of safety, purity, and potency; a full description of manufacturing methods; data establishing stability of the product through the dating period; sample(s) representative of the product to be sold, bartered, or exchanged or offered, sent, carried or brought for sale, barter, or exchange; summaries of results of tests performed on the lot(s) represented by the submitted sample(s); and specimens of the labels enclosures and containers proposed to be used for the product. An application for license shall not be considered as filed until all pertinent information and data shall have been received from the manufacturer by the Bureau of Biologics. In lieu of the procedures described in this paragraph, applications for radioactive biological products shall be handled as set forth in paragraph (b) of this section.

(b) *Radioactive biological products.* In lieu of submitting an establishment and product license for the manufacture of a radioactive biological product, as defined in § 600.3(ee) of this chapter, the manufacturer of such a product shall submit a new drug application to the Director, Division of Oncology and Radiopharmaceutical Drug Products, Bureau of Drugs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852, on form FD-356(H) as set forth in § 314.1(c)(2) of this chapter. For such products, the approval of the new drug application will be in lieu of issuing a product and an establishment license. Compliance with the provisions of Part 314 of this chapter shall be deemed to constitute compliance with the provisions of Subchapter F of this chapter unless the Commissioner makes a determination that a particular regulation from Subchapter F shall be applicable to radioactive drugs containing a biological product, e.g., § 610.2 of this chapter.

PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

6. In § 610.2 by redesignating the present text as paragraph (a) *General* and revising it, and by adding a new paragraph (b). As revised, § 610.2 reads as follows:

§ 610.2 Request for samples and protocols; official release.

(a) *General.* Samples of any lot of any licensed product, except for radioactive biological products, together with the protocols showing results of applicable tests, may at any time be required to be sent to the Director, Bureau of Biologics. Upon notification by the Director, Bureau of Biologics, a manufacturer shall not distribute a lot of a product until the lot is released by the Director, Bureau of Biologics: *Provided*, That the Director, Bureau of Biologics, shall not issue such notification except when deemed necessary for the safety, purity, or potency of the product.

(b) *Radioactive biological products.* Samples of any lot of a radioactive biological product, as defined in § 600.3(ee) of this chapter, together with the protocols showing results of applicable tests, may at any time be required to be sent to the Food and Drug Administration for official release. Upon notification by the Director, Bureau of Drugs, a manufacturer shall not distribute a lot of a radioactive biological product until the lot is released by the Director, Bureau of Drugs: *Provided*, That the Director, Bureau of Drugs shall not issue such notification except when deemed necessary for the safety, purity, or potency of the product.

Since these changes concern internal reassignment of activities and will promote uniform handling of all radioactive drug products, the Commissioner finds that the changes covered by this order are such that, under 5 U.S.C. 553, the notice and comment procedure for rule making are unnecessary and are not prerequisites to this promulgation. In reaching this decision, the Commissioner has considered the facts that less than ten firms currently hold biological product licenses for radioactive biological products, and that all of these firms also hold approved new drug applications. The Commissioner also advises that any person currently preparing a biological product license for a radioactive biological product may submit it within 30 days and thereafter will not be required to resubmit a new drug application for the product.

Interested persons may, however, on or before September 23, 1975, file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20852, written comments in quintuplicate on any portion of the order. Comments received will be available for public inspection at the office noted above during working hours, Monday through Friday. Any changes in this order justified by such comments will be the subject of a further order amending the specific regulations involved.

Effective date. This regulation shall be effective August 25, 1975, except for the requirements for labels and labeling of radioactive biological products. The labels and labeling of any marketed radioactive biological product must comply with the requirements of 21 CFR Part 201 on the date on which such labels and labeling are next printed or July 26, 1975, whichever occurs first.

(Secs. 505, 701(a) 52 Stat. 1052-1053 as amended, 1055 (21 U.S.C. 355, 371(a)); sec. 351, 58 Stat. 702 as amended (42 U.S.C 262))

Dated: July 18, 1975.

A. M. SCHMIDT,
Commissioner of Food and Drugs.

[FR Doc.75-19315 Filed 7-24-75;8:45 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[Docket No. 75N-0069]

RADIOACTIVE DRUGS, INCLUDING BIOLOGICAL PRODUCTS

Notice to Nuclear Pharmacies Regarding the Development of Proposed Regulations and Interim Enforcement Policy

This notice states the interim enforcement policy of the Commissioner of Food and Drugs regarding nuclear pharmacies until definitive regulations on this matter are issued by the Food and Drug Administration. Under the conditions set forth in this notice, the agency will not take regulatory action for the failure of a nuclear pharmacy to comply with the requirements of the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act, except where such regulatory action is necessary to safeguard the public health.

Elsewhere in this issue of the FEDERAL REGISTER, the Commissioner is issuing a final regulation terminating the exemption from new drug requirements for radioactive drugs, including radioactive biological products. As a result, manufacturers and distributors of these products must comply with the requirements of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, and the regulations thereunder, including registration, drug listing, compliance with current good manufacturing practices, marketing under an approved new drug application or biological product license, research under the requirements for investigational drugs, and labeling and advertising requirements. In commenting on the proposal published in the FEDERAL REGISTER of July 29, 1974 (39 FR 27538), which preceded this final regulation, several persons inquired about the legal obligations of "nuclear pharmacies" under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act upon the effective date of the final regulation, especially insofar as these "nuclear pharmacies" may be deemed to be manufacturing or distributing these products other than as part of the compounding and dispensing of drugs in the ordinary practice of pharmacy.

Many radioactive drugs, including biological products, because of their short half-lives, must be prepared in the final dosage form shortly before they are to be used for diagnosis or treatment of disease in man. In addition, the preparation of radioactive drugs requires a special knowledge of radioactive materials, involves the use of special equipment and facilities, and, where reactor-produced radionuclides are involved, requires licensing by the Nuclear Regulatory Commission or an Agreement State. Certain pharmacies, referred to as "nuclear pharmacies," conduct operations which vary from repackaging or preparing radioactive drugs for administration to more extensive and complex manufacturing and compounding procedures. In most cases these nuclear pharmacies are affiliated with, or operated by, hospitals, medical groups, clinics, universities, medical schools, and public health agencies. Some of these pharmacies are not so affiliated, are privately owned, or are operated by several institutions on a cooperative basis. The radioactive drugs prepared by a nuclear pharmacy may be intended solely for use within the institution in which the pharmacy is located, or they may be prepared for distribution to other institutions. For example, a nuclear pharmacy in a university hospital may prepare radioactive drugs for distribution to other hospitals and clinics.

At present, pharmacies are subject to the misbranding and adulteration sections of the Federal Food, Drug, and Cosmetic Act and to the provisions of the Public Health Service Act regarding the licensing of biological products. If they engage in the manufacture of new drugs, they may also be subject to the new drug provisions of the Federal Food, Drug, and Cosmetic Act. Pharmacies are generally exempted under sections 510(g) and 704 (a) of the Federal Food, Drug, and Cosmetic Act from regulations regarding registration, drug listing, inspection, and compliance with current good manufacturing practices where their operations are in compliance with applicable local pharmacy laws and do not involve manufacturing procedures other than in the regular course of their business of dispensing or selling drugs at retail. Application of these rules and exemptions to nuclear pharmacies, which would be an immediate result of the final regulation referred to below, raises numerous complex issues or problems because of the unique nature of operations in nuclear pharmacies.

To clarify the obligations of nuclear pharmacies under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, the Food and Drug Administration is drafting regulations which will define those operations connected with the preparation of radioactive drugs and biological products which will be regarded as manufacturing procedures and not part of the practice of pharmacy. Nuclear pharmacies engaged in such operations will then be subject to regulations regarding registration, drug listing, inspection, new drug applications or biological product licenses, compliance with current good manufacturing practices, and related requirements. Operations not deemed to be manufacturing procedures will also be identified and will thereafter be treated as part of the practice of pharmacy. It is anticipated that these regulations will be proposed in the FEDERAL REGISTER in the near future. Interested persons will be given 60 days to comment on the proposed regulations and all such comments will be considered in the preparation and promulgation of the final regulation.

The Commissioner advises that, until the regulations outlined above are proposed and made final, the Food and Drug Administration will not take regulatory action for the failure of a nuclear pharmacy to comply with the requirements of the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act, so long as the pharmacy (1) complies with applicable local laws regulating the practice of pharmacy and (2) is licensed, where applicable, by the Nuclear Regulatory Commission or an Agreement State to possess, use, or transfer radioactive drugs, except where the Commissioner determines that such regulatory action is necessary to safeguard the public health. The Food and Drug Administration is adopting this policy as an interim measure to avoid any disruption in the practice of nuclear pharmacy and nuclear medicine throughout the United States.

Dated: July 18, 1975.

A. M. SCHMIDT,
Commissioner of Food and Drugs.

[FR Doc.75-19314 Filed 7-24-75;8:45 am]

1032852

Green file

FORM P-4

MEMORANDUM

TO: File DATE: July 29, 1975

SUBJECT: Talk with Mr. Melvin Koons Re Human Studies Committee

COPIES TO:

1. Re-do assurance to say "these" instead of "this." Last "this" is OK.

2. Change Richmond to Postma.

Now I need to retype and Dr. Lushbaugh will take to Postma to sign.

"Legally" Johnson is responsible for ORAU, and Dr. Postmas for ORNL.

1032853

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

Aug 4, 1975

July 25, 1975

TO: Grantees and Research Officers

FROM: Office for Protection from Research Risks,
Office of the Director, NIH, DHEW

SUBJECT: May 22 1975 Request for Revised General Assurance
(Part 46 of Title 45)

This is in regard to the task of updating your General Assurance currently on file with the Department of Health, Education, and Welfare relating to the protection of human subjects in research.

On the basis of the revised statements received in response to our May 22, 1975 request, it appears that further clarification as to the nature of this update would be helpful.

The overall need is for a completely new document revised so as to be in accord with the new changes in Title 45 of the Code of Federal Regulations, Part 46, which are summarized in the March 13, 1975 Federal Register. It is very likely that the agreement on record for your institution was negotiated before the March publication and that some amendments are in order. In this regard, it would be helpful to refer to specific areas of change delineated in our May 22, 1975 communication.

In any event, please submit an entirely new overall package reflecting whatever changes are necessary in each of the components to effect a more accurate state of compliance. Reference to your current agreement will provide a good base for reconstructing an updated document.

To reiterate, the resubmittal should include the components: (1) institutional assurance of compliance statement; (2) implementation and certification procedure involving institutional review board (see especially paragraph (b) of section 46.6); (3) current list of Institutional Review Board members by academic degree, certifications, and relationship to your institution; (4) brief indication of existing or institutional codes to be used as ethical guides in conducting research; (5) optional addendum for including sample forms (informed consent and processing forms).

We trust that this important interim task will not present an undue burden on the staff of your institution. If we can be of help along the way, please let us know (301) 496-7005. If you have already submitted materials, this office will be in further communication with you.

Assurance Management Desk
Office for Protection
from Research Risks
Office of the Director

JUL 31 1975

1032854

Oak Ridge Associated Universities
Incorporated
P.O. Box 117 - Oak Ridge, Tennessee 37830
Telephone 615 483-8411

July 31, 1975

Dr. D. T. Chalkley
Director, Office for Protection
from Research Risks
Office of the Director
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Chalkley:

Enclosed is our revised "Assurance of Compliance," and an up-to-date listing of our Committee on Human Studies with biographical data, as requested in your memo of May 22.

If there is any further information that you need, please let us know.

Sincerely yours,

C. C. Lushbaugh, M.D.
Acting Chairman, Medical
and Health Sciences Division

CCL:fb

Enc.

1032855

Oak Ridge Associated Universities

Incorporated

P.O. Box 117 · Oak Ridge, Tennessee 37830

Telephone 615 483-8411

ASSURANCE OF COMPLIANCE WITH DHEW REGULATIONS ON PROTECTION OF HUMAN SUBJECTS

1. Oak Ridge Associated Universities and Holifield (Oak Ridge) National Laboratory will comply with the Department of Health, Education, and Welfare regulations on Protection of Human Subjects (45 CFR 46 as amended), accordingly:

2. These Institutions have established and will maintain an Institutional Review Board competent to review projects and activities that involve human subjects. The Board shall determine for each activity as planned and conducted whether subjects will be placed at risk and if risk is involved, whether:

The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

The rights and welfare of any subjects will be adequately protected;

Legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provision of the regulation;

The conduct of the activity will be reviewed at timely intervals.

3. These Institutions will provide for Board reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from review of projects or activities in which they have an active role or conflict of interest.

4. These Institutions will encourage continuing constructive communication between the Board and the activity director as a means of safeguarding the rights and welfare of the subjects.

5. These Institutions will have available the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

6. These Institutions acknowledge that they will bear full responsibility for the proper performance of all work and services including the use of human subjects under any grant or contract covered by these assurances, including continuing compliance with pertinent state or local laws, particularly those concerned with informed consent.

1032856

7. These Institutions will maintain appropriate and informative records of the Board's review of applications and activities, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to the review of circumstances that adversely affect the rights or welfare of individual subjects.

8. These Institutions will at least annually reassure themselves through appropriate administrative overview that their practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied and are consistent with the regulation and with the implementation of this assurance as accepted by the Department of Health, Education, and Welfare.

9. This general assurance of compliance applies to the Oak Ridge Associated Universities and the Holifield (Oak Ridge) National Laboratory. Components not named will be requested to submit separate assurances when applying for support of activities to which 45 CFR 46 applies.

OAK RIDGE ASSOCIATED UNIVERSITIES

Philip L. Johnson
(signature of authorized official)

Philip L. Johnson
(name-typewritten)

Executive Director
(titled)

AUG 1 1975
(date)

483-8411, Ext. 201
(telephone number)

HOLIFIELD (OAK RIDGE) NATIONAL LABORATORY

Herman Postma
(signature of authorized official)

Herman Postma
(name-typewritten)

Director
(titled)

JUL 31 1975
(date)

483-8611, Ext. 3-6611
(telephone number)

1032857

ADDENDUM I

EXAMPLE

INSTITUTIONAL ASSURANCE OF COMPLIANCE

This is an EXAMPLE, not a form. PLEASE prepare the Institutional Assurance of Compliance on your *institution's letterhead with the original signature of authorized official.* Mail to Office for Protection from Research Risks, OD, National Institutes of Health, Bethesda, Maryland 20014. Note: It is required that documentation of Assurance Implementation prescribing institutional practices and procedures for protection of human subjects accompany this Assurance of Compliance.

(PLEASE USE INSTITUTIONAL LETTERHEAD)

ASSURANCE OF COMPLIANCE WITH DHEW REGULATIONS ON PROTECTION OF HUMAN SUBJECTS

1. The *(full name of Institution)* will comply with the Department of Health, Education, and Welfare regulations on Protection of Human Subjects (45 CFR 46 as amended*), accordingly:

2. This institution has established and will maintain an Institutional Review Board competent to review projects and activities that involve human subjects. The Board shall determine for each activity as planned and conducted whether subjects will be placed at risk and if risk is involved, whether:

The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

The rights and welfare of any such subjects will be adequately protected;

Legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provision of the regulation;

The conduct of the activity will be reviewed at timely intervals.

3. This Institution will provide for Board reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from review of projects or activities in which they have an active role or conflict of interest.

**Part 46* of *Title 45* of the *Code of Federal Regulations*, as amended - copies available on request from the Office for Protection from Research Risks, OD, NIH, Bethesda, Md. 20014.

4. This Institution will encourage continuing constructive communication between the Board and the activity director as a means of safeguarding the rights and welfare of the subjects.

5. This Institution will have available the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

6. This Institution acknowledges that it will bear full responsibility for the proper performance of all work and services including the use of human subjects under any grant or contract covered by this assurance, including continuing compliance with pertinent state or local laws, particularly those concerned with informed consent.

7. This Institution will maintain appropriate and informative records of the Board's review of applications and activities, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to the review of circumstances that adversely affect the rights or welfare of individual subjects.

8. This Institution will at least annually reassure itself through appropriate administrative overview that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied and are consistent with the regulation and with the implementation of this assurance as accepted by the Department of Health, Education, and Welfare.

9. This general assurance of compliance applies to The *(full name of the institution as used in applying for grants and contracts and the names of all components which have the authority to independently administer grants and contracts and are covered under this assurance)*. Components not named will be requested to submit separate assurances when applying for support of activities to which 45 CFR 46 applies.

_____
(signature of authorized official)

_____
(name-typewritten)

_____
(titled)

_____
(date)

_____
(telephone number)

Dr. Lushbaugh's Copy

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

October 7, 1975

General Assurance
#G1716

C. C. Lushbaugh, M.D.
Acting Chairman, Medical
and Health Sciences Division
Oak Ridge Associated University
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Lushbaugh:

Thanks for your new assurance of compliance and list of board members for human subjects of July 31, 1975. Since you did not include a new set of guidelines nor mention any amendments I assume that the guidelines of January 1972 still stand. Therefore, I have reviewed those guidelines (copy enclosed) and find that they do not quite satisfy present regulations. Enclosed is an outline and checklist with my comments which should be helpful.

Emergent problems should be reported to the board promptly and not only at the annual February meeting. Regular meetings more often than annually are probably needed anyway.

As your board now stands I will have to prohibit review and approval of behavioral sciences projects. If you anticipate such projects please add a couple of psychologists to your board.

Please consider the factors above and those noted on my outline and submit a revised set of guidelines. Call me on 301-496-7005 if you have questions.

Sincerely,

Roy Kinard

Roy Kinard, D.V.M.
Office for Protection
from Research Risks
Office of the Director

Enclosures

1032860

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

August 8, 1975 General Assurance #61716

Committee on Human Studies

C. C. Lushbaugh, M. D.
Acting Chairman, Medical
and Health Sciences Division
Oak Ridge Associated Universities Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

The revised statement of assurance submitted in response to our May 22, 1975 request relating to the above referenced General Assurance number has been received and is being processed for review.

You will be advised of the results of this review or perceived need for additional information shortly.

Assurance Management Desk
Office for Protection
from Research Risks
Office of the Director, NIH
Westwood Building, Room 303
Bethesda, Maryland 20014

copy to C. Richmond ok
FB

1032861

Volume 4 Number 8 August 1975

THE HOSPITAL MEDICAL STAFF

1 P.L. 93-641—Health Care Planning Becomes Mandatory
W. Thomas Berriman

10 California Physicians' Strike Strains Hospital-Staff Relationships
Donald F. Phillips

22 AMA Annual Meeting—Special Report James E. Fague

31 The Organization and Financing of Health Care: Implications for Medical School-Teaching Hospital Agreements—Part 2
E. D. Rosenfeld, M.D., and Thomas P. Weil, Ph.D.

38 Views from the Chairman Bruce W. Evens, M.D.

47 Medicolegal Review—Informed Consent: A Reincarnation
Gregg Orwoll, J.D.

49 Washington Memo

56 Accreditation Clinic John D. Porterfield, M.D.

58 Briefly noted

71 Calendar of Meetings

1032862

mr medicolegal review

by Gregg Orwoll, J.D.

INFORMED CONSENT: A REINCARNATION?

That old bugaboo, the so-called "lack of informed consent claim" is raising its head again with increasing frequency. This type of claim gained popularity in the early 1960s following the much celebrated *Natanson v. Kline*[1] and *Mitchell v. Robinson*[2] decisions in Kansas and Missouri, respectively. Both were decided in 1960 (interestingly, within two days of one another). For several years, it appeared that every plaintiff's malpractice lawyer in the country had found a miracle drug to cure many otherwise questionable malpractice claims. These lawyers believed, or at least hoped, that here was a way, in addition to the doctrine of *res ipsa loquitur*, to "get to the jury" without bringing forth creditable medical expert testimony to satisfy that legal requirement in malpractice cases.

The battle lines were drawn. In state after state efforts were made to obtain decisions that would permit such claims to go to the jury merely on the plaintiff's unsupported claim that he was not warned of the hazards or informed of possible alternative procedures available to him. To the credit of the appellate courts, and much to the relief of physicians throughout the country, in case after case

---

Gregg Orwoll, J.D., is general counsel, Mayo Clinic, Rochester, MN. This material is not intended to be legal advice and should not be used to resolve legal problems. For legal advice, a hospital should consult its attorney.

1032863

decision: all risks potentially affecting the decisions must be unmasked. And to safeguard the patient's interest in achieving his own determination on treatment, the law must itself set the standard for adequate disclosure. . . . In broad outline, we agree that '[a] risk is thus material when a reasonable person, in what the physician knows or should know to be the patient's position, would be likely to attach significance to the risk or cluster of risks in deciding whether or not to forego the proposed therapy.' . . . The factors contributing significance to the dangerousness of a medical technique are, of course, the incidence of injury and the degree of the harm threatened. . . . there is no obligation to communicate those of which persons of average sophistication are aware. Even more clearly, the physician bears no responsibility for discussion of hazards the patient has already discovered, or those having no apparent materiality to patients' decision on therapy. . . .

"Two exceptions to the general rule of disclosure have been noted by the courts. . . . The first comes into play when the patient is unconscious or otherwise incapable of consenting, and harm from a failure to treat is imminent and outweighs any harm threatened by the proposed treatment. . . . The second exception obtains when risk-disclosure poses such a threat of detriment to the patient as to become unfeasible or contraindicated from a medical point of view. . . . Where that is so, the cases have generally held that the physician is armed with a privilege to keep the information from the patient, and we think it clear that portents of that type may justify the physician in action he deems medically warranted. . . . A causal connection exists when, but only when, disclosure of significant risks incidental to treatment would have resulted in a decision against it."

Reliance on forms may be impractical

One more question the physician frequently asks is whether he can satisfy his duty of disclosure by having the patient sign a written form. I really don't think this is a practical solution in most instances.[6] Talk to the patient. Let him ask questions. Have him sign a form if you wish. (If you're dealing with experimental drugs or with federal grant or contract-sponsored human studies, you must.)

The patient's signature on a written form may help prove his

1032864

consent to the procedure, but the physician should not rely on it to satisfy his duty of disclosure. Although written consent forms were used in most of the "informed consent" cases that have reached appellate courts, the courts paid little attention to them. Their concern? What did the physician tell the patient? Did he give him a chance to ask questions? Did he outline the alternatives?

Conclusion

For more than a decade following *Natanson v. Kline* and *Mitchell v. Robinson*, appellate courts were quite uniform in requiring expert testimony in informed consent cases, but in the past four years, courts in several states have done away with this requirement. The next several years will be important ones in this fight. In this summer of discontent for physicians, another change in the law that makes it easier for plaintiffs to recover in malpractice cases simply cannot be justified. The doctrine of informed consent should not be reincarnated.

Just what physicians should tell their patients about the hazards of procedures they propose cannot be described with clarity, but some advice and suggestions are in order: Use your best judgment. Take the patient into your confidence. Talk to him, explain the procedure, outline measurable hazards, mention the alternatives, note the discussion in the record—and pray a little! □

NOTES

1. *Natanson v. Kline*, 186 Kan. 393; 350 P.2d 1093 (1960).
2. *Mitchell v. Robinson*, 334 S.W.2d 11, 79 *A.L.R.2d* 1017 (Mo.,1960).
3. See, e.g., *DiFilippo v. Preston*, 53 Del. 539, 173 A.2d 333 (1961); *Ditlow v. Kaplan*, 181 So.2d 226 (Fla. Dist. Ct. of Appeal 1966); *Grosjean v. Spencer*, 258 Ia. 685, 140 N.W.2d 139 (1966); *Roberts v. Young*, 369 Mich. 133, 119 N.W.2d 627 (1963); *Block v. McVay*, 80 S.D. 469, 126 N.W.2d 808 (1964); *Kaiser v. Suburban Transportation System, et al.*, 65 Wash.2d 461, 398 P.2d 14 (1965); and *Govin v. Hunter*, 374 P.2d 421 (Wyo. 1962).
4. *Williams v. Menehan*, 191 Kan. 6, 379 P.2d 292 (1963); *Aiken v. Clary*, 396 S.W.2d 668 (Mo. 1965).
5. *Canterbury v. Spence et al*, 464 F.2d 772 (D.C. Cir. 1972); *Cobbs v. Grant*, 8 Cal. 3d 229, 104 Cal. Rptr. 505, 502 P.2d 1 (1972); *Cooper v. Roberts*, 220 Pa. Super. 260, 286 A.2d 647 (1971); *Wilkinson v. Vesey*, 110 R.I. 606, 295 A.2d 676 (1972); and *Trogun v. Fruchtman*, 58 Wis.2d 596, 207 N.W.2d 297 (1973). By virtue of the case of *Woods v. Brumlop*, 71 N.M. 221, 377 P.2d 520 (1962), this also appears to be the rule in New Mexico.
6. It doesn't appear to the writer to be practical to attempt to prepare written forms that truly inform for each of the hundreds, perhaps thousands, of different procedures that physicians perform on patients. Informed consent brochures, which include consent forms, are available for some major procedures and may be helpful. But the circumstances of individual patients must be considered, and the patient still must be offered an opportunity to ask questions.

1032865

Put in file "Committee on Human Studies"

PROTECTION of the INDIVIDUAL as a RESEARCH SUBJECT

Grants, awards, contracts

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

1032866

PROTECTION
of the
INDIVIDUAL
as a
RESEARCH SUBJECT

Grants, awards, contracts

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

1032867

FOREWORD

Concern over the rights and welfare of the human being as a subject of research has led to Public Health Service policy to help assure his protection. Any activity which includes such research must provide for the individual's safety, health, and welfare. His rights, including his rights of privacy, must not be infringed. His participation must be voluntary. The direct or potential benefits of the research must outweigh the inherent risks to the individual. This policy applies to all research activities supported through grants, awards, or contracts by the National Institutes of Health, the Health Services and Mental Health Administration, and the Consumer Protection and Environmental Health Service.

The responsibility for assuring this protection when human beings are involved in federally supported research rests with the recipient of the Federal funds (grant, contract, or award). The adequacy of this protection is determined, not by the investigator or program director or any one person, but by a group independent of the activity and the persons conducting it. The group must include the competencies essential to sound judgments on scientific and humanistic values.

Institutions receiving PHS support have been thoroughly cooperative in implementing the PHS policy. Many had already adopted effective measures for protecting the human subject in research. A number of

1032868

the documents submitted to the Public Health Service have included penetrating analyses of the ethical issues in research on and for man. Experience in carrying out the policy, however, revealed the need to define better its applicability, to simplify administrative procedures, and to provide guidelines for institutions concerning the review of research projects. The text which follows states Public Health Service policy as it has been developed since the initial announcement in 1966.

These statements represent the thoughtful advice of many individuals, including officials of PHS grantee institutions, advisory consultants, and internal staff. I believe that we have taken important steps toward protecting the human being who is a subject of research, while encouraging the conduct of excellent research on man.

Correspondence about this policy should be addressed to the Director, Division of Research Grants, National Institutes of Health, Bethesda, Maryland, 20014.

Surgeon General

PROTECTION OF THE INDIVIDUAL AS A RESEARCH SUBJECT

Grants, Awards, or Contracts

Safeguarding the rights and welfare of human subjects involved in research supported by the Public Health Service is the responsibility of the institution to which support is awarded. It is the policy of the Public Health Service that no grant, award, or contract for the support of research involving human subjects shall be made unless the research is given initial and continuing review and approval by an appropriate committee of the applicant institution. This review shall assure that (a) the rights and welfare of the individuals involved are adequately protected, (b) the methods used to obtain informed consent are adequate and appropriate, and (c) the risks to the individual are outweighed by the potential benefit to him or by the importance of the knowledge to be gained.

The institution must provide written assurance to the Public Health Service that it will abide by this policy for all research involving human subjects supported by the Public Health Service. This assurance shall consist of a written statement of compliance with the requirements regarding initial and

1032869

continuing review of research involving human subjects and a description of the institution's review committee structure, its review procedures, and the facilities and personnel available to protect the health and safety of human subjects. In addition to providing the assurance, the institution must also certify to the Public Health Service for each proposal involving human subjects that its committee has reviewed and approved the proposed research before an award may be made.

Since the welfare of the subject is a matter of concern to the Public Health Service as well as to the institution, PHS advisory groups, consultants, and staff will independently review all research involving human subjects, recommending unfavorable action on grants, contracts, or awards if the research presents unacceptable hazards.

Similarly, the institution should be prepared at all times to question the conduct of research, even though previously approved by both the institution and the Public Health Service. The safety and welfare of the subject are paramount.

If any conflict exists between institutional policy, PHS policy, or State or local laws, the more restrictive requirements will be followed.

Research subjects.

A subject is considered to be any human being exposed to any research procedure as the result of the availability of Public Health Service funds, whether provided through

research, training, or other types of grants, awards, or contracts. Subjects may include, therefore, persons involved in behavioral science studies; normal volunteers; donors of services; inpatients and outpatients; living donors of body fluids, organs, and tissues; and members of the general population who may be involved in environmental or epidemiological studies or similar activities.

An individual should generally be accepted as a research subject only after he, or his legally authorized guardian or next of kin, has consented to his participation in the research. Such consent is valid, however, only if the individual is first given a fair explanation of the procedures to be followed, their possible benefits and attendant hazards and discomforts, and the reasons for pursuing the research and its general objectives.

The subject does not abdicate his rights by consenting to participate in a research project. He may withdraw his consent at any time. Further, he has the right to be secure in his person, to receive proper professional care, to enjoy privacy and confidentiality in the use of information about himself, and to be free from undue embarrassment, discomfort, and harassment.

Applicability.

This policy applies to all projects which go beyond the diagnostic and therapeutic needs of the subject, as determined by his attending professional and the institutional committee. Such projects may involve the procurement of human materials or services

1032870

and may be supported by a variety of mechanisms, e.g., research, training, or demonstration grants; general research support grants; and fellowship, traineeship, or contract awards.

The applicability of this policy is most obvious in medical and behavioral science research involving procedures that may induce a potentially harmful altered state or condition. Surgical procedures; the removal of organs or tissues for biopsy, transplantation, or banking; the administration of drugs or radiation; the use of indwelling catheters or electrodes; the requirement of strenuous physical exertion; subjection to deceit, public embarrassment, and humiliation are all examples of procedures which require thorough scrutiny by institutional committees.

There is a wide range of medical, social, and behavorial research in which no immediate physical risk to the subject is involved. However, some of these may impose varying degrees of discomfort, irritation, and harassment. In addition, there may be substantial potential injury to the subject's rights if attention is not given to maintenance of the confidentiality of information obtained from the subject and the protection of the subject from misuse of findings.

There is also research concerned solely with discarded human materials obtained at surgery or in the course of diagnosis or treatment. The use of these materials involves no possible element of risk to the subject. In such instances application of the policy requires only review of the circumstances under which the materials are to be procured.

Cooperative arrangements.

Even if certain aspects of research are to be carried out in another institution, the grantee, contracting, or sponsoring institution is responsible for initial and continuing review of those parts of the study. The review, however, may be carried out in cooperation with appropriate committees or groups within the other institution.

Minimum requirements for an acceptable assurance.

An acceptable assurance consists of two parts:

Formal statement.

A formal statement of compliance with Public Health Service policy must be signed by an appropriate institution official (see Attachment A).

Implementing guidelines.

The institution's description of its own procedures should embody the three headings listed below. The explanatory paragraphs following each heading indicate the type of information which should be supplied.

1) • *Statement of principles concerning the treatment of human subjects.*

It is necessary that the guidelines make reference to the principles the institution will apply in its review of research involving human subjects. The institution may adopt an already existing statement of principles

1032871

(e.g., the Nuremberg Code, the Declaration of Helsinki, the Statement of Ethical Standards in Research of the American Psychological Association) or it may develop its own statement.

- *Description of the review committee.*

The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of the research. The committee may be an existing one, or one especially appointed for the purpose. Institutions may utilize subcommittees to represent major administrative components in those instances where establishment of a single committee is impractical or inadvisable. The institution may utilize staff, consultants, or both. The membership should possess not only broad specific competence to comprehend the nature of the research, but also other competencies necessary in the judgments as to acceptability of the research in terms of institutional regulations, relevant law, standards of professional practice, and community acceptance. The committee's maturity and experience should be such as to justify respect for its advice and counsel.

No individual involved in the conduct of the research activity shall participate in its review, except to provide information to the committee.

Committee members should be identified in the assurance to the Public Health Service in terms of position, earned degrees, board certifications, licensures, memberships, and other indications of experience and competence. Names need not be given.

- *Description of the initial and continuing review procedures to be followed by the committee.*

Timing of review.

Research described in applications and contract proposals should, whenever possible, be given institutional review and approval prior to submission to the Public Health Service. Where review prior to Public Health Service submission is not possible, the review must be made prior to issuance of the award by the Public Health Service. Review of initial applications by institutions which have not previously filed acceptable assurances must be performed after acceptance of the assurance by the Public Health Service.

There may be occasions when a second review by the committee will be required before the research is initiated. For example, a long interval has elapsed between committee review and initiation, or the investigator proposes changes in protocol after the application has been reviewed by the committee but before the research is initiated. Perhaps the investigator has proposed research in a rapidly moving scientific area. The second review, in this case, would determine if changing standards of practice indicate a hazardous procedure unrecognized as such during the initial review (e.g., reduction of acceptable radiation levels).

1032872

Adequacy of the protection of the rights and welfare of the subjects involved.

Institutional committees should carefully examine the research plan to arrive at an independent determination of possible hazards. The committee must be alert to the possibility that investigators, program directors, or contractors may, quite unintentionally, introduce unnecessary or unacceptable hazards, or fail to provide adequate safeguards. This is particularly true of research that crosses disciplinary lines. The committees should consider the research plan as a whole in order to determine that normally minor and acceptable risks are not aggravated by the way it is designed. The severity of the risk from a procedure may vary with the circumstances under which it is carried out. Age, development, size, maturity, intercurrent disease, and other factors with respect to the subject may adversely affect the acceptability of a procedure. Simultaneous or consecutive performance of several minor tests or procedures may add up to a substantial risk. The committees must assure themselves that proper precautions will be taken to deal with emergencies that may develop even in the course of routine procedures.

Relevant to the decision of the committees are those rights of the subject that are defined by law, particularly those concerned with the rights of children and unborn infants; the termination of pregnancy; the use of prisoners, institutionalized, and military personnel; and the donation of tissues and organs.

Methods used to obtain adequate, appropriate, informed consent.

NOTE: In the United States, adherence to the regulations of the Food and Drug Administration (21 CFR 130.37) governing consent in projects involving investigative new drugs (IND) is required by law.

Consent should be obtained, whenever possible, from the subjects themselves. When the subjects are not legally or physically capable of giving informed consent, because of age, mental incapacity, or inability to communicate, or when the attending professional believes that the giving of full information would be contrary to the best interests of the subject, the review committee may consider the validity of consent by next of kin, legal guardians, or by other responsible third parties who are representative of the subject's interests. In the latter instances, careful consideration should be given by the committee not only to the third parties' depth of interest and concern with the subjects' rights and welfare, but also to whether the third parties are authorized to expose the subjects to the risks involved. A parent, for example, may have no authority to expose his child to risk, except for the child's own benefit.

1032813

The review committee should determine if the consent, whether secured as a written document or given orally, or whether the consent is implicit in voluntary participation in a well-advertised activity, is adequate in the light of the risks to the subject, and the circumstances of the research. The review committee should also determine if the information to be given to the subject or to qualified third parties, orally or in writing, is a fair explanation of the procedure, its possible benefits, and its attendant hazards. Where debriefing procedures are considered as a necessary part of the research plan, the committee should ascertain that these will be complete and prompt.

When the sponsoring institution routinely obtains a generalized form of consent for treatment or care, the committee shall determine whether these routine procedures provide an adequate basis for the subject's informed consent to the research procedures involved.

Relative weights of risks versus benefits.

Even though informed consent has been obtained or can be anticipated, the committee shall carefully consider the relative weights of the risks and benefits of the procedures to the subjects. If a procedure may confer a substantial benefit to the subjects, the committee may be justified in permitting them to accept an equally substantial or lesser risk. Where the potential benefits to the

subjects are negligible, or nonexistent, as in some cases of normal volunteers, the committee may be justified in permitting subjects to accept a risk in the interests of humanity. In all instances, careful consideration must be given by the committee to the subjects' motivation in accepting them.

Notification of the committee's decision to the project director.

If the committee's overall recommendation is favorable, it may prescribe restrictions or conditions under which the research may be conducted, define areas of possible pertinent changes in the research plans which should be brought to its attention, and determine the nature and frequency of interim review procedures to insure continued acceptable conduct of the research.

Favorable recommendations by an institutional committee are, of course, always subject to further appropriate review and rejection by institution officials. Unfavorable recommendations, restrictions, or conditions cannot be removed except by the committee or by the action of another appropriate review group described in the assurance filed with the Public Health Service. Under no circumstances shall proposed research, or proposed changes in research plans, not approved by the committee be implemented with Public Health Service funds. The scientist proposing the research should be informed

1032874

of the reasons for any adverse actions taken by the institutional committee.

Continuing review of research.

The committee shall require the project or program director to report to the committee for review any emergent problems or proposed procedural changes which may affect the status of the research with regard to the institution's review criteria. No such changes, except those necessary to eliminate apparent immediate hazards, should be made without prior approval by the committee.

In addition, the committee shall carry out interim review of the conduct of all research in such a manner and at appropriate intervals in the light of apparent risks, existing administrative and supervisory organization, and other factors as to assure itself that its advice is being followed.

The facilities available to protect the health and safety of human subjects.

The assurance should describe in general terms the facilities and personnel available to protect the health and safety of human subjects, particularly those requiring emergency care.

Certification.

An institution sponsoring an application for a grant or an award will submit with the application, or as soon after submission of the application as possible, the following

statement identified by name of investigator, title of project, and assigned number, if known:

> "The (name of institution) reviewed and approved on (date) the procedures in this application which will involve human subjects in accordance with the assurance approved by the Public Health Service. These procedures will also be subject to continuing review as provided for in that assurance."

An institution submitting a contract proposal for research involving human subjects will submit with its proposal, or prior to award, the following statement identifying the contract, the contractor, and the official authorized to sign for the contractor:

> "The (name of institution) reviewed and approved on (date) the procedures in this proposal which will involve human subjects, in accordance with the assurance approved by the Public Health Service. The institution agrees that all work involving the use of human subjects under any contract or any subcontract awarded in response to this proposal will be subject to initial and continuing review as required by Public Health Service policy and as described in its assurance.
> "The contractor shall bear full responsibility for the proper and safe performance of all work and services involving the use of human subjects under this contract. The parties hereto agree that the contractor retains the right to control and direct the performance of all work under this contract. No provision of this contract shall be deemed to constitute the contractor or any subcontractor, agent or employee of the contractor or any other person, organization, institution, or group of any kind whatsoever, as the agent or employee of the government. The contractor agrees that it has entered into this contract and will discharge its obligations, duties, and undertakings and the work pursuant thereto whether requiring professional judgment or otherwise as an independent contractor and without liability on the part of the government."

Records and reports.

The institution is required to keep informative records of group reviews and decisions on the use of human subjects, and to obtain and keep documentary evidence of

1032875

informed consent relating to research carried out with the assistance of Public Health Service financial support. At a minimum these records should include a summary of the factors leading to the group decision. Documentary evidence of informed consent may consist of a record of the decision of the committee as to the type of consent which it considers acceptable. Copies of the information statement, if any, to be given to the subject, where signed consent statements are required, should be retained in institution files. Where oral or implied consents are obtained, notations should be made on official records.

Submission and review of assurance.

Assurances should be forwarded to the Director, Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014, for review and acceptance on behalf of the Public Health Service.

No routine reports to the Public Health Service are required. However, significant changes in policy, procedure, or committee structure shall be promptly reported to the Director, DRG. Review of these changes, or of institutional and other records of performance under the terms and conditions of Public Health Service policy, may require renegotiation of the assurance or such other action as may be appropriate.

EXAMPLE OF A STATEMENT OF COMPLIANCE ATTACHMENT A

Institutional Assurance on Research Involving Human Subjects

The (name of institution) will comply with the principles of the Public Health Service policy with regard to research involving human subjects which requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. It assures the Public Health Service that it will establish and maintain advisory groups competent to review research plans involving human subjects, prior to the initiation of this research, in order to insure adequate safeguards. Group reviews and decisions will be carried out in reference to (1) the rights and welfare of the individuals involved, (2) the appropriateness of the methods used to obtain informed consent, and (3) the risks and potential benefits of the proposed research.

The institution agrees to a continuing exchange of information and advice between the review group and the investigator or director, particularly to deal with proposed changes in research design, and with emergent problems which may alter the investigational situation with regard to the criteria cited above. The institution will assure itself that its policies and the advice of its review groups are followed. It will also provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects involved in research. Records of group review and decision on the use of human subjects and of informed consent will be developed and kept by the institution.

Signed _____

Title _____

Date _____

Enclosures (Implementing Guidelines)

U. S. GOVERNMENT PRINTING OFFICE : 1969 O - 348-095

1032876

Dr. Anthony Girardi, Director
Cancer Research Center
I&I Bldg.
Executive Park Drive

THE UNIVERSITY OF TENNESSEE, KNOXVILLE
KNOXVILLE 37916

OFFICE OF THE VICE CHANCELLOR FOR
GRADUATE STUDIES AND RESEARCH

404 ANDY HOLT TOWER

AREA 615
TELEPHONE 974-3466

MEMORANDUM

TO: Deans and Department Heads

FROM: Hilton A. Smith, Vice Chancellor for Graduate Studies and Research
William Konnert, Chairperson of Committee on Research Participation

RE: Policies and Procedures to be used with Research Proposals which involve Human Subjects

The enclosed packet includes materials outlining the policies and procedures to be used with research proposals in which human subjects are involved. These policies and procedures are in accordance with the general institutional assurance dated July 15, 1975, as amended November 25, 1975 and approved by the Department of Health, Education, and Welfare.

Please note that the Committee on Research Participation meets the second Thursday of each month, and that proposals must be submitted to the chairperson two weeks prior to the meeting date in order to be considered by the Committee. Each department also must have a research review committee with a chairperson. A list of the committee members and the chairperson should be submitted to William Konnert, Room 404, Andy Holt Tower.

The Committee will be distributing material in the near future which hopefully will be helpful to the Departmental Research Review Committees as they develop criteria for determining whether research involving human participants is non-behavioral and/or non-biomedical in nature.

WK:pak

Enclosures (6)
1. Policies and Procedures for Approval of Research Involving Human Subjects
2. Administration of Assurance
3. Form B
4. Form D
5. Declaration of Helsinki
6. Federal Register, Vol. 40, No. 50, March 13, 1975

1032877

THE UNIVERSITY OF TENNESSEE, KNOXVILLE

POLICIES AND PROCEDURES FOR APPROVAL OF RESEARCH INVOLVING HUMAN SUBJECTS

(These policies and procedures are in accordance with the general institutional assurance dated July 15, 1975, as amended November 25, 1975, and approved by the Department of Health, Education, and Welfare.)

I. POLICIES

A. All research, development, and related activities involving human subjects must be reviewed as described prior to conducting any research and for applications for grants to the Department of Health, Education, and Welfare, United States Department of Agriculture, and the American Heart Association prior to submission of proposal. A "related" activity is one labeled other than research or development as, for instance, training, demonstration, improvement, or support, but which nevertheless contains a research and development component

B. The University Committee on Research Participation and all Departmental Committees on Research Participation will apply the broad principles stated in the "Declaration of Helsinki" in their reviews.

II. PROCEDURES

A. Responsibilities of the University Committee on Research Participation

1. After review of the project considering the factors on Form B, the Committee shall determine whether:[1]

   (a) The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;
   (b) the rights and welfare of any such subjects will be adequately protected;
   (c) legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provisions of this part; and
   (d) the conduct of the activity will be reviewed at timely intervals.

2. Review considerations by the Committee shall also include:[2]

   (a) Acceptability in terms of institutional commitments and regulations;
   (b) applicable law;
   (c) standards of professional conduct and practice;
   (d) community attitudes; and
   (e) departmental guidelines for project review.

[1]Fed. Reg., Vol. 40, No. 50, (46.2b), Thursday, March 13, 1975
[2]Fed. Reg., Vol. 40, No. 50, (46.6b1), Thursday, March 13, 1975

1032878

3. The Chairperson will notify the Vice Chancellor for Graduate Studies and Research by letter of the review results with a carbon copy to the Project Director.

   If the Committee recommends changes, the approval will be pending receipt and approval of the revised Form B or a copy of changes, whichever is requested by the Committee.

   If the project is approved, the Office of the Vice Chancellor for Graduate Studies and Research will then verify DHEW 596 by completing items 4, 7, and 8 and sending the form to the proper agency. (Prior to project review by the Committee, the Project Director should send DHEW Form 596 to the Vice Chancellor for Graduate Studies and Research.)

4. The Committee will provide (upon request) advice and counsel to staff working on or contemplating new research.

5. The Committee will meet on the second Thursday of each month for review of new applications and review of continuing projects. Materials must be in the hands of the University Committee Chairperson two weeks previous to each monthly meeting in order to be reviewed at that meeting.

B. Responsibility of all Departments for Research Involving Human Subjects

1. Each department will appoint a Departmental Committee on Research Participation, and names of committee members are to be sent to the Office of the Vice Chancellor for Graduate Studies and Research, 404 Andy Holt Tower. Alternates should be selected to avoid reviewing projects in which they have an active role or conflict of interest.

2. Each Departmental Committee will establish guidelines which will include within their provisions, among others, the departmental criteria for non-behavioral and non-biomedical projects involving human subjects as a basis for approval (gathering of statistics), as well as the definition of subjects at risk as defined in 46.3b.[3] These departmental guidelines will be reviewed and approved by the Committee on Research Participation.

3. Following these guidelines, the Departmental Committee will review all departmental research, development, and related activities involving human subjects (as submitted by Project Director on Form B). In reviewing projects the Departmental Committee will subscribe to the broad principles stated in the "Declaration of Helsinki" and standards of professional ethics.

4. Reports of all projects involving human subjects approved as non-behavioral and non-biomedical by the Departmental Committees will be sent to the Chairperson of the Committee on Research Participation. The Chairperson of the Committee on Research Participation will recommend actions on such projects to the Vice Chancellor for Graduate Studies and Research.

[3]Fed. Reg., Vol. 40, No. 50, (46.3b), Thursday, March 13, 1975

1032879

5. All other approved projects will be referred to the Committee on Research Participation for review.

C. Procedures for and Responsibilities of Project Director

1. Complete Form B (available in Office of the Vice Chancellor for Graduate Studies and Research, 404 Andy Holt Tower) for review by the Departmental Committee on Research Participation. All items on Form B will be considered in evaluation.

2. No project will be evaluated for funding by DHEW without prior approval of the University Committee on Research Participation. Consequently, the timing of the University Committee on Research Participation is important. Until November of 1977, however, there is a provision for approval within the following time limits:[4]

   (a) Certification to DHEW within 30 days after written request;
   (b) certification to DHEW within 90 days after the deadline for submission; and
   (c) certification to DHEW within 90 days after submission if no deadline date is specified.

   On this basis, the Form B should be presented to Departmental Committee in sufficient time to be transmitted to the University Committee on Research Participation by 2 weeks before the regularly scheduled monthly meeting.

3. Following disapproval by the University Committee, options of the Project Director are as follows:

   (a) Revision of the project in accordance with Committee recommendations;
   (b) discussion with the Committee; and/or Vice Chancellor for Graduate Studies and Research; and
   (c) withdrawal of the application.

4. Following approval from the University Committee, the Project Director is responsible for the following:

   (a) Obtaining approval from the University Committee prior to instituting any change in protocol,
   (b) keeping signed consent statements for the duration of the project and for at least 3 years thereafter,
   (c) informing the University Committee of any unexpected physical or psychological effects on subjects for re-evaluation of the protocol approval.

[4]Fed. Reg., Vol. 40, No. 98, Tuesday, May 20, 1975

(d) submitting a statement (Form D)[5] to the University Committee at 12 month intervals attesting to the current status of the project (approved protocol remains in effect, project has been terminated, etc.). For certain projects the Committee may request reports at more frequent intervals. Grant continuation by many agencies is contingent upon continued University Committee review and approval. Form D is the instrument by which continued review is made. It is vital, therefore, that this step is completed.

* * * *

THE UNIVERSITY OF TENNESSEE, KNOXVILLE

ADMINISTRATION OF ASSURANCE
(July 15, 1975, as amended November 25, 1975)

The Vice Chancellor for Graduate Studies and Research is administratively responsible for implementation of the Assurance. Such implementation includes:

1. Appointment of the Committee on Research Participation.

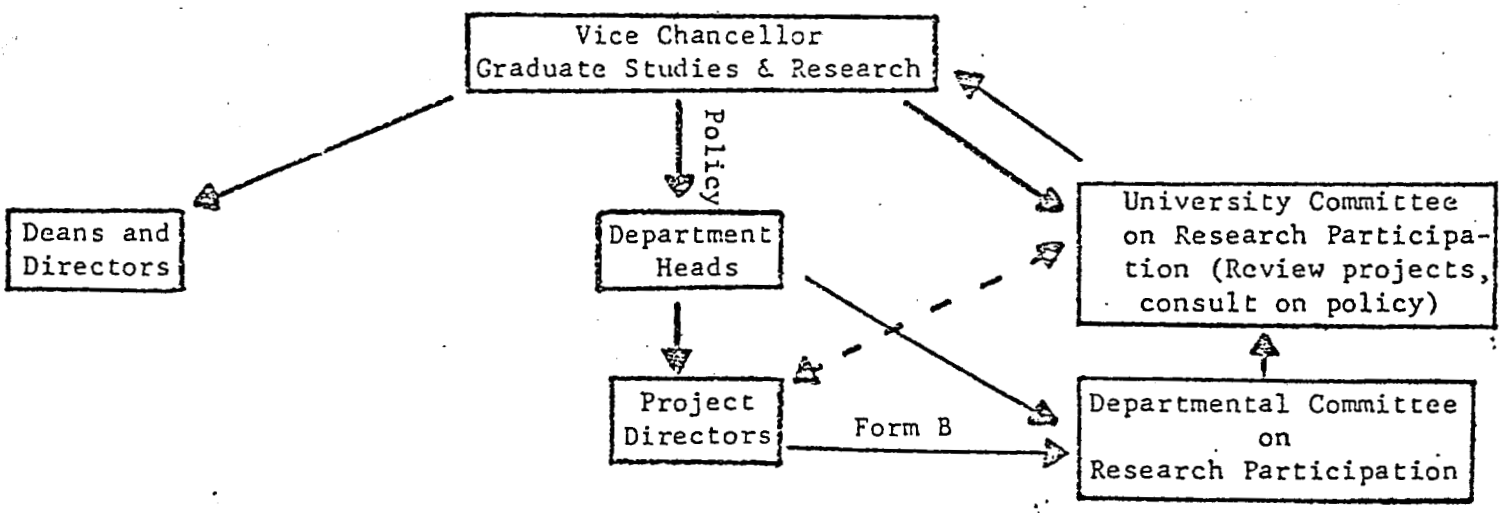
2. Development of policies in consultation with the Committee on Research Participation.

3. Continuing instruction of personnel regarding policies and procedures.

4. Review of Committee on Research Participation recommendations for approval regarding specific projects with options of approval, disapproval or further restrictions on the projects.

5. Maintaining record of decision made by the Committee on Research Participation.

The flow of responsibility and communications is as follows:



Composition of Committee

1. The Committee, the Chairperson, and a Vice-Chairperson will be appointed by the Vice Chancellor for Graduate Studies and Research.

2. The Committee will be composed of 12 members with 4 alternates. Members will be chosen to represent medical, psycho-social,

1032882

humanities and scientific community. Consideration will also be given to legal, religious and local community representation.

3. Term of appointment - 3 years in rotation with potential for reappointment.

Committee on Research Participation to Implement Policy

1. Projects received 2 weeks before regularly scheduled meeting. All projects have prior review by departmental committee.

2. Three reviewers appointed by Chairperson to critically review and make written recommendations (Form C) to Committee at committee meeting prior to voting.

3. Quorum of Committee - 7 members or their alternates. Alternates will be invited to each meeting.

4. Approve departmental policy for review of non-biomedical and non-behavioral projects and determination of risk.[1] A copy of project and departmental review is sent to the Chairperson of the University Committee on Research Participation. Recommendation regarding such projects sent by Chairperson to Vice Chancellor for Graduate Studies and Research.

5. Any project director may request hearing by Committee. Committee may request appearance of project director at review.

6. Option of Committee regarding projects:

   (a) Recommend major changes - resubmit revised Form B to Committee for committee meeting.

   (b) Suggest minor changes - copy of changes to Chairperson - then approval by Chairperson.

   (c) Request "outside specialist consultant" review - refer back to project director.

   (e) Disapprove - Revision of the project in accordance with Committee recommendations; discussion with the Committee; and/or withdrawal of the application.

7. Vote to approve requires majority affirmative votes of those present. Vote to revise includes option of Chairperson or Committee meeting to accept revision.

   Members are ineligible to vote on projects with which they are associated.

[1]Fed. Reg., Vol., 40, No. 50, (46.2b), March 13, 1975

1032883

8. Appeals from decisions of this Committee received by Vice Chancellor for Graduate Studies and Research.

9. The Vice Chancellor for Graduate Studies and Research notified of Committee action by letter which includes CRP #, Agency #, and subject risk statement. A copy of the letter also to the project director and, in the case of USDA projects, to Associate Dean of Agricultural Experiment Station.

10. Annually, Form D is sent to each project director to maintain continuing review of each project.

1032884

FORM B

INSTRUCTIONS AND DEFINITIONS ARE IN ITALICS AND SHOULD NOT APPEAR ON THE COMPLETED FORM.

CRP#_____

Date Received_____

THE UNIVERSITY OF TENNESSEE, KNOXVILLE

Application for Review of Research Involving Human Subjects
(In accordance with general institutional assurance dated
(July 15, 1975, as amended November 25, 1975)

I. Identification of Project: Date:

Project Director and Co-Director:
Title of Project:
Department:
Supporting Agency and Identification Number (if known): *For DHEW grants/ contracts complete DHEW Form 596 (items 1, 2, 3 and 5 and 6 if applicable) and send to Mrs. Janet Krauss, Office of the Vice Chancellor for Graduate Studies and Research, 404 Andy Holt Tower.*
Estimated starting date and completion date:
Grant submission deadline:

II. Objective(s) of Project:

III. Description of Subjects:

Include number of subjects anticipated, criteria for selection and exclusion, age, payments or incentives. Definition from Subtitle A of Title 45 of Code of Federal Regulations is as follows:[1]

> *"Subject at risk" means any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.*

IV. Methods of Procedure:

Include stresses, drugs, or medication, including name and dosage, experimental manipulations, tests or measures, interviews, observations, photographs, recordings, etc. Clearly distinguish between control groups and experimental groups.

[1]Fed. Reg., Vol. 40, No. 50, (46.3b), Thursday, March 13, 1975

1032885

V. Protection Measures:

Include specific controls, screening methods, and follow-up to assure no residual, physical, psychological or social damage to subjects. Include method of protection of anonymity of subjects.

VI. Method of Obtaining "Informed Consent" from Subjects:

Informed consent must be documented and legally effective; a copy of the explanation given to the subject and the consent form used MUST be included with Form B for Committee review.

The definition of informed consent is as follows:[2]

> *"Informed consent" means the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion.*

The basic elements of informed consent are as follows:

1. *A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;*
2. *A description of any attendant discomforts and risks reasonably to be expected;*
3. *A description of any benefits reasonably to be expected;*
4. *A disclosure of any appropriate alternative procedures that might be advantageous for the subject;*
5. *An offer to answer any inquiries concerning the procedures; and*
6. *An instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject.*

In addition, the agreement, written or oral, entered into by the subject, should include no exculpatory language through which the subject is made to waive, or appear to waive, any of his legal rights, including any release of the institution or its agents from liability for negligence.

The actual procedure in obtaining legally effective informed consent and the basis for Committee determinations that the procedures are adequate and appropriate are to be fully documented. The documentation will follow one of the following three forms:[3]

1. *Provision of a written consent document embodying all of the basic elements of informed consent. This form is to be signed by the subject or legally authorized representative.*

[2]Fed. Reg., Vol. 40, No. 50, (46.3c), Thursday, March 13, 1975

[3]Fed. Reg., Vol. 40, No. 50, (46.10), Thursday, March 13, 1975

1032886

2. *Provision of a 'short form' written consent document indicating that the basic elements of informed consent have been presented orally to the subject or his legally authorized representative. Written summaries of what is to be said to the patient are to be approved by the Committee. The 'short form' is to be signed by the subject or his legally authorized representative and by an auditor-witness to the oral presentation and to the subject's signature. A copy of the approved summary, annotated to show any additions, is to be signed by the person officially obtaining the consent and by the auditor-witness.*

3. *Modification of either of the above two primary procedures. All such modifications must be approved by the Committee in the minutes signed by the Committee Chairperson. Criteria for approval of modifications include:*

   a. *that the risk to any subject is minimal;*
   b. *that use of either of the primary procedures for obtaining informed consent would surely invalidate objectives of considerable immediate importance; and*
   c. *that any reasonable alternative means for attaining these objectives would be less advantageous to the subjects.*

VII. Responsibility of Project Director:

By compliance with the policies established by the University Committee on Research Participation, the Project Director subscribes to the broad principles stated in "The Declaration of Helsinki" and standards of professional ethics in all research, development and related activities involving human subjects under the auspices of the University of Tennessee, Knoxville.

a. When appropriate, Form DHEW 596 will be completed and returned to the Office of the Vice Chancellor for Graduate Studies and Research, 404 Andy Holt Tower.
b. Approval will be obtained from the University Committee prior to instituting any change in project protocol.
c. Development of any unexpected risks will be reported to the University Committee.
d. Signed consent statements will be kept for the duration of the project and for at least three years thereafter.
e. A status report (Form D)[4] will be submitted at 12 month intervals, or as requested, attesting to the current status of the project.

1032881

Signature:

Project Director_____

Date_____

[4]Available in the Office of the Vice Chancellor for Graduate Studies and Research, 404 Andy Holt Tower.

VIII. Departmental Review:

COMMENTS/RECOMMENDATIONS:

The application described above has been subjected to departmental review and has been approved.

Signatures:

Department Head_____ Date_____

Chairman, Departmental Committee _____ Date_____

Materials required by the University Committee on Research Participation:

17 copies of Form B

4 copies of technical portion of grant application (omit budget)

4 copies of cover sheet of grant application

Form DHEW 596 to be sent by Project Director to the Office of Graduate Studies and Research, 404 Andy Holt Tower

1032888

FORM D

THE UNIVERSITY OF TENNESSEE, KNOXVILLE

Status Form - Research Involving Human Subjects
Change/Renewal/Termination
(July 15, 1975, as amended November 25, 1975)

Please complete Questions 1 through 5 Date: _____

1. Project Director: _____ Department: _____

2. Project Title: _____

3. Research Participation Committee No.: _____ Date Originally Approved: _____

4. Funding Agency and Number: _____

5. Date Funded: _____ Date Project Initiated: _____

Of the following questions, please complete only those pertinent to the current status of this research project.

6. ☐ Request change in protocol as follows: (Attached revised Form B for changes)

7. ☐ Request renewal of project last approved on _____ (date) with no changes in protocol.

8. ☐ Project terminated on _____ (date).

9. ☐ Describe any unexpected risks to the subjects that may have developed since previous review.

Project Director _____
(Signature) (Date)

Department Chairperson OR
Chairperson of Departmental
Committee _____
(Signature) (Date)

Complete form and return to the Office of the Vice Chancellor of Graduate Studies and Research, 404 Andy Holt Tower.

1032889

D E C L A R A T I O N O F H E L S I N K I

Recommendations Guiding Doctors in Clinical Research

Introduction

It is the mission of the doctor to safeguard the health of the people. His knowledge and conscience are dedicated to the fulfilment of this mission.

The Declaration of Geneva of the World Medical Association binds the doctor with the words: "The health of my patient will be my first consideration" and the International Code of Medical Ethics declares that "Any act or advice which could weaken physical or mental resistance of a human being may be used only in his interest."

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to each doctor in clinical research. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Doctors are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

In the field of clinical research a fundamental distinction must be recognized between clinical research in which the aim is essentially therapeutic for a patient, and the clinical research, the essential object of which is purely scientific and without therapeutic value to the person subjected to the research.

I. Basic Principles

1. Clinical research must conform to the moral and scientific principles that justify medical research and should be based on laboratory and animal experiments or other scientifically established facts.

2. Clinical research should be conducted only by scientifically qualified persons under the supervision of a qualified medical man.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

1032890

II. Clinical Research Combined with Professional Care

1. In the treatment of the sick person, the doctor must be free to use a new therapeutic measure, if in his judgment it offers hope of saving life, re-establishing health, or alleviating suffering.

   If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient has been given a full explanation. In case of legal incapacity, consent should also be procured from the legal guardian; in case of physical incapacity, the permission of the legal guardian replaces that of the patient.

2. The doctor can combine clinical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that clinical research is justified by its therapeutic value for the patient.

III. Non-Therapeutic Clinical Research

1. In the purely scientific application of clinical research carried out on a human being, it is the duty of the doctor to remain the protector of the life and health of that person on whom clinical research is being carried out.

2. The nature, the purpose and the risk of clinical research must be explained to the subject by the doctor.

3a. Clinical research on a human being cannot be undertaken without his free consent after he has been informed; if he is legally incompetent, the consent of the legal guardian should be procured.

3b. The subject of clinical research should be in such a mental, physical and legal state as to be able to exercise fully his power of choice.

3c. Consent should, as a rule, be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject even after consent is obtained.

4a. The investigator must respect the right of each individual to safeguard his personal integrity, especially if the subject is in a dependent relationship to the investigator.

4b. At any time during the course of clinical research, the subject or his guardian should be free to withdraw permission for research to be continued.

   The investigator or the investigating team should discontinue the research if, in his or their judgment, it may, if continued, be harmful to the individual.

OPRR Reports

NIH PHS DHEW

January 1976

The *OPRR Report* has been initiated by the Office for Protection from Research Risks to inform DHEW grantee and contractor institutions of activities concerning the protection of human subjects. The Report will be distributed on an occasional basis and will speak informally to DHEW regulations, to legislation, to court cases and decisions, and to other subjects of a general interest in the protection of human subjects.

CERTIFICATION RESTRICTIONS PLACED ON GENERAL ASSURANCES

A change has been made in the general assurance restriction codes. The code will be shown as a suffix to the general assurance number listed in the *Cumulative List of Organizations and Institutions in Compliance with DHEW Policy and Regulations on Protection of Human Subjects*. This change conforms with the National Research Act, P.L. 93-348, Title II, which specifically applies to both *biomedical* and *behavioral* research, and with the derivative DHEW regulations.

A restriction usually indicates that the Institutional Review Board does not have at least two members with the professional qualifications considered necessary to provide adequate review of research activities in the area of the restriction. Restrictions apply only to activities requiring certification.

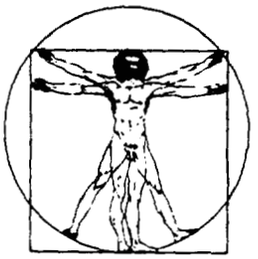
An -XM suffix indicates a restriction in biomedical research; a proposed activity requiring medical expertise to assess risks and benefits and to determine the adequacy of medical services and safeguards cannot be certified under an -XM restriction.

An -XB suffix indicates a restriction in behavioral research; a proposed activity requiring behavioral expertise for assessing risks and benefits and determining the adequacy of clinical services and safeguards cannot be certified under an -XB restriction.

An -XO suffix indicates a restriction that uniquely applies to the institution under the conditions specified in the DHEW assurance approval letter.

1032892

JAN 14 1976



Institutions having IRB's that otherwise meet the requirements of 45 CFR 46.6 will be considered eligible, insofar as Board membership is concerned, for unrestricted DHEW approval when (a) two or more members are licensed to practice medicine (FDA requires that at least two members licensed to administer drugs and at least one member not so licensed serve on the IRB quorum for review of a proposal involving an investigational new drug), and (b) two or more members are identified with competence in the behavioral sciences or related specialties, such as anthropology, psychiatry, psychology, sociology.

Those institutions that have established a committee that does meet requirements for an unrestricted general assurance may request removal of the restriction with submission of an assurance addendum naming additional members to their IRB(s) with the appropriate professional qualifications.

When reporting IRB membership, institutions should follow the format given in the May 22, 1975 OPRR Memorandum. Note that if members are added to the Board, the quorum requirement may be affected and that if replacements are submitted, the member replaced should be identified.

When a proposal to be submitted to DHEW comes within the scope of a restriction, either biomedical or behavioral, the IRB reviewing the proposal must include additional voting members whose qualifications offset the restriction. Their names and qualifications should be reported immediately to OPRR and a statement added under "Notes" on the HEW 596 form certifying IRB review and approval that the additional professionally qualified members have been reported to OPRR. Proposals that come within the certification restrictions that are not preceded or accompanied by appropriate compensating reviewers will be deferred for re-review and recertification.

ONLY AUTHORIZED SIGNATURES RECOGNIZED ON ASSURANCES

> *. . . assurances shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this part . . . .*
>
> *49 FR 11854 45 CFR 46.4(b)*

OPRR does not normally question the credentials of the individual signing the Institutional Assurance of Compliance statement. However, the person signing such a document must in fact have the legal and executive authority to execute such commitments for the institution and all of the components named. Whenever it is not clear that the individual signing the compliance statement has the executive authority to make such institutional commitments, documentation (e.g., a copy of a memorandum signed by the head of the institution clearly delegating such authority) should be provided as an addendum to the Institutional Assurance establishing the basis for such authority.

1032893

When the institution considers it mutually advantageous, because of joint professional staff appointments, common facilities or other considerations, one institution (the affiliating institution, e.g., a veterans administration hospital, a community hospital or an autonomous research institute) may subscribe to the assurance implementing procedures of another institution (the originating institution).

To receive official DHEW recognition of such a relationship (1) the affiliating institution must submit a properly executed "Institutional Assurance of Compliance" with a copy of the assurance implementation procedure of the originating institution including the current membership list of the DHEW approved IRB membership list. The list which may be amended by the originating institution to accommodate the affiliating institution, and (2) a memorandum of understanding signed by authorized officials of both institutions and the chairman of the IRB. The memorandum of understanding must provide for the IRB to review all activities involving human subjects conducted at the affiliating institution and for parallel administration of the assurance implementing procedures at the affiliating institution.

RISK-BENEFIT

DHEW REGULATIONS AMENDED - HUMAN SUBJECTS

Title 45, Code of Federal Regulations, Part 46, 40 FR 51638, November 6, 1975, applies to Section 46.206 of the regulations published August 8, 1975 (40 FR 33526) concerning research, development, and related activities involving fetuses, pregnant women and human *in-vitro* fertilization. The section (46.206) is amended to read: "(a)(2) Except where the purpose of the activity is to meet the health needs of the mother or the particular fetus, the risk to the fetus is minimal and, in all cases, is the least possible risk for achieving the objectives of the activity."

PROPOSED PROCEDURES - TITLE 42 CFR PART 2A

PROTECTION OF IDENTITY - RESEARCH SUBJECTS AND PATIENTS

The proposed amendment introduces procedures under which persons engaged in research on mental health, including research on the use and effect of alcohol and other psychoactive drugs *may* apply for an authorization to protect the privacy of the research subjects by withholding from all persons not connected with the conduct of the research, the names and other identifying characteristics of the subjects.

Interested persons are invited to write, by January 19, 1976 to:

Alcohol, Drug Abuse, and Mental Health Administration
5600 Fishers Lane
Room 13C-06
Rockville, Maryland

1032894

DRR, NIH ISSUES INSTRUCTIONS FOR BRSG

Institutions applying for or receiving awards for Biomedical Research Support Grants (BRSG), have been instructed by the Division of Research Resources, NIH, to report all activities involving human subjects at least 30 days before support begins. Based on the use of form HEW 596, the reporting procedure requires that an initial declaration/assurance/certification accompany the application stating whether or not activities involving human subjects are planned. A similar report must be submitted for each activity proposed or developed later.

The instructions are derived from the regulatory requirements (45 CFR 46), especially sections 46.113, "Applications and proposals lacking definite plans for involvement of human subjects," and 46.114, "Applications and proposals submitted with the intent of not involving human subjects."

Although DRR instructions, reprinted below, were written specifically for the BRSG program, they exemplify the procedure that should be followed whenever sections 46.113 and 46.114 apply or whenever support on any DHEW grant or contract funds are being considered for an activity that has not been previously reviewed or reported to the supporting agency of the DHEW.

APPLICATION FOR BIOMEDICAL RESEARCH SUPPORT GRANT

INSTRUCTIONS FOR COMPLETION OF FORM HEW 596 (Rev 4-75)

"PROTECTION OF HUMAN SUBJECTS, ASSURANCE/CERTIFICATION/DECLARATION"

Note: Read carefully the introductory Statement of Policy on Form HEW 596 (Rev 4-75). For background information, refer to Federal Register 40:11854-11858 March 13, 1975.

Application for a Biomedical Research Support Grant (BRSG) must be accompanied by a properly completed Form HEW 596 (Rev 4-75) indicating proposed involvement (Box 3B) or non-involvement (Box 3A) of human subjects.

I. Institutions with General Assurance

A. Institutions with Unrestricted General Assurance. (Assurance covers both medical and behavioral investigations.)

Before any activity involving human subjects can receive support from BRSG funds, whether it is ongoing, about to be initiated, or will be undertaken later in the grant period, a current certification on Form HEW 596 for each such activity with a copy of each activity plan as reviewed and approved by the Institutional Review Board (IRB)

1032895

must be on file with DHEW. Therefore, enclose the appropriate HEW 596 forms and IRB approved plans for the ongoing and about to be initiated projects with the BRSG application. Plans to involve human subjects in any BRSG supported activity after submission of a BRSG application, must also be reviewed and approved by the IRB and submitted to DHEW (DRR-NIH) with a Form HEW 596 certifying such review and approval at least 30 days prior to actual participation of human subjects in that activity (Box 4B).

B. Institutions with Restricted General Assurance

If there is a restricted general assurance, then institutions cannot propose activities within those restrictions. Restrictions are specified by an XM (restricted from certifying medical research activities), an XB (restricted from certifying behavioral research activities), or, rarely an XO (other restrictions) suffix to institutional assurance numbers. (These suffixes will appear in future issues of the Cumulative List of Institutions in Compliance with DHEW Regulations.) When such restrictions prohibit a proposed activity, the restriction may be removed by submitting HEW Form 596 (Rev 4-75) with a check mark in Box 4A and a request that procedures be initiated to remove the specific restriction.

II. Institutions without General Assurance

If a grantee without general assurance wishes to use the award to support an activity involving human subjects, a Form HEW 596 (Rev 4-75) must be submitted with check mark in Box 4A to initiate procedures necessary to comply with the regulations on protection of human subjects. As part of such compliance, DHEW will request the grantee institution to satisfy the requirements for either a general or special assurance.

III. All Institutions

Before BRSG funds can be used to supplement support of an ongoing project, review, approval, and certification to DHEW must be completed unless the project: 1. is being supported also by another DHEW award, and 2. has been reviewed, approved, and currently is certified to be in compliance with such other DHEW award, and 3. there has been no change in the project since last reviewed, approved, and certified and no change in the project is contemplated at the time of supplementation. Documentation of review, approval, and certification must be part of the BRSG grantee file for each activity involving human subjects that receives either sole or supplemental support from BRSG funds.

All submissions of Form HEW 596 required for use of BRSG funds to support activities involving human subjects in accordance with these instructions should be addressed to:

Biomedical Research Support Grant Program
Division of Research Resources
National Institutes of Health
Bethesda, Maryland 20014
301: 496-6743

FORM HEW 596 TO BE REVISED

Sooner or later, hopefully within eight months, the Form HEW 596 for assurance/certification/declaration will be revised. The Office for Protection from Research Risks encourages those who are using this form to comment on its deficiencies and usefulness for the purposes it is intended to serve. Please note that the form is designated to accommodate institutions not having general assurances as well as those that do have general assurances. Some familiarity with those sections of 45 CFR 46 pertaining to "special assurances" (e.g., section 46.16, cooperative activities) may be helpful in offering suggestions.

It is planned that provision will be made in the next revision of HEW 596 for certification of either the original application or a modified proposal or protocol, a copy of which is to be submitted with the HEW 596.

LEGISLATION ENACTED

NEW YORK - Amendment to the Public Health Law, Chapter 450, 1975. A law, Protection of Human Subjects, was enacted by the 1975 state legislature. The Act is based on DHEW regulations and states (§ 2445) that it does not apply to research which is in compliance with or subject to regulations of any federal agency. Conversely, any institution in compliance with the Act is in compliance with DHEW regulations.

LEGISLATION PENDING

CALIFORNIA - California Assembly Bill No. 2423, 1975-76.
The Human Experimentation Act of 1975 provides that "no person shall be subjected to any medical experiment without his express voluntary consent."

The Act further states that express voluntary consent cannot be given by: persons under 18 years of age; pregnant women; persons confined to any institution, penal

or otherwise; the mentally retarded or those confined to any hospital, nursing home, or home for the elderly or disabled.

Introduced June 25, 1975, the bill was referred to the Committee on Criminal Justice.

LEGAL OPINIONS

There is some confusion in the scientific community as to whether the Department regulations concerning research involving fetuses, pregnant women or *in-vitro* fertilization, published in the *Federal Register* on August 8, 1975, permit investigations: (1) to administer experimental drugs to pregnant women without advising these women ". . . that neither the immediate or delayed effects of the drug are known as long as the investigator and his review committee believe there is little risk to the fetus . . .," and (2) to utilize control groups of unmedicated mothers in research into the effects of obstetric analgesia and anesthesia on the newborn.

The August 8 publication amended the Department's basic regulations (45 CFR Part 46, Subpart A) regarding protection of human subjects by adding a new Subpart B thereto. However, the publication made no significant changes in the pre-existing regulations and, in fact, the new subpart contains a specific statement that its requirements are in addition to those contained in other subparts.

Section 46.109 of the basic regulations continues to require that: "Any institution proposing to place any subject at risk is obligated to obtain and document legally effective informed consent." Informed consent is defined in section 46.103 to include the following elements:

> "(1) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;
> (2) a description of any attendant discomforts and risks reasonably to be expected;
> (3) a description of any benefits reasonably to be expected;
> (4) a disclosure of any appropriate alternative procedures that might be advantageous for the subject;
> (5) an offer to answer any inquiries concerning the procedures; and
> (6) an instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject."

This definition was not modified by the new regulations. Hence, these regulations have not altered the obligation under the pre-existing regulations to secure informed consent from pregnant women involved in research activities. In our view, there is no basis for such a conclusion.

Turning to the second concern, insofar as it is permissible under the Department's regulations (both Subparts A and B) to engage in particular research on medicated mothers to test the effects of obstetric analgesia and anesthesia on the newborn, we are aware of nothing in the regulations which would bar utilization of a control group of unmedicated mothers, assuming the mothers' informed consent was secured. It is assumed that in such circumstances the lack of analgesic or anesthetic medication would not be harmful to, but rather would be likely to benefit, the fetus.

OGC, NIH

PUBLIC ACCESS TO INFORMATION FILED WITH OPRR

DHEW feels especially obliged to deal with any questions or issues that may involve the protection of human subjects as openly and as expeditiously as possible without violating rights to privacy and confidentiality of the individual.

All documents within DHEW that pertain to the implementation of the regulations on protection of human subjects including the institutional assurances and certifications on file with DHEW are considered public documents.

Applications, summary sheets, and project site visit report relating to projects involving human subjects are subject to the same restrictions and privileges accorded to all such documents under the recent decision of the District Court of Appeals.

Certain functions are assigned to the grantee and contracting institutions that provide for the preservation of confidentiality and privacy of the individuals subject to the provisions of applicable law.

Many states have statutory and common law provisions that provide varying degrees of protection to certain confidential records such as those of patients, research data, and committee deliberations.

It is the intention of the Department to respect these preserves.

1032899

NIH REQUIRES DISPOSAL SAFEGUARDS

The National Institutes of Health has developed interim procedures for the disposal of chemical carcinogens at NIH. It is intended that these procedures should compliment specific Department of Health, Education, and Welfare regulations in this area.

The Williams-Steiger Occupational Safety and Health Act of 1970 was enacted to assure safe and healthful working conditions and Executive Order 11612 extended to each Federal agency the requirement that it establish and maintain an effective and comprehensive occupational safety and health program consistent with the standards set in the Act.

Required procedures for the disposal of chemical carcinogenic material at NIH have been developed not only for employee safety, but also for sound environmental management of these materials. Radioactive waste containing chemical carcinogens is disposed of in accordance with provisions of the NIH Radiation Safety Guide. Other carcinogenic waste material is broken down into five categories for disposal purposes: Dilute solutions (0.1%); glassware and equipment; burnable contaminated or potentially contaminated materials; syringes and needles contaminated with chemical carcinogens; and, purchased or synthesized carcinogenic chemicals and dilute non-degradable liquids.

Truly infectious waste that is also contaminated with a chemical carcinogen will be biologically decontaminated by chemical means rather than by autoclave prior to completing the procedures identified.

ANNOUNCEMENTS

INTERNSHIPS

The Institute of Society, Ethics and the Life Sciences offers two programs: a one-month internship in January and a general internship of more than a month, either during the school year or in the summer. Students are provided the opportunity to pursue an individual, self-initiated research project directed and supervised by a staff member.

Interns are students from undergraduate, professional and graduate schools and should be studying for a degree. A prime requirement is an interest in the problems the Institute explores, and the ability to undertake competent independent research in one or more of these areas. An applicant should have some understanding of the philosophical and ethical issues involved before applying.

For summer internships, applications should be postmarked by April 15; for other internships, at least two months before the proposed period. Address applications or inquiries to:

Marc Lappe
Hastings Center
360 Broadway
Hastings-on-Hudson, New York 10706

RESEARCH PRIZE

The Nellie Westerman Prize for Research in Ethics, an annual award for a paper detailing an ethical problem in an investigation involving human subjects, has been announced by the American Federation for Clinical Research. Creative approach to ethical problems will be published in *Clinical Research*.

February 15, 1976, is the deadline for submitting papers to:

Robert J. Levine, M.D.
Department of Medicine
Yale University School of Medicine
333 Cedar Street
New Haven, Connecticut 06510

INTERFACULTY PROGRAM IN MEDICAL ETHICS

Harvard University has established an Interfaculty Program in Medical Ethics under a three-year grant award. The interdisciplinary program, to be administered by the Medical School, is viewed as an opportunity to enhance study in the area and give professional people greater training in the ethical aspects of medicine.

MEETING

The Southern Sociological Society is scheduling a meeting on *Research Risks for Human Subjects* to be held in Miami, April 7-10, 1976. The format of the sessions will permit discussions and exchange of information on the subjects among sociologists. The meeting will be attended by a representative of OPRR.

QUESTIONS AND ANSWERS

Q. Under a protocol approved earlier this year, we have been treating several patients with chronic peptic ulcer and Zollinger-Ellison syndrome with Metiamid, a gastric secretory depressant available

1032901

as an investigational new drug. Within the last few weeks, Metiamid has been withdrawn by the manufacturer because of an accumulation of adverse reactions, and another, Cimetidine, substituted for it under an emergency IND exemption. Because of vacations, we are unable to assemble a quorum of our IRB to review the change in the protocol. Can we take any action without prior approval of the Board?

A. Yes. The Department's regulations provide for prompt reporting to the Board of proposed changes (46.6(d)(2)) and timely review (46.2(b)(4)), but there is no obstruction to emergency changes in protocols necessary in the interests of the patient. Such changes are consistent with the terms of the Declaration of Helsinki (II. 4c) and the Ethical Guidelines for Clinical Investigation of the AMA (2, 3Biii). Under no circumstances should the regulations be construed so as to deny due care to a patient.

Distributed by:

Office for Protection from Research Risks
Office of the Director, NIH
Westwood Building, Room 304
301: 496-7541

1032902

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD. 20014

OFFICIAL BUSINESS
PENALTY FOR PRIVATE USE $300

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.E.W.
HEW 394

U.S.MAIL

GOULD A. ANDREWS, M.D.
CHAIRMAN, MEDICAL DIVISION
OAK RIDGE ASSOCIATED UNIVERSITIES, INC.
P.O. BOX 117
OAK RIDGE, TN 37830

1032903

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
Telephone 615 483-8411

Medical and
Health Sciences
Division

February 18, 1976

Joan B. Woods, M.D.
Oak Ridge Mental Health Center
Oak Ridge, Tennessee 37830

Dear Doctor Woods:

My nomination of you for membership on the ORAU/ORNL Committee on Human Studies has received unanimous approval of the other Committee members. For your information, a complete list is enclosed.

I will be sending you shortly an inquiry concerning possible dates for holding a meeting of the whole committee in Oak Ridge to consider the revised guidelines for Research on Human Subjects to comply with PHS/DHEW Policy on Protection of Human Subjects.

Thank you for your willingness to serve.

Sincerely yours,

C. C. Lushbaugh, M. D.
Chairman, Medical and Health
Sciences Division
Ex Officio Member, ORAU/ORNL
Committee on Human Studies

CCL:fb

Enc.

1032904

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
Telephone 615 483-8411

Medical and
Health Sciences
Division

February 18, 1976

Donald W. Goodwin, Ph.D.
United Church
Chapel-on-the-Hill
Oak Ridge, Tennessee 37830

Dear Doctor Goodwin:

My nomination of you for membership on the ORAU/ORNL Committee on Human Studies has received unanimous approval of the other Committee members. For your information, a complete list is enclosed.

I will be sending you shortly an inquiry concerning possible dates for holding a meeting of the whole committee in Oak Ridge to consider the revised guidelines for Research on Human Subjects to comply with PHS/DHEW Policy on Protection of Human Subjects.

Thank you for your willingness to serve.

Sincerely yours,

C. C. Lushbaugh, M. D., Chairman
Medical and Health Sciences Division
Ex Officio Member, ORAU/ORNL Committee
on Human Studies

CCL:fb

Enc.

1032905

2/20/76

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
Telephone 615 483-8411

Medical and
Health Sciences
Division

Oak Ridge Associated Universities and Oak Ridge National Laboratory
Committee on Human Studies

Gould A. Andrews, M. D., Secretary
Director of Clinical Applications
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

A. Bertrand Brill, M. D., Ph.D.
Associate Professor, Dept. of Medicine
Division of Nuclear Medicine & Physics
Vanderbilt University School of Medicine
Nashville, Tennessee 37203

Donald W. Goodwin, Ph.D.
Minister
United Church
Chapel-on-the-Hill
Oak Ridge, Tennessee 37830

Karl F. Hübner, M. D.
Chief of Outpatient Clinical Studies
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Melvin E. Koons, J. D.
Union Carbide Nuclear Company
Y-12 Area, P. O. Box Y
Building 9704-2
Oak Ridge, Tennessee 37830

Robert D. Lange, M. D., Chairman
Assistant Director
University of Tennessee
Memorial Research Center & Hospital
1924 Alcoa Highway
Knoxville, Tennessee 37920

Thomas A. Lincoln, M. D.
Director, Health Division
Oak Ridge National Laboratory
Building 4500-N, Room K-122
Oak Ridge, Tennessee 37830

Clarence C. Lushbaugh, M. D., ex officio
Chairman, Medical and Health Sciences Div.
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

John B. Storer, M. D.
Director, Biology Division
Oak Ridge National Laboratory
Y-12 Area
Building 9207
Oak Ridge, Tennessee 37830

Joan B. Woods, M. D.
Psychiatrist
Oak Ridge Mental Health Center
Oak Ridge, Tennessee 37830

2.20.76

1032906

May 4, 1976

TO: ORAU/ORNL COMMITTEE ON HUMAN STUDIES

This is to remind you of the scheduled meeting (Tuesday, May 11, 10 a.m., Second Floor Conference Room, ORAU, Medical and Health Sciences Division). We anticipate that the meeting can be concluded by noon unless some unusual problems arise.

New Proposals:

1. Use of ^{11}C-DL-Valine as a potential scanning agent (Dr. Hübner and Dr. Hayes). Relevant dates are included in this mailing. The rather bulky IND (Investigational New Drug) permit is to be sent to the Food and Drug Administration. It is not expected that you read all of it, but for those members of the committee not familiar with these forms, it might be of interest.

2. Discussion of use of chelating agents in radiation accidents involving accidental internal presence of radionuclides (Dr. Lushbaugh). (See attached manuscript by Dr. T. A. Lincoln).

3. Discussion of WR-2721 for human use (Dr. Hayes).

Progress on Previously Approved Proposals:

4. Projects 33, 34, and 35. These rare earth elements have been injected intravenously in the planned doses. Numbers of patients studied so far are Erbium-171, 22 patients; Dysprosium-157, 24 patients; and Thulium-167, 3 patients. We have noted no reactions to these materials. Clinical usefulness is still in doubt. Malignant lesions have some avidity for all of these materials but in most instances the visualization was not as good as was obtained with Gallium-67 in the same patient. It does appear that the newly tried isotopes have little or no localization in the colon and thus might prove superior to Gallium-67 in patients with suspected abdominal lesions. Unfortunately, we have not yet had a chance to study patients with abdominal lesions. It was also observed that Dysprosium-157 shows up bone lesions quite well, including some missed by gallium. However, the dysprosium visualization is not as good as that usually obtained with technetium phosphate preparations.

5. Project 38 was started in November, 1975. Since then we have administered 15 doses of ^{11}C-ACPC ranging from 10 mCi to 40 mCi per patient with the largest volume being 12 ml per dose. To the first ten patients the radiopharmaceutical was given through the tubing of an intravenous infusion of 5%D/0.45%S. There has been no reaction of any type to the injections. There was no discomfort nor any subjective side effects in any of the patients.

   Laboratory tests showed an average excretion of 2.1 percent of the dose between 45 minutes to 2 hours after injection. Radioassays of blood samples showed that 85-90 percent of the activity has left the blood within 5 minutes. Standard hemograms and serum chemistry studies failed

1032907

to show any significant changes. In the future the multiple early laboratory tests will be discontinued. Instead, a pretreatment and 24-hour survey will be made.

So far we have observed some tumor localization of this compound in approximately two-thirds of the patients studied. Concentration of the ^{11}C-ACPC in tumors is not as high as seen with ^{67}Gallium-citrate. Most of the patients included in the study had cancer of the lung. In the future patients with other malignancies may have different results with ^{11}C-ACPC as a tumor scanning agent. Almost all of the scans in this project have been done in conventional gamma mode. We anticipate greatly improved resolution of ^{11}C-ACPC when positron emission transaxial tomography will be available for the evaluation of ^{11}C-ACPC and other positron emitters.

6. Project 41 - Trials of the Line Scanner Developed at ORNL. Approximately 100 patients have been studied, but unfortunately very few of them had thyroid nodules. The techniques for using the new instrument were greatly improved by adjustments made after the clinical trials were started.

At present the instrument gives results that, on the average, equal those from a standard scanner. In individual cases one or the other techniques may prove superior. The radiation from the ^{125}Iodine used for this new procedure is within accepted limits but is higher than would be obtained with ~~^{123}~~ ^{131}Iodine or ^{99m}Technetium.

We are attempting to study a group of patients with palpable thyroid nodules to make a more useful evaluation.

Prepared by G. A. Andrews, M.D., and
Karl F. Hübner, M.D.

May 4, 1976

1032908

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
BETHESDA, MARYLAND 20014

MAY 10 1976

Karl F. Hubner, M.D.
Oak Ridge Associated
Universities
P.O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Hubner:

In response to your recent inquiry regarding submission of Form FD 2830, "Blood Establishment Registration and Product Listing," as long as your establishment does not crossmatch blood, you are not required to register. Thank you for your cooperation

Sincerely,

H. W. Dorsey
Management & Data Systems Staff
Bureau of Biologics

1032909

FORM F-4

MEMORANDUM

TO Mr. Dick Smith DATE July 26, 1976

SUBJECT ORAU Research proposals involving human subjects.

COPIES TO Mr. John Lingerfeld, Dr. C.C.Lushbaugh, Dr.G.A. Andrews, Dr.R.Hayes, Mr.John Crockett

This is an updated list of active research proposals requiring FDA and/or "Human Use Committee " approval.

Proposals

(In order of first committee action.)

Ident.No.	Title	Principal Investigator	Status
2	Clinical Trial of ^{68}Ga-Labeled Ferric Oxide Colloid	Hayes	will be reactivated
9	Tumor Scanning with ^{67}Ga	Hubner	IND no longer required
22.	Comparison of ^{113}In, ^{67}Ga, ^{206}Bi as Tumor Scanning Agents	Hayes	Active
33.	Erbium-171 as a clinical scanning agent for the detection of osseous and non-osseous tumors	Hubner	Active
34.	Thulium-167 as a clinical scanning agent for detecting osseous and non-osseous tumors.	Andrews	Active
35.	Dysprosium-157 as a clinical scanning agent for the detection of osseous and non-osseous tumors	Andrews	Active
38.	Clinical use of ^{11}C-Labeled 1-aminocyclo-pentane carboxylic acid for tumor detection	Hubner	Active
41.	Clinical testing of a line scanning pro-portional counter camera	Andrews	Active
45.	Clinical use of DL-VALINE-1-^{11}C for pancreas visualization	Hubner	Active
46.	Phase I studies of the radioprotective agent S-2 (3-aminopropylamino)ethylphosphorothioic acid (WR-2721)	Andrews	Awaiting approva by UT and UTMRCH Human Use Committees.

Karl F. Hübner, M. D.

1032910

C. Hulbert

FORM P-4

MEMORANDUM

TO Members of ORAU/ORNL Committee on Human Studies DATE July 28, 1976

SUBJECT Appointment of Scott Lawyer to Committee on Human Studies

COPIES TO File

Mr. Scott Lawyer, an attorney well grounded in contractural law, malpractice and human rights has joined the ORAU administrative staff giving us the opportunity to again have a lawyer participate in our evaluations of proposals for experimental studies involving human subjects. I am, therefore, nominating him for the legal slot on the Committee, vacated sometime ago by Mel Koons. Please inform my office of your individual approval or disapproval of this action.

C. C. Lushbaugh, M.D.
Chairman, Medical and
Health Sciences Division

CCL:dgb

1032911

FORM P-4

MEMORANDUM

TO Michael Scott Lawyer DATE 9/29/76

SUBJECT Committee on Human Studies

COPIES TO Dr. Robert Lange, Dr. C. C. Lushbaugh, Dr. Karl Hübner, File

I am sending you a copy of the guidelines concerning the Committee on Human Studies and also an application for a research project. I have talked this over with Dr. Lange, Chairman of the Committee on Human Studies, who suggests that we handle it in this fashion as we have several others in the past.

I feel sure that Dr. Lushbaugh or Dr. Lange will be glad to answer any questions you might have about the Committee's operation. Dr. Hübner would be pleased to answer questions about this specific research project of which he is the senior investigator. I am also available for any questions.

I am sorry that I was not here on the day that you spent considerable time with Dr. Hübner, and I will look forward to seeing you in the future.

Gould Andrews

Gould A. Andrews, M.D.
Secretary, Committee on
Human Studies

GAA:dgb

Enclosures

1032912

CV's - ORAU/ORNL Committee on Human Studies 10/14/76

Name: Gould A. Andrews
Position: Internist, Director of Clinical Applications
School: University of Michigan, A.B., 1940
University of Michigan, M.D., 1943
Licensure: Tennessee
Boards: Internal Medicine, Nuclear Medicine
Memberships: Society for Experimental Biology and Medicine
American Association for Cancer Research
American Thyroid Association
Society of Nuclear Medicine
Southern Society for Clinical Research
American Medical Association
American Association for the Advancement of Science
American Federation for Clinical Research
Fellow, American College of Physicians
American Society of Hematology (1968)
Health Physics Society, East Tennessee Chapter
Tennessee Academy of Science
Tennessee Blood Club

Name: A. Bertrand Brill
Position: Associate Professor of Medicine and Radiology,
Vanderbilt School of Medicine
School: Grinnell, A.B., 1949
University of Utah, M.D., 1956
University of California, Berkeley, Ph.D., 1961
Licensure: Tennessee
Memberships: American Association for the Advancement of Science
Society of Nuclear Medicine
Radiation Research Society
American Thyroid Association
Other Indication of Experience and Competence:
Medical Director, Division of Radiological Health,
U.S. Public Health Service, 1957-1964, Rockville, Md.

Name: Donald W. Goodwin
Position: Minister, United Church, Chapel-on-the-Hill
School: Bangor Theological Seminary, Bachelor of Divinity, 1959
Brown University, Ph.D., 1965
Memberships: Ministerial Standing, United Church of Christ
Additional Information:
Member of various boards which change from time to time

Name: Karl F. Hübner
Position: Internist, Chief of Outpatient Clinical Studies
School: University of Heidelberg, M.D., 1959
Licensure: Tennessee
Memberships: Roane-Anderson County Medical Society
Tennessee Medical Association
American Medical Association

Name: Melvin E. Koons
Position: Executive Assistant to President, Union Carbide Corporation Nuclear Division
School: University of North Dakota, B.A., 1955, Juris Doctor 1961
Admitted to Practice of Law:
North Dakota 1961; Tennessee 1964; Federal District Court, North Dakota 1961; East Tennessee 1964; U. S. Supreme Court, 1966
Memberships: American Bar Association
Public Contracts Section
Federal Bar Association
Government Contracts Committee
R & D Contracts Subcommittee
Tennessee Bar Association
North Dakota Bar Association, Ward County

Name: Robert Lange
Position: Research Professor; Assistant Director, University of Tennessee Memorial Research Center
School: Macalester College, B.A.
Washington University, M.D., 1944
Licensure: Tennessee, Minnesota, Missouri, Georgia
Board: Internal Medicine
Memberships: American Association for the Advancement of Science
American Medical Association
Knoxville Academy of Medicine
Southern Society of Research
Central Society of Clinical Research
American College of Physicians
International Society of Hematology

Name: Michael Scott Lawyer
Position: Staff Attorney, Oak Ridge Associated Universities
School: University of Mississippi, B.P.A., 1968; Juris Doctor, 1970
Admissions: Mississippi, 1970; U. S. District Court, Northern District of Mississippi, 1970
U. S. Court of Military Appeals, 1971
U. S. Tax Court, 1975
U. S. Court of Claims, 1975
U. S. Supreme Court, 1975
Memberships: Federal Bar Association
Government Contracts and Administrative Law Committees
Mississippi Bar Association

Name:	Thomas A. Lincoln
Position:	Director, Health Division, Oak Ridge National Laboratory
School:	Macalester College, St. Paul, Minnesota, B.A. (Chemistry), 1946
	University of Minnesota, Minneapolis, 3.S., 1947; B.M., 1949; and M.D., 1950.
	Rotating Internship, Ancker Hospital, St. Paul, 1949-1950
Licensure:	Tennessee, Minnesota
Board:	American Board of Preventive Medicine, by examination, June 5, 1963
Memberships:	Fellow Industrial Medical Association
	Past President, Tenn. Industrial Medical Association
	American Academy of Occupational Medicine
	American Medical Association
	Past President, Roane-Anderson County Medical Society
	Treasurer, Board of Directors, Oak Ridge Regional Mental Health Center

Name:	Clarence C. Lushbaugh
Position:	Chairman, Medical and Health Sciences Division
	Director, Radiation Emergency Assistance Center/ Training Site (REAC/TS)
School:	University of Chicago, B.S., 1938 (Anatomy)
	University of Chicago, Ph.D., 1942 (Pathology)
	University of Chicago, M.D., 1948 (Pathology)
Licensure:	Tennessee
Memberships:	American Association for the Advancement of Science
	American Society for Experimental Pathology
	Associated Researchers and Clinicians in Cancer
	Society for Experimental Biology and Medicine
	Health Physics Society
	Radiation Research Society
	Society of Nuclear Medicine
	American Medical Society
	Tennessee State Medical Society

Name:	John B. Storer
Position:	Director, Biology Division, Oak Ridge National Laboratory
School:	University of Chicago, M.D., 1947
Memberships:	American Association for Cancer Research
	American Society for Experimental Pathology
	Radiation Research Society
	Society for Experimental Biology and Medicine
	National Council on Radiation Protection and Measurements

Name:	Joan B. Woods
Position:	Psychiatrist, Veterans Administration Hospital, Murfreesboro, Tennessee
School:	University of Chicago School of Medicine, B.S. and M.D., 1960
Licensure:	Tennessee
Boards:	American Board of Psychiatry and Neurology
Memberships:	American Psychiatric Association
	American Medical Association and Subsidiaries

1032915

Name: Edythalena Tompkins
Position: Chief Epidemiologist, ORAU
School: Stanford University, A.B., 1939
Graduate School, 1940-1955
University of Minnesota, Graduate Summer Sessions in Epidemiology 1969 and 1970
Memberships: American Public Health Association
Society for Epidemiological Research
Society for Occupational and Environmental Health
American Thyroid Society

1032916

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

DECEMBER 1, 1976

52ND CUMULATIVE LIST 1976

OF INSTITUTIONS WHICH HAVE ESTABLISHED GENERAL ASSURANCES OF COMPLIANCE WITH DHEW REGULATIONS ON PROTECTION OF HUMAN SUBJECTS

1. INCOMING PROPOSALS - GRANTS OR CONTRACTS

a. If the professional review of a proposal indicates that the project *does not involve* human subjects (box on signature page of application or box 3A of HEW 596), as defined in 45 CFR 46, the application can be processed without further regard to the question of institutional assurances.

b. If the professional review of a proposal indicates that the project *does involve* human subjects (box on signature page of application or box 3B of HEW 596), the next step is to determine whether the institution has checked either box 4A or 4B.

- If 4A is checked, this means that the applicant institution does *not have* an approved assurance on file but will supply documentation and certification of review when requested. This action is initiated by the OPRR, OD, NIH; Westwood Building, Room 303; Bethesda, Maryland 20014; upon receipt of a copy of the proposal from the *operating agency* immediately following an initial review.

- If 4B is checked, this means that the applicant institution has an approved general assurance on file. The fill-in spaces in this paragraph indicate the DHEW general assurance "G" number for the institution as presented in the "Cumulative Listing" and the date when the proposal was certified.

1032917

c. Draft requests for proposals (RFPs or RFAs) should be reviewed to determine whether performance will involve human subjects at risk. If these will be involved, the RFP should include the "Notice to Offerors" required by 41 CFR 3-4.5504(a). Offerings and proposals submitted in response to the RFP should be handled as in 1.b. above.

d. Operating agencies may define "submission date" to fit administrative requirements. It is suggested that sole source responses to RFPs should be considered to be submitted as of the closing date of the RFP and should then be handled as in 1.b. above.

e. Competitive responses to RFPs should be considered to be submitted as of the date of submission of the best and final offer, after establishing the zone of consideration or source selection, and should then proceed as in 1.b. above.

SUBMISSION OF CERTIFICATIONS - Whenever possible, the review and approval by Institutional Review Boards should occur prior to submission of the application or proposal and a certification to that effect should be included in or with the application or proposal itself, preferably on form HEW 596 (Rev. 4/75). Under no circumstances will the review of an application by the Department of Health, Education, and Welfare be completed until certification is received. The point at which review will be deferred or terminated is left to the operating agency involved.

Institutions *having on file* with DHEW an approved general assurance must submit certification within 30 days of the receipt of a written request thereof; and in any event *within 90 days* after the deadline or submission date for which the application or proposal was submitted.

Institutions *not having on file* an approved general assurance will indicate their status by checking box 4A on form HEW 596 accompanying the proposal and *when requested must submit the required assurances of compliance and certification of the review and approval* of the application or proposal by its Institutional Review Board within 30 days of the receipt of a written request from the Office for Protection from Research Risks (OPRR).

3. RESTRICTION CODES are presented as a suffix to the general assurance "G" number. This change conforms with the National Research Act, Public Law 93-348, Title II, which specifically applies to both *biomedical* and *behavioral* research and with the derivative DHEW regulations.

6.

A restriction usually indicates that additional expertise in the Institutional Review Board membership is necessary for particular activities requiring certification.

An XM suffix indicates that the IRB has no or insufficient medical members. A proposed activity requiring medical expertise to assess risks, benefits, and the adequacy of safeguards cannot be certified under an XM restriction.

An XB suffix indicates that the IRB has no or insufficient members expert in the behavioral sciences. A proposed activity requiring behavioral expertise for assessing risks, benefits, and the adequacy of safeguards cannot be certified under an XB restriction.

An XO suffix indicates a restriction that uniquely applies to the institution under conditions of the general assurance agreement [call (301) 496-7005 for details].

When a proposal to be submitted to DHEW comes within the scope of an XM or XB restriction, either biomedical or behavioral, the IRB reviewing the proposal must include additional voting members whose qualifications offset the restriction. Their names and qualifications should be reported immediately to OPRR and a statement added under "Notes" on the HEW 596 form certifying IRB review and approval that the additional professionally qualified members have been reported to OPRR. Proposals that come within the certification restrictions that are not preceded or accompanied by appropriate compensating reviewers will be deferred for rereview and recertification.

4. QUESTIONS with regard to the status of Special or General Assurances of Compliance may be directed to:

Mrs. Florence R. Ober	(301) 496-7005

5. CONSULTATION for Special and General Assurances:

R. C. Backus, Ph.D.	(301) 496-7006
Victor M. Held, Ph.D.	(301) 496-7005
Roy Kinard, D.V.M.	(301) 496-7006
J. R. Marches, Ph.D.	(301) 496-7005

1032919

6. FORMS

Bulk orders for additional copies of HEW 596 should be addressed to:

Chief
Office Services Section
Division of Research Grants
National Institutes of Health
Westwood Building, Room A-17
Bethesda, Maryland 20014

Single copies of HEW 596 can be obtained from OPRR or by duplicating the back pages of this listing.

D. T. Chalkley, Ph.D.
Director, Office for Protection
from Research Risks
Office of the Director
National Institutes of Health

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	PUERTO RICO	
G1348XM	Catholic University of Puerto Rico	Ponce
G0256XB	Puerto Rico, Univ of, Medical Sciences Campus	San Juan Rio Piedras
	RHODE ISLAND	
G0467	Brown University	Providence
*G0318	Rhode Island Hospital	Providence
G2212XB	Roger Williams General Hospital	Providence
	SOUTH CAROLINA	
G2621	Clemson University	Clemson
G0533	South Carolina Department of Mental Health	Columbia
G0240	South Carolina, Medical University of	Charleston
*G0629XO	South Carolina, University of	Columbia
	TENNESSEE	
G0490XM	George Peabody College for Teachers	Nashville
G0393	Meharry Medical College	Nashville
~~*G1716~~	~~Oak Ridge Associated Universities, Inc~~	~~Oak Ridge~~
~~*G1716~~	~~Oak Ridge National Laboratory~~	~~Oak Ridge~~
G0648	St Jude Children's Research Hospital	Memphis
G0170	Tennessee, University of, Center for the Health Sciences	Memphis
G0124	Tennessee, University of - Knoxville	Knoxville
G0401	Vanderbilt University	Nashville
	TEXAS	
G0307	Baylor College of Medicine	Houston
*G1843	Bexar County Hospital District	San Antonio
G0398XM	Houston, University of	Houston

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Revised General Assurance in Negotiation With OPRR

1032921

DEC 22 1976

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

General Assurance G1716

December 20, 1976

Crockett
for action per
discussion

Clarence C. Lushbaugh, M.D.
Acting Chairman
Medical and Health Sciences Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Doctor Lushbaugh:

Please note that your institution is marked *. You are among the few in your state or region who have not yet submitted an acceptable revised general assurance according to the regulations of 1975. The regulations state: "General assurances will be required from institutions having a significant number of concurrent DHEW-supported projects or activities involving human subjects." We have set no deadline yet, but I think it is reasonable to expect award of new grants to your institution to be cut off sometime in the future. Please see what you can do to resolve this matter.

Sincerely yours,

Roy Kinard, D.V.M.
Office for Protection
from Research Risks
Office of the Director

Enclosure
"52nd Cumulative List . . ."

cc:
Mr. Philip L. Johnson
Executive Director
Oak Ridge Associated Universities, Inc.

1032922

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

See page 18.

DECEMBER 1, 1976

52ND CUMULATIVE LIST 1976

OF INSTITUTIONS WHICH HAVE ESTABLISHED GENERAL ASSURANCES OF COMPLIANCE WITH DHEW REGULATIONS ON PROTECTION OF HUMAN SUBJECTS

1. INCOMING PROPOSALS - GRANTS OR CONTRACTS

a. If the professional review of a proposal indicates that the project *does not involve* human subjects (box on signature page of application or box 3A of HEW 596), as defined in 45 CFR 46, the application can be processed without further regard to the question of institutional assurances.

b. If the professional review of a proposal indicates that the project *does involve* human subjects (box on signature page of application or box 3B of HEW 596), the next step is to determine whether the institution has checked either box 4A or 4B.

- If 4A is checked, this means that the applicant institution does *not have* an approved assurance on file but will supply documentation and certification of review when requested. This action is initiated by the OPRR, OD, NIH; Westwood Building, Room 303; Bethesda, Maryland 20014; upon receipt of a copy of the proposal from the *operating agency* immediately following an initial review.

- If 4B is checked, this means that the applicant institution has an approved general assurance on file. The fill-in spaces in this paragraph indicate the DHEW general assurance "G" number for the institution as presented in the "Cumulative Listing" and the date when the proposal was certified.

1032923

c. Draft requests for proposals (RFPs or RFAs) should be reviewed to determine whether performance will involve human subjects at risk. If these will be involved, the RFP should include the "Notice to Offerors" required by 41 CFR 3-4.5504(a). Offerings and proposals submitted in response to the RFP should be handled as in 1.b. above.

d. Operating agencies may define "submission date" to fit administrative requirements. It is suggested that sole source responses to RFPs should be considered to be submitted as of the closing date of the RFP and should then be handled as in 1.b. above.

e. Competitive responses to RFPs should be considered to be submitted as of the date of submission of the best and final offer, after establishing the zone of consideration or source selection, and should then proceed as in 1.b. above.

SUBMISSION OF CERTIFICATIONS - Whenever possible, the review and approval by Institutional Review Boards should occur prior to submission of the application or proposal and a certification to that effect should be included in or with the application or proposal itself, preferably on form HEW 596 (Rev. 4/75). Under no circumstances will the review of an application by the Department of Health, Education, and Welfare be completed until certification is received. The point at which review will be deferred or terminated is left to the operating agency involved.

Institutions *having on file* with DHEW an approved general assurance must submit certification within 30 days of the receipt of a written request thereof; and in any event *within 90 days* after the deadline or submission date for which the application or proposal was submitted.

Institutions *not having on file* an approved general assurance will indicate their status by checking box 4A on form HEW 596 accompanying the proposal and *when requested must submit the required assurances of compliance and certification of the review and approval* of the application or proposal by its Institutional Review Board within 30 days of the receipt of a written request from the Office for Protection from Research Risks (OPRR).

3. RESTRICTION CODES are presented as a suffix to the general assurance "G" number. This change conforms with the National Research Act, Public Law 93-348, Title II, which specifically applies to both *biomedical* and *behavioral* research and with the derivative DHEW regulations.

A restriction usually indicates that additional expertise in the Institutional Review Board membership is necessary for particular activities requiring certification.

An XM suffix indicates that the IRB has no or insufficient medical members. A proposed activity requiring medical expertise to assess risks, benefits, and the adequacy of safeguards cannot be certified under an XM restriction.

An XB suffix indicates that the IRB has no or insufficient members expert in the behavioral sciences. A proposed activity requiring behavioral expertise for assessing risks, benefits, and the adequacy of safeguards cannot be certified under an XB restriction.

An XO suffix indicates a restriction that uniquely applies to the institution under conditions of the general assurance agreement [call (301) 496-7005 for details].

When a proposal to be submitted to DHEW comes within the scope of an XM or XB restriction, either biomedical or behavioral, the IRB reviewing the proposal must include additional voting members whose qualifications offset the restriction. Their names and qualifications should be reported immediately to OPRR and a statement added under "Notes" on the HEW 596 form certifying IRB review and approval that the additional professionally qualified members have been reported to OPRR. Proposals that come within the certification restrictions that are not preceded or accompanied by appropriate compensating reviewers will be deferred for rereview and recertification.

4. QUESTIONS with regard to the status of Special or General Assurances of Compliance may be directed to:

Mrs. Florence R. Ober	(301) 496-7005

5. CONSULTATION for Special and General Assurances:

R. C. Backus, Ph.D.	(301) 496-7006
Victor M. Held, Ph.D.	(301) 496-7005
Roy Kinard, D.V.M.	(301) 496-7006
J. R. Marches, Ph.D.	(301) 496-7005

6. FORMS

Bulk orders for additional copies of HEW 596 should be addressed to:

Chief
Office Services Section
Division of Research Grants
National Institutes of Health
Westwood Building, Room A-17
Bethesda, Maryland 20014

Single copies of HEW 596 can be obtained from OPRR or by duplicating the back pages of this listing.

D. T. Chalkley, Ph.D.
Director, Office for Protection
from Research Risks
Office of the Director
National Institutes of Health

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	ALABAMA	
G0198	Alabama, University of, Birmingham	Birmingham
*G0610	Alabama, University of, Tuscaloosa	University
G0055	Tuskegee Institute	Tuskegee Inst
	ARIZONA	
G0799XM	Arizona State University	Tempe
G0026	Arizona, University of	Tucson
*G1287	St Joseph's Hospital and Medical Center	Phoenix
	ARKANSAS	
*G0336	Arkansas, University of, Medical Center	Little Rock
	CALIFORNIA	
G0784XM	American Institutes for Research	Palo Alto
*G0261XO	California Department of Public Health	Berkeley
*G0420XO	California State University, San Diego	San Diego
*G0278	California, University of, Berkeley	Berkeley
*G0195	California, University of, Davis	Davis
*G0380	California, University of, Irvine	Irvine
*G0238	California, University of, Los Angeles	Los Angeles
*G0193XO	California, University of, Riverside	Riverside
*G0389	California, University of, San Diego	La Jolla
G0155	California, University of, San Francisco	San Francisco
*G0282	California, University of, Santa Barbara	Santa Barbara
G0205XM	California, University of, Santa Cruz	Santa Cruz
*G0028	Camarillo State Hospital	Camarillo
G0234	Cedars-Sinai Medical Center	Los Angeles
*G2564	Charles R. Drew Postgraduate Medical School	Los Angeles
*G0135	Children's Hospital of Los Angeles	Los Angeles
*G0287	Children's Hospital of San Francisco	San Francisco
*G0009	City of Hope National Medical Center	Duarte

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032927

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G2259XO	Far West Laboratory for Educational Research and Development	San Francisco
*G1838	Huntington Inst of Applied Medical Research	Pasadena
*G1838	Huntington Memorial Hospital	Pasadena
*G2400	Institute of Medical Sciences	San Francisco
*G2367	John Wesley County Hospital Attending Staff Association	Los Angeles
*G0214	Kaiser Foundation Research Institute Including Its Regional Divisions in Northern California, Southern California, and Oregon	Oakland
*G0226	Loma Linda University	La Sierra
*G0226	Loma Linda University	Loma Linda
G0359XB	Los Angeles County Harbor General Hospital, Professional Staff Association of	Torrance
*G0213	Los Angeles County Hospital-University of Southern California Medical Center, Professional Staff Association of	Los Angeles
*G2564	Martin Luther King, Jr. General Hospital and Its Staff Association Foundation	Los Angeles
*G0367XO	Mental Research Institute	Palo Alto
*G0145	Mount Zion Hospital and Medical Center	San Francisco
*G0710	Pacific State Hospital	Pomona
*G2400	Pacific, Univ of, School of Dentistry	San Francisco
*G2400	Pacific, Univ of, School of Medical Sciences	San Francisco
*G0082	Palo Alto Medical Research Foundation	Palo Alto
*G1838	Pasadena Hospital Association, Ltd	Pasadena
*G2400	Presbyterian Hospital of the Pacific Medical Center, Inc	San Francisco
*G0067	Rancho Los Amigos Hospital and Its Professional Staff Association	Downey
*G1416XO	Rand Corporation	Santa Monica
*G1096	Salk Institute	San Diego
*G0420XO	San Diego State University Foundation	San Diego
G1472XM	Scientific Analysis Corporation (Including the Institute for Scientific Analysis and Performance Sites in Berkeley, Los Angeles, and San Diego)	San Francisco
G0108XB	Scripps Clinic and Research Foundation	La Jolla
G0201	Sonoma State Hospital	Eldridge

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032928

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0122	Southern California, University of	Los Angeles
*G0378	Stanford Research Institute	Menlo Park
G0011	Stanford University	Stanford
G1620	Veterans Administration Hospital-Long Beach	Long Beach
G1796	Veterans Administration Hospital-Sepulveda	Sepulveda
*G1658	Veterans Administration Hospital-Wadsworth	Los Angeles
*G1591XO	Wright Institute	Berkeley
	COLORADO	
G2823XB	Colorado Regional Cancer Center, Inc	Denver
*G1144XO	Colorado State University	Fort Collins
G0455	Colorado, University of	Boulder
*G0268	Colorado, University of, Medical Center	Denver
*G0277XO	Denver, University of	Denver
G0267	National Asthma Center	Denver
*G0068XO	National Jewish Hospital	Denver
	CONNECTICUT	
G0039	Connecticut, University of	Storrs
G1966	Connecticut, University of, Health Center	Farmington-Hartford
G1533	Connecticut Valley Hospital	Middletown
G0007	Institute of Living	Hartford
G0003	John B. Pierce Fdn of Connecticut, Inc	New Haven
G0821	Saint Francis Hospital	Hartford
G2895XB	Waterbury Hospital Health Center	Waterbury
*G0243	Yale University	New Haven
	DELAWARE	
G0148	Delaware Division of Mental Health of the Department of Health and Social Services	Delaware City
G0013	Delaware, University of	Newark

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032929

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	DISTRICT OF COLUMBIA	
G0784XM	American Institutes for Research	Washington
G1398XB	American National Red Cross	Washington
G1674XM	Bureau of Social Science Research, Inc	Washington
*G0365XO	Catholic University of America	Washington
G0042	Children's Hospital of D.C., Research Foundation of	Washington
*G1249XO	Gallaudet College	Washington
G0294	George Washington University	Washington
G0228	Georgetown University	Washington
G0841	Howard University	Washington
G1989	National Academy of Sciences, Including National Academy of Engineering, Institute of Medicine, and National Research Council	Washington
G1036XM	National Children's Center, Inc	Washington
*G0180	Washington Hospital Center	Washington
	FLORIDA	
G2905	Florida State Department of Health and Rehabilitative Services	Tallahassee
*G0119XO	Florida State University	Tallahassee
G0382	Florida, University of	Gainesville
G0840XB	Miami Heart Institute	Miami Beach
G0301	Miami, University of	Coral Gables
G0301	Miami, University of	Miami
G0275XB	Mt Sinai Medical Center of Greater Miami	Miami Beach
G2321	Papanicolaou Cancer Research Institute	Miami
G1065	South Florida, University of	Fort Myers St Petersburg Sarasota Tampa
	GEORGIA	
*G0138	Emory Univ Division of Basic Health Sciences	Atlanta
*G0622	Emory Univ Graduate Sch of Arts and Sciences	Atlanta

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032930

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0138	Emory Univ Nell Hodgson Woodruff School of Nursing	Atlanta
*G0595	Emory Univ School of Dentistry	Atlanta
*G0138	Emory Univ School of Medicine	Atlanta
G0197	Georgia Dept of Human Resources, All Units	Atlanta
G0151XB	Georgia, Medical College of	Augusta
G0248	Georgia, University of	Athens
*G1467	Grady Memorial Hospital	Atlanta
	HAWAII	
*G0104XO	Hawaii, University of	Honolulu
	IDAHO	
*G1869	Mountain States Tumor Institute	Boise
	ILLINOIS	
G0395	American Dental Assn and ADA Health Fdn	Chicago
G0332XM	Anna Mental Health and Developmental Center	Anna
G1626	Chicago, University of (Division of Biological Sciences and Pritzker School of Medicine, Division of Social Sciences, School of Social Service Administration, and Related Units)	Chicago
G0114	Children's Memorial Hospital	Chicago
G0430	Downey Veterans Administration Hospital	Downey
G0182	Evanston Hospital	Evanston
G0430	Health Sciences, Univ of/Chicago Medical Sch	Chicago
G0053	Hektoen Institute for Medical Research	Chicago
G1561	Illinois State Psychiatric Institute	Chicago
G0345	Illinois, University of, at Chicago Circle	Chicago
G0291	Illinois, University of, Medical Center Campus, Including Rockford School of Medicine, Peoria School of Medicine, and Sch of Basic Medical Sciences, Urbana-Champaign	Chicago

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032931

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0102	Illinois, Univ of, at Urbana-Champaign	Urbana
*G1373XO	Lincoln Developmental Center	Lincoln
G0095	Michael Reese Hospital and Medical Center	Chicago
G0518XM	Northern Illinois University	DeKalb
*G0190	Northwestern University	Chicago
*G0190	Northwestern University	Evanston
G0175	Rush-Presbyterian-St Luke's Medical Center	Chicago
*G0309	Southern Illinois University	Carbondale
G2606XM	Southern Illinois University	Edwardsville
*G1970XO	Western Illinois University	Macomb
	INDIANA	
*G0314XO	Depauw University	Greencastle
G0945XM	Fort Wayne State Hosp and Training Center	Ft Wayne
G0185	Indiana Univ and Indiana Univ Foundation	Bloomington Indianapolis
G0185	Indiana University (Law School)	Indianapolis
G0185	Indiana Univ-Purdue Univ (Medical Facility)	Indianapolis
G0185	Indiana University Regional Campuses at Fort Wayne, Gary, Kokomo, New Albany, Richmond, and South Bend	
G1397	Indianapolis Center for Advanced Research	Indianapolis
G0883	Larue D. Carter Memorial Hospital	Indianapolis
G1697XM	Marion County Assn for Retarded Children, Inc	Indianapolis
C1246XB	Methodist Hospital of Indiana, Inc	Indianapolis
*G1176	New Castle State Hospital	New Castle
G1119	Notre Dame, University of	Notre Dame
G0131	Purdue Univ and Purdue Research Foundation	West Lafayette
	IOWA	
*G0343XO	Iowa State Univ of Science and Technology	Ames
G0209	Iowa, University of	Iowa City
*G0856XO	Woodward State Hospital-School	Woodward
	KANSAS	
G0038	Kansas State University	Manhattan

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032932

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0157XO	Kansas, University of	Lawrence
*G0229	Kansas, University of, Medical Center	Kansas City
G0081	Menninger Foundation	Topeka
	KENTUCKY	
G0223	Kentucky, Univ of, and the Research Foundation	Lexington
G0527	Louisville, University of, Except School of Medicine, and Louisville, University of, Foundation, Inc	Louisville
G0023	Louisville, University of, Schools of Medicine and Dentistry	Louisville
	LOUISIANA	
G0442XB	Alton Ochsner Medical Foundation	New Orleans
*G0262XO	Louisiana State Univ and A & M College System	Baton Rouge
*G2428XO	Louisiana State Univ in Baton Rouge	Baton Rouge
*G2485	Louisiana State Univ Medical Center	New Orleans
G0137XM	Pinecrest State School	Pineville
G0018	Tulane Medical Center	New Orleans
G2386	Tulane University Except Medical Center	New Orleans
	MAINE	
G3007	Eastern Maine Medical Center	Bangor
G0513	Maine Medical Center	Portland
	MARYLAND	
G0402	Baltimore City Hospitals	Baltimore
G0186	Friends Medical Science Research Center, Inc	Baltimore
G0640	Institute for Behavioral Research, Inc	Silver Spring
G0352	Johns Hopkins Univ Faculty of Arts and Sciences	Baltimore
G0274	Johns Hopkins Univ School of Hygiene and Public Health	Baltimore

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032933

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0174	Johns Hopkins Univ School of Medicine and Johns Hopkins Hospital	Baltimore
*G0326	Maryland, Univ of, Baltimore Campus	Baltimore
G0296	Maryland, Univ of, College Park Campus	College Park
G0400	Sinai Hospital of Baltimore, Inc	Baltimore
	MASSACHUSETTS	
G0784XM	American Institutes for Research	Cambridge
G0286	Beth Israel Hospital	Boston
*G0554	Boston City Hospital	Boston
*G0554	Boston Department of Health and Hospitals	Boston
*G0554	Boston Division of Community Health Services	Boston
G0488	Boston Hospital for Women	Boston
G0783	Boston Mental Health Foundation, Inc	Boston
G0783	Boston State Hospital	Boston
G0322	Boston Univ, Charles River Campus	Boston
G0550	Boston Univ Medical Center	Boston
G0550	Boston Univ School of Graduate Dentistry	Boston
G0550	Boston Univ School of Medicine	Boston
G0132XM	Brandeis University	Waltham
G2396XB	Center for Blood Research, Inc	Boston
G0406	Children's Hospital Medical Center	Boston
*G0117XO	Clark University	Worcester
G0098	Danvers State Hospital	Hathorne
G2042	Eunice Kennedy Shriver Center	Waltham
G0410XB	Eye Research Institute of Retina Foundation	Boston
G0412XB	Forsyth Dental Center	Boston
G2397	Harvard Medical Sch and Sch of Dental Medicine	Boston
G2238	Harvard Univ, Faculty of Arts and Sciences	Cambridge
G2494XM	Harvard Univ, Graduate School of Education	Cambridge
G2398XB	Harvard Univ, School of Public Health	Boston
G2573	Harvard Univ, University Health Services	Cambridge
G0791XB	Joslin Diabetes Foundation, Inc	Boston
G0087XB	Lahey Clinic Foundation, Inc	Boston
G0449XB	Lemuel Shattuck Hospital	Jamaica Plain
*G0554	Long Island Chronic Disease Hospital	Boston Harbor
G2304XO	Mass Developmental Disabilities Council	Boston
*G0212	Massachusetts Eye and Ear Infirmary	Boston

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032934

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0167	Massachusetts General Hospital	Boston
G0097	Massachusetts Institute of Technology	Cambridge
G0597	Massachusetts Mental Health Center	Boston
G0597	Massachusetts Mental Health Research Corp	Boston
G0147XM	Massachusetts, University of - Amherst	Amherst
G2736	Massachusetts, University of, Medical School	Worcester
*G0554	Mattapan Chronic Disease Hospital	Mattapan
G0576	McLean Hospital	Belmont
G0494XB	New England Deaconess Hospital	Boston
G0133	New England Medical Center Hospital	Boston
G0297	Northeastern University	Boston
G0429	Peter Bent Brigham Hospital Division of the Affiliated Hospitals Center, Inc	Boston
G2515XM	Research Institute for Educational Problems	Cambridge
G0404XB	Robert B. Brigham Hospital	Boston
G0771	Sidney Farber Cancer Institute, Inc	Boston
G0351XB	St Margaret's Hospital for Women	Boston
*G0554	Trustees of Health & Hosps, City of Boston	Boston
G2107	Tufts-New England Medical Center	Boston
G2379	Tufts University - Boston	Boston
*G0266XO	Tufts University - Medford	Medford
G0550	University Hospital, Inc	Boston
G2042	Walter E. Fernald State School	Belmont
G0085	Worcester Foundation for Experimental Biology	Shrewsbury
	MICHIGAN	
G0363	Child Research Center of Michigan	Detroit
G0363	Children's Hospital of Michigan	Detroit
G0497XM	Detroit, University of	Detroit
G0357	Edsel B. Ford Institute for Medical Research	Detroit
G0357	Henry Ford Hospital	Detroit
G0101	Lafayette Clinic	Detroit
G0656XB	Michigan Cancer Foundation	Detroit
*G0615	Michigan Department of Public Health	Lansing
G0384	Michigan State University	East Lansing
G0295	Michigan, University of	Ann Arbor
G0255	Michigan, University of	Dearborn
G0255	Michigan, University of	Flint

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032935

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0008	Sinai Hospital of Detroit	Detroit
*G2483	Veterans Administration Hospital-Ann Arbor	Ann Arbor
G0354	Wayne State University	Detroit
G0720	Western Michigan University	Kalamazoo
	MINNESOTA	
G0065XB	Hennepin County Medical Center	Minneapolis
G0041	Mayo Foundation	Rochester
G0065XB	Minneapolis Medical Research Foundation, Inc	Minneapolis
G0463	Minnesota, University of	Austin
G0463	Minnesota, University of	Duluth
G0463	Minnesota, University of	Minneapolis
G0463	Minnesota, University of	Morris
G0463	Minnesota, University of	St Paul
G0463	Minnesota, University of, Technical College	Crookston
G0463	Minnesota, University of, Technical College	Waseca
	MISSISSIPPI	
*G0561XO	Mississippi, University of	University
G0366XB	Mississippi, University of, Medical Center	Jackson
	MISSOURI	
G2791XM	American Nurses' Association, Inc	Kansas City
*G0298	Cancer Research Center	Columbia
*G0298	Ellis Fischel State Cancer Hospital	Columbia
*G0424	Jewish Hospital of St Louis	St Louis
*G0292XO	Missouri, University of, Except Medical Center	Columbia
*G0292	Missouri, University of, Medical Center, Including Missouri Institute of Psychiatry	Columbia
*G0292	Missouri, University of	Kansas City
*G0292XO	Missouri, University of	Rolla
*G0292XO	Missouri, University of	St Louis
*G0292	Missouri, University of, Regional Medical Programs, All Campuses	

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Revised General Assurance in Negotiation With OPRR

1032936

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0356	St Louis University	St Louis
*G2056	Veterans Administration Hospital-Kansas City	Kansas City
*G0279	Washington University	St Louis
G2351XB	Washington University School of Medicine	St Louis
	NEBRASKA	
*G1120	Creighton University	Omaha
G0407	Nebraska, Univ of, Including the Medical Ctr	Omaha
G0407	Nebraska, Univ of, Including the State Univ of Nebraska	Lincoln
	NEVADA	
G0762XM	Nevada, University of, Reno Campus	Reno
	NEW HAMPSHIRE	
G0427XM	Dartmouth College Faculty of Arts & Sciences	Hanover
G0227	Dartmouth Medical School	Hanover
	NEW JERSEY	
G0492XB	Institute for Medical Research	Camden
G0349	New Jersey, College of Medicine & Dentistry of	Newark
G0349	New Jersey Dental School	Jersey City
G0349	New Jersey Medical School	Newark
G0837	Newark Beth Israel Medical Center	Newark
G0570XM	Princeton University	Princeton
G0349	Rutgers Medical School	Piscataway
G0300	Rutgers, The State Univ of New Jersey	Camden
G0300	Rutgers, The State Univ of New Jersey	New Brunswick
G0300	Rutgers, The State Univ of New Jersey	Newark

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032937

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	NEW MEXICO	
*G0472	New Mexico, University of	Albuquerque
*G0353	New Mexico, University of, Health Sciences Group-School of Medicine, Colleges of Pharmacy and Nursing	Albuquerque
	NEW YORK	
G0217	Albany Medical College of Union University	Albany
G2129	American Health Foundation	New York
G1064XB	Associated Universities, Inc, Including Brookhaven National Laboratory	Upton
G2116XM	Barnard College	New York
G0341	Beth Israel Medical Center	New York
G2277XM	Child Welfare League of America, Inc	New York
G0381	Children's Hospital of Buffalo	Buffalo
G0437XM	Columbia Univ, Except Health Sciences Division	New York
G0034	Columbia Univ Health Sciences Division, Including College of Physicians and Surgeons, Schools of Public Health and Nursing, Faculty of Medicine, and Oral and Dental Surgery	New York
G0063	Cornell Univ, Except Medical College	Ithaca
G0245	Cornell University Medical College	New York
G0109XB	Eastman Dental Center	Rochester
G2912XB	Genesee Hospital	Rochester
G2887XB	Health Research, Inc, Albany Division	Albany
G2904	Health Research, Inc, Roswell Park Division	Buffalo
G2887XB	Helen Hayes Hospital	West Haverstraw
G0621	Hospital for Joint Diseases and Medical Center, Including the Research Institute for Skeletomuscular Diseases	New York
G0047	Hospital for Special Surgery	New York
G2920	ICD Rehabilitation and Research Center	New York
G1005XO	Jewish Board of Guardians	New York
G0369	Kingsbrook Jewish Medical Center and Isaac Albert Research Institute	Brooklyn
G2375	Long Island Jewish-Hillside Medical Center	New Hyde Park

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032938

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0397	Maimonides Medical Center	Brooklyn
G0086	Mary Imogene Bassett Hospital	Cooperstown
G0383XB	Memorial Hosp for Cancer and Allied Diseases	New York
G0059	Montefiore Hospital and Medical Center	New York
G0139	Mount Sinai School of Medicine of CUNY	New York
G2518XB	Nassau County Medical Center, Including Meadowbrook Medical Education and Research Foundation, Inc	East Meadow
G0173XM	New School for Social Research	New York
G0526XB	New York Blood Center of the Community Blood Council of Greater New York, Inc	New York
G1370XB	New York City Department of Health	New York
G0765XM	New York, City Univ of	New York
G0765XM	New York, City Univ of, Baruch College	New York
G0765XM	New York, City Univ of, Bronx Cmty College	Bronx
G0765XM	New York, City Univ of, Brooklyn College	Brooklyn
G0765XM	New York, City Univ of, City College	New York
G0765XM	New York, City Univ of, Graduate School and University Center	New York
G0765XM	New York, City Univ of, Herbert H. Lehman College	Bronx
G0765XM	New York, City Univ of, Hunter College	New York
G0765XM	New York, City Univ of, John Jay College of Criminal Justice	New York
G0765XM	New York, City Univ of, Kingsborough Community College	Brooklyn
G0765XM	New York, City Univ of, Manhattan Cmty College	New York
G0765XM	New York, City Univ of, Medgar Evers College	Brooklyn
G0765XM	New York, City Univ of, New York City Community College	Brooklyn
G0765XM	New York, City Univ of, Queens College	Flushing
G0765XM	New York, City Univ of, Queensborough Community College	New York
G0765XM	New York, City Univ of, Research Foundation	New York
G0765XM	New York, City Univ of, Staten Island Community College	Staten Island
G0765XM	New York, City Univ of, York College	Jamaica
G2887XB	New York Dept of Health and Regional Offices	Albany
G0208	New York Medical College-Flower and Fifth Avenue Hospitals, Metropolitan Hospital, and Bird S. Coler Memorial Hospital	New York

RESTRICTION CODE

XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032939

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0374XM	New York, State Univ of, at Albany	Albany
G0508	New York, State Univ of, at Binghamton	Binghamton
G0163	New York, State Univ of, at Buffalo	Buffalo
G0596	New York, State Univ of, at Stony Brook	Stony Brook
G0474	New York, State Univ of, College at Brockport	Brockport
G0506XM	New York, State Univ of, College at Buffalo	Buffalo
G0259XM	New York, State Univ of, College at Cortland	Cortland
G0386XM	New York, State Univ of, College at Oswego	Oswego
G0457	New York, State Univ of, College of Arts and Science at Geneseo	Geneseo
G0220	New York, State Univ of, College of Environmental Science and Forestry	Syracuse
G0305	New York, State Univ of, Downstate Medical Ctr	Brooklyn
G0127	New York, State Univ of, Upstate Medical Ctr	Syracuse
G0390XO	New York Univ, Exclusive of the Medical Ctr	New York
G0405	New York University Medical Center	New York
G0788	North Shore Hospital	Manhasset
G2887XB	Oxford Home for Veterans and Their Dependents	Oxford
G2247	Public Health Research Institute of the City of New York, Inc	New York
G2375	Queens Hospital Center	Jamaica
G1001	Rensselaer Polytechnic Institute	Troy
G0624	Research Foundation for Mental Hygiene, Inc (NYS Dept of Mental Hygiene) Including	Albany
	New York State Psychiatric Institute	New York
	Long Island Research Institute	Central Islip
	NYS Institute for Basic Research in Mental Retardation	Staten Island
	Research Institute on Alcoholism	Buffalo
	Rockland Research Institute	Orangeburg
	Marcy Psychiatric Ctr, Research Division	Marcy
	Creedmoor Inst for Psychobiologic Studies	Queens Village
G0172	Rochester, University of	Rochester
G0230	Rockefeller University	New York
G2036	Rockland County Health & Social Svcs Complex	Pomona
G0491	Roosevelt Hospital	New York
G2904	Roswell Park Memorial Institute	Buffalo
G0536XB	Sloan-Kettering Institute for Cancer Research	New York
G0076	St Luke's Hospital Center	New York
G2972XB	St Mary's Hospital	Rochester

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032940

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0376	St Vincent's Hosp and Medical Ctr of New York	New York
G0280XM	Syracuse University	Syracuse
G0373XM	Teachers College, Columbia University	New York
G2438XB	Trudeau Institute	Saranac Lake
G2045	Veterans Administration Hospital-Northport	Northport
G0002	Yeshiva Univ, Albert Einstein College of Med	Bronx
	NORTH CAROLINA	
G0191	Duke University Medical Center	Durham
G2242	North Carolina A & T State University	Greensboro
G0285	North Carolina State University at Raleigh	Raleigh
G0177	North Carolina, Univ of, at Chapel Hill	Chapel Hill
G0242	Wake Forest Univ, Bowman Gray Sch of Medicine	Winston-Salem
G1087	Wake Forest Univ, Except School of Medicine	Winston-Salem
G0078	Western Carolina Center	Morganton
	OHIO	
G0485	Akron, University of	Akron
G0683XM	Battelle Columbus Laboratories of the Battelle Memorial Institute	Columbus
G2843XB	Cancer Center, Inc	Cleveland
G1167	Case Western Reserve University	Cleveland
G0088	Children's Hospital Medical Center	Cincinnati
G0249	Children's Hospital Research Foundation, Inc	Columbus
G0667XM	Cincinnati, Univ of, Except Medical Center	Cincinnati
G0337	Cincinnati, Univ of, Medical Center, Including Colleges of Medicine, Nursing, and Health and Pharmacy	Cincinnati
*G0502	Cleveland Clinic Fdn & Educational Fdn	Cleveland
G0171	Cleveland Psychiatric Institute	Cleveland
G0160	Fels Research Institute	Yellow Springs
G1936XB	Jewish Hospital of Cincinnati, Including the School of Nursing, Children's Psychiatric Center, and May Institute for Medical Research	Cincinnati
G0542	Kent State University	Kent

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032941

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0269XB	Mount Sinai Hospital of Cleveland	Cleveland
G0121	Ohio Agricultural Research & Development Ctr	Wooster
G0121	Ohio State University and Research Foundation	Columbus
G0662XB	St Luke's Hospital Association (United Methodist Church)	Cleveland
G0350XB	University Hospitals of Cleveland	Cleveland
G2907XM	Youngstown State University	Youngstown
	OKLAHOMA	
*G0327	Oklahoma Medical Research Foundation	Oklahoma City
*G2402XO	Oklahoma, University of	Norman
*G0241	Oklahoma, University of, Health Sciences Ctr	Oklahoma City
	OREGON	
*G0134	Good Samaritan Hospital and Medical Center	Portland
*G0214	Kaiser Foundation Research Institute	Portland
G0043XB	Medical Research Foundation of Oregon and Oregon Regional Primate Research Center	Portland
*G2399XO	Northwest Regional Educational Laboratory	Portland
*G0505XO	Oregon Research Institute	Eugene
G0111XM	Oregon State University	Corvallis
G0288XM	Oregon, University of, Graduate School	Eugene
G2931	Oregon, University of, Health Sciences Center, Including Schools of Medicine, Dentistry, and Nursing	Portland
	PENNSYLVANIA	
G0125	Albert Einstein Medical Center, Northern Div	Philadelphia
G0952XB	Allegheny General Hospital	Pittsburgh
G0784XM	American Institutes for Research	Pittsburgh
G0338	Arthur P. Noyes Research Foundation	Norristown
G0436XM	Bucknell University	Lewisburg
G1218	Carnegie-Mellon University	Pittsburgh

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032942

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0129	Children's Hospital of Philadelphia (Joseph Stokes, Jr., Research Inst of)	Philadelphia
G0360XB	Children's Hospital of Pittsburgh	Pittsburgh
G1556	Franklin Institute	Philadelphia
G0475	Hahnemann Medical College and Hospital	Philadelphia
G0936	H. K. Cooper Institute for Oral-Facial Anomalies and Communicative Disorders (Lancaster Cleft Palate Clinic)	Lancaster
G0045	Institute for Cancer Research (Fox Chase Cancer Center and American Oncologic Hosp)	Philadelphia
G0273XB	Lankenau Hospital	Philadelphia
G0189XB	Magee-Womens Hospital	Pittsburgh
G2121XM	Marywood College	Scranton
G0057XB	Montefiore Hospital	Pittsburgh
G0338	Norristown State Hospital	Norristown
G0333	Pennsylvania Hospital	Philadelphia
G0222	Pennsylvania, Medical College of	Philadelphia
G0573	Pennsylvania State Univ & Commonwealth Camps	University Park
G1668	Pennsylvania State Univ, Milton S. Hershey Medical Center	Hershey
G0012	Pennsylvania, University of	Philadelphia
G1531	Philadelphia Department of Public Health	Philadelphia
G0044	Philadelphia General Hospital	Philadelphia
G0324	Philadelphia Geriatric Center	Philadelphia
G0344	Philadelphia Psychiatric Center	Philadelphia
G0881	Philadelphia State Hospital	Philadelphia
G1532	Pittsburgh Child Guidance Center	Pittsburgh
G2929	Pittsburgh, University Health Center of	Pittsburgh
G0418	Pittsburgh, University of	Pittsburgh
G2200	Presbyterian-University Hospital	Pittsburgh
G0465	Presbyterian-Univ of Pennsylvania Medical Ctr	Philadelphia
G2264XM	Research for Better Schools, Inc	Philadelphia
G0795	St Joseph's Hospital	Lancaster
G2880	Temple Univ, Excluding the Health Sciences Ctr	Philadelphia
G2879	Temple University Health Sciences Center	Philadelphia
G0049	Thomas Jefferson Univ, All Components	Philadelphia
G0362XB	Wills Eye Hospital and Research Institute	Philadelphia
G0054XB	Wistar Institute	Philadelphia

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032943

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	PUERTO RICO	
G1348XM	Catholic University of Puerto Rico	Ponce
G0256XB	Puerto Rico, Univ of, Medical Sciences Campus	San Juan Rio Piedras
	RHODE ISLAND	
G0467	Brown University	Providence
*G0318	Rhode Island Hospital	Providence
G2212XB	Roger Williams General Hospital	Providence
	SOUTH CAROLINA	
G2621	Clemson University	Clemson
G0533	South Carolina Department of Mental Health	Columbia
G0240	South Carolina, Medical University of	Charleston
*G0629XO	South Carolina, University of	Columbia
	TENNESSEE	
G0490XM	George Peabody College for Teachers	Nashville
G0393	Meharry Medical College	Nashville
*G1716	Oak Ridge Associated Universities, Inc	Oak Ridge
*G1716	Oak Ridge National Laboratory	Oak Ridge
G0648	St Jude Children's Research Hospital	Memphis
G0170	Tennessee, University of, Center for the Health Sciences	Memphis
G0124	Tennessee, University of - Knoxville	Knoxville
G0401	Vanderbilt University	Nashville
	TEXAS	
G0307	Baylor College of Medicine	Houston
*G1843	Bexar County Hospital District	San Antonio
G0398XM	Houston, University of	Houston

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Revised General Assurance in Negotiation With OPRR

1032944

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G2344XO	Southwest Educational Development Corporation (AKA Southwest Educational Development Lab)	Austin
G1045	Texas A & M University and Research Foundation, College Station Campus Only	College Station
*G0590	Texas Institute for Rehabilitation and Research	Houston
G0564	Texas Tech University Complex (Texas Tech Univ and Texas Tech Univ Sch of Medicine)	Lubbock
*G1121XO	Texas, University of, at Arlington	Arlington
G0123	Texas, University of, at Austin	Austin
G0113	Texas, University of, Cancer Center (and its M.D. Anderson Hospital and Tumor Institute)	Houston
G2615	Texas, University of, Health Science Center at Dallas	Dallas
*G2760	Texas, University of, Health Science Center at Houston	Houston
*G2255	Texas, University of, Health Science Center at San Antonio, Including Medical School, Dental School, and Graduate School of Biomedical Sciences	San Antonio
G0107	Texas, Univ of, Medical Branch at Galveston	Galveston
	UTAH	
*G0933XO	Brigham Young University	Provo
*G2426	Deseret Fdn for Medical Education & Research	Salt Lake City
*G0235	Utah, University of	Salt Lake City
	VERMONT	
G0194	Vermont, University of, and State Agricultural College	Burlington
G2335XB	Veterans Administration Ctr-White River Junction	White River Jct
	VIRGINIA	
G2275XM	Human Resources Research Organization	Alexandria
G0239	Virginia Commonwealth University (All Schools and Divisions)	Richmond
*G0306	Virginia, University of	Charlottesville

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032945

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	WASHINGTON	
*G0522	Children's Orthopedic Hosp and Medical Ctr	Seattle
G2627XB	Fred Hutchinson Cancer Research Center	Seattle
G0029XB	Pacific Northwest Research Foundation	Seattle
*G0900	Virginia Mason Research Center, Including Mason Clinic and Virginia Mason Hospital	Seattle
G1717	Washington Department of Social and Health Services, All Components	Olympia
*G0105XO	Washington State University	Pullman
*G0299	Washington, University of	Seattle
	WEST VIRGINIA	
G0431	West Virginia University	Morgantown
	WISCONSIN	
G0315	Central Wisconsin Colony and Training School	Madison
G2891XB	Columbia Hospital	Milwaukee
G0387	Marquette University	Milwaukee
G0763	Mendota Mental Health Institute	Madison
G3010XB	Mount Sinai Medical Center of Milwaukee	Milwaukee
G0503	Southern Wisconsin Colony and Training School	Union Grove
*G0077	Wisconsin, Medical College of	Milwaukee
G0319	Wisconsin, University of, Madison Campus	Madison
G2106XM	Wisconsin, University of, Parkside	Kenosha
	SWITZERLAND	
*G1137	World Health Organization	Geneva

TOTAL NUMBER OF INSTITUTIONS AND COMPONENTS WITH ACCEPTABLE GENERAL ASSURANCES — 501

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1032946

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☐ FOLLOWUP ☐ REVISION

☐ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☐ RENEWAL ☐ CONTINUATION

APPLICATION IDENTIFICATION NUMBER *(If known)*

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of Public Law 93-348, as implemented by Part 46 of Title 45 of the Code of Federal Regulations, as amended, (45 CFR 46). Administration of the DHEW policy and regulation is the responsibility of the Office for Protection from Research Risks, National Institutes of Health, Bethesda, Md 20014.

1. TITLE OF PROPOSAL OR ACTIVITY

2. PRINCIPAL INVESTIGATOR/ACTIVITY DIRECTOR/FELLOW

3. DECLARATION THAT HUMAN SUBJECTS EITHER WOULD OR WOULD NOT BE INVOLVED

☐ A. NO INDIVIDUALS WHO MIGHT BE CONSIDERED HUMAN SUBJECTS, INCLUDING THOSE FROM WHOM ORGANS, TISSUES, FLUIDS, OR OTHER MATERIALS WOULD BE DERIVED, OR WHO COULD BE IDENTIFIED BY PERSONAL DATA, WOULD BE INVOLVED IN THE PROPOSED ACTIVITY. (IF NO HUMAN SUBJECTS WOULD BE INVOLVED, CHECK THIS BOX AND PROCEED TO ITEM 7. PROPOSALS DETERMINED BY THE AGENCY TO INVOLVE HUMAN SUBJECTS WILL BE RETURNED.)

☐ B. HUMAN SUBJECTS WOULD BE INVOLVED IN THE PROPOSED ACTIVITY AS EITHER: ☐ NONE OF THE FOLLOWING, OR INCLUDING: ☐ MINORS, ☐ FETUSES, ☐ ABORTUSES, ☐ PREGNANT WOMEN, ☐ PRISONERS, ☐ MENTALLY RETARDED, ☐ MENTALLY DISABLED. UNDER SECTION 6. COOPERATING INSTITUTIONS, ON REVERSE OF THIS FORM, GIVE NAME OF INSTITUTION AND NAME AND ADDRESS OF OFFICIAL(S) AUTHORIZING ACCESS TO ANY SUBJECTS IN FACILITIES NOT UNDER DIRECT CONTROL OF THE APPLICANT OR OFFERING INSTITUTION.

4. DECLARATION OF ASSURANCE STATUS/CERTIFICATION OF REVIEW

☐ A. THIS INSTITUTION HAS NOT PREVIOUSLY FILED AN ASSURANCE AND ASSURANCE IMPLEMENTING PROCEDURES FOR THE PROTECTION OF HUMAN SUBJECTS WITH THE DHEW THAT APPLIES TO THIS APPLICATION OR ACTIVITY. ASSURANCE IS HEREBY GIVEN THAT THIS INSTITUTION WILL COMPLY WITH REQUIREMENTS OF *DHEW Regulation 45 CFR 46*, THAT IT HAS ESTABLISHED AN INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS AND, WHEN REQUESTED, WILL SUBMIT TO DHEW DOCUMENTATION AND CERTIFICATION OF SUCH REVIEWS AND PROCEDURES AS MAY BE REQUIRED FOR IMPLEMENTATION OF THIS ASSURANCE FOR THE PROPOSED PROJECT OR ACTIVITY.

☐ B. THIS INSTITUTION HAS AN APPROVED GENERAL ASSURANCE (DHEW ASSURANCE NUMBER _____) OR AN ACTIVE SPECIAL ASSURANCE FOR THIS ONGOING ACTIVITY, ON FILE WITH DHEW. THE SIGNER CERTIFIES THAT ALL ACTIVITIES IN THIS APPLICATION PROPOSING TO INVOLVE HUMAN SUBJECTS HAVE BEEN REVIEWED AND APPROVED BY THIS INSTITUTION'S INSTITUTIONAL REVIEW BOARD IN A CONVENED MEETING ON THE DATE OF _____ IN ACCORDANCE WITH THE REQUIREMENTS OF THE *Code of Federal Regulations on Protection of Human Subjects (45 CFR 46)*. THIS CERTIFICATION INCLUDES, WHEN APPLICABLE, REQUIREMENTS FOR CERTIFYING FDA STATUS FOR EACH INVESTIGATIONAL NEW DRUG TO BE USED (SEE REVERSE SIDE OF THIS FORM).

THE INSTITUTIONAL REVIEW BOARD HAS DETERMINED, AND THE INSTITUTIONAL OFFICIAL SIGNING BELOW CONCURS THAT:

EITHER ☐ HUMAN SUBJECTS WILL NOT BE AT RISK; OR ☐ HUMAN SUBJECTS WILL BE AT RISK.

5. AND 6. SEE REVERSE SIDE

7. NAME AND ADDRESS OF INSTITUTION

8. TITLE OF INSTITUTIONAL OFFICIAL	TELEPHONE NUMBER
SIGNATURE OF INSTITUTIONAL OFFICIAL	DATE

HEW-596 (Rev. 4-75)

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO REQUESTING AGENCY.

10329H1

5. INVESTIGATIONAL NEW DRUGS - ADDITIONAL CERTIFICATION REQUIREMENT

SECTION 46.17 OF TITLE 45 OF THE Code of Federal Regulations states, "Where an organization is required to prepare or to submit a certification . . . and the proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 130.3(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received."

INVESTIGATIONAL NEW DRUG CERTIFICATION

TO CERTIFY COMPLIANCE WITH FDA REQUIREMENTS FOR PROPOSED USE OF INVESTIGATIONAL NEW DRUGS IN ADDITION TO CERTIFICATION OF INSTITUTIONAL REVIEW BOARD APPROVAL, THE FOLLOWING REPORT FORMAT SHOULD BE USED FOR EACH IND: (ATTACH ADDITIONAL IND CERTIFICATIONS AS NECESSARY).

- IND FORMS FILED: ☐ FDA 1571, ☐ FDA 1572, ☐ FDA 1573

- NAME OF IND AND SPONSOR _____

- DATE OF 30-DAY EXPIRATION OR FDA WAIVER
  (FUTURE DATE REQUIRES FOLLOWUP REPORT TO AGENCY) _____

- FDA RESTRICTION _____

- SIGNATURE OF INVESTIGATOR _____ DATE _____

6. COOPERATING INSTITUTIONS - ADDITIONAL REPORTING REQUIREMENT

SECTION 46.16 OF TITLE 45 OF THE *Code of Federal Regulations* IMPOSES SPECIAL REQUIREMENTS ON THE CONDUCT OF STUDIES OR ACTIVITIES IN WHICH THE GRANTEE OR PRIME CONTRACTOR OBTAINS ACCESS TO ALL OR SOME OF THE SUBJECTS THROUGH COOPERATING INSTITUTIONS NOT UNDER ITS CONTROL. IN ORDER THAT THE DHEW BE FULLY INFORMED, THE FOLLOWING REPORT IS REQUESTED WHEN APPLICABLE.

USE FOLLOWING REPORT FORMAT FOR EACH INSTITUTION OTHER THAN GRANTEE OR CONTRACTING INSTITUTION WITH RESPONSIBILITY FOR HUMAN SUBJECTS PARTICIPATING IN THIS ACTIVITY: (ATTACH ADDITIONAL REPORT SHEETS AS NECESSARY).

INSTITUTIONAL AUTHORIZATION FOR ACCESS TO SUBJECTS

- SUBJECTS: STATUS (WARDS, RESIDENTS, EMPLOYEES, PATIENTS, ETC.) _____

NUMBER _____ AGE RANGE _____

NAME OF OFFICIAL (PLEASE PRINT) _____

TITLE _____ TELEPHONE _____

NAME AND ADDRESS OF COOPERATING INSTITUTION _____

- OFFICIAL SIGNATURE _____

NOTES: *(e.g., report of modification in proposal as submitted to agency affecting human subjects involvement)*

1032948

Guidelines of June 1972
Acceptable
Not accepted [illegible]

GENERAL HUMAN SUBJECTS ASSURANCE
OUTLINE AND CHECKLIST

I. ASSURANCE OF COMPLIANCE NEW 1975
(follow example)

- Institution & Components (example--9)
- Signed by Responsible Officer and Dated

II. IMPLEMENTING GUIDELINES
(Policies & Procedures)

- Code or principles

- Definitions

Not absolutely required but very helpful to board & staff

§ 46.6 Minimum requirements for general assurances.

General assurances shall be submitted in such form and manner as the Secretary may require. The institution must include, as part of its general assurance, implementing guidelines that specifically provide for:

(a) A statement of principles which will govern the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may include appropriate existing codes or declarations, or statements formulated by the institution itself. It is to be understood that no such principles supersede DHEW policy or applicable law.

§ 46.3 Definitions.

(b) "Subject at risk" means any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

(c) "Informed consent" means the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. The basic elements of information necessary to such consent include:

(1) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;

(2) a description of any attendant discomforts and risks reasonably to be expected;

(3) a description of any benefits reasonably to be expected;

(4) a disclosure of any appropriate alternative procedures that might be advantageous for the subject;

(5) an offer to answer any inquiries concerning the procedures; and

(6) an instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject.

1032949

IMPLEMENTING GUIDELINES continued

Board Functions

46.6

(b) An Institutional Review Board or Board structure which will conduct initial and continuing reviews in accordance with the policy outlined in § 46.2.

(c) Procedures which the institution will follow in its initial and continuing review of applications, proposals, and activities.

Initial and continuing review

of all human experimentation-not limited to DHEW (P.L. 93-348)

The Secretary shall by regulation require that each entity which applies for a grant or contract under this Act for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit in or with its application for such grant or contract assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an 'Institutional Review Board') to review biomedical and behavioral research involving human subjects conducted at or sponsored by such entity in order to protect the rights of human subjects of such research.

46.2

(b) This review shall determine whether these subjects will be placed at risk, and, if risk is involved, whether:

(1) The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

(2) the rights and welfare of any such subjects will be adequately protected;

(3) legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provisions of this part; and

(4) the conduct of the activity will be reviewed at timely intervals.

Consider risks

benefits

rights

welfare

consent

timely review

In future, review before submission of applications to DHEW will be required. Then each project should have a review schedule set by the board.

1032950

IMPLEMENTING GUIDELINES continued

Board Functions continued

Review consent procedures and determine that consent is adequate and appropriate

- not exculpatory

- standard written form
- short form
- modified

Could you send a copy of an ideal or previously used consent form?

1032951

§ 46.9 Obligation to obtain informed consent; prohibition of exculpatory clauses.

Any institution proposing to place any subject at risk is obligated to obtain and document legally effective informed consent. No such informed consent, oral or written, obtained under an assurance provided pursuant to this part shall include any exculpatory language through which the subject is made to waive, or to appear to waive, any of his legal rights, including any release of the institution or its agents from liability for negligence.

§ 46.10 Documentation of informed consent.

The actual procedure utilized in obtaining legally effective informed consent and the basis for Institutional Review Board determinations that the procedures are adequate and appropriate shall be fully documented. The documentation of consent will employ one of the following three forms:

(a) Provision of a written consent document embodying all of the basic elements of informed consent. This may be read to the subject or to his legally authorized representative, but in any event he or his legally authorized representative must be given adequate opportunity to read it. This document is to be signed by the subject or his legally authorized representative. Sample copies of the consent form as approved by the Board are to be retained in its records.

(b) Provision of a "short form" written consent document indicating that the basic elements of informed consent have been presented orally to the subject or his legally authorized representative. Written summaries of what is to be said to the patient are to be approved by the Board. The short form is to be signed by the subject or his legally authorized representative and by an auditor witness to the oral presentation and to the subject's signature. A copy of the approved summary, annotated to show any additions, is to be signed by the persons officially obtaining the consent and by the auditor witness. Sample copies of the consent form and of the summaries as approved by the Board are to be retained in its records.

(c) Modification of either of the primary procedures outlined in paragraphs (a) and (b) of this section. Granting of permission to use modified procedures imposes additional responsibility upon the Board and the institution to establish: (1) that the risk to any subject is minimal, (2) that use of either of the primary procedures for obtaining informed consent would surely invalidate objectives of considerable immediate importance, and (3) that any reasonable alternative means for attaining these objectives would be less advantageous to the subjects. The Board's reasons for permitting the use of modified procedures must be individually and specifically documented in the minutes and in reports of Board actions to the files of the institution. All such modifications should be regularly reconsidered as a function of continuing review and as required for annual review, with documentation of reaffirmation, revision, or discontinuation, as appropriate.

46.6

IMPLEMENTING GUIDELINES continued

Board Members NEW 1975

varied backgrounds

XE

medical

behavioral

mature, experienced

know regulations, law, standards of conduct, community attitudes

identified - degrees, occupation, employer, representative capacity

no conflicting interest

not all employees or associated
not all same profession

Quorum defined --will convene and discuss projects

Such Board structure or Board shall meet the following requirements:

(1) The Board must be composed of not less than five persons with varying backgrounds to assure complete and adequate review of activities commonly conducted by the institution. The Board must be sufficiently qualified through the maturity, experience, and expertise of its members and diversity of its membership to insure respect for its advice and counsel for safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific activities, the Board must be able to ascertain the acceptability of applications and proposals in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. The Board must therefore include persons whose concerns are in these areas.

(2) The Board members shall be identified to DHEW by name; earned degrees, if any; position or occupation; representative capacity; and by other pertinent indications of experience such as board certification, licenses, etc., sufficient to describe each member's chief anticipated contributions to Board deliberations. Any employment or other relationship between each member and the institution shall be identified, i.e., full-time employee, part-time employee, member of governing panel or board, paid consultant, unpaid consultant. Changes in Board membership shall be reported to DHEW in such form and at such times as the Secretary may require.

(3) No member of a Board shall be involved in either the initial or continuing review of an activity in which he has a conflicting interest, except to provide information requested by the Board.

(4) No Board shall consist entirely of persons who are officers, employees, or agents, of, or are otherwise associated with the institution, apart from their membership on the Board.

(5) No Board shall consist entirely of members of a single professional group.

(6) The quorum of the Board shall be defined, but may in no event be less than a majority of the total membership duly convened to carry out the Board's responsibilities under the terms of the assurance.

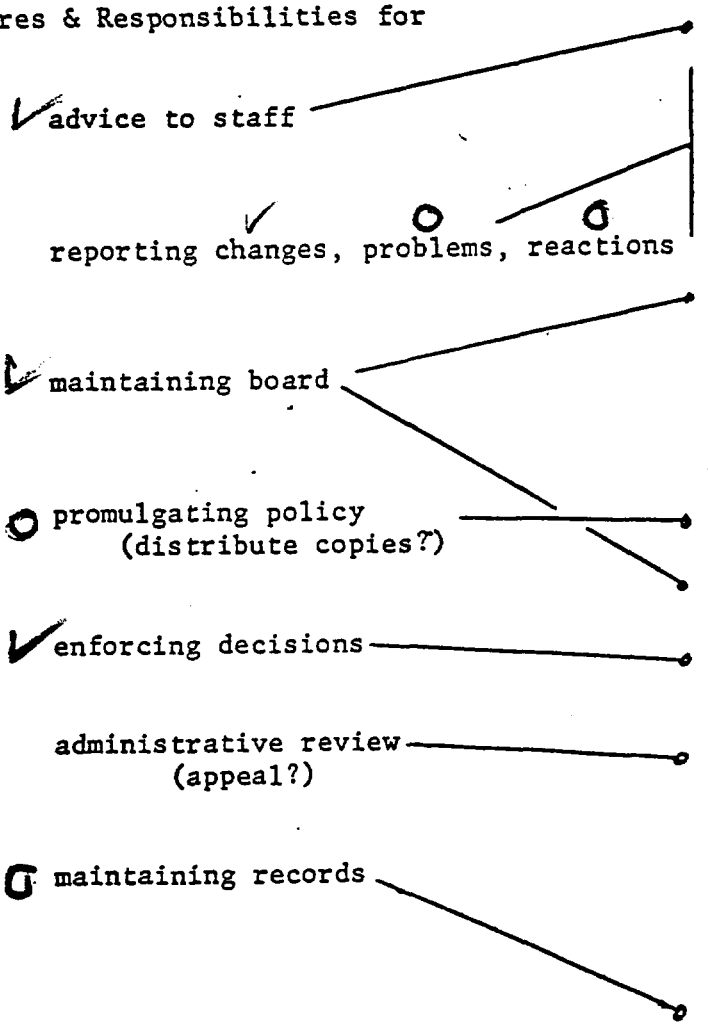
Too many MD's - should consider adding some of these: clergyman
woman
Community or entjet representative
psychologist

1032952

IMPLEMENTING GUIDELINES continued

46.6

Procedures & Responsibilities for



(d) Procedures which the Board will follow (1) to provide advice and counsel to activity directors and investigators with regard to the Board's actions, (2) to insure prompt reporting to the Board of proposed changes in an activity and of unanticipated problems involving risk to subjects or others, and (3) to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labelled drugs, or to medical devices are promptly reported to DHEW.

(e) Procedures which the institution will follow to maintain an active and effective Board and to implement its recommendations.

§ 46.18 Institution's executive responsibility.

Specific executive functions to be conducted by the institution include policy development and promulgation and continuing indoctrination of personnel. Appropriate administrative assistance and support shall be provided for the Board's functions. Implementation of the Board's recommendations through appropriate administrative action and followup is a condition of DHEW approval of an assurance. Board approvals, favorable actions, and recommendations are subject to review and to disapproval or further restriction by the institution officials. Board disapprovals, restrictions, or conditions cannot be rescinded or removed except by action of a Board described in the assurance approved by DHEW.

§ 46.19 Institution's records; confidentiality.

(a) Copies of all documents presented or required for initial and continuing review by the Institutional Review Board, such as Board minutes, records of subject's consent, transmittals on actions, instructions, and conditions resulting from Board deliberations addressed to the activity director, are to be retained by the institution, subject to the terms and conditions of grant and contract awards.

1032953

Put in file "Committee on Human Studies"

PROTECTION of the INDIVIDUAL as a RESEARCH SUBJECT

Grants, awards, contracts

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

1032954

PROTECTION
of the
INDIVIDUAL
as a
RESEARCH SUBJECT

Grants, awards, contracts

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

1032955

FOREWORD

Concern over the rights and welfare of the human being as a subject of research has led to Public Health Service policy to help assure his protection. Any activity which includes such research must provide for the individual's safety, health, and welfare. His rights, including his rights of privacy, must not be infringed. His participation must be voluntary. The direct or potential benefits of the research must outweigh the inherent risks to the individual. This policy applies to all research activities supported through grants, awards, or contracts by the National Institutes of Health, the Health Services and Mental Health Administration, and the Consumer Protection and Environmental Health Service.

The responsibility for assuring this protection when human beings are involved in federally supported research rests with the recipient of the Federal funds (grant, contract, or award). The adequacy of this protection is determined, not by the investigator or program director or any one person, but by a group independent of the activity and the persons conducting it. The group must include the competencies essential to sound judgments on scientific and humanistic values.

Institutions receiving PHS support have been thoroughly cooperative in implementing the PHS policy. Many had already adopted effective measures for protecting the human subject in research. A number of

1032956

the documents submitted to the Public Health Service have included penetrating analyses of the ethical issues in research on and for man. Experience in carrying out the policy, however, revealed the need to define better its applicability, to simplify administrative procedures, and to provide guidelines for institutions concerning the review of research projects. The text which follows states Public Health Service policy as it has been developed since the initial announcement in 1966.

These statements represent the thoughtful advice of many individuals, including officials of PHS grantee institutions, advisory consultants, and internal staff. I believe that we have taken important steps toward protecting the human being who is a subject of research, while encouraging the conduct of excellent research on man.

Correspondence about this policy should be addressed to the Director, Division of Research Grants, National Institutes of Health, Bethesda, Maryland, 20014.

Surgeon General

PROTECTION OF THE INDIVIDUAL AS A RESEARCH SUBJECT

Grants, Awards, or Contracts

Safeguarding the rights and welfare of human subjects involved in research supported by the Public Health Service is the responsibility of the institution to which support is awarded. It is the policy of the Public Health Service that no grant, award, or contract for the support of research involving human subjects shall be made unless the research is given initial and continuing review and approval by an appropriate committee of the applicant institution. This review shall assure that (a) the rights and welfare of the individuals involved are adequately protected, (b) the methods used to obtain informed consent are adequate and appropriate, and (c) the risks to the individual are outweighed by the potential benefit to him or by the importance of the knowledge to be gained.

The institution must provide written assurance to the Public Health Service that it will abide by this policy for all research involving human subjects supported by the Public Health Service. This assurance shall consist of a written statement of compliance with the requirements regarding initial and

1032957

continuing review of research involving human subjects and a description of the institution's review committee structure, its review procedures, and the facilities and personnel available to protect the health and safety of human subjects. In addition to providing the assurance, the institution must also certify to the Public Health Service for each proposal involving human subjects that its committee has reviewed and approved the proposed research before an award may be made.

Since the welfare of the subject is a matter of concern to the Public Health Service as well as to the institution, PHS advisory groups, consultants, and staff will independently review all research involving human subjects, recommending unfavorable action on grants, contracts, or awards if the research presents unacceptable hazards.

Similarly, the institution should be prepared at all times to question the conduct of research, even though previously approved by both the institution and the Public Health Service. The safety and welfare of the subject are paramount.

If any conflict exists between institutional policy, PHS policy, or State or local laws, the more restrictive requirements will be followed.

Research subjects.

A subject is considered to be any human being exposed to any research procedure as the result of the availability of Public Health Service funds, whether provided through

research, training, or other types of grants, awards, or contracts. Subjects may include, therefore, persons involved in behavioral science studies; normal volunteers; donors of services; inpatients and outpatients; living donors of body fluids, organs, and tissues; and members of the general population who may be involved in environmental or epidemiological studies or similar activities.

An individual should generally be accepted as a research subject only after he, or his legally authorized guardian or next of kin, has consented to his participation in the research. Such consent is valid, however, only if the individual is first given a fair explanation of the procedures to be followed, their possible benefits and attendant hazards and discomforts, and the reasons for pursuing the research and its general objectives.

The subject does not abdicate his rights by consenting to participate in a research project. He may withdraw his consent at any time. Further, he has the right to be secure in his person, to receive proper professional care, to enjoy privacy and confidentiality in the use of information about himself, and to be free from undue embarrassment, discomfort, and harassment.

Applicability.

This policy applies to all projects which go beyond the diagnostic and therapeutic needs of the subject, as determined by his attending professional and the institutional committee. Such projects may involve the procurement of human materials or services

1032958

and may be supported by a variety of mechanisms, e.g., research, training, or demonstration grants; general research support grants; and fellowship, traineeship, or contract awards.

The applicability of this policy is most obvious in medical and behavioral science research involving procedures that may induce a potentially harmful altered state or condition. Surgical procedures; the removal of organs or tissues for biopsy, transplantation, or banking; the administration of drugs or radiation; the use of indwelling catheters or electrodes; the requirement of strenuous physical exertion; subjection to deceit, public embarrassment, and humiliation are all examples of procedures which require thorough scrutiny by institutional committees.

There is a wide range of medical, social, and behavorial research in which no immediate physical risk to the subject is involved. However, some of these may impose varying degrees of discomfort, irritation, and harassment. In addition, there may be substantial potential injury to the subject's rights if attention is not given to maintenance of the confidentiality of information obtained from the subject and the protection of the subject from misuse of findings.

There is also research concerned solely with discarded human materials obtained at surgery or in the course of diagnosis or treatment. The use of these materials involves no possible element of risk to the subject. In such instances application of the policy requires only review of the circumstances under which the materials are to be procured.

Cooperative arrangements.

Even if certain aspects of research are to be carried out in another institution, the grantee, contracting, or sponsoring institution is responsible for initial and continuing review of those parts of the study. The review, however, may be carried out in cooperation with appropriate committees or groups within the other institution.

Minimum requirements for an acceptable assurance.

An acceptable assurance consists of two parts:

Formal statement.

A formal statement of compliance with Public Health Service policy must be signed by an appropriate institution official (see Attachment A).

Implementing guidelines.

The institution's description of its own procedures should embody the three headings listed below. The explanatory paragraphs following each heading indicate the type of information which should be supplied.

1) • *Statement of principles concerning the treatment of human subjects.*

It is necessary that the guidelines make reference to the principles the institution will apply in its review of research involving human subjects. The institution may adopt an already existing statement of principles

1032959

(e.g., the Nuremberg Code, the Declaration of Helsinki, the Statement of Ethical Standards in Research of the American Psychological Association) or it may develop its own statement.

- *Description of the review committee.*

The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of the research. The committee may be an existing one, or one especially appointed for the purpose. Institutions may utilize subcommittees to represent major administrative components in those instances where establishment of a single committee is impractical or inadvisable. The institution may utilize staff, consultants, or both. The membership should possess not only broad specific competence to comprehend the nature of the research, but also other competencies necessary in the judgments as to acceptability of the research in terms of institutional regulations, relevant law, standards of professional practice, and community acceptance. The committee's maturity and experience should be such as to justify respect for its advice and counsel.

No individual involved in the conduct of the research activity shall participate in its review, except to provide information to the committee.

Committee members should be identified in the assurance to the Public Health Service in terms of position, earned degrees, board certifications, licensures, memberships, and other indications of experience and competence. Names need not be given.

- *Description of the initial and continuing review procedures to be followed by the committee.*

Timing of review.

Research described in applications and contract proposals should, whenever possible, be given institutional review and approval prior to submission to the Public Health Service. Where review prior to Public Health Service submission is not possible, the review must be made prior to issuance of the award by the Public Health Service. Review of initial applications by institutions which have not previously filed acceptable assurances must be performed after acceptance of the assurance by the Public Health Service.

There may be occasions when a second review by the committee will be required before the research is initiated. For example, a long interval has elapsed between committee review and initiation, or the investigator proposes changes in protocol after the application has been reviewed by the committee but before the research is initiated. Perhaps the investigator has proposed research in a rapidly moving scientific area. The second review, in this case, would determine if changing standards of practice indicate a hazardous procedure unrecognized as such during the initial review (e.g., reduction of acceptable radiation levels).

1032960

Adequacy of the protection of the rights and welfare of the subjects involved.

Institutional committees should carefully examine the research plan to arrive at an independent determination of possible hazards. The committee must be alert to the possibility that investigators, program directors, or contractors may, quite unintentionally, introduce unnecessary or unacceptable hazards, or fail to provide adequate safeguards. This is particularly true of research that crosses disciplinary lines. The committees should consider the research plan as a whole in order to determine that normally minor and acceptable risks are not aggravated by the way it is designed. The severity of the risk from a procedure may vary with the circumstances under which it is carried out. Age, development, size, maturity, intercurrent disease, and other factors with respect to the subject may adversely affect the acceptability of a procedure. Simultaneous or consecutive performance of several minor tests or procedures may add up to a substantial risk. The committees must assure themselves that proper precautions will be taken to deal with emergencies that may develop even in the course of routine procedures.

Relevant to the decision of the committees are those rights of the subject that are defined by law, particularly those concerned with the rights of children and unborn infants; the termination of pregnancy; the use of prisoners, institutionalized, and military personnel; and the donation of tissues and organs.

Methods used to obtain adequate, appropriate, informed consent.

NOTE: In the United States, adherence to the regulations of the Food and Drug Administration (21 CFR 130.37) governing consent in projects involving investigative new drugs (IND) is required by law.

Consent should be obtained, whenever possible, from the subjects themselves. When the subjects are not legally or physically capable of giving informed consent, because of age, mental incapacity, or inability to communicate, or when the attending professional believes that the giving of full information would be contrary to the best interests of the subject, the review committee may consider the validity of consent by next of kin, legal guardians, or by other responsible third parties who are representative of the subject's interests. In the latter instances, careful consideration should be given by the committee not only to the third parties' depth of interest and concern with the subjects' rights and welfare, but also to whether the third parties are authorized to expose the subjects to the risks involved. A parent, for example, may have no authority to expose his child to risk, except for the child's own benefit.

1032961

The review committee should determine if the consent, whether secured as a written document or given orally, or whether the consent is implicit in voluntary participation in a well-advertised activity, is adequate in the light of the risks to the subject, and the circumstances of the research. The review committee should also determine if the information to be given to the subject or to qualified third parties, orally or in writing, is a fair explanation of the procedure, its possible benefits, and its attendant hazards. Where debriefing procedures are considered as a necessary part of the research plan, the committee should ascertain that these will be complete and prompt.

When the sponsoring institution routinely obtains a generalized form of consent for treatment or care, the committee shall determine whether these routine procedures provide an adequate basis for the subject's informed consent to the research procedures involved.

Relative weights of risks versus benefits.

Even though informed consent has been obtained or can be anticipated, the committee shall carefully consider the relative weights of the risks and benefits of the procedures to the subjects. If a procedure may confer a substantial benefit to the subjects, the committee may be justified in permitting them to accept an equally substantial or lesser risk. Where the potential benefits to the

subjects are negligible, or nonexistent, as in some cases of normal volunteers, the committee may be justified in permitting subjects to accept a risk in the interests of humanity. In all instances, careful consideration must be given by the committee to the subjects' motivation in accepting them.

Notification of the committee's decision to the project director.

If the committee's overall recommendation is favorable, it may prescribe restrictions or conditions under which the research may be conducted, define areas of possible pertinent changes in the research plans which should be brought to its attention, and determine the nature and frequency of interim review procedures to insure continued acceptable conduct of the research.

Favorable recommendations by an institutional committee are, of course, always subject to further appropriate review and rejection by institution officials. Unfavorable recommendations, restrictions, or conditions cannot be removed except by the committee or by the action of another appropriate review group described in the assurance filed with the Public Health Service. Under no circumstances shall proposed research, or proposed changes in research plans, not approved by the committee be implemented with Public Health Service funds. The scientist proposing the research should be informed

1032962

of the reasons for any adverse actions taken by the institutional committee.

Continuing review of research.

The committee shall require the project or program director to report to the committee for review any emergent problems or proposed procedural changes which may affect the status of the research with regard to the institution's review criteria. No such changes, except those necessary to eliminate apparent immediate hazards, should be made without prior approval by the committee.

In addition, the committee shall carry out interim review of the conduct of all research in such a manner and at appropriate intervals in the light of apparent risks, existing administrative and supervisory organization, and other factors as to assure itself that its advice is being followed.

The facilities available to protect the health and safety of human subjects.

The assurance should describe in general terms the facilities and personnel available to protect the health and safety of human subjects, particularly those requiring emergency care.

Certification.

An institution sponsoring an application for a grant or an award will submit with the application, or as soon after submission of the application as possible, the following statement identified by name of investigator, title of project, and assigned number, if known:

> "The (name of institution) reviewed and approved on (date) the procedures in this application which will involve human subjects in accordance with the assurance approved by the Public Health Service. These procedures will also be subject to continuing review as provided for in that assurance."

An institution submitting a contract proposal for research involving human subjects will submit with its proposal, or prior to award, the following statement identifying the contract, the contractor, and the official authorized to sign for the contractor:

> "The (name of institution) reviewed and approved on (date) the procedures in this proposal which will involve human subjects, in accordance with the assurance approved by the Public Health Service. The institution agrees that all work involving the use of human subjects under any contract or any subcontract awarded in response to this proposal will be subject to initial and continuing review as required by Public Health Service policy and as described in its assurance.
>
> "The contractor shall bear full responsibility for the proper and safe performance of all work and services involving the use of human subjects under this contract. The parties hereto agree that the contractor retains the right to control and direct the performance of all work under this contract. No provision of this contract shall be deemed to constitute the contractor or any subcontractor, agent or employee of the contractor or any other person, organization, institution, or group of any kind whatsoever, as the agent or employee of the government. The contractor agrees that it has entered into this contract and will discharge its obligations, duties, and undertakings and the work pursuant thereto whether requiring professional judgment or otherwise as an independent contractor and without liability on the part of the government."

Records and reports.

The institution is required to keep informative records of group reviews and decisions on the use of human subjects, and to obtain and keep documentary evidence of

1032963

informed consent relating to research carried out with the assistance of Public Health Service financial support. At a minimum these records should include a summary of the factors leading to the group decision. Documentary evidence of informed consent may consist of a record of the decision of the committee as to the type of consent which it considers acceptable. Copies of the information statement, if any, to be given to the subject, where signed consent statements are required, should be retained in institution files. Where oral or implied consents are obtained, notations should be made on official records.

Submission and review of assurance.

Assurances should be forwarded to the Director, Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014, for review and acceptance on behalf of the Public Health Service.

No routine reports to the Public Health Service are required. However, significant changes in policy, procedure, or committee structure shall be promptly reported to the Director, DRG. Review of these changes, or of institutional and other records of performance under the terms and conditions of Public Health Service policy, may require renegotiation of the assurance or such other action as may be appropriate.

EXAMPLE OF A STATEMENT OF COMPLIANCE ATTACHMENT A

Institutional Assurance on Research Involving Human Subjects

The (name of institution) will comply with the principles of the Public Health Service policy with regard to research involving human subjects which requires a review independent of the investigator or director to safeguard the rights and welfare of those subjects. It assures the Public Health Service that it will establish and maintain advisory groups competent to review research plans involving human subjects, prior to the initiation of this research, in order to insure adequate safeguards. Group reviews and decisions will be carried out in reference to (1) the rights and welfare of the individuals involved, (2) the appropriateness of the methods used to obtain informed consent, and (3) the risks and potential benefits of the proposed research.

The institution agrees to a continuing exchange of information and advice between the review group and the investigator or director, particularly to deal with proposed changes in research design, and with emergent problems which may alter the investigational situation with regard to the criteria cited above. The institution will assure itself that its policies and the advice of its review groups are followed. It will also provide whatever professional attention or facilities are required to safeguard the rights and welfare of human subjects involved in research. Records of group review and decision on the use of human subjects and of informed consent will be developed and kept by the institution.

Signed _____

Title _____

Date _____

Enclosures (Implementing Guidelines)

U. S. GOVERNMENT PRINTING OFFICE : 1969 O - 348-095

1032964

ORAU-30021 (2 of 2)

ORAU/ORNL
COMMITTEE ON HUMAN STUDIES
BUSINESS FILE
(FILE 2)

REPOSITORY OAK RIDGE INSTITUTE FOR SCIENCE + EDUCATION, MEDICAL SCIENCES DIV
ORAU/ORNL NAT'L LAB
COLLECTION COMMITTEE OF HUMAN STUDIES
BOX No. VANCE ROAD FACILITY, RM. 202A
FOLDER ORAU-30021 FILE 2 of 2

1032965

1977

REPOSITORY Oak Ridge Institute for Science and Education, Medical Sciences Division
Oak Ridge Associated Universities/Oak Ridge
COLLECTION National Lab Committee of Human Studies

BOX No. Vance Road Facility, Room 202A
No folder title.
FOLDER Document no. ORAU-30021. File 2 of 2

1032966

Committee Members and Their Responsible Area

(On January 1, 1977, the following members constituted the Committee and had these stated responsibilities.)

O Robert Lange, M.D. (Univ. Tenn.), Chairman, Extramural Representative
Gould A. Andrews, M.D. (ORAU), Secretary
OO John B. Storer, M.D., Official ORNL Representative
OO C. C. Lushbaugh, Ph.D., M.D., Official ORAU Representative
O A. Bertrand Brill (Vanderbilt Univ.), Extramural Representative
* Melvin E. Koons (UCNC), Lawyer
* M. Scott Lawyer (ORAU), Lawyer
O* Donald W. Goodwin, Ph.D. (United Church, O.R.), Minister
OW Joan B. Woods, M.D. (VA Hosp., Murfreesboro), Psychiatrist
Thomas A. Lincoln, M.D. (ORNL), Occupational Medicine
Karl F. Hübner, M.D. (ORAU), Clinical Research
*W Edythalena Tompkins, A.B. (ORAU), Epidemiology

O - Extramural member
OO - Institutional representative
* - Non-M.D. member
W - Woman member

1032967

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
Telephone 615 483-8411

Medical and
Health Sciences
Division

January 17, 1977

Roy Kinard, D.V.M.
Office for Protection from Research
Risks
Office of the Director
Department of Health, Education, and Welfare
Public Health Service
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Kinard:

It was most helpful to talk with you today and have you resolve my remaining problems concerning our need to get our General Assurance (G1716) into complete compliance with HEW guidelines. I particularly appreciate your willingness to take a look at a draft just completed of the reorganized guidelines for this Committee on Human Studies. Accordingly, I am including with this letter a copy of this tentative revision for your criticism. I am simultaneously sending our Committee members a copy for their information and comments. I am hoping that with this informal approach we can obtain formal acceptance of our General Assurance by 1 February.

I appreciate your help in my meeting this goal.

Sincerely,

C. C. Lushbaugh, M.D.
Chairman, Medical and
Health Sciences Division

CCL:fb

Enc.

cc: Dr. P. L. Johnson, Executive Director, ORAU
Dr. C. R. Richmond, ORNL
Committee Members

1032968

Annex Items

Annex 1 Definitions
Annex 2 FR 40
Annex 3 FR 41
Annex 4 CVs of present Committee members
Annex 5 Summarized Committee assignments
Annex 6 Block diagram of the bi-institutional Committee structure, administration, lines of authority and present membership and functional identities
Annex 7 Application for approval
Annex 8 Example of a typical informed consent form for a specific project
Annex 9 HEW Form 596
Annex 10 Review and Action Form

1032969

DEFINITIONS

(a) "Institution" means any public or private institution or agency (including Federal, State, and local government agencies).

(b) "Subject at risk" means any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

(c) "Informed consent" means the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. The basic elements of information necessary to such consent include:

(1) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;

(2) a description of any attendant discomforts and risks reasonably to be expected;

(3) a description of any benefits reasonably to be expected;

(4) a disclosure of any appropriate alternative procedures that might be advantageous for the subject;

(5) an offer to answer any inquiries concerning the procedures; and

(6) an instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject.

(d) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(e) "DHEW" means the Department of Health, Education, and Welfare.

( ) "ERDA" means the Energy Research and Development Administration.

(f) "Approved assurance" means a document that fulfills the requirements of this part and is approved by the Secretary.

(g) "Certification" means the official institutional notification to DHEW in accordance with the requirements of this part that a project or activity involving human subjects at risk has been reviewed and approved by the institution in accordance with the "approved assurance" on file at DHEW.

(h) "Legally authorized representative" means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to such subject's participation in the particular activity or procedure.

federal register

THURSDAY, MARCH 13, 1975

WASHINGTON, D.C.

Volume 40 ▪ Number 50

PART II

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Office of the Secretary

▪

PROTECTION OF HUMAN SUBJECTS

Technical Amendments

1032971

Title 45—Public Welfare

SUBTITLE A—DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, GENERAL ADMINISTRATION

PART 46—PROTECTION OF HUMAN SUBJECTS

Technical Amendments

On May 30, 1974, final regulations were published in the FEDERAL REGISTER (39 FR 18914) relating to protection of human subjects in research, development, and related activities supported by Department of Health, Education, and Welfare grants and contracts. Shortly thereafter, on July 12, 1974, the National Research Act, Public Law 93-348, was enacted. Although the Conference Report on the bill (H.R. 7724) which later became Pub. L. 93-348 expressed satisfaction with the regulations (H. Rep. No. 93-1148, at p. 26), section 212(a) of said Law added a new section 474(a) to the Public Health Service Act, which provides as follows:

The Secretary shall by regulation require that each entity which applies for a grant or contract under this Act for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit in or with its application for such grant or contract assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an 'Institutional Review Board') to review biomedical and behavioral research involving human subjects conducted at or sponsored by such entity in order to protect the rights of human subjects of such research.

Section 212(b) of Pub. L. 93-348 further stated that the regulations required to carry out section 474(a) shall apply with respect to applications for grants and contracts under the Public Health Service Act submitted after promulgation of such regulations.

The regulations published on May 30, 1974, codified at 45 CFR Part 46, would with minor, technical changes fully implement section 474(a). This would be accomplished by: (1) amending the citation of AUTHORITY to refer to section 474(a), (2) substituting references to "institutions" and "Institutional Review Boards" for existing references to "organizations" and "committees" and making related changes, and (3) revising 45 CFR 46.7, 46.11(a), and 46.12 to take account of the requirement in section 474 (a) that an assurance concerning establishment of a Board must in all cases be submitted in or with the application. Since Part 46 was published initially as a notice of proposed rulemaking (38 FR 27882), and since the aforesaid changes would be minor and technical in nature, it is unnecessary to publish such changes as a notice of proposed rulemaking. The Department therefore finds that good cause exists for dispensing with this step.

Accordingly, the regulations published in the FEDERAL REGISTER on May 30, 1974 and codified at 45 CFR Part 46, as so amended, are hereby adopted as final regulations implementing section 474(a) of the Public Health Service Act, effective March 13, 1975.

Dated: February 14, 1975.

THEODORE COOPER,
Acting Assistant Secretary for Health.

Approved: March 7, 1975.

CASPAR W. WEINBERGER,
Secretary.

Therefore, Subtitle A of Title 45 of the Code of Federal Regulations is amended by revising Part 46 to read as follows:

Sec.
46.1 Applicability.
46.2 Policy.
46.3 Definitions.
46.4 Submission of assurances.
46.5 Types of assurances.
46.6 Minimum requirements for general assurances.
46.7 Minimum requirements for special assurances.
46.8 Evaluation and disposition of assurances.
46.9 Obligation to obtain informed consent; prohibition of exculpatory clauses.
46.10 Documentation of informed consent.
46.11 Submission and certification of applications and proposals, general assurances.
46.12 Submission and certification of applications and proposals, special assurances.
46.13 Applications and proposals lacking definite plans for involvement of human subjects.
46.14 Applications and proposals submitted with the intent of not involving human subjects.
46.15 Evaluation and disposition of applications and proposals.
46.16 Cooperative activities.
46.17 Investigational new drug 30-day delay requirement.
46.18 Institution's executive responsibility.
46.19 Institution's records; confidentiality.
46.20 Reports.
46.21 Early termination of awards; evaluation of subsequent applications and proposals.
46.22 Conditions.

AUTHORITY: 5 U.S.C. 301; sec. 474(a), 88 Stat. 352 (42 U.S.C. 2891-3(a)).

§ 46.1 Applicability.

(a) The regulations in this part are applicable to all Department of Health, Education, and Welfare grants and contracts supporting research, development, and related activities in which human subjects are involved.

(b) The Secretary may, from time to time, determine in advance whether specific programs, methods, or procedures to which this part is applicable place subjects at risk, as defined in § 46.3(b). Such determinations will be published as notices in the FEDERAL REGISTER and will be included in an appendix to this part.

§ 46.2 Policy.

(a) Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless an Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of this part.

(b) This review shall determine whether these subjects will be placed at risk, and, if risk is involved, whether:

(1) The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

(2) the rights and welfare of any such subjects will be adequately protected;

(3) legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provisions of this part; and

(4) the conduct of the activity will be reviewed at timely intervals.

(c) No grant or contract involving human subjects at risk shall be made to an individual unless he is affiliated with or sponsored by an institution which can and does assume responsibility for the subjects involved.

§ 46.3 Definitions.

(a) "Institution" means any public or private institution or agency (including Federal, State, and local government agencies).

(b) "Subject at risk" means any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

(c) "Informed consent" means the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. The basic elements of information necessary to such consent include:

(1) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;

(2) a description of any attendant discomforts and risks reasonably to be expected;

(3) a description of any benefits reasonably to be expected;

(4) a disclosure of any appropriate alternative procedures that might be advantageous for the subject;

(5) an offer to answer any inquiries concerning the procedures; and

(6) an instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject.

(d) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(e) "DHEW" means the Department of Health, Education, and Welfare.

(f) "Approved assurance" means a document that fulfills the requirements of this part and is approved by the Secretary.

(g) "Certification" means the official institutional notification to DHEW in accordance with the requirements of this part that a project or activity involving human subjects at risk has been reviewed and approved by the institution in accordance with the "approved assurance" on file at DHEW.

(h) "Legally authorized representative" means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to such subject's participation in the particular activity or procedure.

§ 46.4 Submission of assurances.

(a) Recipients or prospective recipients of DHEW support under a grant or contract involving subjects at risk shall provide written assurance acceptable to DHEW that they will comply with DHEW policy as set forth in this part. Each assurance shall embody a statement of compliance with DHEW requirements for initial and continuing Institutional Review Board review of the supported activities; a set of implementing guidelines, including identification of the Board and a description of its review procedures; or, in the case of special assurances concerned with single, activities or projects, a report of initial findings of the Board and of its proposed continuing review procedures.

(b) Such assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this part, and shall be filed in such form and manner as the Secretary may require.

§ 46.5 Types of assurances.

(a) *General assurances.* A general assurance describes the review and implementation procedures applicable to all DHEW-supported activities conducted by an institution regardless of the number, location, or types of its components or field activities. General assurances will be required from institutions having a significant number of concurrent DHEW-supported projects or activities involving human subjects.

(b) *Special assurances.* A special assurance will, as a rule, describe those review and implementation procedures applicable to a single activity or project. A special assurance will not be solicited or accepted from an institution which has on file with DHEW an approved general assurance.

§ 46.6 Minimum requirements for general assurances.

General assurances shall be submitted in such form and manner as the Secretary may require. The institution must include, as part of its general assurance, implementing guidelines that specifically provide for:

(a) A statement of principles which will govern the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may include appropriate existing codes or declarations, or statements formulated by the institution itself. It is to be understood that no such principles supersede DHEW policy or applicable law.

(b) An Institutional Review Board or Board structure which will conduct initial and continuing reviews in accordance with the policy outlined in § 46.2. Such Board structure or Board shall meet the following requirements:

(1) The Board must be composed of not less than five persons with varying backgrounds to assure complete and adequate review of activities commonly conducted by the institution. The Board must be sufficiently qualified through the maturity, experience, and expertise of its members and diversity of its membership to insure respect for its advice and counsel for safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific activities, the Board must be able to ascertain the acceptability of applications and proposals in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. The Board must therefore include persons whose concerns are in these areas.

(2) The Board members shall be identified to DHEW by name; earned degrees, if any; position or occupation; representative capacity; and by other pertinent indications of experience such as board certification, licenses, etc., sufficient to describe each member's chief anticipated contributions to Board deliberations. Any employment or other relationship between each member and the institution shall be identified, i.e., full-time employee, part-time employee, member of governing panel or board, paid consultant, unpaid consultant. Changes in Board membership shall be reported to DHEW in such form and at such times as the Secretary may require.

(3) No member of a Board shall be involved in either the initial or continuing review of an activity in which he has a conflicting interest, except to provide information requested by the Board.

(4) No Board shall consist entirely of persons who are officers, employees, or agents, of, or are otherwise associated with the institution, apart from their membership on the Board.

(5) No Board shall consist entirely of members of a single professional group.

(6) The quorum of the Board shall be defined, but may in no event be less than a majority of the total membership duly convened to carry out the Board's responsibilities under the terms of the assurance.

(c) Procedures which the institution will follow in its initial and continuing review of applications, proposals, and activities.

(d) Procedures which the Board will follow (1) to provide advice and counsel to activity directors and investigators with regard to the Board's actions, (2) to insure prompt reporting to the Board of proposed changes in an activity and of unanticipated problems involving risk to subjects or others, and (3) to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labelled drugs, or to medical devices, are promptly reported to DHEW.

(e) Procedures which the institution will follow to maintain an active and effective Board and to implement its recommendations.

§ 46.7 Minimum requirements for special assurances.

Special assurances shall be submitted in such form and manner as the Secretary may require. An acceptable special assurance shall:

(a) Identify the specific grant or contract involved by its full title; and by the name of the activity or project director, principal investigator, fellow, or other person immediately responsible for the conduct of the activity.

(b) Include a statement, executed by an appropriate institutional official, indicating that the institution has established an Institutional Review Board satisfying the requirements of § 46.6(b).

(c) Describe the makeup of the Board and the training, experience, and background of its members, as required by § 46.6(b)(2).

(d) Describe in general terms the risks to subjects that the Board recognizes as inherent in the activity, and justify its decision that these risks are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant the Board's decision to permit the subject to accept these risks.

(e) Describe the informed consent procedures to be used and attach documentation as required by § 46.10.

(f) Describe procedures which the Board will follow to insure prompt reporting to the Board of proposed changes in the activity and of any unanticipated problems, involving risks to subjects or others and to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labelled drugs, or to medical devices are promptly reported to DHEW.

(g) Indicate at what time intervals the Board will meet to provide for continuing review. Such review must occur no less than annually.

(h) Be signed by the individual members of the Board and be endorsed by an appropriate institutional official.

§ 46.8 Evaluation and disposition of assurances.

(a) All assurances submitted in accordance with §§ 46.6 and 46.7 shall be

1032973

evaluated by the Secretary through such officers and employees of DHEW and such experts or consultants engaged for this purpose as he determines to be appropriate. The Secretary's evaluation shall take into consideration, among other pertinent factors, the adequacy the proposed. Institutional Review Board in the light of the anticipated scope of the applicant institution's activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in the light of the probable risks, and the size and complexity of the institution.

(b) On the basis of his evaluation of an assurance pursuant to paragraph (a) of this section, the Secretary shall (1) approve, (2) enter into negotiations to develop a more satisfactory assurance, or (3) disapprove. With respect to approved assurances, the Secretary may determine the period during which any particular assurance or class of assurances shall remain effective or otherwise condition or restrict his approval. With respect to negotiations, the Secretary may, pending completion of negotiations for a general assurance, require an institution otherwise eligible for such an assurance, to submit special assurances.

§ 46.9 Obligation to obtain informed consent; prohibition of exculpatory clauses.

Any institution proposing to place any subject at risk is obligated to obtain and document legally effective informed consent. No such informed consent, oral or written, obtained under an assurance provided pursuant to this part shall include any exculpatory language through which the subject is made to waive, or to appear to waive, any of his legal rights, including any release of the institution or its agents from liability for negligence.

§ 46.10 Documentation of informed consent.

The actual procedure utilized in obtaining legally effective informed consent and the basis for Institutional Review Board determinations that the procedures are adequate and appropriate shall be fully documented. The documentation of consent will employ one of the following three forms:

(a) Provision of a written consent document embodying all of the basic elements of informed consent. This may be read to the subject or to his legally authorized representative, but in any event he or his legally authorized representative must be given adequate opportunity to read it. This document is to be signed by the subject or his legally authorized representative. Sample copies of the consent form as approved by the Board are to be retained in its records.

(b) Provision of a "short form" written consent document indicating that the basic elements of informed consent have been presented orally to the subject or his legally authorized representative. Written summaries of what is to be said to the patient are to be approved by the Board. The short form is to be signed by the subject or his legally authorized representative and by an auditor witness to the oral presentation and to the subject's signature. A copy of the approved summary, annotated to show any additions, is to be signed by the persons officially obtaining the consent and by the auditor witness. Sample copies of the consent form and of the summaries as approved by the Board are to be retained in its records.

(c) Modification of either of the primary procedures outlined in paragraphs (a) and (b) of this section. Granting of permission to use modified procedures imposes additional responsibility upon the Board and the institution to establish: (1) that the risk to any subject is minimal, (2) that use of either of the primary procedures for obtaining informed consent would surely invalidate objectives of considerable immediate importance, and (3) that any reasonable alternative means for attaining these objectives would be less advantageous to the subjects. The Board's reasons for permitting the use of modified procedures must be individually and specifically documented in the minutes and in reports of Board actions to the files of the institution. All such modifications should be regularly reconsidered as a function of continuing review and as required for annual review, with documentation of reaffirmation, revision, or discontinuation, as appropriate.

§ 46.11 Submission and certification of applications and proposals, general assurances.

(a) *Timely review.* Any institution having an approved general assurance shall indicate in each application or proposal for support of activities covered by this part (or in a separate document submitted with such application or proposal) that it has on file with DHEW such an assurance. In addition, unless the Secretary otherwise provides, each such application or proposal must be given review and, when found to involve subjects at risk, approval, prior to submission to DHEW. In the event the Secretary provides for the performance of institutional review of an application or proposal after its submission to DHEW, processing of such application or proposal by DHEW will under no circumstances be completed until such institutional review and approval has been certified. Except where the institution determines that human subjects are not involved, the application or proposal should be appropriately certified in the spaces provided on forms, or one of the following certifications, as appropriate, should be typed on the lower or right hand margin of the page bearing the name of an official authorized to sign or execute applications or proposals for the institution.

Human Subjects: Reviewed, Not at Risk.

(Date)

Human Subjects: Reviewed, At Risk, Approved

(Date)

(b) *Applications and proposals not certified.* Applications and proposals not properly certified, or submitted as not involving human subjects and found by the operating agency to involve human subjects, will be returned to the institution concerned.

§ 46.12 Submission and certification of applications and proposals, special assurances.

(a) Except as provided in paragraph (b) of this section, institutions not having an approved general assurance shall submit in or with each application or proposal for support of activities covered by this part a separate special assurance and certification of its review and approval.

(b) If the Secretary so provides, the assurance which must be submitted in or with the application or proposal under paragraph (a) of this section need satisfy only the requirements of § 46.7(a) and § 46.7(b) of this part. Under such circumstances, processing of such application or proposal by DHEW will not be completed until a further assurance satisfying the remaining requirements of § 46.7 has been submitted to DHEW.

(c) An assurance and certification prepared in accordance with this part and approved by DHEW shall be considered to have met the requirement for certification for the initial grant or contract period concerned. If the terms of the grant or contract recommend additional support periods, each application or proposal for continuation or renewal of support must satisfy the requirements of this section or § 46.11 whichever is applicable at the time of its submission.

§ 46.13 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications or proposals are submitted with the knowledge that subjects are to be involved within the support period, but definite plans for this involvement would not normally be set forth in the application or proposal. These include such activities as (a) institutional type grants where selection of projects is the responsibility of the institution, (b) training grants where training projects remain to be selected, and (c) research, pilot, or developmental studies in which involvement depends upon such things as the completion of instruments, or of prior animal studies, or upon the purification of compounds. Such applications or proposals shall be reviewed and certified in the same manner as more definitive applications or proposals. The initial certification indicates institutional approval of the applications or proposals as submitted, and commits the institution to later review of the plans when completed. Such later review and certification to DHEW should be completed prior to the beginning of the budget period during which actual involvement of human subjects is to begin. Review and certification to DHEW must in any event be completed prior to involvement of human subjects.

1032974

§ 46.14 Applications and proposals submitted with the intent of not involving human subjects.

If an application or proposal does not anticipate involving or intend to involve human subjects, no certification should be included with the initial submission of the application or proposal. In those instances, however, when later it becomes appropriate to use all or part of awarded funds for one or more activities which will involve subjects, each such activity shall be reviewed and approved in accordance with the assurance of the institution prior to the involvement of subjects. In addition, no such activity shall be undertaken until the institution has submitted to DHEW: (a) a certification that the activity has been reviewed and approved in accordance with this part, and (b) a detailed description of the proposed activity (including any protocol or similar document). Also, where support is provided by project grants or contracts, subjects shall not be involved prior to certification and institutional receipt of DHEW approval and, in the case of contracts, prior to negotiation and approval of an amended contract description of work.

§ 46.15 Evaluation and disposition of applications and proposals.

(a) Notwithstanding any prior review, approval, and certification by the institution all applications or proposals involving human subjects at risk submitted to DHEW shall be evaluated by the Secretary for compliance with this part through such officers and employees of the Department and such experts or consultants engaged for this purpose as he determines to be appropriate. This evaluation may take into account, among other pertinent factors, the apparent risks to the subjects, the adequacy of protection against these risks, the potential benefits of the activity to the subjects and to others, and the importance of the knowledge to be gained.

(b) Disposition. On the basis of his evaluation of an application or proposal pursuant to paragraph (a) of this section and subject to such approval or recommendation by or consultation with appropriate councils, committees, or other bodies as may be required by law, the Secretary shall (1) approve, (2) defer for further evaluation, or (3) disapprove support of the proposed activity in whole or in part. With respect to any approved grant or contract, the Secretary may impose conditions, including restrictions on the use of certain procedures, or certain subject groups, or requiring use of specified safeguards or informed consent procedures when in his judgment such conditions are necessary for the protection of human subjects.

§ 46.16 Cooperative activities.

Cooperative activities are those which involve institutions in addition to the grantee or prime contractor (such as a contractor under a grantee or a subcontractor under a prime contractor). If, in such instances, the grantee or prime contractor obtains access to all or some of the subjects involved through one or more cooperating institutions, the basic DHEW policy applies and the grantee or prime contractor remains responsible for safeguarding the rights and welfare of the subjects.

(a) *Institution with approved general assurance.* Initial and continuing review by the institution may be carried out by one or a combination of procedures:

(1) Cooperating institution with approved general assurance. When the cooperating institution has on file with DHEW an approved general assurance, the grantee or contractor may, in addition to its own review, request the cooperating institution to conduct an independent review and to report its recommendations on those aspects of the activity that concern individuals for whom the cooperating institution has responsibility under its own assurance to the grantee's or contractor's Institutional Review Board. The grantee or contractor may, at its discretion, concur with or further restrict the recommendations of the cooperating institution. It is the responsibility of the grantee or contractor to maintain communication with the Boards of the cooperating institution. However, the cooperating institution shall promptly notify the grantee or contracting institution whenever the cooperating institution finds the conduct of the project or activity within its purview unsatisfactory.

(2) Cooperating institution with no approved general assurance. When the cooperating institution does not have an approved general assurance on file with DHEW, the DHEW may require the submission of a general or special assurance which, if approved, will permit the grantee or contractor to follow the procedure outlined in the preceding subparagraph.

(3) Interinstitutional joint review. The grantee or contracting institution may wish to develop an agreement with cooperating institutions to provide for an Institutional Review Board with representatives from cooperating institutions. Representatives of cooperating institutions may be appointed as ad hoc members of the grantee or contracting institution's existing Institutional Review Board or, if cooperation is on a frequent or continuing basis as between a medical school and a group of affiliated hospitals, appointments for extended periods may be made. All such cooperative arrangements must be approved by DHEW as part of a general assurance, or as an amendment to a general assurance.

(b) *Institutions with special assurances.* While responsibility for initial and continuing review necessarily lies with the grantee or contracting institution, DHEW may also require approved assurances from those cooperating institutions having immediate responsibility for subjects.

If the cooperating institution has on file with DHEW an approved general assurance, the grantee or contractor shall request the cooperating institution to conduct its own independent review of those aspects of the project or activity which will involve human subjects for which it has responsibility. Such a request shall be in writing and should provide for direct notification of the grantee's or contractor's Institutional Review Board in the event that the cooperating institution's Board finds the conduct of the activity to be unsatisfactory. If the cooperating institution does not have an approved general assurance on file with DHEW, it must submit to DHEW a general or special assurance which is determined by DHEW to comply with the provisions of this part.

§ 46.17 Investigational new drug 30-day delay requirement.

Where an institution is required to prepare or to submit a certification under §§ 46.11, 46.12, 46.13, or 46.14 and the application or proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 312.1(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received.

§ 46.18 Institution's executive responsibility.

Specific executive functions to be conducted by the institution include policy development and promulgation and continuing indoctrination of personnel. Appropriate administrative assistance and support shall be provided for the Board's functions. Implementation of the Board's recommendations through appropriate administrative action and followup is a condition of DHEW approval of an assurance. Board approvals, favorable actions, and recommendations are subject to review and to disapproval or further restriction by the institution officials. Board disapprovals, restrictions, or conditions cannot be rescinded or removed except by action of a Board described in the assurance approved by DHEW.

§ 46.19 Institution's records; confidentiality.

(a) Copies of all documents presented or required for initial and continuing review by the Institutional Review Board, such as Board minutes, records of subject's consent, transmittals on actions, instructions, and conditions resulting from Board deliberations addressed to the activity director, are to be retained by the institution, subject to the terms and conditions of grant and contract awards.

(b) Except as otherwise provided by law information in the records or possession of an institution acquired in con-

nection with an activity covered by this part, which information refers to or can be identified with a particular subject, may not be disclosed except:

(1) with the consent of the subject or his legally authorized representative; or

(2) as may be necessary for the Secretary to carry out his responsibilities under this part.

§ 46.20 Reports.

Each institution with an approved assurance shall provide the Secretary with such reports and other information as the Secretary may from time to time prescribe.

§ 46.21 Early termination of awards; evaluation of subsequent applications and proposals.

(a) If, in the judgment of the Secretary an institution has failed materially to comply with the terms of this policy with respect to a particular DHEW grant or contract, he may require that said grant or contract be terminated or suspended in the manner prescribed in applicable grant or procurement regulations.

(b) In evaluating applications or proposals for support of activities covered by this part, the Secretary may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) whether the applicant or offeror has been subject to a termination or suspension under paragraph (a) of this section, (2) whether the applicant or offeror or the person who would direct the scientific and technical aspects of an activity has in the judgment of the Secretary failed materially to discharge his, her, or its responsibility for the protection of the rights and welfare of subjects in his, her, or its care (whether or not DHEW funds were involved), and (3) whether, where past deficiencies have existed in discharging such responsibility, adequate steps have, in the judgment of the Secretary been taken to eliminate these deficiencies.

§ 46.22 Conditions.

The Secretary may with respect to any grant or contract or any class of grants or contracts impose additional conditions prior to or at the time of any award when in his judgment such conditions are necessary for the protection of human subjects.

[FR Doc.75-6621 Filed 3-12-75;8:45 am]

1032976

knowledge of the Animal and Plant Health Inspection Service.

Therefore, pursuant to the authority conferred upon the Deputy Administrator, Veterinary Services, Animal and Plant Health Inspection Service by § 97.1 of the regulations concerning overtime services relating to imports and exports (9 CFR 97.1), administrative instructions 9 CFR 97.2 (1976 ed.), as amended January 21, 1976 (41 FR 3074), April 16, 1976 (41 FR 16145), and July 23, 1976 (41 FR 30321), prescribing the commuted traveltime that shall be included in each period of overtime or holiday duty, are hereby amended by adding to or deleting from the respective lists therein as follows:

§ 97.2 Administrative instructions prescribing commuted traveltime.

* * * * *

WITHIN METROPOLITAN AREA

ONE HOUR

Add:

Los Angeles, California and Los Angeles Airport (served from Lawndale, California).

Add:

Madison, Wisconsin.

Delete:

Mobile, Alabama.

OUTSIDE METROPOLITAN AREA

TWO HOURS

Add:

Vernon, California (served from Lawndale, California).

Add:

Los Angeles Harbor, San Pedro, California: including Long Beach, Wilmington, and Terminal Island (served from Lawndale, California).

Add:

Middleton, Wisconsin (served from Madison, Wisconsin).

Add:

Sauk City, Wisconsin (served from Madison, Wisconsin).

Add:

Watertown, Wisconsin (served from Madison, Wisconsin).

THREE HOURS

Add:

Chilton, Wisconsin (served from Markesan, Wisconsin).

Add:

Hartford, Wisconsin (served from Markesan, Wisconsin).

Add:

Mineral Point, Wisconsin (served from Madison and Wauzeka Wisconsin).

Add:

Monroe, Wisconsin (served from Madison, Wisconsin).

Add:

Ontario, California (served from Lawndale, California).

Add:

Watertown, Wisconsin (served from Markesan, Wisconsin).

FOUR HOURS

Add:

Edwards Air Force Base, California (served from Lawndale, California).

Add:

Hartford, Wisconsin (served from Madison, Wisconsin).

Add:

Hueneme, California (served from Lawndale, California).

Add:

Milwaukee, Wisconsin (served from Madison, Wisconsin).

Add:

Newport Beach, California (served from Lawndale, California).

Add:

Sheboygan Falls, Wisconsin (served from Markesan, Wisconsin).

Delete:

Juda, Wisconsin (served from Madison, Wisconsin.)

Delete:

Sheboygan Falls, Wisconsin (served from Milwaukee and Ripon, Wisconsin).

FIVE HOURS

Add:

March Field, California (served from Lawndale, California).

Delete:

Juda, Wisconsin (served from Sauk City, Wisconsin).

SIX HOURS

Add:

Antelope Wells, New Mexico (served from Roswell and Socorro, New Mexico).

Add:

Chilton, Wisconsin (served from Madison, Wisconsin).

Add:

Columbus, New Mexico (served from Roswell and Socorro, New Mexico).

Add:

San Luis Obispo, California (served from Lawndale, California).

TEN HOURS

Delete:

Barron, Wisconsin (served from Sauk City, Wisconsin).

(64 Stat. 561; 7 U.S.C. 2260.)

Effective date. The foregoing amendments shall become effective November 30, 1976.

It is to the benefit of the public that these instructions be made effective at the earliest practicable date. It does not appear that public participation in this rulemaking proceeding would make additional relevant information available to the Department.

Accordingly, pursuant to 5 U.S.C. 553, it is found upon good cause that notice and public procedure on these instructions are impracticable, unnecessary, and contrary to the public interest and good cause is found for making them effective less than 30 days after publication in the FEDERAL REGISTER.

Done at Washington, D.C., this 23rd day of November 1976.

NOTE.—The Animal and Plant Health Inspection Service has determined that this document does not contain a major proposal requiring preparation of an Inflation Impact Statement under Executive Order 11821 and OMB Circular A-107.

PIERRE A. CHALOUX,
Acting Deputy Administrator,
Veterinary Services.

[FR Doc.76-35184 Filed 11-29-76;8:45 am]

Title 10—Energy

CHAPTER III—ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION

PART 745—PROTECTION OF HUMAN SUBJECTS

Adoption of Final Regulations

On August 17, 1976, a document entitled, "Protection of Human Subjects Proposed Regulations," (10 CFR Part 705—now 10 CFR Part 745) was published in the FEDERAL REGISTER (41 FR 34778). These proposed regulations have been altered in §§ 705.6, 705.10, 705.11, 705.16, and 705.19 (now 745.6, 745.10, 745.11, 745.16, and 745.19) as a result of comments received.

The proposed regulations intend to ensure the rights and welfare of human subjects in research activities supported by ERDA. Adequate review and approval of activities involving human subjects is primarily the responsibility of the institution which receives or is accountable to ERDA for the funds awarded.

Although ERDA intended to substantially duplicate the policies and procedures adopted by HEW (40 FR 11854, March 13, 1975), comments received in response to the proposed regulation identified differences that needed to be resolved between the two sets of regulations. The most significant issues were the membership requirements of the institutional review board (745.6) and the retention of records (745.19). To eliminate the problems caused by these differences, these and other ERDA sections have been altered to conform to the HEW regulations.

Accordingly, with the incorporated changes, the proposed regulations are adopted as set forth below.

Effective date: November 30, 1976.

JAMES L. LIVERMAN,
Assistant Administrator
for Environment and Safety.

The proposed regulations are adopted as follows:

Sec.

745.1 Applicability.
745.2 Policy.
745.3 Definitions.
745.4 Submission of assurances.
745.5 Types of assurances.
745.6 Minimum requirements for general assurances.
745.7 Minimum requirements for special assurances.

Sec.
745.8 Evaluation and disposition of assurances.
745.9 Obligation to obtain informed consent; prohibition of exculpatory clauses.
745.10 Documentation of informed consent.
745.11 Submission and certification of applications and proposals—general assurances.
745.12 Submission and certification of applications and proposals—special assurances.
745.13 Applications and proposals lacking definite plans for involvement of human subjects.
745.14 Applications and proposals submitted with the intent of not involving human subjects.
745.15 Evaluation and disposition of applications and proposals.
745.16 Cooperative activities.
745.17 Investigation new drug 30-day delay requirement.
745.18 Institution's executive responsibility.
745.19 Institution's records; confidentiality.
745.20 Reports.
745.21 Early termination of awards; evaluation of subsequent applications proposals.
745.22 Conditions.

AUTHORITY: Sec. 105(a) Energy Reorganization Act of 1974, Pub. L. 93-438.

§ 745.1 Applicability.

(a) The regulations in this part are applicable to all Energy Research and Development Administration (ERDA) agreements including, but not limited to, grants and contracts supporting research, development, and related activities within the United States and its territories in which human subjects are involved.

(b) For agreements supporting activities outside the United States and its territories in which human subjects are involved, the requirements of this part shall apply to the maximum extent practicable as determined by the Administrator on a case-by-case basis, taking into account the relevant laws and practices of the foreign nation in which the activity will be conducted.

(c) The Administrator may, from time to time, determine in advance whether specific programs, methods, or procedures to which this part is applicable place subjects at risk, as defined in § 745.3(b). Such determinations will be published as notices in the FEDERAL REGISTER and will be included in an appendix to this part.

§ 745.2 Policy.

(a) Safeguarding the rights and welfare of subjects at risk in activities supported under ERDA agreements is primarily the responsibility of the institution which receives, or is accountable to ERDA for, the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of ERDA that no activity involving human subjects within the United States and its territories to be supported by ERDA agreements shall be undertaken unless an Institutional Review Board has reviewed and approved such activity, and the institution has submitted to ERDA a certification of such review and approval, in accordance with the requirements of this part.

(b) This review shall determine whether these subjects will be placed at risk, and, if risk is involved, whether:

(1) the risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

(2) the rights and welfare of any such subjects will be adequately protected;

(3) legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provisions of this part; and

(4) the conduct of the activity will be reviewed at timely intervals.

(c) No agreement involving human subjects at risk shall be awarded to an individual unless he is affiliated with or sponsored by an institution which can and does assume responsibility for the subjects involved.

§ 745.3 Definitions.

(a) "Institution" means any public or private institution or agency (including Federal, State, and local government agencies).

(b) "Subject at risk" means any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

(c) "Informed consent" means the knowing consent of an individual or his legally authorized representative so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. The basic elements of information necessary to such consent include:

(1) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;

(2) a description of any attendant discomforts and risks reasonably to be pected;

(3) a description of any benefits reasonably to be expected;

(4) a disclosure of any appropriate alternative procedures that might be advantageous for the subject;

(5) an offer to answer any inquiries concerning the procedures; and

(6) an instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject.

(d) "ERDA" means the Energy Research and Development Administration.

(e) "Administrator" means the Administrator of ERDA or any other officer or employee of ERDA to whom authority has been delegated.

(f) "Agreement" means a grant, contract, cooperative agreement, or any other instrument under which ERDA provides funds or other resources for projects or efforts involving human subjects.

(g) "Approved assurance" means a document that fulfills the requirements of this part and is approved by the Administrator.

(h) "Certification" means the official institutional notification to ERDA in accordance with the requirements of this part that a project or activity involving human subjects at risk has been reviewed and approved by the institution in accordance with the "approved assurance" on file at ERDA.

(i) "Legally authorized representative" means an individual or judicial, or other body authorized under applicable law to consent on behalf of a prospective subject to such subject's participation in the particular activity or procedure.

§ 745.4 Submission of assurances.

(a) Recipients or prospective recipients of ERDA support under any agreement involving subjects at risk shall provide written assurance acceptable to ERDA that they will comply with ERDA policy as set forth in this part. Each assurance shall embody (1) A statement of compliance with ERDA requirements for initial and continuing Institutional Review Board review of the supported activities; and (2) A set of implementing guidelines, including identification of the Board and a description of its review procedures; or, in the case of special assurance concerned with single activities or projects, a report of initial findings of the Board and of its proposed continuing review procedures.

(b) Such assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this part, and shall be filed in such form and manner as the Administrator may require.

§ 745.5 Types of assurances.

(a) *General assurances.* A general assurance describes the review and implementation procedures applicable to all ERDA-supported activities conducted by an institution, regardless of the number, location, or types of its components or field activities. General assurances will be required from institutions having a significant number of concurrent ERDA-supported projects or activities involving human subjects.

(b) *Special assurances.* A special assurance will, as a rule, describe those review and implementation procedures applicable to a single activity or project. A special assurance will not be solicited or accepted from an institution which has on file with ERDA an approved general assurance.

§ 745.6 Minimum requirements for general assurances.

General assurances shall be submitted in such form and manner as the Administrator may require. The institution must include, as part of its general as-

10329718

surance, implementing guidelines that specifically provide for:

(a) A statement of principles which will govern the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may include appropriate existing codes or declarations, or statements formulated by the institution itself. It is to be understood that no such principles supersede ERDA policy or applicable law.

(b) An Institutional Review Board or Board structure which will conduct initial and continuing reviews in accordance with the policy outlined in § 745.2. Such a Board or Board structure shall meet the following requirements:

(1) The Board must be composed of not less than five persons with varying backgrounds to assure complete and adequate review of activities commonly conducted by the institution. The Board must be sufficiently qualified through the maturity, experience, and expertise of its members, and diversity of its membership, to insure respect for its advice and counsel for safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific activities, the Board must be able to ascertain the acceptability of applications and proposals in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. The Board must, therefore, include persons whose concerns are in these areas.

(2) The Board members shall be identified to ERDA by name; earned degrees, if any; position or occupation; representative capacity; and by other pertinent indications of experience, such as board certification, licenses, etc., sufficient to describe each member's chief anticipated contributions to Board deliberations. Any employment or other relationship between each member and the institution shall be identified, i.e., full-time employee, part-time employee, member of governing panel or board, paid consultant, or unpaid consultant. Changes in Board membership shall be reported to ERDA in such form and at such times as the Administrator may require.

(3) No member of a Board shall be involved in either the initial or continuing review of an activity in which he has a conflicting interest, except to provide information requested by the Board.

(4) No Board shall consist entirely of persons who are officers, employees, or agents of, or are otherwise associated with, the institution, apart from their membership on the Board.

(5) No Board shall consist entirely of members of a single professional group.

(6) The quorum of the Board shall be defined, but may in no event be less than a majority of the total membership duly convened to carry out the Board's responsibilities under the terms of the assurance.

(c) Procedures which the institution will follow in its initial and continuing review of applications, proposals, and activities.

(d) Procedures which the Board will follow: (1) To provide advice and counsel to activity directors and investigators with regard to the Board's actions, (2) To insure prompt reporting to the Board of proposed changes in an activity, and of unanticipated problems involving risk to subjects or others, and (3) To insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope-labelled drugs, or to medical devices, are promptly reported to ERDA.

(e) Procedures which the institution will follow to maintain an active and effective Board and to implement its recommendations.

§ 745.7 Minimum requirements for special assurances.

Special assurances shall be submitted in such form and manner as the Administrator may require. An acceptable special assurance shall:

(a) Identify the specific agreement involved by its full title and by the name of the activity or project director, principal investigator, fellow, or other person immediately responsible for the conduct of the activity.

(b) Include a statement, executed by an appropriate institutional official, indicating that the institution has established an Institutional Review Board satisfying the requirements of § 745.6(b).

(c) Describe the makeup of the Board and the training, experience, and background of its members as required by § 745.6(b)(2).

(d) Describe, in general terms, the risks to subjects that the Board recognizes as inherent in the activity, and justify its decision that these risks are so outweighed by the sum of the benefit to the subject, and the importance of the knowledge to be gained, as to warrant the Board's decision to permit the subject to accept these risks.

(e) Describe the informed consent procedures to be used, and attach documentation as required by § 745.10.

(f) Describe procedures which the Board will follow to insure prompt reporting to the Board of proposed changes in the activity, and of any unanticipated problems involving risks to subjects or others, to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope-labelled drugs, or to medical devices, are promptly reported to ERDA.

(g) Indicate at what time intervals the Board will meet to provide for continuing review. Such review must occur no less than annually.

(h) Be signed by the individual members of the Board and be endorsed by an appropriate institutional official.

§ 745.8 Evaluation and disposition of assurances.

(a) All assurances submitted in accordance with §§ 745.6 and 745.7 shall be evaluated by the Administrator through such officers and employees of ERDA as he determines to be appropriate. The Administrator's evaluation shall take into consideration, among other pertinent factors, the adequacy of the proposed Institutional Review Board in light of the anticipated scope of the applicant institution's activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

(b) On the basis of his evaluation of an assurance, pursuant to paragraph (a) of this section, the Administrator shall: (1) Approve, (2) Enter into negotiations to develop a more satisfactory assurance, or (3) Disapprove. With respect to approved assurances, the Administrator may determine the period during which any particular assurance or class of assurances shall remain effective or otherwise condition or restrict his approval. With respect to negotiations, the Administrator may, pending completion of negotiations for a general assurance, require an institution, otherwise eligible for such an assurance, to submit specific assurances.

§ 745.9 Obligation to obtain informed consent; prohibition of exculpatory clauses.

Any institution proposing to place any subject at risk is obligated to obtain and document legally effective informed consent. No such informed consent, oral or written, obtained under an assurance provided pursuant to this part shall include any exculpatory language through which the subject is made to waive, or to appear to waive, any of his legal rights including any release of the institution or its agents from liability for negligence.

§ 745.10 Documentation of informed consent.

The actual procedure utilized in obtaining legally effective informed consent and the basis for Institutional Review Board determinations that the procedures are adequate and appropriate shall be fully documented. The documentation of consent will employ one of the following three forms:

(a) Provision of a written consent document embodying all of the basic elements of informed consent. This may be read to the subject or to his legally authorized representative, but in any event he or his legally authorized representative must be given adequate opportunity to read it. This document is to be signed by the subject or his legally authorized representative. Sample copies of the consent form, as approved by the Board, are to be retained in its records.

(b) Provision of a "short form" written consent document indicating that the basic elements of informed consent have been presented orally to the subject or his legally authorized representative. Written summaries of what is to be said to the subject are to be approved by the Board. The short form is to be signed by the subject or his legally authorized representative and by an auditor witness to the oral presentation and to the subject's signature. A copy of the approved summary, annotated to show any additions, is to be signed by the persons officiating obtaining the consent and by the auditor witness. Sample copies of the consent

1032979

prime contractor. If, in such instances, the grantee or prime contractor obtains access to all or some of the subjects involved through one or more cooperating institutions, the basic ERDA policy applies and the grantee or prime contractor remains responsible for safeguarding the rights and welfare of the subjects.

(a) *Institutions with approved general assurances.* Initial and continuing review by the institution may be carried out by one or a combination of procedures:

(1) *Cooperating institution with approved general assurance.* When the cooperating institution has on file with ERDA an approved general assurance, the grantee or prime contractor may, in addition to its own review, request the cooperating institution to conduct an independent review, and to report its recommendations on those aspects of the activity that concern individuals for whom the cooperating institution has responsibility under its own assurance to the grantee's or prime contractor's Institutional Review Board. The grantee or prime contractor may, at its discertion, concur with or further restrict the recommendations of the cooperating institution. It is the responsibility of the grantee or prime contractor to maintain communication with the Boards of the cooperating institution. However, the cooperating institution shall promptly notify the grantee or contracting institution whenever the cooperating institution finds the conduct of the project or activity within its purview to be unsatisfactory.

(2) *Cooperating institution with no approved general assurance.* When the cooperating institution does not have an approved general asusrance on file with ERDA, ERDA may require the submission of a general or special assurance which, if approved, will permit the grantee or prime contractor to follow the procedure outlined in the preceding subparagraph.

(3) *Interinstitutional joint review.* The grantee or prime contracting institution may wish to develop an agreement with cooperating institutions to provide for an Institutional Review Board with representatives from cooperating institutions. Representatives of cooperating institutions may be appointed as ad hoc members of the grantee or contracting institution's existing Institutional Review Board or, if cooperating is on a frequent or continuing basis, as between a medical school and a group of affiliated hospitals, appointments for extended periods may be made. All such cooperative arrangements must be approved by ERDA as part of a general assurance, or as an amendment to a general assurance.

(b) *Institutions with special assurances.* While responsibility for initial and continuing review necessarily lies with the grantee or prime contracting institution, ERDA may also require approved assurance from those cooperating institutions having immediate responsibility for subjects. If the cooperating institution has on file with ERDA an approved general assurance, the grantee or prime contractor shall request the cooperating institution to conduct its own independent review of those aspects of the project or activity which will involve human subjects for which it has responsibility. Such a request shall be in writing and should provide for direct notification of the grantee's or pmime contractor's Institutional Review Board in the event that the cooperating institution's Board finds the conduct of the activity to be unsatisfactory. If the cooperating institution does not have an approved general assurance on file with ERDA, it must submit to ERDA a general or special assurance which is determined by ERDA to comply with the provisions of this part.

§ 745.17 Investigational new drug 30-day delay requirement.

Where an institution is required to prepare or to submit a certification under §§ 745.11, 745.12, 745.13, or 745.14, and the application or proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification, together with a statement that the 30-day delay required by 21 CFR 312.1(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to ERDA upon such expiration, or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received.

§ 745.18 Institution's executive responsibility.

Specific executive functions to be conducted by the institution include policy development and promulgation and continuing indoctrination of personnel. Appropriate administrative assistance and support shall be provided for the Board's functions. Implementation of the Board's recommendations through appropriate administrative action and follow-up is a condition of ERDA approval of an assurance. Board approvals, favorable actions, and recommendations are subject to review and to disapproval or further restriction by the institution officials. Board disapprovals, restrictions, or conditions cannot be rescinded or removed except by action of a Board described in the assurance approved by ERDA.

§ 745.19 Institution's records: confidentiality.

(a) Copies of all documents presented, or required for initial and continuing review by the Institutional Review Board, and documents such as Board minutes, records of subject's consent, transmittals on actions, instructions, and conditions resulting from Board deliberations addressed to the activity director, are to be retained by the institution permanently unless permission is obtained from the Administrator to destroy specific records.

(b) Except as otherwise provided by law, information in the records or possession of an institution acquired in connection with an activity covered by this part, which information refers to or can be identified with a particular subject, may not be disclosed except:

(1) with the consent of the subject or his legally authorized representative; or

(2) as may be necessary for the Administrator to carry out his responsibilities under this part.

§ 745.20 Reports.

Each institution with an approved assurance shall provide the Administrator with such reports and other information as the Administrator may, from time to time, prescribe.

§ 745.21 Early termination of awards: evaluation of subsequent applications and proposals.

(a) If, in the judgment of the Administrator, an institution has failed materially to comply with the terms of this policy with respect to a particular ERDA agreement, he may require that said agreement be terminated or suspended in the manner prescribed in applicable regulations.

(b) In evaluating applications or proposals for support of activities covered by this part, the Administrator may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) Whether the applicant or offeror has been subject to a termination or suspension under paragraph (a) of this section, (2) Whether the applicant, offeror, or the person who would direct the scientific and technical aspects of an activity has, in the judgment of the Administrator, failed materially to discharge his, her, or its responsibility for the protection of the rights and welfare of subjects in his, her, or its care (whether or not ERDA funds were involved, and (3) Whether, where past deficiencies have existed in discharging such responsibility, adequate steps have in the judgment of the Administrator been taken to eliminate these deficiencies.

§ 745.22 Conditions.

The Administrator may, with respect to any agreement or any class of agreements, impose additional conditions prior to or at the time of any award when in his judgment such conditions are necessary for the protection of human subjects.

[FR Doc.76-35154 Filed 11-29-76;8:45 am]

Title 12—Banks and Banking

CHAPTER I—COMPTROLLER OF THE CURRENCY, DEPARTMENT OF THE TREASURY

PART 4—DESCRIPTION OF OFFICE, PROCEDURES, PUBLIC INFORMATION

Revision of List of Forms Currently in Use

This amendment is issued under authority of the National Bank Act, 12 U.S.C. 1 et seq., pursuant to the requirement of 5 U.S.C. 552 that each agency publish in the FEDERAL REGISTER descriptions of agency forms and instructions which are available to and which may be obtained by the public. The amendment

prime contractor. If, in such instances, the grantee or prime contractor obtains access to all or some of the subjects involved through one or more cooperating institutions, the basic ERDA policy applies and the grantee or prime contractor remains responsible for safeguarding the rights and welfare of the subjects.

(a) *Institutions with approved general assurances.* Initial and continuing review by the institution may be carried out by one or a combination of procedures:

(1) *Cooperating institution with approved general assurance.* When the cooperating institution has on file with ERDA an approved general assurance, the grantee or prime contractor may, in addition to its own review, request the cooperating institution to conduct an independent review, and to report its recommendations on those aspects of the activity that concern individuals for whom the cooperating institution has responsibility under its own assurance to the grantee's or prime contractor's Institutional Review Board. The grantee or prime contractor may, at its discretion, concur with or further restrict the recommendations of the cooperating institution. It is the responsibility of the grantee or prime contractor to maintain communication with the Boards of the cooperating institution. However, the cooperating institution shall promptly notify the grantee or contracting institution whenever the cooperating institution finds the conduct of the project or activity within its purview to be unsatisfactory.

(2) *Cooperating institution with no approved general assurance.* When the cooperating institution does not have an approved general assurance on file with ERDA, ERDA may require the submission of a general or special assurance which, if approved, will permit the grantee or prime contractor to follow the procedure outlined in the preceding subparagraph.

(3) *Interinstitutional joint review.* The grantee or prime contracting institution may wish to develop an agreement with cooperating institutions to provide for an Institutional Review Board with representatives from cooperating institutions. Representatives of cooperating institutions may be appointed as ad hoc members of the grantee or contracting institution's existing Institutional Review Board or, if cooperating is on a frequent or continuing basis, as between a medical school and a group of affiliated hospitals, appointments for extended periods may be made. All such cooperative arrangements must be approved by ERDA as part of a general assurance, or as an amendment to a general assurance.

(b) *Institutions with special assurances.* While responsibility for initial and continuing review necessarily lies with the grantee or prime contracting institution, ERDA may also require approved assurance from those cooperating institutions having immediate responsibility for subjects. If the cooperating institution has on file with ERDA an approved general assurance, the grantee or prime contractor shall request the cooperating institution to conduct its own independent review of those aspects of the project or activity which will involve human subjects for which it has responsibility. Such a request shall be in writing and should provide for direct notification of the grantee's or pmime contractor's Institutional Review Board in the event that the cooperating institution's Board finds the conduct of the activity to be unsatisfactory. If the cooperating institution does not have an approved general assurance on file with ERDA, it must submit to ERDA a general or special assurance which is determined by ERDA to comply with the provisions of this part.

§ 745.17 Investigational new drug 30-day delay requirement.

Where an institution is required to prepare or to submit a certification under §§ 745.11, 745.12, 745.13, or 745.14, and the application or proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification, together with a statement that the 30-day delay required by 21 CFR 312.1(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to ERDA upon such expiration, or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received.

§ 745.18 Institution's executive responsibility.

Specific executive functions to be conducted by the institution include policy development and promulgation and continuing indoctrination of personnel. Appropriate administrative assistance and support shall be provided for the Board's functions. Implementation of the Board's recommendations through appropriate administrative action and follow-up is a condition of ERDA approval of an assurance. Board approvals, favorable actions, and recommendations are subject to review and to disapproval or further restriction by the institution officials. Board disapprovals, restrictions, or conditions cannot be rescinded or removed except by action of a Board described in the assurance approved by ERDA.

§ 745.19 Institution's records: confidentiality.

(a) Copies of all documents presented, or required for initial and continuing review by the Institutional Review Board, and documents such as Board minutes, records of subject's consent, transmittals on actions, instructions, and conditions resulting from Board deliberations addressed to the activity director, are to be retained by the institution permanently unless permission is obtained from the Administrator to destroy specific records.

(b) Except as otherwise provided by law, information in the records or possession of an institution acquired in connection with an activity covered by this part, which information refers to or can be identified with a particular subject, may not be disclosed except:

(1) with the consent of the subject or his legally authorized representative; or

(2) as may be necessary for the Administrator to carry out his responsibilities under this part.

§ 745.20 Reports.

Each institution with an approved assurance shall provide the Administrator with such reports and other information as the Administrator may, from time to time, prescribe.

§ 745.21 Early termination of awards: evaluation of subsequent applications and proposals.

(a) If, in the judgment of the Administrator, an institution has failed materially to comply with the terms of this policy with respect to a particular ERDA agreement, he may require that said agreement be terminated or suspended in the manner prescribed in applicable regulations.

(b) In evaluating applications or proposals for support of activities covered by this part, the Administrator may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) Whether the applicant or offeror has been subject to a termination or suspension under paragraph (a) of this section, (2) Whether the applicant, offeror, or the person who would direct the scientific and technical aspects of an activity has, in the judgment of the Administrator, failed materially to discharge his, her, or its responsibility for the protection of the rights and welfare of subjects in his, her, or its care (whether or not ERDA funds were involved, and (3) Whether, where past deficiencies have existed in discharging such responsibility, adequate steps have in the judgment of the Administrator been taken to eliminate these deficiencies.

§ 745.22 Conditions.

The Administrator may, with respect to any agreement or any class of agreements, impose additional conditions prior to or at the time of any award when in his judgment such conditions are necessary for the protection of human subjects.

[FR Doc.76-35154 Filed 11-29-76;8:45 am]

Title 12—Banks and Banking

CHAPTER I—COMPTROLLER OF THE CURRENCY, DEPARTMENT OF THE TREASURY

PART 4—DESCRIPTION OF OFFICE, PROCEDURES, PUBLIC INFORMATION

Revision of List of Forms Currently in Use

This amendment is issued under authority of the National Bank Act, 12 U.S.C. 1 et seq., pursuant to the requirement of 5 U.S.C. 552 that each agency publish in the FEDERAL REGISTER descriptions of agency forms and instructions which are available to and which may be obtained by the public. The amendment

CV's - ORAU/ORNL Committee on Human Studies 10/14/76

Name: Gould A. Andrews
Position: Internist, Director of Clinical Applications
School: University of Michigan, A.B., 1940
University of Michigan, M.D., 1943
Licensure: Tennessee
Boards: Internal Medicine, Nuclear Medicine
Memberships: Society for Experimental Biology and Medicine
American Association for Cancer Research
American Thyroid Association
Society of Nuclear Medicine
Southern Society for Clinical Research
American Medical Association
American Association for the Advancement of Science
American Federation for Clinical Research
Fellow, American College of Physicians
American Society of Hematology (1968)
Health Physics Society, East Tennessee Chapter
Tennessee Academy of Science
Tennessee Blood Club

Name: A. Bertrand Brill
Position: Associate Professor of Medicine and Radiology,
Vanderbilt School of Medicine
School: Grinnell, A.B., 1949
University of Utah, M.D., 1956
University of California, Berkeley, Ph.D., 1961
Licensure: Tennessee
Memberships: American Association for the Advancement of Science
Society of Nuclear Medicine
Radiation Research Society
American Thyroid Association
Other Indication of Experience and Competence:
Medical Director, Division of Radiological Health,
U.S. Public Health Service, 1957-1964, Rockville, Md.

Name: Donald W. Goodwin
Position: Minister, United Church, Chapel-on-the-Hill
School: Bangor Theological Seminary, Bachelor of Divinity, 1959
Brown University, Ph.D., 1965
Memberships: Ministerial Standing, United Church of Christ
Additional Information:
Member of various boards which change from time to time

Name: Karl F. Hübner
Position: Internist, Chief of Outpatient Clinical Studies
School: University of Heidelberg, M.D., 1959
Licensure: Tennessee
Memberships: Roane-Anderson County Medical Society
Tennessee Medical Association
American Medical Association

Name: Melvin E. Koons
Position: Executive Assistant to President, Union Carbide Corporation Nuclear Division
School: University of North Dakota, B.A., 1955, Juris Doctor 1961
Admitted to Practice of Law:
North Dakota 1961; Tennessee 1964; Federal District Court, North Dakota 1961; East Tennessee 1964; U. S. Supreme Court, 1966
Memberships: American Bar Association
Public Contracts Section
Federal Bar Association
Government Contracts Committee
R & D Contracts Subcommittee
Tennessee Bar Association
North Dakota Bar Association, Ward County

Name: Robert Lange
Position: Research Professor; Assistant Director, University of Tennessee Memorial Research Center
School: Macalester College, B.A.
Washington University, M.D., 1944
Licensure: Tennessee, Minnesota, Missouri, Georgia
Board: Internal Medicine
Memberships: American Association for the Advancement of Science
American Medical Association
Knoxville Academy of Medicine
Southern Society of Research
Central Society of Clinical Research
American College of Physicians
International Society of Hematology

Name: Michael Scott Lawyer
Position: Staff Attorney, Oak Ridge Associated Universities
School: University of Mississippi, B.P.A., 1968; Juris Doctor, 1970
Admissions: Mississippi, 1970; U. S. District Court, Northern District of Mississippi, 1970
U. S. Court of Military Appeals, 1971
U. S. Tax Court, 1975
U. S. Court of Claims, 1975
U. S. Supreme Court, 1975
Memberships: Federal Bar Association
Government Contracts and Administrative Law Committees
Mississippi Bar Association

1032983

Name:	Thomas A. Lincoln
Position:	Director, Health Division, Oak Ridge National Laboratory
School:	Macalester College, St. Paul, Minnesota, B.A. (Chemistry), 1946 University of Minnesota, Minneapolis, B.S., 1947; B.M., 1949; and M.D., 1950. Rotating Internship, Ancker Hospital, St. Paul, 1949-1950
Licensure:	Tennessee, Minnesota
Board:	American Board of Preventive Medicine, by examination, June 5, 1963
Memberships:	Fellow Industrial Medical Association Past President, Tenn. Industrial Medical Association American Academy of Occupational Medicine American Medical Association Past President, Roane-Anderson County Medical Society Treasurer, Board of Directors, Oak Ridge Regional Mental Health Center

Name:	Clarence C. Lushbaugh
Position:	Chairman, Medical and Health Sciences Division Director, Radiation Emergency Assistance Center/ Training Site (REAC/TS)
School:	University of Chicago, B.S., 1938 (Anatomy) University of Chicago, Ph.D., 1942 (Pathology) University of Chicago, M.D., 1948 (Pathology)
Licensure:	Tennessee
Memberships:	American Association for the Advancement of Science American Society for Experimental Pathology Associated Researchers and Clinicians in Cancer Society for Experimental Biology and Medicine Health Physics Society Radiation Research Society Society of Nuclear Medicine American Medical Society Tennessee State Medical Society

Name:	John B. Storer
Position:	Director, Biology Division, Oak Ridge National Laboratory
School:	University of Chicago, M.D., 1947
Memberships:	American Association for Cancer Research American Society for Experimental Pathology Radiation Research Society Society for Experimental Biology and Medicine National Council on Radiation Protection and Measurements

Name:	Joan B. Woods
Position:	Psychiatrist, Veterans Administration Hospital, Murfreesboro, Tennessee
School:	University of Chicago School of Medicine, B.S. and M.D., 1960
Licensure:	Tennessee
Boards:	American Board of Psychiatry and Neurology
Memberships:	American Psychiatric Association American Medical Association and Subsidiaries

1032984

Committee Members and Their Responsible Area

(On January 1, 1977, the following members constituted the Committee and had these stated responsibilities.)

O Robert Lange, M.D. (Univ. Tenn.), Chairman, Extramural Representative
Gould A. Andrews, M.D. (ORAU), Secretary
OO John B. Storer, M.D., Official ORNL Representative
OO C. C. Lushbaugh, Ph.D., M.D., Official ORAU Representative
O A. Bertrand Brill (Vanderbilt Univ.), Extramural Representative
* Melvin E. Koons (UCNC), Lawyer
* M. Scott Lawyer (ORAU), Lawyer
O* Donald W. Goodwin, Ph.D. (United Church, O.R.), Minister
OW Joan B. Woods, M.D. (VA Hosp., Murfreesboro), Psychiatrist
Thomas A. Lincoln, M.D. (ORNL), Occupational Medicine
Karl F. Hübner, M.D. (ORAU), Clinical Research
*W Edythalena Tompkins, A.B. (ORAU), Epidemiology

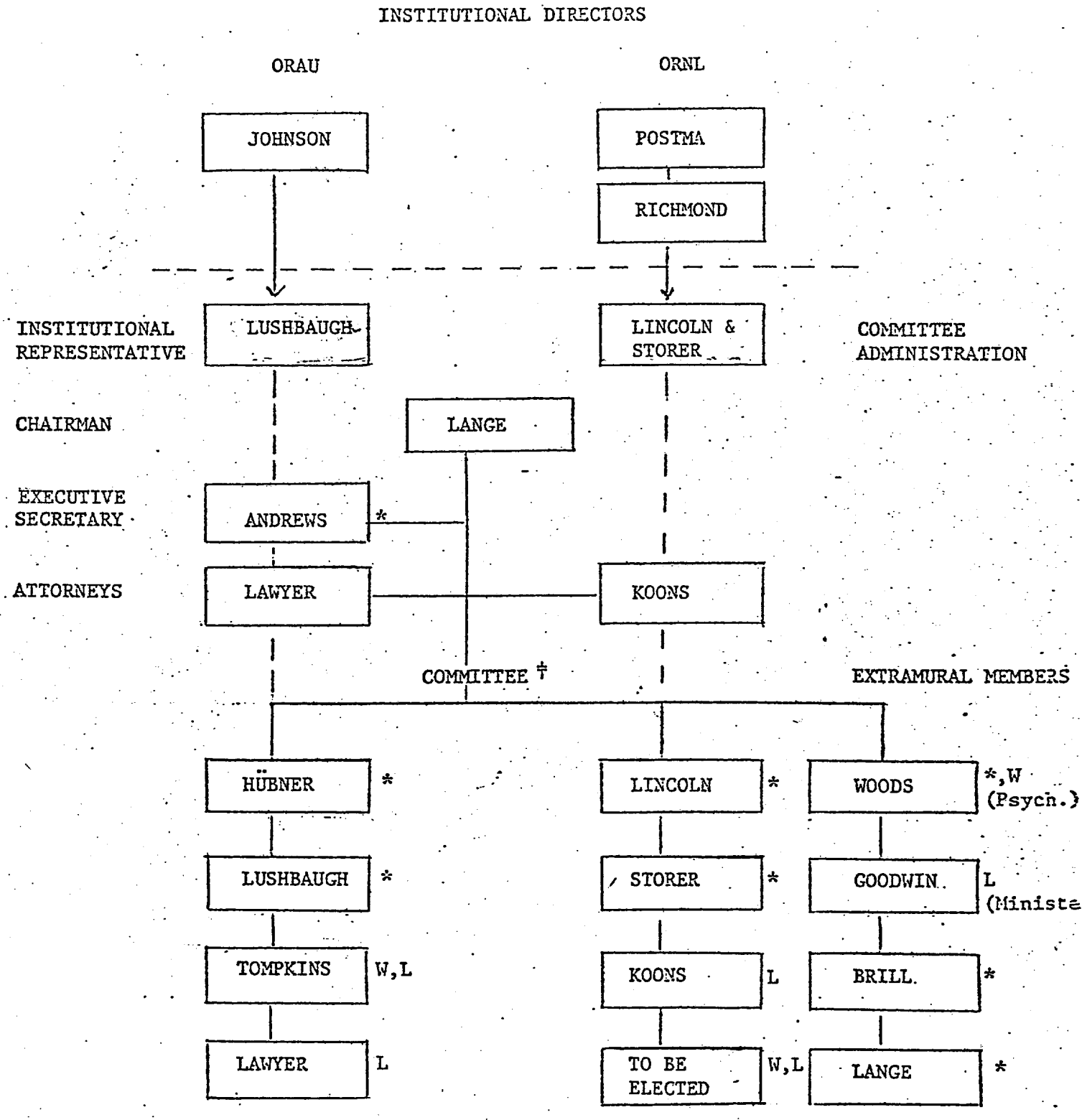
O - Extramural member
OO - Institutional representative
* - Non-M.D. member
W - Woman member

1032985

Annex 6 – Block diagram of the bi-institutional Committee Structure, administration, lines of authority and present membership and functional identities

BLOCK DIAGRAM OF ADMINISTRATIVE AND MEMBERSHIP STRUCTURE OF

ORAU/ORNL COMMITTEE ON HUMAN STUDIES 1977



1032986

* = M.D.
W = Woman
L = Layperson

†ON ORNL PROPOSALS, ORNL AFFILIATES DO NOT VOTE:
ON ORAU PROPOSALS, ORAU AFFILIATES DO NOT VOTE.

Ident. No._____

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date_____

Principal Investigator: _____

Co-Investigators: _____

_____

_____

_____

Title of Project: _____

_____

Use Following Format (Submit Original and 8 Copies)

I. Objectives of Experiment:

(Include statement why experiment must be done in humans, and expected benefits from the knowledge.)

II. Methods of Procedure:

Brief description of methods, all medications including name and dose range, number and types of subjects anticipated, time for single session, total number of sessions, total duration of study, methods used to screen subjects, etc.

III. Possible Hazards and their Evaluation:

IV. Radioisotopes and New Drugs

If the study involves radioisotopes, indicate action of the Isotopes Committee. If new drugs are involved, indicate that appropriate application to FDA has been made.

See page 2

1032987

Title of Project: _____

Ident. No. _____

V. Responsibility of Principal Investigator:

Include statement of your procedures for protecting rights of the patients and gaining informed consent.

The principal investigator will follow the procedures of the Committee on Human Studies in obtaining "informed consent" from the subjects under study. The investigator recognizes that he retains the primary responsibility for safe-guarding the interests of the participants under study. Any significant changes in methods of procedure or of the development of unexpected risks will be brought to the attention of the Committee on Human Studies.

Starting Date_____

Signatures: _____Principal Investigator

_____ Co-Investigator

_____ "

_____ "

_____ "

_____ "

DIVISION REVIEW:

The application described above has been reviewed and approved.

Official signing for the institution:

Signature_____

Title _____

Institution_____

Date _____

1032988

(Revised January 1972)

MEDICAL AND HEALTH SCIENCES DIVISION
OAK RIDGE ASSOCIATED UNIVERSITIES
Oak Ridge, Tennessee

Annex 8 Example of a typical informed consent form for a specific project

Consent for Experimental Test

I authorize the performance upon _____
(myself or name of patient)
of the following test: Phase I radiopharmaceutical tests of DL-valine-1-^{11}C for pancreas visualization.

The nature and purpose of the test, the risks involved, and the possibilities of complications have been explained to me. I understand that this test is not a treatment for my disorder nor is it being done primarily for my benefit, rather that the test is for experimental purposes. Further, I understand that any information gained from doing this test becomes the property of ORAU and may be published in the scientific literature at the discretion of the staff of the Medical and Health Sciences Division, Oak Ridge Associated Universities.

DATE _____ _____
(Patient or person authorized to consent for patient)

WITNESS: _____

_____

I have talked with _____ about the proposed test to be given including the following:

1. This is a new radioactive drug: DL-Valine-1-^{11}C.
2. The drug contains the radioactive isotope ^{11}C and an organic chemical in quantities much less than those required to produce any measurable chemical effect in the body. Patient should feel no effect from the drug.
3. The radiation dose will be approximately 0.25-0.5 rad to the whole body.
4. Blood samples (2 ml) will be drawn at intervals during a period of 1-1/2 hours after administration.
5. Whole body counts and scans will be made over a 2-hr period.
6. The patient may withdraw from the test at any time.

DATE: _____ _____
Investigator

1032989

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☐ FOLLOWUP ☐ REVISION

☐ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☐ RENEWAL ☐ CONTINUATION

APPLICATION IDENTIFICATION NUMBER *(If known)*

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of Public Law 93-348, as implemented by Part 46 of Title 45 of the Code of Federal Regulations, as amended, (45 CFR 46). Administration of the DHEW policy and regulation is the responsibility of the Office for Protection from Research Risks, National Institutes of Health, Bethesda, Md 20014.

1. TITLE OF PROPOSAL OR ACTIVITY

2. PRINCIPAL INVESTIGATOR/ACTIVITY DIRECTOR/FELLOW

3. DECLARATION THAT HUMAN SUBJECTS EITHER WOULD OR WOULD NOT BE INVOLVED

☐ A. NO INDIVIDUALS WHO MIGHT BE CONSIDERED HUMAN SUBJECTS, INCLUDING THOSE FROM WHOM ORGANS, TISSUES, FLUIDS, OR OTHER MATERIALS WOULD BE DERIVED, OR WHO COULD BE IDENTIFIED BY PERSONAL DATA, WOULD BE INVOLVED IN THE PROPOSED ACTIVITY. (IF NO HUMAN SUBJECTS WOULD BE INVOLVED, CHECK THIS BOX AND PROCEED TO ITEM 7. PROPOSALS DETERMINED BY THE AGENCY TO INVOLVE HUMAN SUBJECTS WILL BE RETURNED.)

☐ B. HUMAN SUBJECTS WOULD BE INVOLVED IN THE PROPOSED ACTIVITY AS EITHER: ☐ NONE OF THE FOLLOWING, OR INCLUDING: ☐ MINORS, ☐ FETUSES, ☐ ABORTUSES, ☐ PREGNANT WOMEN, ☐ PRISONERS, ☐ MENTALLY RETARDED, ☐ MENTALLY DISABLED. UNDER SECTION 6. COOPERATING INSTITUTIONS, ON REVERSE OF THIS FORM, GIVE NAME OF INSTITUTION AND NAME AND ADDRESS OF OFFICIAL(S) AUTHORIZING ACCESS TO ANY SUBJECTS IN FACILITIES NOT UNDER DIRECT CONTROL OF THE APPLICANT OR OFFERING INSTITUTION.

DECLARATION OF ASSURANCE STATUS/CERTIFICATION OF REVIEW

☐ A. THIS INSTITUTION HAS NOT PREVIOUSLY FILED AN ASSURANCE AND ASSURANCE IMPLEMENTING PROCEDURES FOR THE PROTECTION OF HUMAN SUBJECTS WITH THE DHEW THAT APPLIES TO THIS APPLICATION OR ACTIVITY. ASSURANCE IS HEREBY GIVEN THAT THIS INSTITUTION WILL COMPLY WITH REQUIREMENTS OF *DHEW Regulation 45 CFR 46*, THAT IT HAS ESTABLISHED AN INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS AND, WHEN REQUESTED, WILL SUBMIT TO DHEW DOCUMENTATION AND CERTIFICATION OF SUCH REVIEWS AND PROCEDURES AS MAY BE REQUIRED FOR IMPLEMENTATION OF THIS ASSURANCE FOR THE PROPOSED PROJECT OR ACTIVITY.

☐ B. THIS INSTITUTION HAS AN APPROVED GENERAL ASSURANCE (DHEW ASSURANCE NUMBER _____) OR AN ACTIVE SPECIAL ASSURANCE FOR THIS ONGOING ACTIVITY, ON FILE WITH DHEW. THE SIGNER CERTIFIES THAT ALL ACTIVITIES IN THIS APPLICATION PROPOSING TO INVOLVE HUMAN SUBJECTS HAVE BEEN REVIEWED AND APPROVED BY THIS INSTITUTION'S INSTITUTIONAL REVIEW BOARD IN A CONVENED MEETING ON THE DATE OF _____ IN ACCORDANCE WITH THE REQUIREMENTS OF THE *Code of Federal Regulations on Protection of Human Subjects (45 CFR 46)*. THIS CERTIFICATION INCLUDES, WHEN APPLICABLE, REQUIREMENTS FOR CERTIFYING FDA STATUS FOR EACH INVESTIGATIONAL NEW DRUG TO BE USED (SEE REVERSE SIDE OF THIS FORM).

THE INSTITUTIONAL REVIEW BOARD HAS DETERMINED, AND THE INSTITUTIONAL OFFICIAL SIGNING BELOW CONCURS THAT:

EITHER ☐ HUMAN SUBJECTS WILL NOT BE AT RISK; OR ☐ HUMAN SUBJECTS WILL BE AT RISK.

5. AND 6. SEE REVERSE SIDE

7. NAME AND ADDRESS OF INSTITUTION

8. TITLE OF INSTITUTIONAL OFFICIAL	TELEPHONE NUMBER
SIGNATURE OF INSTITUTIONAL OFFICIAL	DATE

HEW-596 (Rev. 4-75)

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO REQUESTING AGENCY.

1032990

5. INVESTIGATIONAL NEW DRUGS - ADDITIONAL CERTIFICATION REQUIREMENT

SECTION 46.17 OF TITLE 45 OF THE Code of Federal Regulations states, "Where an organization is required to prepare or to submit a certification . . . and the proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 130.3(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received."

INVESTIGATIONAL NEW DRUG CERTIFICATION

TO CERTIFY COMPLIANCE WITH FDA REQUIREMENTS FOR PROPOSED USE OF INVESTIGATIONAL NEW DRUGS IN ADDITION TO CERTIFICATION OF INSTITUTIONAL REVIEW BOARD APPROVAL, THE FOLLOWING REPORT FORMAT SHOULD BE USED FOR EACH IND (ATTACH ADDITIONAL IND CERTIFICATIONS AS NECESSARY).

- IND FORMS FILED: ☐ FDA 1571, ☐ FDA 1572, ☐ FDA 1573

- NAME OF IND AND SPONSOR _____

- DATE OF 30-DAY EXPIRATION OR FDA WAIVER
  (FUTURE DATE REQUIRES FOLLOWUP REPORT TO AGENCY) _____

- FDA RESTRICTION _____

- SIGNATURE OF INVESTIGATOR _____ DATE _____

6. COOPERATING INSTITUTIONS - ADDITIONAL REPORTING REQUIREMENT

SECTION 46.116 OF TITLE 45 OF THE *Code of Federal Regulations* IMPOSES SPECIAL REQUIREMENTS ON THE CONDUCT OF STUDIES OR ACTIVITIES IN WHICH THE GRANTEE OR PRIME CONTRACTOR OBTAINS ACCESS TO ALL OR SOME OF THE SUBJECTS THROUGH COOPERATING INSTITUTIONS NOT UNDER ITS CONTROL. IN ORDER THAT THE DHEW BE FULLY INFORMED, THE FOLLOWING REPORT IS REQUESTED WHEN APPLICABLE.

USE FOLLOWING REPORT FORMAT FOR EACH INSTITUTION OTHER THAN GRANTEE OR CONTRACTING INSTITUTION WITH RESPONSIBILITY FOR HUMAN SUBJECTS PARTICIPATING IN THIS ACTIVITY: (ATTACH ADDITIONAL REPORT SHEETS AS NECESSARY).

INSTITUTIONAL AUTHORIZATION FOR ACCESS TO SUBJECTS

- SUBJECTS: STATUS (WARDS, RESIDENTS, EMPLOYEES, PATIENTS, ETC.) _____

NUMBER _____ AGE RANGE _____

NAME OF OFFICIAL (PLEASE PRINT) _____

TITLE _____ TELEPHONE _____

NAME AND ADDRESS OF COOPERATING INSTITUTION _____

- OFFICIAL SIGNATURE _____

NOTES: *(e.g., report of modification in proposal as submitted to agency affecting human subjects involvement)*

1032991

GPO : 1975 O - 574-849

REVIEW AND ACTION

ORAU/ORNL Committee on Human Studies

Principal Investigator _____ Ident. No. _____

Project Title _____

_____

1. In the opinion of this committee the risks to the rights and welfare of the subjects in this project or activity are:

   The committee states that adequate safeguards against these risks have been provided.

2. In the opinion of the committee the potential benefits of this activity to the subjects outweigh any probable risks. This opinion is justified by the following reasons:

3. In the opinion of the committee the following informed consent procedures will be adequate and appropriate:

4. The committee seeks continuing communication with the investigator(s) on this project along the following lines:

5. Other committee comments:

Approve _____

Disapprove _____

_____
Chairman of Committee

_____
Date

1032992

(Revised January 1972)

Dr. L.

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
Telephone 615 483-8411

Medical and
Health Sciences
Division

January 21, 1977

To the ORAU/ORNL Committee on Human Studies

As you can see from Dr. Kinard's letter of December 20, and Dr. Chalkley's form letter and list of accepted assurances to DHEW, ours at that time was considered unacceptable. This was principally because our guidelines were not as restrictive and regulatory as those published by HEW in the Federal Register.

I took it upon myself in the interest of expediency and the urgency reflected in Dr. Kinard's remarks about new funding to rewrite our guidelines. I used the HEW FR and ERDA FR guidelines, as well as a letter from Dr. Kinard (received in October 1975) that gave the Committee constructive criticism of the 1972 guidelines. Somehow we did not follow these suggestions as thoroughly as we should have.

Please read this material at your earliest convenience and return your comments as soon as possible. If you have none, please phone my secretary, Mrs. F. Banner, and tell her so.

Please note (especially C. Richmond) the innovation of "institutional members" with delegated responsibility from the institutional directors. This is needed for obtaining staff compliance with these HEW and ERDA directives, since the Committee itself cannot block funds of investigators who did not respond constructively to Committee criticisms and disapprovals. Also note ORNL's need to nominate a nonmedical woman (preferably black) to the vacant slot indicated in the block diagram. Also note that there is great urgency for a meeting of this Committee to meet and take care of these problems.

Sincerely,

C. C. Lushbaugh, M.D.

CCL:fb

Enc.

cc: Dr. Philip L. Johnson, ORAU
Dr. Chester Richmond, ORNL
(for Dr. Herman Postma)

1032993

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

General Assurance G1716XB

January 27, 1977

Herman Postma, Ph.D.
Director
Oak Ridge National Laboratory
Building 4500N
P. O. Box X
Oak Ridge, Tennessee 37830

Dear Doctor Postma:

The Department of Health, Education, and Welfare has approved a general institutional assurance dated August 1, 1975, as amended January 17, 1977, submitted by the Oak Ridge National Laboratory in compliance with the requirements for the protection of human subjects prescribed in Part 46 of Title 45 of the Code of Federal Regulations (45 CFR 46).

Approval of this assurance is restricted to proposals and activities that do not involve behavioral science studies. This restriction is reflected by the suffix XB on your general assurance number. If your Institutional Review Board is faced with the necessity of reviewing a proposal in this area, it should get in touch with this office for advice.

The implementing procedures submitted in support of the assurance are accepted subject to the issuance of additional or superseding regulations, and further negotiation as may be considered desirable. It is essential that proposed changes in membership of the Institutional Review Board, and changes in institutional policies, or in procedures for protection of the rights and welfare of human subjects be reported to this office.

This assurance supersedes previous assurances and is effective immediately for all applications hereafter submitted for new and renewal of DHEW support of activities involving human subjects, and will become effective within the ensuing year for current activities as each such activity is the subject of continuing interim review by the Institutional Review Board and prior to application for continuation of support for the activity.

Approval of the assurance will remain in effect until superseded or terminated by either your institution or the Department following appropriate advance notification.

1032994

We are prepared to assist you in any way we can in your institutional efforts to provide for the protection of human subjects. Please call us on Area Code 301, 496-7005 if you feel we can be of service to you.

Sincerely yours,

D. T. Chalkley, Ph.D.
Director, Office for Protection
from Research Risks
Office of the Director

cc:
Clarence C. Lushbaugh, M.D.
Acting Chairman
Medical and Health Sciences Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

Philip L. Johnson, Ph.D.
Executive Director
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

General Assurance G1716XB

January 27, 1977

Philip L. Johnson, Ph.D.
Executive Director
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Doctor Johnson:

The Department of Health, Education, and Welfare has approved a general institutional assurance dated August 1, 1975, as amended January 17, 1977, submitted by the Oak Ridge Associated Universities in compliance with the requirements for the protection of human subjects prescribed in Part 46 of Title 45 of the Code of Federal Regulations (45 CFR 46).

Approval of this assurance is restricted to proposals and activities that do not involve behavioral science studies. This restriction is reflected by the suffix XB on your general assurance number. If your Institutional Review Board is faced with the necessity of reviewing a proposal in this area, it should get in touch with this office for advice.

The implementing procedures submitted in support of the assurance are accepted subject to the issuance of additional or superseding regulations, and further negotiation as may be considered desirable. It is essential that proposed changes in membership of the Institutional Review Board, and changes in institutional policies, or in procedures for protection of the rights and welfare of human subjects be reported to this office.

This assurance supersedes previous assurances and is effective immediately for all applications hereafter submitted for new and renewal of DHEW support of activities involving human subjects, and will become effective within the ensuing year for current activities as each such activity is the subject of continuing interim review by the Institutional Review Board and prior to application for continuation of support for the activity.

Approval of the assurance will remain in effect until superseded or terminated by either your institution or the Department following appropriate advance notification.

1032996

We are prepared to assist you in any way we can in your institutional efforts to provide for the protection of human subjects. Please call us on Area Code 301, 496-7005 if you feel we can be of service to you.

Sincerely yours,

D. T. Chalkley, Ph.D.
Director, Office for Protection
from Research Risks
Office of the Director

cc:
Herman Postma, Ph.D.
Director
Oak Ridge National Laboratory
Building 4500N
P. O. Box X
Oak Ridge, Tennessee 37830

Clarence C. Lushbaugh, M.D.
Acting Chairman
Medical and Health Sciences Division
Oak Ridge Associated Universities, Inc.
P. O. Box 117
Oak Ridge, Tennessee 37830

1032997

See page 18

Date _____

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

Copies to _____

APRIL 1, 1977

53RD CUMULATIVE LIST 1977

OF INSTITUTIONS WHICH HAVE ESTABLISHED

GENERAL ASSURANCES

OF COMPLIANCE WITH DHEW REGULATIONS ON

PROTECTION OF HUMAN SUBJECTS

1. INCOMING PROPOSALS - GRANTS OR CONTRACTS

a. If the professional review of a proposal indicates that the project *does not involve* human subjects (box on signature page of application or box 3A of HEW 596), as defined in 45 CFR 46, the application can be processed without further regard to the question of institutional assurances.

b. If the professional review of a proposal indicates that the project *does involve* human subjects (box on signature page of application or box 3B of HEW 596), the next step is to determine whether the institution has checked either box 4A or 4B.

- If 4A is checked, this means that the applicant institution does *not have* an approved assurance on file but will supply documentation and certification of review when requested. This action is initiated by the OPRR, OD, NIH; Westwood Building, Room 303; Bethesda, Maryland 20014; upon receipt of a copy of the proposal from the *operating agency* immediately following an initial review.

- If 4B is checked, this means that the applicant institution has an approved general assurance on file. The fill-in spaces in this paragraph indicate the DHEW general assurance "G" number for the institution as presented in the "Cumulative Listing" and the date when the proposal was certified.

1032998

c. Draft requests for proposals (RFPs or RFAs) should be reviewed to determine whether performance will involve human subjects at risk. If these will be involved, the RFP should include the "Notice to Offerors" required by 41 CFR 3-4.5504(a). Offerings and proposals submitted in response to the RFP should be handled as in 1.b. above.

d. Operating agencies may define "submission date" to fit administrative requirements. It is suggested that sole source responses to RFPs should be considered to be submitted as of the closing date of the RFP and should then be handled as in 1.b. above.

e. Competitive responses to RFPs should be considered to be submitted as of the date of submission of the best and final offer, after establishing the zone of consideration or source selection, and should then proceed as in 1.b. above.

2. SUBMISSION OF CERTIFICATIONS - Whenever possible, the review and approval by Institutional Review Boards should occur prior to submission of the application or proposal and a certification to that effect should be included in or with the application or proposal itself, preferably on form HEW 596 (Rev. 4/75). Under no circumstances will the review of an application by the Department of Health, Education, and Welfare be completed until certification is received. The point at which review will be deferred or terminated is left to the operating agency involved.

Institutions *having on file* with DHEW an approved general assurance must submit certification within 30 days of the receipt of a written request thereof; and in any event *within 90 days* after the deadline or submission date for which the application or proposal was submitted.

Institutions *not having on file* an approved general assurance will indicate their status by checking box 4A on form HEW 596 accompanying the proposal and *when requested must submit the required assurances of compliance and certification of the review and approval* of the application or proposal by its Institutional Review Board within 30 days of the receipt of a written request from the Office for Protection from Research Risks (OPRR).

3. RESTRICTION CODES are presented as a suffix to the general assurance "G" number. This change conforms with the National Research Act, Public Law 93-348, Title II, which specifically applies to both *biomedical* and *behavioral* research and with the derivative DHEW regulations.

A restriction usually indicates that additional expertise in the Institutional Review Board membership is necessary for particular activities requiring certification.

An XM suffix indicates that the IRB has no or insufficient medical members. A proposed activity requiring medical expertise to assess risks, benefits, and the adequacy of safeguards cannot be certified under an XM restriction.

An XB suffix indicates that the IRB has no or insufficient members expert in the behavioral sciences. A proposed activity requiring behavioral expertise for assessing risks, benefits, and the adequacy of safeguards cannot be certified under an XB restriction.

An XO suffix indicates a restriction that uniquely applies to the institution under conditions of the general assurance agreement [call (301) 496-7005 for details].

When a proposal to be submitted to DHEW comes within the scope of an XM or XB restriction, either biomedical or behavioral, the IRB reviewing the proposal must include additional voting members whose qualifications offset the restriction. Their names and qualifications should be reported immediately to OPRR and a statement added under "Notes" on the HEW 596 form certifying IRB review and approval that the additional professionally qualified members have been reported to OPRR. Proposals that come within the certification restrictions that are not preceded or accompanied by appropriate compensating reviewers will be deferred for rereview and recertification.

4. QUESTIONS with regard to the status of Special or General Assurances of Compliance may be directed to:

Mrs. Florence R. Ober	(301) 496-7005

5. CONSULTATION for Special and General Assurances:

R. C. Backus, Ph.D.	(301) 496-7006
Victor M. Held, Ph.D.	(301) 496-7005
Roy Kinard, D.V.M.	(301) 496-7006
J. R. Marches, Ph.D.	(301) 496-7005

6. FORMS

Bulk orders for additional copies of HEW 596 should be addressed to:

Chief
Office Services Section
Division of Research Grants
National Institutes of Health
Westwood Building, Room A-17
Bethesda, Maryland 20014

Single copies of HEW 596 can be obtained from OPRR or by duplicating the back pages of this listing.

D. T. Chalkley, Ph.D.
Director, Office for Protection
from Research Risks
Office of the Director
National Institutes of Health

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	ALABAMA	
G0198	Alabama, University of, Birmingham	Birmingham
G0610	Alabama, University of	University
G0055	Tuskegee Institute	Tuskegee Inst
	ARIZONA	
G0799XM	Arizona State University	Tempe
G0026	Arizona, University of	Tucson
*G1287	St Joseph's Hospital and Medical Center	Phoenix
	ARKANSAS	
*G0336	Arkansas, University of, Medical Center	Little Rock
	CALIFORNIA	
G0784XM	American Institutes for Research	Palo Alto
*G0261XO	California Department of Health	Sacramento
G0278	California, University of, Berkeley	Berkeley
*G0195	California, University of, Davis	Davis
*G0380	California, University of, Irvine	Irvine
*G0238	California, University of, Los Angeles	Los Angeles
*G0193XO	California, University of, Riverside	Riverside
*G0389	California, University of, San Diego	La Jolla
G0155	California, University of, San Francisco	San Francisco
*G0282	California, University of, Santa Barbara	Santa Barbara
G0205XM	California, University of, Santa Cruz	Santa Cruz
*G0028	Camarillo State Hospital	Camarillo
G0234	Cedars-Sinai Medical Center	Los Angeles
*G2564	Charles R. Drew Postgraduate Medical School	Los Angeles
*G0135	Children's Hospital of Los Angeles	Los Angeles
*G0287	Children's Hospital of San Francisco	San Francisco
*G0009	City of Hope National Medical Center	Duarte
*G2259XO	Far West Laboratory for Educational Research and Development	San Francisco

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033002

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G1838	Huntington Inst of Applied Medical Research	Pasadena
*G1838	Huntington Memorial Hospital	Pasadena
*G2400	Institute of Medical Sciences	San Francisco
*G2367	John Wesley County Hospital Attending Staff Association	Los Angeles
*G0214	Kaiser Foundation Research Institute Including Its Regional Divisions in Northern California, Southern California, and Oregon	Oakland
G0226	Loma Linda University	Loma Linda
G0226	Loma Linda University (La Sierra Campus)	Riverside
G0359XB	Los Angeles County Harbor General Hospital, Professional Staff Association of	Torrance
*G0213	Los Angeles County Hospital-University of Southern California Medical Center, Professional Staff Association of	Los Angeles
*G2564	Martin Luther King, Jr. General Hospital and Its Staff Association Foundation	Los Angeles
*G0367XO	Mental Research Institute	Palo Alto
*G0145	Mount Zion Hospital and Medical Center	San Francisco
*G0710	Pacific State Hospital	Pomona
*G2400	Pacific, Univ of, School of Dentistry	San Francisco
*G2400	Pacific, Univ of, School of Medical Sciences	San Francisco
*G0082	Palo Alto Medical Research Foundation	Palo Alto
*G1838	Pasadena Hospital Association, Ltd	Pasadena
*G2400	Presbyterian Hospital of the Pacific Medical Center, Inc	San Francisco
*G0067	Rancho Los Amigos Hospital and Its Professional Staff Association	Downey
*G1416XO	Rand Corporation	Santa Monica
*G1096	Salk Institute	San Diego
G0420	San Diego State University	San Diego
G0420	San Diego State University Foundation	San Diego
G1472XM	Scientific Analysis Corporation (Including the Institute for Scientific Analysis and Performance Sites in Berkeley, Los Angeles, and San Diego)	San Francisco
G0108XB	Scripps Clinic and Research Foundation	La Jolla
G0201	Sonoma State Hospital	Eldridge
*G0122	Southern California, University of	Los Angeles

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033003

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0378	Stanford Research Institute	Menlo Park
G0011	Stanford University	Stanford
G1620	Veterans Administration Hospital-Long Beach	Long Beach
G1796	Veterans Administration Hospital-Sepulveda	Sepulveda
*G1658	Veterans Administration Hospital-Wadsworth	Los Angeles
*G1591XO	Wright Institute	Berkeley
	COLORADO	
G2823XB	Colorado Regional Cancer Center, Inc	Denver
*G1144XO	Colorado State University	Fort Collins
G0455	Colorado, University of	Boulder
*G0268	Colorado, University of, Medical Center	Denver
*G0277XO	Denver, University of	Denver
G0267	National Asthma Center	Denver
*G0068XO	National Jewish Hospital	Denver
	CONNECTICUT	
G0672XB	Connecticut State Department of Health	Hartford
G0039	Connecticut, University of	Storrs
G1966	Connecticut, University of, Health Center	Farmington-Hartford
G1533	Connecticut Valley Hospital	Middletown
G0007	Institute of Living	Hartford
G0003	John B. Pierce Fdn of Connecticut, Inc	New Haven
G0821	Saint Francis Hospital	Hartford
G2895XB	Waterbury Hospital Health Center	Waterbury
*G0243	Yale University	New Haven
	DELAWARE	
G0148	Delaware Division of Mental Health of the Department of Health and Social Services	Delaware City
G0013	Delaware, University of	Newark

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Revised General Assurance in Negotiation With OPRR

1033004

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	DISTRICT OF COLUMBIA	
G0784XM	American Institutes for Research	Washington
G1398XB	American National Red Cross	Washington
G1674XM	Bureau of Social Science Research, Inc	Washington
*G0365XO	Catholic University of America	Washington
G0042	Children's Hospital of D.C., Research Foundation of	Washington
G1249	Gallaudet College	Washington
G0294	George Washington University	Washington
G0228	Georgetown University	Washington
G0841	Howard University	Washington
G1989	National Academy of Sciences, Including National Academy of Engineering, Institute of Medicine, and National Research Council	Washington
G1036XM	National Children's Center, Inc	Washington
*G0180	Washington Hospital Center	Washington
	FLORIDA	
G2905	Florida State Department of Health and Rehabilitative Services	Tallahassee
*G0119XO	Florida State University	Tallahassee
G0382	Florida, University of	Gainesville
G0840XB	Miami Heart Institute	Miami Beach
G0301	Miami, University of	Coral Gables
G0301	Miami, University of	Miami
G0275XB	Mt Sinai Medical Center of Greater Miami	Miami Beach
G2321	Papanicolaou Cancer Research Institute	Miami
G1065	South Florida, University of	Fort Myers St Petersburg Sarasota Tampa
	GEORGIA	
*G0138	Emory Univ Division of Basic Health Sciences	Atlanta
*G0622	Emory Univ Graduate Sch of Arts and Sciences	Atlanta

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033005

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0138	Emory Univ Nell Hodgson Woodruff School of Nursing	Atlanta
*G0595	Emory Univ School of Dentistry	Atlanta
*G0138	Emory Univ School of Medicine	Atlanta
G0197	Georgia Dept of Human Resources, All Units	Atlanta
G0151XB	Georgia, Medical College of	Augusta
G0248	Georgia, University of	Athens
*G1467	Grady Memorial Hospital	Atlanta
	HAWAII	
*G0104XO	Hawaii, University of	Honolulu
	IDAHO	
*G1869	Mountain States Tumor Institute	Boise
	ILLINOIS	
G0395	American Dental Assn and ADA Health Fdn	Chicago
G0332XM	Anna Mental Health and Developmental Center	Anna
G1626	Chicago, University of (Division of Biological Sciences and Pritzker School of Medicine, Division of Social Sciences, School of Social Service Administration, and Related Units)	Chicago
G0114	Children's Memorial Hospital	Chicago
G0430	Downey Veterans Administration Hospital	Downey
G0182	Evanston Hospital	Evanston
G0430	Health Sciences, Univ of/Chicago Medical Sch	Chicago
G0053	Hektoen Institute for Medical Research	Chicago
G1561	Illinois State Psychiatric Institute	Chicago
G0345	Illinois, University of, at Chicago Circle	Chicago
G0291	Illinois, University of, Medical Center Campus, Including Rockford School of Medicine, Peoria School of Medicine, and Sch of Basic Medical Sciences, Urbana-Champaign	Chicago

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033006

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0102	Illinois, Univ of, at Urbana-Champaign	Urbana
G1373XM	Lincoln Developmental Center	Lincoln
G2369	Loyola University Medical Center	Maywood
G0095	Michael Reese Hospital and Medical Center	Chicago
G0518XM	Northern Illinois University	DeKalb
*G0190	Northwestern University	Chicago
*G0190	Northwestern University	Evanston
G0175	Rush-Presbyterian-St Luke's Medical Center	Chicago
G0309	Southern Illinois University	Carbondale
G2606XM	Southern Illinois University	Edwardsville
G0309	Southern Illinois Univ School of Medicine	Springfield
*G1970XO	Western Illinois University	Macomb
	INDIANA	
*G0314XO	Depauw University	Greencastle
G0945XM	Fort Wayne State Hosp and Training Center	Ft Wayne
G0185	Indiana Univ and Indiana Univ Foundation	Bloomington Indianapolis
G0185	Indiana University (Law School)	Indianapolis
G0185	Indiana Univ-Purdue Univ (Medical Facility)	Indianapolis
G0185	Indiana University Regional Campuses at Fort Wayne, Gary, Kokomo, New Albany, Richmond, and South Bend	
G1397	Indianapolis Center for Advanced Research	Indianapolis
G0883	Larue D. Carter Memorial Hospital	Indianapolis
G1697XM	Marion County Assn for Retarded Children, Inc	Indianapolis
G1246XB	Methodist Hospital of Indiana, Inc	Indianapolis
*G1176	New Castle State Hospital	New Castle
G1119	Notre Dame, University of	Notre Dame
G0131	Purdue Univ and Purdue Research Foundation	West Lafayette
	IOWA	
*G0343XO	Iowa State Univ of Science and Technology	Ames
G0209	Iowa, University of	Iowa City
*G0856XO	Woodward State Hospital-School	Woodward

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033007

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	KANSAS	
G0038	Kansas State University	Manhattan
*G0157XO	Kansas, University of	Lawrence
*G0229	Kansas, University of, Medical Center	Kansas City
G0081	Menninger Foundation	Topeka
	KENTUCKY	
G0223	Kentucky, Univ of, and the Research Foundation	Lexington
G0527	Louisville, University of, Except School of Medicine, and Louisville, University of, Foundation, Inc	Louisville
G0023	Louisville, University of, Schools of Medicine and Dentistry	Louisville
	LOUISIANA	
G0442XB	Alton Ochsner Medical Foundation	New Orleans
*G0262XO	Louisiana State Univ and A & M College System	Baton Rouge
*G2428XO	Louisiana State Univ in Baton Rouge	Baton Rouge
*G2485	Louisiana State Univ Medical Center	New Orleans
G0137XM	Pinecrest State School	Pineville
G0018	Tulane Medical Center	New Orleans
G2386	Tulane University Except Medical Center	New Orleans
	MAINE	
G3007	Eastern Maine Medical Center	Bangor
G0513	Maine Medical Center	Portland
	MARYLAND	
G0402	Baltimore City Hospitals	Baltimore
G0186	Friends Medical Science Research Center, Inc	Baltimore
G0640	Institute for Behavioral Research, Inc	Silver Spring

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033008

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0352	Johns Hopkins Univ Faculty of Arts and Sciences	Baltimore
G0274	Johns Hopkins Univ School of Hygiene and Public Health	Baltimore
G0174	Johns Hopkins Univ School of Medicine and Johns Hopkins Hospital	Baltimore
G0326	Maryland, Univ of, at Baltimore	Baltimore
G0296	Maryland, Univ of, at College Park	College Park
G0400	Sinai Hospital of Baltimore, Inc	Baltimore
	MASSACHUSETTS	
G0784XM	American Institutes for Research	Cambridge
G0286	Beth Israel Hospital	Boston
G0554	Boston City Hospital	Boston
G0554	Boston Department of Health and Hospitals	Boston
G0554	Boston Division of Community Health Services	Boston
G0488	Boston Hospital for Women, a Division of the Affiliated Hospitals Center, Inc	Boston
G0783	Boston Mental Health Foundation, Inc	Boston
G0783	Boston State Hospital	Boston
G0322	Boston Univ, Charles River Campus	Boston
G0550	Boston Univ Medical Center	Boston
G0550	Boston Univ School of Graduate Dentistry	Boston
G0550	Boston Univ School of Medicine	Boston
G0132XM	Brandeis University	Waltham
G2396XB	Center for Blood Research, Inc	Boston
G0406	Children's Hospital Medical Center	Boston
*G0117XO	Clark University	Worcester
G0098	Danvers State Hospital	Hathorne
G2042	Eunice Kennedy Shriver Center	Waltham
G0410XB	Eye Research Institute of Retina Foundation	Boston
G0412XB	Forsyth Dental Center	Boston
G2397	Harvard Medical Sch and Sch of Dental Medicine	Boston
G2238	Harvard Univ, Faculty of Arts and Sciences	Cambridge
G2494XM	Harvard Univ, Graduate School of Education	Cambridge
G2398XB	Harvard Univ, School of Public Health	Boston
G2573	Harvard Univ, University Health Services	Cambridge
G0791XB	Joslin Diabetes Foundation, Inc	Boston
G0087XB	Lahey Clinic Foundation, Inc	Boston

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Revised General Assurance in Negotiation With OPRR

1033009

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0449XB	Lemuel Shattuck Hospital	Jamaica Plain
G0554	Long Island Chronic Disease Hospital	Boston Harbor
G2304XO	Mass Developmental Disabilities Council	Boston
G0212XB	Massachusetts Eye and Ear Infirmary	Boston
G0167	Massachusetts General Hospital	Boston
G0097	Massachusetts Institute of Technology	Cambridge
G0597	Massachusetts Mental Health Center	Boston
G0597	Massachusetts Mental Health Research Corp	Boston
G0147XM	Massachusetts, University of - Amherst	Amherst
G2736	Massachusetts, University of, Medical School	Worcester
G0554	Mattapan Chronic Disease Hospital	Mattapan
G0576	McLean Hospital	Belmont
G0494XB	New England Deaconess Hospital	Boston
G0133	New England Medical Center Hospital	Boston
G0297	Northeastern University	Boston
G0429XB	Peter Bent Brigham Hospital Division of the Affiliated Hospitals Center, Inc	Boston
G3018XB	Pondville Hospital	Walpole (Norfolk)
G2515XM	Research Institute for Educational Problems	Cambridge
G0404XB	Robert B. Brigham Hospital, a Division of the Affiliated Hospitals Center, Inc	Boston
G0771	Sidney Farber Cancer Institute, Inc	Boston
G0351XB	St Margaret's Hospital for Women	Boston
G0554	Trustees of Health & Hosps, City of Boston, Inc	Boston
G2107	Tufts-New England Medical Center	Boston
G2379	Tufts University - Boston	Boston
*G0266XO	Tufts University - Medford	Medford
G0550	University Hospital, Inc	Boston
G2042	Walter E. Fernald State School	Belmont
G0085	Worcester Foundation for Experimental Biology	Shrewsbury
	MICHIGAN	
G0363	Child Research Center of Michigan	Detroit
G0363	Children's Hospital of Michigan	Detroit
G0497XM	Detroit, University of	Detroit
G0357	Edsel B. Ford Institute for Medical Research	Detroit
G0357	Henry Ford Hospital	Detroit
G0101	Lafayette Clinic	Detroit

RESTRICTION CODE
XM — No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033010

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0656XB	Michigan Cancer Foundation	Detroit
G0615	Michigan Department of Public Health	Lansing
G0384	Michigan State University	East Lansing
G0295	Michigan, University of	Ann Arbor
G0295	Michigan, University of	Dearborn
G0295	Michigan, University of	Flint
G0008	Sinai Hospital of Detroit	Detroit
G2483XB	Veterans Administration Hospital-Ann Arbor	Ann Arbor
G0354	Wayne State University	Detroit
G0720	Western Michigan University	Kalamazoo
	MINNESOTA	
G0065XB	Hennepin County Medical Center	Minneapolis
G0041	Mayo Foundation	Rochester
G0065XB	Minneapolis Medical Research Foundation, Inc	Minneapolis
G0463	Minnesota, University of	Austin
G0463	Minnesota, University of	Duluth
G0463	Minnesota, University of	Minneapolis
G0463	Minnesota, University of	Morris
G0463	Minnesota, University of	St Paul
G0463	Minnesota, University of, Technical College	Crookston
G0463	Minnesota, University of, Technical College	Waseca
	MISSISSIPPI	
*G0561XO	Mississippi, University of	University
G0366	Mississippi, University of, Medical Center	Jackson
	MISSOURI	
G2791XM	American Nurses' Association, Inc	Kansas City
*G0298	Cancer Research Center	Columbia
*G0298	Ellis Fischel State Cancer Hospital	Columbia
*G0424	Jewish Hospital of St Louis	St Louis
*G0292XO	Missouri, University of, Except Medical Center	Columbia

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033011

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0292	Missouri, University of, Medical Center, Including Missouri Institute of Psychiatry	Columbia
*G0292	Missouri, University of	Kansas City
*G0292XO	Missouri, University of	Rolla
*G0292XO	Missouri, University of	St Louis
*G0292	Missouri, University of, Regional Medical Programs, All Campuses	
*G0356	St Louis University	St Louis
*G2056	Veterans Administration Hospital-Kansas City	Kansas City
*G0279	Washington University	St Louis
G2351	Washington University School of Medicine	St Louis
	NEBRASKA	
G1120	Creighton University	Omaha
G0407	Nebraska, Univ of, Including the Medical Ctr	Omaha
G0407	Nebraska, Univ of, Including the State Univ of Nebraska	Lincoln
	NEVADA	
G0762XM	Nevada, University of, Reno Campus	Reno
	NEW HAMPSHIRE	
G0427XM	Dartmouth College Faculty of Arts & Sciences	Hanover
G0227	Dartmouth Medical School	Hanover
	NEW JERSEY	
G0492XB	Institute for Medical Research	Camden
G0349	New Jersey, College of Medicine & Dentistry of	Newark
G0349	New Jersey Dental School	Jersey City
G0349	New Jersey Medical School	Newark
G0837	Newark Beth Israel Medical Center	Newark
G0570XM	Princeton University	Princeton

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033012

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0349	Rutgers Medical School	Piscataway
G0300	Rutgers, The State Univ of New Jersey	Camden
G0300	Rutgers, The State Univ of New Jersey	New Brunswick
G0300	Rutgers, The State Univ of New Jersey	Newark
	NEW MEXICO	
*G0472	New Mexico, University of	Albuquerque
*G0353	New Mexico, University of, Health Sciences Group-School of Medicine, Colleges of Pharmacy and Nursing	Albuquerque
	NEW YORK	
G0217	Albany Medical College of Union University	Albany
G2129	American Health Foundation	New York
G1064XB	Associated Universities, Inc, Including Brookhaven National Laboratory	Upton
G2116XM	Barnard College	New York
G0341	Beth Israel Medical Center	New York
G2277XM	Child Welfare League of America, Inc	New York
G0381	Children's Hospital of Buffalo	Buffalo
G0437XM	Columbia Univ, Except Health Sciences Division	New York
G0034	Columbia Univ Health Sciences Division, Including College of Physicians and Surgeons, Schools of Public Health and Nursing, Faculty of Medicine, and Oral and Dental Surgery	New York
G0063	Cornell Univ, Except Medical College	Ithaca
G0245	Cornell University Medical College	New York
G0109XB	Eastman Dental Center	Rochester
G2912XB	Genesee Hospital	Rochester
G2887XB	Health Research, Inc, Albany Division	Albany
G2904	Health Research, Inc, Roswell Park Division	Buffalo
G2887XB	Helen Hayes Hospital	West Haverstraw
G0621	Hospital for Joint Diseases and Medical Center, Including the Research Institute for Skeletomuscular Diseases	New York

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033013

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0047	Hospital for Special Surgery	New York
G2920	ICD Rehabilitation and Research Center	New York
G1005XO	Jewish Board of Guardians	New York
G0369	Kingsbrook Jewish Medical Center and Isaac Albert Research Institute	Brooklyn
G2375	Long Island Jewish-Hillside Medical Center	New Hyde Park
G0397	Maimonides Medical Center	Brooklyn
G0086	Mary Imogene Bassett Hospital	Cooperstown
G0383XB	Memorial Hosp for Cancer and Allied Diseases	New York
G0059	Montefiore Hospital and Medical Center	New York
G0139	Mount Sinai School of Medicine of CUNY	New York
G2518XB	Nassau County Medical Center, Including Meadowbrook Medical Education and Research Foundation, Inc	East Meadow
G0173XM	New School for Social Research	New York
G0526XB	New York Blood Center of the Community Blood Council of Greater New York, Inc	New York
G1370XB	New York City Department of Health	New York
G0765XM	New York, City Univ of	New York
G0765XM	New York, City Univ of, Baruch College	New York
G0765XM	New York, City Univ of, Bronx Cmty College	Bronx
G0765XM	New York, City Univ of, Brooklyn College	Brooklyn
G0765XM	New York, City Univ of, City College	New York
G0765XM	New York, City Univ of, Graduate School and University Center	New York
G0765XM	New York, City Univ of, Herbert H. Lehman College	Bronx
G0765XM	New York, City Univ of, Hunter College	New York
G0765XM	New York, City Univ of, John Jay College of Criminal Justice	New York
G0765XM	New York, City Univ of, Kingsborough Community College	Brooklyn
G0765XM	New York, City Univ of, Manhattan Cmty College	New York
G0765XM	New York, City Univ of, Medgar Evers College	Brooklyn
G0765XM	New York, City Univ of, New York City Community College	Brooklyn
G0765XM	New York, City Univ of, Queens College	Flushing
G0765XM	New York, City Univ of, Queensborough Community College	New York
G0765XM	New York, City Univ of, Research Foundation	New York

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033014

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0765XM	New York, City Univ of, Staten Island Community College	Staten Island
G0765XM	New York, City Univ of, York College	Jamaica
G2887XB	New York Dept of Health and Regional Offices	Albany
G0208	New York Medical College-Flower and Fifth Avenue Hospitals, Metropolitan Hospital, and Bird S. Coler Memorial Hospital	New York
G0374XM	New York, State Univ of, at Albany	Albany
G0508	New York, State Univ of, at Binghamton	Binghamton
G0163	New York, State Univ of, at Buffalo	Buffalo
G0596	New York, State Univ of, at Stony Brook	Stony Brook
G0474	New York, State Univ of, College at Brockport	Brockport
G0506XM	New York, State Univ of, College at Buffalo	Buffalo
G0259XM	New York, State Univ of, College at Cortland	Cortland
G0386XM	New York, State Univ of, College at Oswego	Oswego
G0457	New York, State Univ of, College of Arts and Science at Geneseo	Geneseo
G0220	New York, State Univ of, College of Environmental Science and Forestry	Syracuse
G0305	New York, State Univ of, Downstate Medical Ctr	Brooklyn
G0127	New York, State Univ of, Upstate Medical Ctr	Syracuse
G0390XO	New York Univ, Exclusive of the Medical Ctr	New York
G0405	New York University Medical Center	New York
G0788	North Shore Hospital	Manhasset
G2887XB	Oxford Home for Veterans and Their Dependents	Oxford
G2247	Public Health Research Institute of the City of New York, Inc	New York
G2375	Queens Hospital Center	Jamaica
G1001	Rensselaer Polytechnic Institute	Troy
G0624	Research Foundation for Mental Hygiene, Inc (NYS Dept of Mental Hygiene) Including	Albany
	New York State Psychiatric Institute	New York
	Long Island Research Institute	Central Islip
	NYS Institute for Basic Research in Mental Retardation	Staten Island
	Research Institute on Alcoholism	Buffalo
	Rockland Research Institute	Orangeburg
	Marcy Psychiatric Ctr, Research Division	Marcy
	Creedmoor Inst for Psychobiologic Studies	Queens Village

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033015

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0172	Rochester, University of	Rochester
G0230	Rockefeller University	New York
G2036	Rockland County Health & Social Svcs Complex	Pomona
G0491	Roosevelt Hospital	New York
G2904	Roswell Park Memorial Institute	Buffalo
G0536XB	Sloan-Kettering Institute for Cancer Research	New York
G0076	St Luke's Hospital Center	New York
G2972XB	St Mary's Hospital	Rochester
G0376	St Vincent's Hosp and Medical Ctr of New York	New York
G0280XM	Syracuse University	Syracuse
G0373XM	Teachers College, Columbia University	New York
G2438XB	Trudeau Institute	Saranac Lake
G2045	Veterans Administration Hospital-Northport	Northport
G0002	Yeshiva Univ, Albert Einstein College of Med	Bronx
	NORTH CAROLINA	
G0191	Duke University Medical Center	Durham
G2242	North Carolina A & T State University	Greensboro
G0285	North Carolina State University at Raleigh	Raleigh
G0177	North Carolina, Univ of, at Chapel Hill	Chapel Hill
G0242	Wake Forest Univ, Bowman Gray Sch of Medicine	Winston-Salem
G1087	Wake Forest Univ, Except School of Medicine	Winston-Salem
G0078	Western Carolina Center	Morganton
	OHIO	
G0485	Akron, University of	Akron
G0683XM	Battelle Columbus Laboratories of the Battelle Memorial Institute	Columbus
G2843XB	Cancer Center, Inc	Cleveland
G1167	Case Western Reserve University	Cleveland
G0088	Children's Hospital Medical Center	Cincinnati
G0249	Children's Hospital Research Foundation, Inc	Columbus
G0667XM	Cincinnati, Univ of, Except Medical Center	Cincinnati
G0337	Cincinnati, Univ of, Medical Center, Including Colleges of Medicine, Nursing, and Health and Pharmacy	Cincinnati

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033016

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0502	Cleveland Clinic Fdn & Educational Fdn	Cleveland
G0171	Cleveland Psychiatric Institute	Cleveland
G0160	Fels Research Institute	Yellow Springs
G1936XB	Jewish Hospital of Cincinnati, Including the School of Nursing, Children's Psychiatric Center, and May Institute for Medical Research	Cincinnati
G0542	Kent State University	Kent
G1724XB	Medical College of Ohio at Toledo	Toledo
G0269XB	Mount Sinai Hospital of Cleveland	Cleveland
G0121	Ohio Agricultural Research & Development Ctr	Wooster
G0121	Ohio State University and Research Foundation	Columbus
G0662XB	St Luke's Hospital Association (United Methodist Church)	Cleveland
G0350XB	University Hospitals of Cleveland	Cleveland
G2907XM	Youngstown State University	Youngstown
	OKLAHOMA	
*G0327	Oklahoma Medical Research Foundation	Oklahoma City
*G2402XO	Oklahoma, University of	Norman
*G0241	Oklahoma, University of, Health Sciences Ctr	Oklahoma City
	OREGON	
*G0214	Kaiser Foundation Research Institute	Portland
G0043XB	Medical Research Foundation of Oregon and Oregon Regional Primate Research Center	Portland
*G2399XO	Northwest Regional Educational Laboratory	Portland
*G0505XO	Oregon Research Institute	Eugene
G0111XM	Oregon State University	Corvallis
G0288XM	Oregon, University of, Graduate School	Eugene
G2931	Oregon, University of, Health Sciences Center, Including Schools of Medicine, Dentistry, and Nursing	Portland

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033017

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	PENNSYLVANIA	
G0125	Albert Einstein Medical Center, Northern Div	Philadelphia
G0952XB	Allegheny General Hospital	Pittsburgh
G0784XM	American Institutes for Research	Pittsburgh
G0338	Arthur P. Noyes Research Foundation	Norristown
G0436XM	Bucknell University	Lewisburg
G1218	Carnegie-Mellon University	Pittsburgh
G0129	Children's Hospital of Philadelphia (Joseph Stokes, Jr., Research Inst of)	Philadelphia
G0360XB	Children's Hospital of Pittsburgh	Pittsburgh
G1556	Franklin Institute	Philadelphia
G0475	Hahnemann Medical College and Hospital	Philadelphia
G0936	H. K. Cooper Institute for Oral-Facial Anomalies and Communicative Disorders (Lancaster Cleft Palate Clinic)	Lancaster
G0045	Institute for Cancer Research (Fox Chase Cancer Center and American Oncologic Hosp)	Philadelphia
G0273XB	Lankenau Hospital	Philadelphia
G0189XB	Magee-Womens Hospital	Pittsburgh
G2121XM	Marywood College	Scranton
G0057XB	Montefiore Hospital	Pittsburgh
G0338	Norristown State Hospital	Norristown
G0333	Pennsylvania Hospital	Philadelphia
G0222	Pennsylvania, Medical College of	Philadelphia
G0573	Pennsylvania State Univ & Commonwealth Camps	University Park
G1668	Pennsylvania State Univ, Milton S. Hershey Medical Center	Hershey
G0012	Pennsylvania, University of	Philadelphia
G1531	Philadelphia Department of Public Health	Philadelphia
G0044	Philadelphia General Hospital	Philadelphia
G0324	Philadelphia Geriatric Center	Philadelphia
G0344	Philadelphia Psychiatric Center	Philadelphia
G0881	Philadelphia State Hospital	Philadelphia
G1532	Pittsburgh Child Guidance Center	Pittsburgh
G2929	Pittsburgh, University Health Center of	Pittsburgh
G0418	Pittsburgh, University of	Pittsburgh
G2200	Presbyterian-University Hospital	Pittsburgh
G0465	Presbyterian-Univ of Pennsylvania Medical Ctr	Philadelphia

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033018

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G2264XM	Research for Better Schools, Inc	Philadelphia
G0795	St Joseph's Hospital	Lancaster
G2880	Temple Univ, Excluding the Health Sciences Ctr	Philadelphia
G2879	Temple University Health Sciences Center	Philadelphia
G0049	Thomas Jefferson Univ, All Components	Philadelphia
G0362XB	Wills Eye Hospital and Research Institute	Philadelphia
G0054XB	Wistar Institute	Philadelphia
	PUERTO RICO	
G1348XM	Catholic University of Puerto Rico	Ponce
G0256XB	Puerto Rico, Univ of, Medical Sciences Campus	San Juan Rio Piedras
	RHODE ISLAND	
G0467	Brown University	Providence
*G0318	Rhode Island Hospital	Providence
G2212XB	Roger Williams General Hospital	Providence
	SOUTH CAROLINA	
G2621	Clemson University	Clemson
G0533	South Carolina Department of Mental Health	Columbia
G0240	South Carolina, Medical University of	Charleston
*G0629XO	South Carolina, University of	Columbia
	TENNESSEE	
G0490XM	George Peabody College for Teachers	Nashville
G0393	Meharry Medical College	Nashville
G1716XB	Oak Ridge Associated Universities	Oak Ridge
G1716XB	Oak Ridge National Laboratory	Oak Ridge
G0648	St Jude Children's Research Hospital	Memphis
G0170	Tennessee, University of, Center for the Health Sciences	Memphis

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033019

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0124	Tennessee, University of - Knoxville	Knoxville
G0401	Vanderbilt University	Nashville
	TEXAS	
G0307	Baylor College of Medicine	Houston
*G1843	Bexar County Hospital District	San Antonio
G0398XM	Houston, University of	Houston
*G2344XO	Southwest Educational Development Corporation (AKA Southwest Educational Development Lab)	Austin
G1045	Texas A & M University and Research Foundation, College Station Campus Only	College Station
G3027	Texas Department of Public Welfare	Austin
*G0590	Texas Institute for Rehabilitation and Research	Houston
G0564	Texas Tech University Complex (Texas Tech Univ and Texas Tech Univ Sch of Medicine)	Lubbock
*G1121XO	Texas, University of, at Arlington	Arlington
G0123	Texas, University of, at Austin	Austin
G0113	Texas, University of, Cancer Center (and its M.D. Anderson Hospital and Tumor Institute)	Houston
G2615	Texas, University of, Health Science Center at Dallas	Dallas
*G2760	Texas, University of, Health Science Center at Houston	Houston
*G2255	Texas, University of, Health Science Center at San Antonio, Including Medical School, Dental School, and Graduate School of Biomedical Sciences	San Antonio
G0107	Texas, Univ of, Medical Branch at Galveston	Galveston
	UTAH	
*G0933XO	Brigham Young University	Provo
*G2426	Deseret Fdn for Medical Education & Research	Salt Lake City
*G0235	Utah, University of	Salt Lake City

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033020

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	VERMONT	
G0194	Vermont, University of, and State Agricultural College	Burlington
G2335XB	Veterans Administration Ctr-White River Junction	White River Jct
	VIRGINIA	
G2275XM	Human Resources Research Organization	Alexandria
G0239	Virginia Commonwealth University (All Schools and Divisions)	Richmond
G0306	Virginia, University of	Charlottesville
	WASHINGTON	
*G0522	Children's Orthopedic Hosp and Medical Ctr	Seattle
G2627XB	Fred Hutchinson Cancer Research Center	Seattle
G0029XB	Pacific Northwest Research Foundation	Seattle
*G0900	Virginia Mason Research Center, Including Mason Clinic and Virginia Mason Hospital	Seattle
G1717	Washington Department of Social and Health Services, All Components	Olympia
*G0105XO	Washington State University	Pullman
*G0299	Washington, University of	Seattle
	WEST VIRGINIA	
G0431	West Virginia University	Morgantown
	WISCONSIN	
G0315	Central Wisconsin Colony and Training School	Madison
G2891XB	Columbia Hospital	Milwaukee

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033021

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0387	Marquette University	Milwaukee
G0763	Mendota Mental Health Institute	Madison
G3010XB	Mount Sinai Medical Center of Milwaukee	Milwaukee
G0503	Southern Wisconsin Colony and Training School	Union Grove
G0077	Wisconsin, Medical College of, Inc	Milwaukee
G0319	Wisconsin, University of, Madison Campus	Madison
G2106XM	Wisconsin, University of, Parkside	Kenosha
	SWITZERLAND	
*G1137	World Health Organization	Geneva

TOTAL NUMBER OF INSTITUTIONS AND COMPONENTS WITH ACCEPTABLE GENERAL ASSURANCES — 506

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Revised General Assurance in Negotiation With OPRR

1033022

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☐ FOLLOWUP ☐ REVISION

☐ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☐ RENEWAL ☐ CONTINUATION

APPLICATION IDENTIFICATION NUMBER *(If known)*

_____

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of Public Law 93-348, as implemented by Part 46 of Title 45 of the Code of Federal Regulations, as amended, (45 CFR 46). Administration of the DHEW policy and regulation is the responsibility of the Office for Protection from Research Risks, National Institutes of Health, Bethesda, Md 20014.

1. TITLE OF PROPOSAL OR ACTIVITY

2. PRINCIPAL INVESTIGATOR/ACTIVITY DIRECTOR/FELLOW

3. DECLARATION THAT HUMAN SUBJECTS EITHER WOULD OR WOULD NOT BE INVOLVED

☐ A. NO INDIVIDUALS WHO MIGHT BE CONSIDERED HUMAN SUBJECTS, INCLUDING THOSE FROM WHOM ORGANS, TISSUES, FLUIDS, OR OTHER MATERIALS WOULD BE DERIVED, OR WHO COULD BE IDENTIFIED BY PERSONAL DATA, WOULD BE INVOLVED IN THE PROPOSED ACTIVITY. (IF NO HUMAN SUBJECTS WOULD BE INVOLVED, CHECK THIS BOX AND PROCEED TO ITEM 7. PROPOSALS DETERMINED BY THE AGENCY TO INVOLVE HUMAN SUBJECTS WILL BE RETURNED.)

☐ B. HUMAN SUBJECTS WOULD BE INVOLVED IN THE PROPOSED ACTIVITY AS EITHER: ☐ NONE OF THE FOLLOWING, OR INCLUDING: ☐ MINORS, ☐ FETUSES, ☐ ABORTUSES, ☐ PREGNANT WOMEN, ☐ PRISONERS, ☐ MENTALLY RETARDED, ☐ MENTALLY DISABLED. UNDER SECTION 6. COOPERATING INSTITUTIONS, ON REVERSE OF THIS FORM, GIVE NAME OF INSTITUTION AND NAME AND ADDRESS OF OFFICIAL(S) AUTHORIZING ACCESS TO ANY SUBJECTS IN FACILITIES NOT UNDER DIRECT CONTROL OF THE APPLICANT OR OFFERING INSTITUTION.

DECLARATION OF ASSURANCE STATUS/CERTIFICATION OF REVIEW

☐ A. THIS INSTITUTION HAS NOT PREVIOUSLY FILED AN ASSURANCE AND ASSURANCE IMPLEMENTING PROCEDURES FOR THE PROTECTION OF HUMAN SUBJECTS WITH THE DHEW THAT APPLIES TO THIS APPLICATION OR ACTIVITY. ASSURANCE IS HEREBY GIVEN THAT THIS INSTITUTION WILL COMPLY WITH REQUIREMENTS OF *DHEW Regulation 45 CFR 46*, THAT IT HAS ESTABLISHED AN INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS AND, WHEN REQUESTED, WILL SUBMIT TO DHEW DOCUMENTATION AND CERTIFICATION OF SUCH REVIEWS AND PROCEDURES AS MAY BE REQUIRED FOR IMPLEMENTATION OF THIS ASSURANCE FOR THE PROPOSED PROJECT OR ACTIVITY.

☐ B. THIS INSTITUTION HAS AN APPROVED GENERAL ASSURANCE (DHEW ASSURANCE NUMBER _____) OR AN ACTIVE SPECIAL ASSURANCE FOR THIS ONGOING ACTIVITY, ON FILE WITH DHEW. THE SIGNER CERTIFIES THAT ALL ACTIVITIES IN THIS APPLICATION PROPOSING TO INVOLVE HUMAN SUBJECTS HAVE BEEN REVIEWED AND APPROVED BY THIS INSTITUTION'S INSTITUTIONAL REVIEW BOARD IN A CONVENED MEETING ON THE DATE OF _____ IN ACCORDANCE WITH THE REQUIREMENTS OF THE *Code of Federal Regulations on Protection of Human Subjects (45 CFR 46)*. THIS CERTIFICATION INCLUDES, WHEN APPLICABLE, REQUIREMENTS FOR CERTIFYING FDA STATUS FOR EACH INVESTIGATIONAL NEW DRUG TO BE USED (SEE REVERSE SIDE OF THIS FORM).

THE INSTITUTIONAL REVIEW BOARD HAS DETERMINED, AND THE INSTITUTIONAL OFFICIAL SIGNING BELOW CONCURS THAT:

EITHER ☐ HUMAN SUBJECTS WILL NOT BE AT RISK; OR ☐ HUMAN SUBJECTS WILL BE AT RISK.

5. AND 6. SEE REVERSE SIDE

7. NAME AND ADDRESS OF INSTITUTION

8. TITLE OF INSTITUTIONAL OFFICIAL	TELEPHONE NUMBER
SIGNATURE OF INSTITUTIONAL OFFICIAL	DATE

HEW-596 (Rev. 4-75)

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO REQUESTING AGENCY.

1033023

550

5. INVESTIGATIONAL NEW DRUGS - ADDITIONAL CERTIFICATION REQUIREMENT

SECTION 46.17 OF TITLE 45 OF THE Code of Federal Regulations states, "Where an organization is required to prepare or to submit a certification . . . and the proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 130.3(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received."

INVESTIGATIONAL NEW DRUG CERTIFICATION

TO CERTIFY COMPLIANCE WITH FDA REQUIREMENTS FOR PROPOSED USE OF INVESTIGATIONAL NEW DRUGS IN ADDITION TO CERTIFICATION OF INSTITUTIONAL REVIEW BOARD APPROVAL, THE FOLLOWING REPORT FORMAT SHOULD BE USED FOR EACH IND: (ATTACH ADDITIONAL IND CERTIFICATIONS AS NECESSARY).

- IND FORMS FILED: ☐ FDA 1571, ☐ FDA 1572, ☐ FDA 1573

- NAME OF IND AND SPONSOR _____

- DATE OF 30-DAY EXPIRATION OR FDA WAIVER
  (FUTURE DATE REQUIRES FOLLOWUP REPORT TO AGENCY) _____

- FDA RESTRICTION _____

- SIGNATURE OF INVESTIGATOR _____ DATE _____

6. COOPERATING INSTITUTIONS - ADDITIONAL REPORTING REQUIREMENT

SECTION 46.16 OF TITLE 45 OF THE *Code of Federal Regulations* IMPOSES SPECIAL REQUIREMENTS ON THE CONDUCT OF STUDIES OR ACTIVITIES IN WHICH THE GRANTEE OR PRIME CONTRACTOR OBTAINS ACCESS TO ALL OR SOME OF THE SUBJECTS THROUGH COOPERATING INSTITUTIONS NOT UNDER ITS CONTROL. IN ORDER THAT THE DHEW BE FULLY INFORMED, THE FOLLOWING REPORT IS REQUESTED WHEN APPLICABLE.

USE FOLLOWING REPORT FORMAT FOR EACH INSTITUTION OTHER THAN GRANTEE OR CONTRACTING INSTITUTION WITH RESPONSIBILITY FOR HUMAN SUBJECTS PARTICIPATING IN THIS ACTIVITY: (ATTACH ADDITIONAL REPORT SHEETS AS NECESSARY).

INSTITUTIONAL AUTHORIZATION FOR ACCESS TO SUBJECTS

- SUBJECTS: STATUS (WARDS, RESIDENTS, EMPLOYEES, PATIENTS, ETC.) _____

NUMBER _____ AGE RANGE _____

NAME OF OFFICIAL (PLEASE PRINT) _____

TITLE _____ TELEPHONE _____

NAME AND ADDRESS OF COOPERATING INSTITUTION _____

- OFFICIAL SIGNATURE _____

NOTES: *(e.g., report of modification in proposal as submitted to agency affecting human subjects involvement)*

1033024

GPO : 1975 O - 574-849

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
Telephone 615 483-8411

Medical and
Health Sciences
Division

April 7, 1977

Dr. Roy Kinard
Office for Protection from
Research Risks
Office of the Director
Department of Health, Education,
and Welfare
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Kinard:

As a follow-up of your correspondence and conversations with Dr. Lushbaugh concerning our general assurrance (No. G1716), I am writing to inform you that a psychologist has joined our Committee on Human Studies. Dr. William Calhoun is Chairman of the Department of Psychology at The University of Tennessee, Knoxville, and I am sending you a copy of his letter accepting a position on the Committee. We also have on the Committee a psychiatrist, Dr. Joan B. Woods, of Murfreesboro, Tennessee.

We believe that this addition to the Committee brings us completely in line with the regulations of 1975 and the suggestions that have been made and that we are, therefore, in complete compliance. If there is anything further that is required, we would appreciate having you inform us about it.

Thank you for your assistance in this matter.

Sincerely,

Gould Andrews

Gould A. Andrews, M.D.

GAA:dgb

Enclosure

1033025

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

General Assurance G1716

April 12, 1977

Gould A. Andrews, M.D.
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Doctor Andrews:

Thanks for your letter of April 7 reporting appointment of Dr. Calhoun to your human subjects review board. This change is acceptable as a revision to your general assurance G1716 and the behavioral sciences restriction (XB) is removed.

Sincerely yours,

Roy Kinard

Roy Kinard, D.V.M.
Office for Protection
from Research Risks
Office of the Director

Enclosure
Suggested Format for Submitting IRB Member Roster

cc:
Clarence C. Lushbaugh, M.D.
Acting Chairman
Medical and Health Sciences Division
Oak Ridge Associated Universities

Herman Postma, Ph.D.
Director
Oak Ridge National Laboratory
Building 4500N
P. O. Box X
Oak Ridge, Tennessee 37830

1033026

APR 14 1976

LETTERHEAD OF INSTITUTION

Institutional General Assurance No. G1716 Date _____

INSTITUTIONAL REVIEW BOARD MEMBER ROSTER

[Instructions: Please use this format for reporting Institutional Review Board members and alternates to DHEW (OPRR). The report for each member should be limited to the information indicated. *Please do not send curriculum vitae bibliographies or detailed information other than that indicated.*]

Name of Institutional Officer (other than chairperson) to whom correspondence concerning Board affairs should be addressed _____ *(name typewritten)* _____.

Regular Member		Alternate Member
Name (typewritten): _____ *Earned degrees:* _____ *Position or Occupation:* _____ *Board certification, licenses, etc.:* _____ *Relationship to institution:* _____ *Representative capacity:* _____	OR	Designated Alternate (if any)

NOTES: (a) The IRB must consist of not less than FIVE members identified as above.

(b) Alternate members (if any) should be similarly identified and keyed to a particular member(s).

(c) The "Representative capacity" line should be used to indicate whether the individual serves the IRB as an investigator, administrator, practitioner, lawyer, ethicist, or in other capacities such as community representative.

(d) An IRB member may serve in more than one representative capacity.

(e) The Chairman of the IRB *must be identified.*

(f) IRBs reviewing activities involving the use of investigational new drugs (INDs) *must include at least two individuals licensed to administer drugs, and one person not so licensed.* Review for other purposes should utilize IRBs of equal or greater breadth.

(g) No IRB may be composed *entirely of members from the same professional group or entirely of members employed either full or part-time by the institution.*

(h) When updating an existing committee, *please submit a new roster, listing the full membership as it currently stands.*

1033027

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

See page 19

AUGUST 1, 1977

54TH CUMULATIVE LIST 1977

OF INSTITUTIONS WHICH HAVE ESTABLISHED

GENERAL ASSURANCES

OF COMPLIANCE WITH DHEW REGULATIONS ON

PROTECTION OF HUMAN SUBJECTS

1. INCOMING PROPOSALS - GRANTS OR CONTRACTS

a. If the professional review of a proposal indicates that the project *does not involve* human subjects (box on signature page of application or box 3A of HEW 596), as defined in 45 CFR 46, the application can be processed without further regard to the question of institutional assurances.

b. If the professional review of a proposal indicates that the project *does involve* human subjects (box on signature page of application or box 3B of HEW 596), the next step is to determine whether the institution has checked either box 4A or 4B.

- If 4A is checked, this means that the applicant institution does *not have* an approved assurance on file but will supply documentation and certification of review when requested. This action is initiated by the OPRR, OD, NIH; Westwood Building, Room 303; Bethesda, Maryland 20014; upon receipt of a copy of the proposal from the *operating agency* immediately following an initial review.

- If 4B is checked, this means that the applicant institution has an approved general assurance on file. The fill-in spaces in this paragraph indicate the DHEW general assurance "G" number for the institution as presented in the "Cumulative Listing" and the date when the proposal was certified.

1033028

c. Draft requests for proposals (RFPs or RFAs) should be reviewed to determine whether performance will involve human subjects at risk. If these will be involved, the RFP should include the "Notice to Offerors" required by 41 CFR 3-4.5504(a). Offerings and proposals submitted in response to the RFP should be handled as in 1.b. above.

d. Operating agencies may define "submission date" to fit administrative requirements. It is suggested that sole source responses to RFPs should be considered to be submitted as of the closing date of the RFP and should then be handled as in 1.b. above.

e. Competitive responses to RFPs should be considered to be submitted as of the date of submission of the best and final offer, after establishing the zone of consideration or source selection, and should then proceed as in 1.b. above.

2. SUBMISSION OF CERTIFICATIONS - Whenever possible, the review and approval by Institutional Review Boards should occur prior to submission of the application or proposal and a certification to that effect should be included in or with the application or proposal itself, preferably on form HEW 596 (Rev. 4/75). Under no circumstances will the review of an application by the Department of Health, Education, and Welfare be completed until certification is received. The point at which review will be deferred or terminated is left to the operating agency involved.

Institutions *having on file* with DHEW an approved general assurance must submit certification within 30 days of the receipt of a written request thereof; and in any event *within 60 days* after the deadline or submission date for which the application or proposal was submitted.

Institutions *not having on file* an approved general assurance will indicate their status by checking box 4A on form HEW 596 accompanying the proposal and *when requested must submit the required assurances of compliance and certification of the review and approval* of the application or proposal by its Institutional Review Board within 30 days of the receipt of a written request from the Office for Protection from Research Risks (OPRR).

3. RESTRICTION CODES are presented as a suffix to the general assurance "G" number. This change conforms with the National Research Act, Public Law 93-348, Title II, which specifically applies to both *biomedical* and *behavioral* research and with the derivative DHEW regulations.

A restriction usually indicates that additional expertise in the Institutional Review Board membership is necessary for particular activities requiring certification.

An XM suffix indicates that the IRB has no or insufficient medical members. A proposed activity requiring medical expertise to assess risks, benefits, and the adequacy of safeguards cannot be certified under an XM restriction.

An XB suffix indicates that the IRB has no or insufficient members expert in the behavioral sciences. A proposed activity requiring behavioral expertise for assessing risks, benefits, and the adequacy of safeguards cannot be certified under an XB restriction.

An XO suffix indicates a restriction that uniquely applies to the institution under conditions of the general assurance agreement [call (301) 496-7005 for details].

When a proposal to be submitted to DHEW comes within the scope of an XM or XB restriction, either biomedical or behavioral, the IRB reviewing the proposal must include additional voting members whose qualifications offset the restriction. Their names and qualifications should be reported immediately to OPRR and a statement added under "Notes" on the HEW 596 form certifying IRB review and approval that the additional professionally qualified members have been reported to OPRR. Proposals that come within the certification restrictions that are not preceded or accompanied by appropriate compensating reviewers will be deferred for rereview and recertification.

4. QUESTIONS with regard to the status of Special or General Assurances of Compliance may be directed to:

Mrs. Florence R. Ober	(301) 496-7005

5. CONSULTATION for Special and General Assurances:

R. C. Backus, Ph.D.	(301) 496-7006
Victor M. Held, Ph.D.	(301) 496-7005
Roy Kinard, D.V.M.	(301) 496-7006
J. R. Marches, Ph.D.	(301) 496-7005

6. FORMS

Bulk orders for additional copies of HEW 596 should be addressed to:

Chief
Office Services Section
Division of Research Grants
National Institutes of Health
Westwood Building, Room A-17
Bethesda, Maryland 20014

Single copies of HEW 596 can be obtained from OPRR or by duplicating the back pages of this listing.

D. T. Chalkley, Ph.D.
Director, Office for Protection
from Research Risks
Office of the Director
National Institutes of Health

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	ALABAMA	
G0198	Alabama, University of, Birmingham	Birmingham
G0610	Alabama, University of	University
G0055	Tuskegee Institute	Tuskegee Inst
	ARIZONA	
G0799XM	Arizona State University	Tempe
G0026	Arizona, University of	Tucson
*G1287	St Joseph's Hospital and Medical Center	Phoenix
	ARKANSAS	
*G0336	Arkansas, University of, Medical Center	Little Rock
	CALIFORNIA	
G0784XM	American Institutes for Research	Palo Alto
*G0261XO	California Department of Health	Sacramento
G0278	California, University of, Berkeley	Berkeley
*G0195	California, University of, Davis	Davis
*G0380	California, University of, Irvine	Irvine
*G0238	California, University of, Los Angeles	Los Angeles
*G0193XO	California, University of, Riverside	Riverside
*G0389	California, University of, San Diego	La Jolla
G0155	California, University of, San Francisco	San Francisco
*G0282	California, University of, Santa Barbara	Santa Barbara
G0205XM	California, University of, Santa Cruz	Santa Cruz
*G0028	Camarillo State Hospital	Camarillo
G0234	Cedars-Sinai Medical Center	Los Angeles
*G2564	Charles R. Drew Postgraduate Medical School	Los Angeles
G0135	Childrens Hospital of Los Angeles	Los Angeles
*G0287	Children's Hospital of San Francisco	San Francisco
*G0009	City of Hope National Medical Center	Duarte
*G2259XO	Far West Laboratory for Educational Research and Development	San Francisco

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033032

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G1838	Huntington Inst of Applied Medical Research	Pasadena
*G1838	Huntington Memorial Hospital	Pasadena
G0432	Institute for Medical Research	San Jose
*G2400	Institute of Medical Sciences	San Francisco
*G2367	John Wesley County Hospital Attending Staff Association	Los Angeles
*G0214	Kaiser Foundation Research Institute Including Its Regional Divisions in Northern California, Southern California, and Oregon	Oakland
G0226	Loma Linda University	Loma Linda
G0226	Loma Linda University (La Sierra Campus)	Riverside
G0359XB	Los Angeles County Harbor General Hospital, Professional Staff Association of	Torrance
*G0213	Los Angeles County Hospital-University of Southern California Medical Center, Professional Staff Association of	Los Angeles
*G2564	Martin Luther King, Jr. General Hospital and Its Staff Association Foundation	Los Angeles
*G0367XO	Mental Research Institute	Palo Alto
*G0145	Mount Zion Hospital and Medical Center	San Francisco
*G0710	Pacific State Hospital	Pomona
*G2400	Pacific, Univ of, School of Dentistry	San Francisco
*G2400	Pacific, Univ of, School of Medical Sciences	San Francisco
*G0082	Palo Alto Medical Research Foundation	Palo Alto
*G1838	Pasadena Hospital Association, Ltd	Pasadena
*G2400	Presbyterian Hospital of the Pacific Medical Center, Inc	San Francisco
*G0067	Rancho Los Amigos Hospital and Its Professional Staff Association	Downey
G1416	Rand Corporation	Santa Monica
*G1096	Salk Institute	San Diego
G0420	San Diego State University	San Diego
G0420	San Diego State University Foundation	San Diego
G1472XM	Scientific Analysis Corporation (Including the Institute for Scientific Analysis and Performance Sites in Berkeley, Los Angeles, and San Diego)	San Francisco
G0108XB	Scripps Clinic and Research Foundation	La Jolla
G0201	Sonoma State Hospital	Eldridge
*G0122	Southern California, University of	Los Angeles

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033033

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0378	Stanford Research Institute	Menlo Park
G0011	Stanford University	Stanford
G0010	USPHS Hospital, San Francisco	San Francisco
G1620	Veterans Administration Hospital-Long Beach	Long Beach
G1796	Veterans Administration Hospital-Sepulveda	Sepulveda
*G1658	Veterans Administration Hospital-Wadsworth	Los Angeles
*G1591XO	Wright Institute	Berkeley
	COLORADO	
G2823XB	Colorado Regional Cancer Center, Inc	Denver
G1144	Colorado State University	Fort Collins
G0455	Colorado, University of	Boulder
G0268XB	Colorado, University of, Medical Center	Denver
G0277XM	Denver, University of (Colorado Seminary)	Denver
G0267	National Asthma Center	Denver
G0068	National Jewish Hospital and Research Center	Denver
	CONNECTICUT	
G0672XB	Connecticut State Department of Health	Hartford
G0039	Connecticut, University of	Storrs
G1966	Connecticut, University of, Health Center	Farmington-Hartford
G1533	Connecticut Valley Hospital	Middletown
G0007	Institute of Living	Hartford
G0003	John B. Pierce Fdn of Connecticut, Inc	New Haven
G0821	Saint Francis Hospital	Hartford
G2895XB	Waterbury Hospital Health Center	Waterbury
*G0243	Yale University	New Haven
	DELAWARE	
G0148	Delaware Division of Mental Health of the Department of Health and Social Services	Delaware City
G0013	Delaware, University of	Newark
G2480XB	Wilmington Medical Center, Inc	Wilmington

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033034

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	DISTRICT OF COLUMBIA	
G0784XM	American Institutes for Research	Washington
G1398XB	American National Red Cross	Washington
G1674XM	Bureau of Social Science Research, Inc	Washington
G0365XM	Catholic University of America	Washington
G0042	Children's Hospital of D.C., Research Foundation of	Washington
G1249	Gallaudet College	Washington
G0294	George Washington University	Washington
G0228	Georgetown University	Washington
G0841	Howard University	Washington
G1989	National Academy of Sciences, Including National Academy of Engineering, Institute of Medicine, and National Research Council	Washington
G1036XM	National Children's Center, Inc	Washington
G3045XO	Veterans Administration Central Office (NCI CANCER THERAPY PROJECTS ONLY)	Washington
*G0180	Washington Hospital Center	Washington
	FLORIDA	
G2905	Florida State Department of Health and Rehabilitative Services	Tallahassee
*G0119XO	Florida State University	Tallahassee
G0382	Florida, University of	Gainesville
G0840XB	Miami Heart Institute	Miami Beach
G0301	Miami, University of	Coral Gables
G0301	Miami, University of	Miami
G0275	Mt Sinai Medical Center of Greater Miami	Miami Beach
G2321	Papanicolaou Cancer Research Institute	Miami
G1065	South Florida, University of	Fort Myers St Petersburg Sarasota Tampa
	GEORGIA	
*G0138	Emory Univ Division of Basic Health Sciences	Atlanta

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033035

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
*G0622	Emory Univ Graduate Sch of Arts and Sciences	Atlanta
*G0138	Emory Univ Nell Hodgson Woodruff School of Nursing	Atlanta
*G0595	Emory Univ School of Dentistry	Atlanta
*G0138	Emory Univ School of Medicine	Atlanta
G0197	Georgia Dept of Human Resources, All Units	Atlanta
G0151XB	Georgia, Medical College of	Augusta
G0248	Georgia, University of	Athens
*G1467	Grady Memorial Hospital	Atlanta
	HAWAII	
G0104	Hawaii, University of (Including the Entire System and the Research Corporation)	Honolulu
	IDAHO	
*G1869	Mountain States Tumor Institute	Boise
	ILLINOIS	
G0395	American Dental Assn and ADA Health Fdn	Chicago
G0332XM	Anna Mental Health and Developmental Center	Anna
G1626	Chicago, University of (Division of Biological Sciences and Pritzker School of Medicine, Division of Social Sciences, School of Social Service Administration, and Related Units)	Chicago
G0114	Children's Memorial Hospital	Chicago
G0430	Downey Veterans Administration Hospital	Downey
G0182	Evanston Hospital	Evanston
G0430	Health Sciences, Univ of/Chicago Medical Sch	Chicago
G0053	Hektoen Institute for Medical Research	Chicago
G1561	Illinois State Psychiatric Institute	Chicago
G0345	Illinois, University of, at Chicago Circle	Chicago
G0291	Illinois, University of, Medical Center Campus, Including Rockford School of Medicine, Peoria School of Medicine, and Sch of Basic Medical Sciences, Urbana-Champaign	Chicago

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033036

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0102	Illinois, Univ of, at Urbana-Champaign	Urbana
G1373XM	Lincoln Developmental Center	Lincoln
G2369	Loyola University Medical Center	Maywood
G0095	Michael Reese Hospital and Medical Center	Chicago
G2763	Mount Sinai Hospital Medical Center of Chicago	Chicago
G0518XM	Northern Illinois University	DeKalb
*G0190	Northwestern University	Chicago
*G0190	Northwestern University	Evanston
G0175	Rush-Presbyterian-St Luke's Medical Center	Chicago
G0309	Southern Illinois University	Carbondale
G2606XM	Southern Illinois University	Edwardsville
G0309	Southern Illinois Univ School of Medicine	Springfield
G1970XM	Western Illinois University	Macomb
	INDIANA	
G0314XM	DePauw University	Greencastle
G0945XM	Fort Wayne State Hosp and Training Center	Ft Wayne
G0185	Indiana Univ and Indiana Univ Foundation	Bloomington Indianapolis
G0185	Indiana University (Law School)	Indianapolis
G0185	Indiana Univ-Purdue Univ (Medical Facility)	Indianapolis
G0185	Indiana University Regional Campuses at Fort Wayne, Gary, Kokomo, New Albany, Richmond, and South Bend	
G1397	Indianapolis Center for Advanced Research	Indianapolis
G0883	Larue D. Carter Memorial Hospital	Indianapolis
G1697XM	Marion County Assn for Retarded Children, Inc	Indianapolis
G1246XB	Methodist Hospital of Indiana, Inc	Indianapolis
*G1176	New Castle State Hospital	New Castle
G1119	Notre Dame, University of	Notre Dame
G0131	Purdue Univ and Purdue Research Foundation	West Lafayette
	IOWA	
*G0343XO	Iowa State Univ of Science and Technology	Ames
G0209	Iowa, University of	Iowa City
*G0856XO	Woodward State Hospital-School	Woodward

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033037

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	KANSAS	
G0038	Kansas State University	Manhattan
*G0157XO	Kansas, University of	Lawrence
G0229	Kansas, University of, Medical Center College of Health Sciences and Hospital	Kansas City
G0081	Menninger Foundation	Topeka
	KENTUCKY	
G0223	Kentucky, Univ of, and the Research Foundation	Lexington
G0527	Louisville, University of, Except School of Medicine, and Louisville, University of, Foundation, Inc	Louisville
G0023	Louisville, University of, Schools of Medicine and Dentistry	Louisville
	LOUISIANA	
G0442XB	Alton Ochsner Medical Foundation	New Orleans
*G0262XO	Louisiana State Univ and A & M College System	Baton Rouge
*G2428XO	Louisiana State Univ in Baton Rouge	Baton Rouge
*G2485	Louisiana State Univ Medical Center	New Orleans
G0137XM	Pinecrest State School	Pineville
G0018	Tulane Medical Center	New Orleans
G2386	Tulane University Except Medical Center	New Orleans
G0010	USPHS Hospital (National Leprosarium)	Carville
G0010	USPHS Hospital, New Orleans	New Orleans
	MAINE	
G3007	Eastern Maine Medical Center	Bangor
G0513	Maine Medical Center	Portland

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	MARYLAND	
G0402	Baltimore City Hospitals	Baltimore
G0010	Division of Hospitals and Clinics, BMS, DHEW (Includes 9 USPHS Hospitals and 26 Outpatient Clinics)	West Hyattsville
G0186	Friends Medical Science Research Center, Inc	Baltimore
G0640	Institute for Behavioral Research, Inc	Silver Spring
G0352	Johns Hopkins Univ Faculty of Arts and Sciences	Baltimore
G0274	Johns Hopkins Univ School of Hygiene and Public Health	Baltimore
G0174	Johns Hopkins Univ School of Medicine and Johns Hopkins Hospital	Baltimore
G0326	Maryland, Univ of, at Baltimore	Baltimore
G0296	Maryland, Univ of, at College Park	College Park
G0400	Sinai Hospital of Baltimore, Inc	Baltimore
G0010	USPHS Hospital, Baltimore	Baltimore
	MASSACHUSETTS	
G0784XM	American Institutes for Research	Cambridge
G0286	Beth Israel Hospital	Boston
G0554	Boston City Hospital	Boston
G0554	Boston Department of Health and Hospitals	Boston
G0554	Boston Division of Community Health Services	Boston
G0488	Boston Hospital for Women, a Division of the Affiliated Hospitals Center, Inc	Boston
G0783	Boston Mental Health Foundation, Inc	Boston
G0783	Boston State Hospital	Boston
G0322XM	Boston Univ, Charles River Campus	Boston
G0550	Boston Univ Medical Center	Boston
G0550	Boston Univ School of Graduate Dentistry	Boston
G0550	Boston Univ School of Medicine	Boston
G0132XM	Brandeis University	Waltham
G2396XB	Center for Blood Research, Inc	Boston
G0406	Children's Hospital Medical Center	Boston
G0117XM	Clark University	Worcester
G0098	Danvers State Hospital	Hathorne
G2042	Eunice Kennedy Shriver Center	Waltham
G0410XB	Eye Research Institute of Retina Foundation	Boston

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033039

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0412XB	Forsyth Dental Center	Boston
G2397	Harvard Medical Sch and Sch of Dental Medicine	Boston
G2238	Harvard Univ, Faculty of Arts and Sciences	Cambridge
G2494XM	Harvard Univ, Graduate School of Education	Cambridge
G2398XB	Harvard Univ, School of Public Health	Boston
G2573	Harvard Univ, University Health Services	Cambridge
G0791XB	Joslin Diabetes Foundation, Inc	Boston
G0087XB	Lahey Clinic Foundation, Inc	Boston
G0449XB	Lemuel Shattuck Hospital	Jamaica Plain
G0554	Long Island Chronic Disease Hospital	Boston Harbor
G2304XO	Mass Developmental Disabilities Council	Boston
G0212XB	Massachusetts Eye and Ear Infirmary	Boston
G0167	Massachusetts General Hospital	Boston
G0097	Massachusetts Institute of Technology	Cambridge
G0597	Massachusetts Mental Health Center	Boston
G0597	Massachusetts Mental Health Research Corp	Boston
G0147XM	Massachusetts, University of - Amherst	Amherst
G2736	Massachusetts, University of, Medical School	Worcester
G0554	Mattapan Chronic Disease Hospital	Mattapan
G0576	McLean Hospital	Belmont
G0494XB	New England Deaconess Hospital	Boston
G0133	New England Medical Center Hospital	Boston
G0297	Northeastern University	Boston
G0429XB	Peter Bent Brigham Hospital Division of the Affiliated Hospitals Center, Inc	Boston
G3018XB	Pondville Hospital	Walpole (Norfolk)
G2515XM	Research Institute for Educational Problems	Cambridge
G0404XB	Robert B. Brigham Hospital, a Division of the Affiliated Hospitals Center, Inc	Boston
G0771	Sidney Farber Cancer Institute, Inc	Boston
G0351XB	St Margaret's Hospital for Women	Boston
G0554	Trustees of Health & Hosps, City of Boston, Inc	Boston
G2107	Tufts-New England Medical Center	Boston
G2379	Tufts University - Boston	Boston
*G0266XO	Tufts University - Medford	Medford
G0550	University Hospital, Inc	Boston
G0010	USPHS Hospital, Boston	Boston
G2042	Walter E. Fernald State School	Belmont
G0085	Worcester Foundation for Experimental Biology	Shrewsbury

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033040

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	MICHIGAN	
G0363	Child Research Center of Michigan	Detroit
G0363	Children's Hospital of Michigan	Detroit
G0497XM	Detroit, University of	Detroit
G0357	Edsel B. Ford Institute for Medical Research	Detroit
G0357	Henry Ford Hospital	Detroit
G0101	Lafayette Clinic	Detroit
G0656XB	Michigan Cancer Foundation	Detroit
G0615	Michigan Department of Public Health	Lansing
G0384	Michigan State University	East Lansing
G0295	Michigan, University of	Ann Arbor
G0295	Michigan, University of	Dearborn
G0295	Michigan, University of	Flint
G1009XM	Oakland University	Rochester
G0008	Sinai Hospital of Detroit	Detroit
G2483XB	Veterans Administration Hospital-Ann Arbor	Ann Arbor
G0354	Wayne State University	Detroit
G0720	Western Michigan University	Kalamazoo
	MINNESOTA	
G0065XB	Hennepin County Medical Center	Minneapolis
G0041	Mayo Foundation	Rochester
G0065XB	Minneapolis Medical Research Foundation, Inc	Minneapolis
G0463	Minnesota, University of	Austin
G0463	Minnesota, University of	Duluth
G0463	Minnesota, University of	Minneapolis
G0463	Minnesota, University of	Morris
G0463	Minnesota, University of	St Paul
G0463	Minnesota, University of, Technical College	Crookston
G0463	Minnesota, University of, Technical College	Waseca
	MISSISSIPPI	
*G0561XO	Mississippi, University of	University
G0366	Mississippi, University of, Medical Center	Jackson
G0366	Veterans Administration Center	Jackson

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033041

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	MISSOURI	
G2791XM	American Nurses' Association, Inc	Kansas City
*G0298	Cancer Research Center	Columbia
*G0298	Ellis Fischel State Cancer Hospital	Columbia
G0424	Jewish Hospital of St Louis	St Louis
*G0292XO	Missouri, University of, Except Medical Center	Columbia
*G0292	Missouri, University of, Medical Center, Including Missouri Institute of Psychiatry	Columbia
*G0292	Missouri, University of	Kansas City
*G0292XO	Missouri, University of	Rolla
*G0292XO	Missouri, University of	St Louis
*G0292	Missouri, University of, Regional Medical Programs, All Campuses	
*G0356	St Louis University	St Louis
*G2056	Veterans Administration Hospital-Kansas City	Kansas City
G0279XM	Washington University (Excluding Schools of Medicine and Dentistry)	St Louis
G2351	Washington University School of Medicine	St Louis
	NEBRASKA	
G1120	Creighton University	Omaha
G0407	Nebraska, Univ of, Including the Medical Ctr	Omaha
G0407	Nebraska, Univ of, Including the State Univ of Nebraska	Lincoln
	NEVADA	
G0762XM	Nevada, University of, Reno Campus	Reno
	NEW HAMPSHIRE	
G0427XM	Dartmouth College Faculty of Arts & Sciences	Hanover
G0227	Dartmouth Medical School	Hanover

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033042

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	NEW JERSEY	
G0981XM	Educational Testing Service	Princeton
G0492XB	Institute for Medical Research	Camden
G0349	New Jersey, College of Medicine & Dentistry of	Newark
G0349	New Jersey Dental School	Jersey City
G0349	New Jersey Medical School	Newark
G0837	Newark Beth Israel Medical Center	Newark
G0570XM	Princeton University	Princeton
G0349	Rutgers Medical School	Piscataway
G0300	Rutgers, The State Univ of New Jersey	Camden
G0300	Rutgers, The State Univ of New Jersey	New Brunswick
G0300	Rutgers, The State Univ of New Jersey	Newark
	NEW MEXICO	
*G0472	New Mexico, University of	Albuquerque
*G0353	New Mexico, University of, Health Sciences Group-School of Medicine, Colleges of Pharmacy and Nursing	Albuquerque
	NEW YORK	
G0217	Albany Medical College of Union University	Albany
G2129	American Health Foundation	New York
G1064XB	Associated Universities, Inc, Including Brookhaven National Laboratory	Upton
G2116XM	Barnard College	New York
G0341	Beth Israel Medical Center	New York
G1831XM	Center for Policy Research, Inc	New York
G2277XM	Child Welfare League of America, Inc	New York
G0381	Children's Hospital of Buffalo	Buffalo
G0437XM	Columbia Univ, Except Health Sciences Division	New York
G0034	Columbia Univ Health Sciences Division, Including College of Physicians and Surgeons, Schools of Public Health and Nursing, Faculty of Medicine, and Oral and Dental Surgery	New York

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033043

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0063	Cornell Univ, Except Medical College	Ithaca
G0245	Cornell University Medical College	New York
G0109XB	Eastman Dental Center	Rochester
G2912XB	Genesee Hospital	Rochester
G2887XB	Health Research, Inc, Albany Division	Albany
G2904	Health Research, Inc, Roswell Park Division	Buffalo
G2887XB	Helen Hayes Hospital	West Haverstraw
G2475XB	Highland Hospital of Rochester	Rochester
G0621	Hospital for Joint Diseases and Medical Center, Including the Research Institute for Skeletomuscular Diseases	New York
G0047	Hospital for Special Surgery	New York
G2920	ICD Rehabilitation and Research Center	New York
G1005XO	Jewish Board of Guardians	New York
G0369	Kingsbrook Jewish Medical Center and Isaac Albert Research Institute	Brooklyn
G2375	Long Island Jewish-Hillside Medical Center	New Hyde Park
G0397	Maimonides Medical Center	Brooklyn
G0086	Mary Imogene Bassett Hospital	Cooperstown
G0383XB	Memorial Hosp for Cancer and Allied Diseases	New York
G0059	Montefiore Hospital and Medical Center	New York
G0139	Mount Sinai School of Medicine of CUNY	New York
G2518XB	Nassau County Medical Center, Including Meadowbrook Medical Education and Research Foundation, Inc	East Meadow
G0173XM	New School for Social Research	New York
G0526XB	New York Blood Center, Inc	New York
G1370XB	New York City Department of Health	New York
G0765XM	New York, City Univ of	New York
G0765XM	New York, City Univ of, Baruch College	New York
G0765XM	New York, City Univ of, Bronx Cmty College	Bronx
G0765XM	New York, City Univ of, Brooklyn College	Brooklyn
G0765XM	New York, City Univ of, City College	New York
G0765XM	New York, City Univ of, Graduate School and University Center	New York
G0765XM	New York, City Univ of, Herbert H. Lehman College	Bronx
G0765XM	New York, City Univ of, Hunter College	New York
G0765XM	New York, City Univ of, John Jay College of Criminal Justice	New York

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033044

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0765XM	New York, City Univ of, Kingsborough Community College	Brooklyn
G0765XM	New York, City Univ of, Manhattan Cmty College	New York
G0765XM	New York, City Univ of, Medgar Evers College	Brooklyn
G0765XM	New York, City Univ of, New York City Community College	Brooklyn
G0765XM	New York, City Univ of, Queens College	Flushing
G0765XM	New York, City Univ of, Queensborough Community College	New York
G0765XM	New York, City Univ of, Research Foundation	New York
G0765XM	New York, City Univ of, Staten Island Community College	Staten Island
G0765XM	New York, City Univ of, York College	Jamaica
G2887XB	New York Dept of Health and Regional Offices	Albany
G0208	New York Medical College-Flower and Fifth Avenue Hospitals, Metropolitan Hospital, and Bird S. Coler Memorial Hospital	New York
G0374XM	New York, State Univ of, at Albany	Albany
G0508	New York, State Univ of, at Binghamton	Binghamton
G0163	New York, State Univ of, at Buffalo	Buffalo
G0596	New York, State Univ of, at Stony Brook	Stony Brook
G0474	New York, State Univ of, College at Brockport	Brockport
G0506XM	New York, State Univ of, College at Buffalo	Buffalo
G0259XM	New York, State Univ of, College at Cortland	Cortland
G0386XM	New York, State Univ of, College at Oswego	Oswego
G0457	New York, State Univ of, College of Arts and Science at Geneseo	Geneseo
G0220	New York, State Univ of, College of Environmental Science and Forestry	Syracuse
G0305	New York, State Univ of, Downstate Medical Ctr	Brooklyn
G0127	New York, State Univ of, Upstate Medical Ctr	Syracuse
G0390XO	New York Univ, Exclusive of the Medical Ctr	New York
G0405	New York University Medical Center	New York
G0788	North Shore Hospital	Manhasset
G2887XB	Oxford Home for Veterans and Their Dependents	Oxford
G2247	Public Health Research Institute of the City of New York, Inc	New York
G2375	Queens Hospital Center	Jamaica
G1001	Rensselaer Polytechnic Institute	Troy

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033045

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0624	Research Foundation for Mental Hygiene, Inc (NYS Dept of Mental Hygiene) Including	Albany
	New York State Psychiatric Institute	New York
	Long Island Research Institute	Central Islip
	NYS Institute for Basic Research in Mental Retardation	Staten Island
	Research Institute on Alcoholism	Buffalo
	Rockland Research Institute	Orangeburg
	Marcy Psychiatric Ctr, Research Division	Marcy
	Creedmoor Inst for Psychobiologic Studies	Queens Village
G0172	Rochester, University of	Rochester
G0230	Rockefeller University	New York
G2036	Rockland County Health & Social Svcs Complex	Pomona
G0491	Roosevelt Hospital	New York
G2904	Roswell Park Memorial Institute	Buffalo
G0536XB	Sloan-Kettering Institute for Cancer Research	New York
G0076	St Luke's Hospital Center	New York
G2972XB	St Mary's Hospital	Rochester
G0376	St Vincent's Hosp and Medical Ctr of New York	New York
G0280XM	Syracuse University	Syracuse
G0373XM	Teachers College, Columbia University	New York
G2438XB	Trudeau Institute	Saranac Lake
G0010	USPHS Hospital, Staten Island	New York
G2045	Veterans Administration Hospital-Northport	Northport
G0002	Yeshiva Univ, Albert Einstein College of Med	Bronx
	NORTH CAROLINA	
G0191	Duke University Medical Center and Duke University Exclusive of the Medical Center	Durham
G2242	North Carolina A & T State University	Greensboro
G0285	North Carolina State University at Raleigh	Raleigh
G0177	North Carolina, Univ of, at Chapel Hill	Chapel Hill
G0242	Wake Forest Univ, Bowman Gray Sch of Medicine	Winston-Salem
G1087	Wake Forest Univ, Except School of Medicine	Winston-Salem
G0078	Western Carolina Center	Morganton

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033046

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	OHIO	
G0485	Akron, University of	Akron
G0683XM	Battelle Columbus Laboratories of the Battelle Memorial Institute	Columbus
G2843XB	Cancer Center, Inc	Cleveland
G1167	Case Western Reserve University	Cleveland
G0088	Children's Hospital Medical Center	Cincinnati
G0249	Children's Hospital Research Foundation, Inc	Columbus
G0667XM	Cincinnati, Univ of, Except Medical Center	Cincinnati
G0337	Cincinnati, Univ of, Medical Center, Including Colleges of Medicine, Nursing, and Health and Pharmacy	Cincinnati
G0502XB	Cleveland Clinic Foundation and Cleveland Clinic Educational Foundation	Cleveland
G0171	Cleveland Psychiatric Institute	Cleveland
G0160	Fels Research Institute	Yellow Springs
G1936XB	Jewish Hospital of Cincinnati, Including the School of Nursing, Children's Psychiatric Center, and May Institute for Medical Research	Cincinnati
G0542	Kent State University	Kent
G1724	Medical College of Ohio at Toledo	Toledo
G0269XB	Mount Sinai Hospital of Cleveland	Cleveland
G0121	Ohio Agricultural Research & Development Ctr	Wooster
G0121	Ohio State University and Research Foundation	Columbus
G0662XB	St Luke's Hospital Association (United Methodist Church)	Cleveland
G0350XB	University Hospitals of Cleveland	Cleveland
G2907XM	Youngstown State University	Youngstown
	OKLAHOMA	
*G0327	Oklahoma Medical Research Foundation	Oklahoma City
*G2402XO	Oklahoma, University of	Norman
*G0241	Oklahoma, University of, Health Sciences Ctr	Oklahoma City

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033047

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	OREGON	
*G0214	Kaiser Foundation Research Institute	Portland
G0043XB	Medical Research Foundation of Oregon and Oregon Regional Primate Research Center	Portland
*G2399XO	Northwest Regional Educational Laboratory	Portland
G0505XM	Oregon Research Institute	Eugene
G0111XM	Oregon State University	Corvallis
G0288XM	Oregon, University of, Graduate School	Eugene
G2931	Oregon, University of, Health Sciences Center, Including Schools of Medicine, Dentistry, and Nursing	Portland
	PENNSYLVANIA	
G0125	Albert Einstein Medical Center, Northern Div	Philadelphia
G0952XB	Allegheny General Hospital	Pittsburgh
G0784XM	American Institutes for Research	Pittsburgh
G0338	Arthur P. Noyes Research Foundation	Norristown
G0436XM	Bucknell University	Lewisburg
G1218	Carnegie-Mellon University	Pittsburgh
G0129	Children's Hospital of Philadelphia (Joseph Stokes, Jr., Research Inst of)	Philadelphia
G0360XB	Children's Hospital of Pittsburgh	Pittsburgh
G1556	Franklin Institute	Philadelphia
G0475	Hahnemann Medical College and Hospital	Philadelphia
G0936	H. K. Cooper Institute for Oral-Facial Anomalies and Communicative Disorders (Lancaster Cleft Palate Clinic)	Lancaster
G0045	Institute for Cancer Research (Fox Chase Cancer Center and American Oncologic Hosp)	Philadelphia
G0273XB	Lankenau Hospital	Philadelphia
G0189XB	Magee-Womens Hospital	Pittsburgh
G2121XM	Marywood College	Scranton
G0057XB	Montefiore Hospital	Pittsburgh
G0338	Norristown State Hospital	Norristown
G0333	Pennsylvania Hospital	Philadelphia
G0222	Pennsylvania, Medical College of	Philadelphia
G0573	Pennsylvania State Univ & Commonwealth Camps	University Park

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033048

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G1668	Pennsylvania State Univ, Milton S. Hershey Medical Center	Hershey
G0012	Pennsylvania, University of	Philadelphia
G1531	Philadelphia Department of Public Health	Philadelphia
G0044	Philadelphia General Hospital	Philadelphia
G0324	Philadelphia Geriatric Center	Philadelphia
G0344	Philadelphia Psychiatric Center	Philadelphia
G0881	Philadelphia State Hospital	Philadelphia
G1532	Pittsburgh Child Guidance Center	Pittsburgh
G2929	Pittsburgh, University Health Center of	Pittsburgh
G0418	Pittsburgh, University of	Pittsburgh
G2200	Presbyterian-University Hospital	Pittsburgh
G0465	Presbyterian-Univ of Pennsylvania Medical Ctr	Philadelphia
G2264XM	Research for Better Schools, Inc	Philadelphia
G0795	St Joseph's Hospital	Lancaster
G2880	Temple Univ, Excluding the Health Sciences Ctr	Philadelphia
G2879	Temple University Health Sciences Center	Philadelphia
G0049	Thomas Jefferson Univ, All Components	Philadelphia
G0362XB	Wills Eye Hospital and Research Institute	Philadelphia
G0054XB	Wistar Institute	Philadelphia
	PUERTO RICO	
G1348XM	Catholic University of Puerto Rico	Ponce
G0256XB	Puerto Rico, Univ of, Medical Sciences Campus	San Juan Rio Piedras
	RHODE ISLAND	
G0467	Brown University	Providence
*G0318	Rhode Island Hospital	Providence
G2212XB	Roger Williams General Hospital	Providence
	SOUTH CAROLINA	
G2621	Clemson University	Clemson
G0533	South Carolina Department of Mental Health	Columbia
G0240	South Carolina, Medical University of	Charleston
*G0629XO	South Carolina, University of	Columbia

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	TENNESSEE	
G0490XM	George Peabody College for Teachers	Nashville
G0393	Meharry Medical College	Nashville
G1716	Oak Ridge Associated Universities	Oak Ridge
G1716	Oak Ridge National Laboratory	Oak Ridge
G0648	St Jude Children's Research Hospital	Memphis
G0170	Tennessee, University of, Center for the Health Sciences	Memphis
G0124	Tennessee, University of - Knoxville	Knoxville
G0401	Vanderbilt University	Nashville
	TEXAS	
G0307	Baylor College of Medicine	Houston
*G1843	Bexar County Hospital District	San Antonio
G0398XM	Houston, University of	Houston
*G2344XO	Southwest Educational Development Corporation (AKA Southwest Educational Development Lab)	Austin
G1045	Texas A & M University and Research Foundation, College Station Campus Only	College Station
G3027	Texas Department of Public Welfare	Austin
*G0590	Texas Institute for Rehabilitation and Research	Houston
G0564	Texas Tech University Complex (Texas Tech Univ and Texas Tech Univ Sch of Medicine)	Lubbock
*G1121XO	Texas, University of, at Arlington	Arlington
G0123	Texas, University of, at Austin	Austin
G0113	Texas, University of, Cancer Center (and its M.D. Anderson Hospital and Tumor Institute)	Houston
G2615	Texas, University of, Health Science Center at Dallas	Dallas
*G2760	Texas, University of, Health Science Center at Houston	Houston
*G2255	Texas, University of, Health Science Center at San Antonio, Including Medical School, Dental School, and Graduate School of Biomedical Sciences	San Antonio
G0107	Texas, Univ of, Medical Branch at Galveston	Galveston
G0010	USPHS Hospital, Galveston	Galveston

RESTRICTION CODE
XM — No Medical or IND Studies
XB — No Behavioral Studies
XO — Other Restriction (Call 301-496-7005)
* — Final Acceptance of Revisions Pending

1033050

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☐ FOLLOWUP ☐ REVISION

☐ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☐ RENEWAL ☐ CONTINUATION

APPLICATION IDENTIFICATION NUMBER *(If known)*

_____

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of Public Law 93-348, as implemented by Part 46 of Title 45 of the Code of Federal Regulations, as amended, (45 CFR 46). Administration of the DHEW policy and regulation is the responsibility of the Office for Protection from Research Risks, National Institutes of Health, Bethesda, Md 20014.

1. TITLE OF PROPOSAL OR ACTIVITY

2. PRINCIPAL INVESTIGATOR/ACTIVITY DIRECTOR/FELLOW

3. DECLARATION THAT HUMAN SUBJECTS EITHER WOULD OR WOULD NOT BE INVOLVED

☐ A. NO INDIVIDUALS WHO MIGHT BE CONSIDERED HUMAN SUBJECTS, INCLUDING THOSE FROM WHOM ORGANS, TISSUES, FLUIDS, OR OTHER MATERIALS WOULD BE DERIVED, OR WHO COULD BE IDENTIFIED BY PERSONAL DATA, WOULD BE INVOLVED IN THE PROPOSED ACTIVITY. (IF NO HUMAN SUBJECTS WOULD BE INVOLVED, CHECK THIS BOX AND PROCEED TO ITEM 7. PROPOSALS DETERMINED BY THE AGENCY TO INVOLVE HUMAN SUBJECTS WILL BE RETURNED.)

☐ B. HUMAN SUBJECTS WOULD BE INVOLVED IN THE PROPOSED ACTIVITY AS EITHER: ☐ NONE OF THE FOLLOWING, OR INCLUDING: ☐ MINORS, ☐ FETUSES, ☐ ABORTUSES, ☐ PREGNANT WOMEN, ☐ PRISONERS, ☐ MENTALLY RETARDED, ☐ MENTALLY DISABLED. UNDER SECTION 5. COOPERATING INSTITUTIONS, ON REVERSE OF THIS FORM, GIVE NAME OF INSTITUTION AND NAME AND ADDRESS OF OFFICIAL(S) AUTHORIZING ACCESS TO ANY SUBJECTS IN FACILITIES NOT UNDER DIRECT CONTROL OF THE APPLICANT OR OFFERING INSTITUTION.

4. DECLARATION OF ASSURANCE STATUS/CERTIFICATION OF REVIEW

☐ A. THIS INSTITUTION HAS NOT PREVIOUSLY FILED AN ASSURANCE AND ASSURANCE IMPLEMENTING PROCEDURES FOR THE PROTECTION OF HUMAN SUBJECTS WITH THE DHEW THAT APPLIES TO THIS APPLICATION OR ACTIVITY. ASSURANCE IS HEREBY GIVEN THAT THIS INSTITUTION WILL COMPLY WITH REQUIREMENTS OF *DHEW Regulation 45 CFR 46*, THAT IT HAS ESTABLISHED AN INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS AND, WHEN REQUESTED, WILL SUBMIT TO DHEW DOCUMENTATION AND CERTIFICATION OF SUCH REVIEWS AND PROCEDURES AS MAY BE REQUIRED FOR IMPLEMENTATION OF THIS ASSURANCE FOR THE PROPOSED PROJECT OR ACTIVITY.

☐ B. THIS INSTITUTION HAS AN APPROVED GENERAL ASSURANCE (DHEW ASSURANCE NUMBER _____) OR AN ACTIVE SPECIAL ASSURANCE FOR THIS ONGOING ACTIVITY, ON FILE WITH DHEW. THE SIGNER CERTIFIES THAT ALL ACTIVITIES IN THIS APPLICATION PROPOSING TO INVOLVE HUMAN SUBJECTS HAVE BEEN REVIEWED AND APPROVED BY THIS INSTITUTION'S INSTITUTIONAL REVIEW BOARD IN A CONVENED MEETING ON THE DATE OF _____ IN ACCORDANCE WITH THE REQUIREMENTS OF THE *Code of Federal Regulations on Protection of Human Subjects (45 CFR 46)*. THIS CERTIFICATION INCLUDES, WHEN APPLICABLE, REQUIREMENTS FOR CERTIFYING FDA STATUS FOR EACH INVESTIGATIONAL NEW DRUG TO BE USED (SEE REVERSE SIDE OF THIS FORM).

THE INSTITUTIONAL REVIEW BOARD HAS DETERMINED, AND THE INSTITUTIONAL OFFICIAL SIGNING BELOW CONCURS THAT:

EITHER ☐ HUMAN SUBJECTS WILL NOT BE AT RISK; OR ☐ HUMAN SUBJECTS WILL BE AT RISK.

5. AND 6. SEE REVERSE SIDE

7. NAME AND ADDRESS OF INSTITUTION

8. TITLE OF INSTITUTIONAL OFFICIAL	TELEPHONE NUMBER
SIGNATURE OF INSTITUTIONAL OFFICIAL	DATE

HEW-596 (Rev. 4-75)

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO REQUESTING AGENCY.

1033051

5. INVESTIGATIONAL NEW DRUGS - ADDITIONAL CERTIFICATION REQUIREMENT

SECTION 46.17 OF TITLE 45 OF THE Code of Federal Regulations states, "Where an organization is required to prepare or to submit a certification . . . and the proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 130.3(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received."

INVESTIGATIONAL NEW DRUG CERTIFICATION

TO CERTIFY COMPLIANCE WITH FDA REQUIREMENTS FOR PROPOSED USE OF INVESTIGATIONAL NEW DRUGS IN ADDITION TO CERTIFICATION OF INSTITUTIONAL REVIEW BOARD APPROVAL, THE FOLLOWING REPORT FORMAT SHOULD BE USED FOR EACH IND: (ATTACH ADDITIONAL IND CERTIFICATIONS AS NECESSARY).

- IND FORMS FILED: ☐ FDA 1571, ☐ FDA 1572, ☐ FDA 1573

- NAME OF IND AND SPONSOR _____

- DATE OF 30-DAY EXPIRATION OR FDA WAIVER
  (FUTURE DATE REQUIRES FOLLOWUP REPORT TO AGENCY) _____

- FDA RESTRICTION _____

- SIGNATURE OF INVESTIGATOR _____ DATE _____

6. COOPERATING INSTITUTIONS - ADDITIONAL REPORTING REQUIREMENT

SECTION 46.16 OF TITLE 45 OF THE *Code of Federal Regulations* IMPOSES SPECIAL REQUIREMENTS ON THE CONDUCT OF STUDIES OR ACTIVITIES IN WHICH THE GRANTEE OR PRIME CONTRACTOR OBTAINS ACCESS TO ALL OR SOME OF THE SUBJECTS THROUGH COOPERATING INSTITUTIONS NOT UNDER ITS CONTROL. IN ORDER THAT THE DHEW BE FULLY INFORMED, THE FOLLOWING REPORT IS REQUESTED WHEN APPLICABLE.

USE FOLLOWING REPORT FORMAT FOR EACH INSTITUTION OTHER THAN GRANTEE OR CONTRACTING INSTITUTION WITH RESPONSIBILITY FOR HUMAN SUBJECTS PARTICIPATING IN THIS ACTIVITY: (ATTACH ADDITIONAL REPORT SHEETS AS NECESSARY).

INSTITUTIONAL AUTHORIZATION FOR ACCESS TO SUBJECTS

- SUBJECTS: STATUS (WARDS, RESIDENTS, EMPLOYEES, PATIENTS, ETC.) _____

NUMBER _____ AGE RANGE _____

NAME OF OFFICIAL (PLEASE PRINT) _____

TITLE _____ TELEPHONE _____

NAME AND ADDRESS OF COOPERATING INSTITUTION _____

- OFFICIAL SIGNATURE _____

NOTES: *(e.g., report of modification in proposal as submitted to agency affecting human subjects involvement)*

1033052

Rec. 11-28-77
cc: Dr. Hübner
Dianne /HSI

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

General Assurance G1716

November 23, 1977

C. C. Lushbaugh
Medical and Health Sciences Division
Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Lushbaugh:

Thanks for your letter of November 7, 1977 reporting changes in membership of your human subjects review board and explaining the quorum arrangement. All this is acceptable and your letter is now on file as an amendment to your general assurance G1716.

There is nothing wrong with all thirteen members, including representatives from ORAU and ORNL, participating regularly in most board actions. Only an individual who may have a close and possible conflicting interest in a project being reviewed need be left out. In fact it is very likely that a member's field of competence is more important than his affiliation in decisions about quorum composition. If you care to change your system just let us know.

Sincerely,

Roy Kinard

Roy Kinard, D.V.M.
Office for Protection
from Research Risks
Office of the Director

Enclosure: IRB Member Form

1033053

INSTITUTIONAL REVIEW BOARD ROSTER

[Instructions: Please use this format. Do not send curriculum vitae, bibliographies, or detailed information other than that indicated.]

NAME OF INSTITUTION _____
(typewritten)

GENERAL ASSURANCE NUMBER

G 1716 _____

DATE: _____

Institutional Officer (other than chairperson to whom correspondence should be addressed)

_____
(Name - typewritten)

_____
(Title - typewritten)

Regular Member		Alternate Member
Name (typewritten): _____ Earned Degrees: _____ Position or Occupation: _____ Board certification, licenses, etc.: _____ Relationship to institution: _____ Representative capacity: _____	____	Designated Alternate (if any)
Name (typewritten): _____ Earned Degrees: _____ Position or Occupation: _____ Board certification, licenses, etc.: _____ Relationship to institution: _____ Representative capacity: _____	____	Designated Alternate (if any)
Name (typewritten): _____ Earned Degrees: _____ Position or Occupation: _____ Board certification, licenses, etc.: _____ Relationship to institution: _____ Representative capacity: _____	____	Designated Alternate (if any)

(Add Continuation Pages as Necessary)

1033054

(CONTINUATION PAGE)

Regular Member		Alternate Member
Name (typewritten): _____		
Earned Degrees: _____		
Position or Occupation: _____		Designated Alternate
Board certification, licenses: __	——	(if any)
Relationship to institution: ____		
Representative capacity: _____		

(Repeat as Needed)

NOTES:

(a) The IRB must consist of not less than FIVE members identified as above.

(b) Alternate members (if any) should be similarly identified and keyed to a particular member(s).

(c) The "Representative capacity" line should be used to indicate whether the individual serves the IRB as an investigator, administrator, practitioner, lawyer, ethicist, or in other capacities such as community representative.

(d) An IRB member may serve in more than one representative capacity.

(e) The Chairman of the IRB *must be identified.*

(f) IRBs reviewing activities involving the use of investigational new drugs (INDs) *must include at least two individuals licensed to administer drugs, and one person who is not so licensed.* Review for other purposes should utilize IRBs of equal or greater breadth.

(g) No IRB may be composed *entirely of members from the same professional group or entirely of members employed either full or part-time by the institution.*

(h) When updating an existing committee, *please submit a new roster, listing the full membership as it currently stands.*

1978

1033056

ORAU/ORNL
COMMITTEE ON HUMAN STUDIES
MEDICAL SCIENCES DIVISION
BUSINESS FILE 2
1978: NO DOCUMENTS

1033057

1033058

Rec 5/3/79

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

Dianne

May 1, 1979

59TH CUMULATIVE LIST 1979

OF INSTITUTIONS WHICH HAVE ESTABLISHED

GENERAL ASSURANCES

OF COMPLIANCE WITH HEW REGULATIONS ON

PROTECTION OF HUMAN SUBJECTS

see page 21

1. INCOMING PROPOSALS - GRANTS OR CONTRACTS

a. If the professional review of a proposal indicates that the project *does not involve* human subjects (box on signature page of application or box 3A of HEW-596), as defined in 45 CFR 46, the application can be processed without further regard to the question of institutional assurances.

b. If the professional review of a proposal indicates that the project *does involve* human subjects (box on signature page of application or box 3B of HEW-596), the next step is to determine whether the institution has checked either box 4A or 4B.

- If 4A is checked, this means that the applicant institution does *not have* an approved assurance on file but will supply documentation and certification of review when requested. This action is initiated by the OPRR, OD, NIH; Westwood Bldg., Room 303; Bethesda, Maryland 20205; upon receipt of a copy of the proposal and summary statement from the *operating agency* immediately following an initial review.

- If 4B is checked, this means that the applicant institution has an approved general assurance on file. The fill-in spaces in this paragraph indicate the HEW general assurance "G" number for the institution as presented in the "Cumulative Listing" and the date when the proposal was certified.

1033059

c. Draft requests for proposals (RFPs or RFAs) should be reviewed to determine whether performance will involve human subjects at risk. If these will be involved, the RFP should include the "Notice to Offerors" required by 41 CFR 3-4.5504(a). Offerings and proposals submitted in response to the RFP should be handled as in 1.b. above.

d. Operating agencies may define "submission date" to fit administrative requirements. It is suggested that sole source responses to RFPs should be considered to be submitted as of the closing date of the RFP and should then be handled as in 1.b. above.

e. Competitive responses to RFPs should be considered to be submitted as of the date of submission of the best and final offer, after establishing the zone of consideration or source selection, and should then proceed as in 1.b. above.

2. SUBMISSION OF CERTIFICATIONS - Whenever possible, the review and approval by Institutional Review Boards should occur prior to submission of the application or proposal and a certification to that effect should be included in or with the application or proposal itself, preferably on form HEW-596 (Rev. 4/75). Under no circumstances will the review of an application by the Department of Health, Education, and Welfare be completed until certification is received. The point at which review will be deferred or terminated is left to the operating agency involved.

Institutions having on file with HEW an approved general assurance must submit certification within 30 days of the receipt of a written request thereof; and in any event *within 60 days* after the deadline or submission date for which the application or proposal was submitted.

Institutions not having on file an approved general assurance will indicate their status by checking box 4A on form HEW-596 accompanying the proposal *and when requested must submit the required assurances of compliance and certification of the review and approval* of the application or proposal by its Institutional Review Board within 30 days of the receipt of a written request from the Office for Protection from Research Risks (OPRR).

3. RESTRICTION CODES are presented as a suffix to the general assurance "G" number. This change conforms with the National Research Act, Public Law 93-348, Title II, which specifically applies to both *biomedical* and *behavioral* research and with the derivative HEW regulations.

A restriction usually indicates that additional expertise in the Institutional Review Board membership is necessary for particular activities requiring certification.

An XM suffix indicates that the IRB has no or insufficient medical members. A proposed activity requiring medical expertise to assess risks, benefits, and the adequacy of safeguards cannot be certified under an XM restriction.

An XB suffix indicates that the IRB has no or insufficient members expert in the behavioral sciences. A proposed activity requiring behavioral expertise for assessing risks, benefits, and the adequacy of safeguards cannot be certified under an XB restriction.

An XO suffix indicates a restriction that uniquely applies to the institution under conditions of the general assurance agreement [call (301) 496-7005 for details].

When a proposal to be submitted to HEW comes within the scope of an XM or XB restriction, either biomedical or behavioral, the IRB reviewing the proposal must include additional voting members whose qualifications offset the restriction. Their names and qualifications should be reported immediately to OPRR and a statement added under "Notes" on the HEW-596 form certifying IRB review and approval that the additional professionally qualified members have been reported to OPRR. Proposals that come within the certification restrictions that are not preceded or accompanied by appropriate compensating reviewers will be deferred for rereview and recertification.

4. QUESTIONS with regard to the status of Special or General Assurances of Compliance may be directed to:

Mrs. Florence R. Ober	(301) 496-7005

5. CONSULTATION for Special and General Assurances:

Roy Kinard, D.V.M.	(301) 496-7006
J. R. Marches, Ph.D.	(301) 496-7005

6. FORMS

Bulk orders for additional copies of HEW 596 should be addressed to:

Chief
Office Services Section
Division of Research Grants
National Institutes of Health
Westwood Building, Room A-17
Bethesda, Maryland 20205

Single copies of HEW 596 can be obtained from OPRR or by duplicating the back pages of this listing.

Charles R. McCarthy, Ph.D.
Director
Office for Protection
from Research Risks
Office of the Director
National Institutes of Health

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	ALABAMA	
G0198	Alabama, University of, Birmingham	Birmingham
G0610	Alabama, University of	University
G2522XB	South Alabama, University of, Including the Medical Center	Mobile
G0055	Tuskegee Institute	Tuskegee Inst
	ARIZONA	
G0799XM	Arizona State University	Tempe
G0026	Arizona, University of	Tucson
G1287XB	St. Joseph's Hospital and Medical Center, Including Barrow Neurological Institute	Phoenix
	ARKANSAS	
*G0336	Arkansas, University of, Medical Center	Little Rock
	CALIFORNIA	
G0784XM	American Institutes for Research	Palo Alto
G0261	California State Health and Welfare Agency Department of Health Services Department of Mental Health Department of Developmental Services Department of Social Services Department of Alcohol and Drug Abuse Office of Statewide Health Planning and Development	Sacramento
G0278	California, University of, Berkeley	Berkeley
G0195	California, University of, Davis	Davis
G0380	California, University of, Irvine	Irvine
G0238	California, University of, Los Angeles	Los Angeles
G0193	California, University of, Riverside	Riverside
*G0389	California, University of, San Diego	La Jolla
G0155	California, University of, San Francisco	San Francisco
G0282	California, University of, Santa Barbara	Santa Barbara

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033063

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0205XM	California, University of, Santa Cruz	Santa Cruz
G0234	Cedars-Sinai Medical Center	Los Angeles
*G2564	Charles R. Drew Postgraduate Medical School	Los Angeles
G0135	Childrens Hospital of Los Angeles	Los Angeles
*G0287	Children's Hospital of San Francisco	San Francisco
G0009	City of Hope National Medical Center	Duarte
*G2259XO	Far West Laboratory for Educational Research and Development	San Francisco
G0432	Institute for Medical Research	San Jose
G2169XM	Institute for Research in Social Behavior	Oakland
*G2400	Institute of Medical Sciences	San Francisco
*G2367	John Wesley County Hospital Attending Staff Association	Los Angeles
G0214	Kaiser Foundation Research Institute, a Division of Kaiser Foundation Hospitals, and Kaiser Foundation Hospitals in Northern California, Southern California, Oregon, and Hawaii	Oakland
G0278	Lawrence Berkeley Laboratory University of California	Berkeley
G0226	Loma Linda University	Loma Linda
G0226	Loma Linda University (La Sierra Campus)	Riverside
G0359XB	Los Angeles County Harbor General Hospital, Professional Staff Association of	Torrance
*G0213	Los Angeles County Hospital-University of Southern California Medical Center, Professional Staff Association of	Los Angeles
*G2564	Martin Luther King, Jr. General Hospital and Its Staff Association Foundation	Los Angeles
*G0367XO	Mental Research Institute	Palo Alto
*G0145	Mount Zion Hospital and Medical Center	San Francisco
G2961	Northern California Cancer Program	Palo Alto
*G2400	Pacific, Univ of, School of Dentistry	San Francisco
*G2400	Pacific, Univ of, School of Medical Sciences	San Francisco
G0082XB	Palo Alto Medical Research Foundation	Palo Alto
*G2400	Presbyterian Hospital of the Pacific Medical Center, Inc	San Francisco
*G0067	Rancho Los Amigos Hospital and Its Professional Staff Association	Downey
G1416	Rand Corporation	Santa Monica
*G1096	Salk Institute	San Diego

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033064

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0420	San Diego State University	San Diego
G0420	San Diego State University Foundation	San Diego
G1472XM	Scientific Analysis Corporation (Including the Institute for Scientific Analysis and Performance Sites in Berkeley, Los Angeles, and San Diego)	San Francisco
G0108XB	Scripps Clinic and Research Foundation	La Jolla
*G0122	Southern California, University of	Los Angeles
G0378	SRI International	Menlo Park
G0011	Stanford University	Stanford
G0010	USPHS Hospital, San Francisco	San Francisco
G1620	Veterans Administration Hospital-Long Beach	Long Beach
G1796	Veterans Administration Hospital-Sepulveda	Sepulveda
G1658XB	Veterans Administration Wadsworth Medical Center	Los Angeles
*G1591XO	Wright Institute	Berkeley
	COLORADO	
G0845	Children's Hospital of Denver	Denver
G2823XB	Colorado Regional Cancer Center, Inc	Denver
G1144	Colorado State University	Fort Collins
G0455XM	Colorado, University of	Boulder
G0268	Colorado, University of, Medical Center	Denver
G0277XM	Denver, University of (Colorado Seminary)	Denver
G0267	National Asthma Center	Denver
G0068	National Jewish Hospital and Research Center	Denver
	CONNECTICUT	
G0672XB	Connecticut State Department of Health	Hartford
G0039	Connecticut, University of	Storrs
G1966	Connecticut, University of, Health Center	Farmington-Hartford
G1533	Connecticut Valley Hospital	Middletown
G0331XB	Hartford Hospital	Hartford
G0007	Institute of Living	Hartford
G0003	John B. Pierce Fdn of Connecticut, Inc	New Haven

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033065

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0821	Saint Francis Hospital	Hartford
G2895	Waterbury Hospital Health Center	Waterbury
*G0243	Yale University	New Haven
	DELAWARE	
G0148	Delaware Division of Mental Health of the Department of Health and Social Services	New Castle
G0013	Delaware, University of	Newark
G2480XB	Wilmington Medical Center, Inc	Wilmington
	DISTRICT OF COLUMBIA	
G0784XM	American Institutes for Research	Washington
G1398XB	American National Red Cross	Washington
G1674XM	Bureau of Social Science Research, Inc	Washington
G0365XM	Catholic University of America	Washington
G0042	Children's Hospital of D.C., Research Foundation of	Washington
G1249	Gallaudet College	Washington
G0294	George Washington University	Washington
G0228	Georgetown University	Washington
G0841	Howard University	Washington
G1989	National Academy of Sciences, Including National Academy of Engineering, Institute of Medicine, and National Research Council	Washington
G1036XM	National Children's Center, Inc	Washington
G3045XO	Veterans Administration Central Office (NCI-VA COOP CANCER THERAPY PROJECTS ONLY)	Washington
G0180	Washington Hospital Center	Washington
	FLORIDA	
G2905	Florida State Department of Health and Rehabilitative Services	Tallahassee
G0119	Florida State University	Tallahassee
G0382	Florida, University of	Gainesville
G0840XB	Miami Heart Institute	Miami Beach

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033066

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0301	Miami, University of	Coral Gables
G0301	Miami, University of	Miami
G0275	Mt Sinai Medical Center of Greater Miami	Miami Beach
G2321	Papanicolaou Cancer Research Institute	Miami
G1065	South Florida, University of	Fort Myers
		St Petersburg
		Sarasota
		Tampa
	GEORGIA	
*G0138	Emory Univ Division of Basic Health Sciences	Atlanta
G0622	Emory Univ Graduate Sch of Arts and Sciences	Atlanta
*G0138	Emory Univ Nell Hodgson Woodruff School of Nursing	Atlanta
G0595	Emory Univ School of Dentistry	Atlanta
*G0138	Emory Univ School of Medicine	Atlanta
G0197	Georgia Dept of Human Resources, All Units	Atlanta
G0520	Georgia Institute of Technology, Including its Engineering Experiment Station, and its Georgia Tech Research Institute	Atlanta
G0151	Georgia, Medical College of	Augusta
G0248	Georgia, University of	Athens
*G1467	Grady Memorial Hospital	Atlanta
	HAWAII	
G0104	Hawaii, University of (Including the Entire System and the Research Corporation)	Honolulu
G0214	Kaiser Foundation Hospital	Honolulu
	IDAHO	
G0218XM	Idaho, University of	Moscow
*G1869	Mountain States Tumor Institute	Boise

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033067

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	ILLINOIS	
G0395	American Dental Assn and ADA Health Fdn	Chicago
G0332XM	Anna Mental Health and Developmental Center	Anna
G1626	Chicago, University of (Division of Biological Sciences and Pritzker School of Medicine, Division of Social Sciences, School of Social Service Administration, and Related Units)	Chicago
G0114	Children's Memorial Hospital	Chicago
G0430	Downey Veterans Administration Hospital	Downey
G0182	Evanston Hospital	Evanston
G0430	Health Sciences, Univ of/Chicago Medical Sch	Chicago
G0053	Hektoen Institute for Medical Research	Chicago
G2959	Illinois Cancer Council	Chicago
G1561	Illinois State Psychiatric Institute	Chicago
G0345	Illinois, University of, at Chicago Circle	Chicago
G0291	Illinois, University of, Medical Center Campus, Including Rockford School of Medicine, Peoria School of Medicine, and Sch of Basic Medical Sciences, Urbana-Champaign	Chicago
G0102	Illinois, Univ of, at Urbana-Champaign	Urbana
G1373XM	Lincoln Developmental Center	Lincoln
G2369	Loyola University Medical Center	Maywood
G0095	Michael Reese Hospital and Medical Center	Chicago
G2763	Mount Sinai Hospital Medical Center of Chicago	Chicago
G0518XM	Northern Illinois University	DeKalb
G0190	Northwestern Memorial Hospital	Chicago
G0190	Northwestern University	Chicago
G0190	Northwestern University	Evanston
G0190	Rehabilitation Institute of Chicago	Chicago
G0175	Rush-Presbyterian-St Luke's Medical Center	Chicago
G0309	Southern Illinois University	Carbondale
G2606XM	Southern Illinois University	Edwardsville
G0309	Southern Illinois Univ School of Medicine	Springfield
G0190	VA Lakeside Hospital of Chicago	Chicago
G1970XM	Western Illinois University	Macomb

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033068

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	INDIANA	
G0314XM	DePauw University	Greencastle
G0945	Fort Wayne State Hosp and Training Center	Ft Wayne
G0185	Indiana Univ and Indiana Univ Foundation	Bloomington Indianapolis
G0185	Indiana University (Law School)	Indianapolis
G0185	Indiana Univ-Purdue Univ (Medical Facility)	Indianapolis
G0185	Indiana University Regional Campuses at Fort Wayne, Gary, Kokomo, New Albany, Richmond, and South Bend	
G1397	Indianapolis Center for Advanced Research	Indianapolis
G0883	Larue D. Carter Memorial Hospital	Indianapolis
G1697	Marion County Assn for Retarded Citizens, Inc	Indianapolis
G1246XB	Methodist Hospital of Indiana, Inc	Indianapolis
G1119	Notre Dame, University of	Notre Dame
G0131	Purdue Univ and Purdue Research Foundation	West Lafayette
	IOWA	
*G0343XO	Iowa State Univ of Science and Technology	Ames
G0209	Iowa, University of	Iowa City
*G0856XO	Woodward State Hospital-School	Woodward
	KANSAS	
G0038	Kansas State University	Manhattan
*G0157XO	Kansas, University of - Lawrence Campus	Lawrence
G0229	Kansas, University of, Medical Center College of Health Sciences and Hospital	Kansas City
G0081	Menninger Foundation	Topeka

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033069

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	KENTUCKY	
G0223	Kentucky, Univ of, and the Research Foundation	Lexington
G0527	Louisville, University of, and Louisville, University of, Foundation, Inc; Except Schools of Med and Dent	Louisville
G0023	Louisville, University of, Schools of Medicine and Dentistry	Louisville
G0223	Veterans Administration Hospital	Lexington
	LOUISIANA	
G0442	Alton Ochsner Medical Foundation	New Orleans
*G0262XO	Louisiana State Univ and A & M College System	Baton Rouge
*G2428XO	Louisiana State Univ in Baton Rouge	Baton Rouge
*G2485	Louisiana State Univ Medical Center	New Orleans
G0137XM	Pinecrest State School	Pineville
G0018	Tulane Medical Center	New Orleans
G2386	Tulane University Except Medical Center	New Orleans
G0010	USPHS Hospital (National Leprosarium)	Carville
G0010	USPHS Hospital, New Orleans	New Orleans
	MAINE	
G3007	Eastern Maine Medical Center	Bangor
G0513	Maine Medical Center	Portland
	MARYLAND	
G0402	Baltimore City Hospitals	Baltimore
G0010	Division of Hospitals and Clinics, BMS, DHEW (Includes 9 USPHS Hospitals and 26 Outpatient Clinics)	West Hyattsville
G3109XB	Frederick Cancer Research Center	Frederick
G0186	Friends Medical Science Research Center, Inc	Baltimore
G0640	Institute for Behavioral Research, Inc	Silver Spring

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033070

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G2857	John F. Kennedy Institute for Handicapped Children	Baltimore
G0352	Johns Hopkins Univ Faculty of Arts and Sciences	Baltimore
G0274	Johns Hopkins Univ School of Hygiene and Public Health and Faculty of Health Services	Baltimore
G0174	Johns Hopkins Univ School of Medicine and Johns Hopkins Hospital	Baltimore
G0326	Maryland, Univ of, at Baltimore	Baltimore
G0296	Maryland, Univ of, at College Park	College Park
G0400	Sinai Hospital of Baltimore, Inc	Baltimore
G0010	USPHS Hospital, Baltimore	Baltimore
	MASSACHUSETTS	
G0784XM	American Institutes for Research	Cambridge
G0286	Beth Israel Hospital	Boston
G0554	Boston City Hospital	Boston
G0554	Boston Department of Health and Hospitals	Boston
G0554	Boston Division of Community Health Services	Boston
G0488	Boston Hospital for Women, a Division of the Affiliated Hospitals Center, Inc	Boston
G0783	Boston Mental Health Foundation, Inc	Boston
G0783	Boston State Hospital	Boston
G0322XM	Boston Univ, Charles River Campus	Boston
G0550	Boston Univ Medical Center	Boston
G0550	Boston Univ School of Graduate Dentistry	Boston
G0550	Boston Univ School of Medicine	Boston
G0132XM	Brandeis University	Waltham
G2396XB	Center for Blood Research, Inc	Boston
G0406	Children's Hospital Medical Center	Boston
G0117XM	Clark University	Worcester
G0098	Danvers State Hospital	Hathorne
G2042	Eunice Kennedy Shriver Center	Waltham
G0410XB	Eye Research Institute of Retina Foundation	Boston
G0412XB	Forsyth Dental Center	Boston
G2397	Harvard Medical Sch and Sch of Dental Medicine	Boston
G2238	Harvard Univ, Faculty of Arts and Sciences	Cambridge
G2494XM	Harvard Univ, Graduate School of Education	Cambridge

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033071

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G2398	Harvard Univ, School of Public Health	Boston
G2573	Harvard Univ, University Health Services	Cambridge
G0791XB	Joslin Diabetes Foundation, Inc	Boston
G0087XB	Lahey Clinic Foundation, Inc	Boston
G0449XB	Lemuel Shattuck Hospital	Jamaica Plain
G0554	Long Island Chronic Disease Hospital	Boston Harbor
G2304XO	Mass Developmental Disabilities Council	Boston
G0212XB	Massachusetts Eye and Ear Infirmary	Boston
G0167	Massachusetts General Hospital	Boston
G0097	Massachusetts Institute of Technology	Cambridge
G0597	Massachusetts Mental Health Center	Boston
G0597	Massachusetts Mental Health Research Corp	Boston
G0147	Massachusetts, University of - Amherst	Amherst
G2736	Massachusetts, University of, Medical School	Worcester
G0554	Mattapan Chronic Disease Hospital	Mattapan
G0576	McLean Hospital	Belmont
G3123	Mount Auburn Hospital	Cambridge
G0494XB	New England Deaconess Hospital	Boston
G0133	New England Medical Center Hospital	Boston
G3064	North Charles Mental Health Research & Training Foundation, Inc	Cambridge
G0297	Northeastern University	Boston
G0429XB	Peter Bent Brigham Hospital Division of the Affiliated Hospitals Center, Inc	Boston
G3018XB	Pondville Hospital	Walpole (Norfolk)
G2515XM	Research Institute for Educational Problems	Cambridge
G0404XB	Robert B. Brigham Hospital, a Division of the Affiliated Hospitals Center, Inc	Boston
G0771	Sidney Farber Cancer Institute, Inc	Boston
G0351XB	St Margaret's Hospital for Women	Boston
G0554	Trustees of Health & Hosps, City of Boston, Inc	Boston
G2107	Tufts-New England Medical Center	Boston
G2379	Tufts University - Boston	Boston
*G0266XO	Tufts University - Medford	Medford
G0550	University Hospital, Inc	Boston
G0010	USPHS Hospital, Boston	Boston
G2042	Walter E. Fernald State School	Belmont
G0085	Worcester Foundation for Experimental Biology	Shrewsbury

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033072

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	MICHIGAN	
G0363	Child Research Center of Michigan	Detroit
G0363	Children's Hospital of Michigan	Detroit
G0497XM	Detroit, University of	Detroit
G0357	Edsel B. Ford Institute for Medical Research	Detroit
G0357	Henry Ford Hospital	Detroit
G0101	Lafayette Clinic	Detroit
G0656XB	Michigan Cancer Foundation	Detroit
G0615	Michigan Department of Public Health	Lansing
G0384	Michigan State University	East Lansing
G0295	Michigan, University of	Ann Arbor
G0295	Michigan, University of	Dearborn
G0295	Michigan, University of	Flint
G1009XM	Oakland University	Rochester
G0008	Sinai Hospital of Detroit	Detroit
G2483	Veterans Administration Medical Center-Ann Arbor	Ann Arbor
G0354	Wayne State University	Detroit
G0720	Western Michigan University	Kalamazoo
	MINNESOTA	
G0065	Hennepin County Medical Center	Minneapolis
G0041	Mayo Foundation	Rochester
G0065	Minneapolis Medical Research Foundation, Inc	Minneapolis
G0463	Minnesota, University of	Austin
G0463	Minnesota, University of	Duluth
G0463	Minnesota, University of	Minneapolis
G0463	Minnesota, University of	Morris
G0463	Minnesota, University of	St Paul
G0463	Minnesota, University of, Technical College	Crookston
G0463	Minnesota, University of, Technical College	Waseca

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033073

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	MISSISSIPPI	
G0561XM	Mississippi, University of (Main Campus)	University
G0366	Mississippi, University of, Medical Center	Jackson
G0366	Veterans Administration Center	Jackson
	MISSOURI	
G2791XM	American Nurses' Association, Inc	Kansas City
G0298XB	Cancer Research Center	Columbia
G0298XB	Ellis Fischel State Cancer Hospital	Columbia
G0424	Jewish Hospital of St Louis	St Louis
G0320XB	Kirksville College of Osteopathic Medicine	Kirksville
G2936XB	Missouri Cancer Programs	Columbia
G0292	Missouri, University of	Columbia
G0292	Missouri, University of	Kansas City
G0292	Missouri, University of	Rolla
G0292	Missouri, University of	St Louis
*G0356	St Louis University	St Louis
*G2056	Veterans Administration Med Ctr - Kansas City	Kansas City
G0279XM	Washington University (Excluding Schools of Medicine and Dentistry)	St Louis
G2351	Washington University School of Medicine	St Louis
	NEBRASKA	
G1120	Creighton University	Omaha
G3112	Father Flanagan's Boys' Home	Boys Town
G0407	Nebraska, Univ of, Including the Medical Ctr	Omaha
G0407	Nebraska, Univ of, Including the State Univ of Nebraska	Lincoln
	NEVADA	
G0762XM	Nevada, University of, Reno Campus	Reno

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033074

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	NEW HAMPSHIRE	
G0427XM	Dartmouth College Faculty of Arts & Sciences	Hanover
G0227	Dartmouth Medical School	Hanover
	NEW JERSEY	
G0981XM	Educational Testing Service	Princeton
G0492XB	Institute for Medical Research	Camden
G0349	New Jersey, College of Medicine & Dentistry of	Newark
G0349	New Jersey Dental School	Newark
G0349	New Jersey Medical School	Newark
G0837	Newark Beth Israel Medical Center	Newark
G0570XM	Princeton University	Princeton
G0349	Rutgers Medical School	Piscataway
G0300	Rutgers, The State Univ of New Jersey	Camden
G0300	Rutgers, The State Univ of New Jersey	New Brunswick
G0300	Rutgers, The State Univ of New Jersey	Newark
	NEW MEXICO	
*G0472	New Mexico, University of	Albuquerque
*G0353	New Mexico, University of, Health Sciences Group-School of Medicine, Colleges of Pharmacy and Nursing	Albuquerque
	NEW YORK	
G0217	Albany Medical College of Union University	Albany
G2129	American Health Foundation	New York
G1064XB	Associated Universities, Inc, Including Brookhaven National Laboratory	Upton
G2116XM	Barnard College	New York
G0341	Beth Israel Medical Center	New York
G1831XM	Center for Policy Research, Inc	New York

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033075

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G2277XM	Child Welfare League of America, Inc	New York
G0381	Children's Hospital of Buffalo	Buffalo
G0437XM	Columbia Univ, Except Health Sciences Division	New York
G0034	Columbia Univ Health Sciences and Presbyterian Hospital	New York
G0063XM	Cornell Univ, Except Medical College	Ithaca
G0245	Cornell University Medical College	New York
G0109XO	Eastman Dental Center	Rochester
G2912	Genesee Hospital	Rochester
G2887XB	Health Research, Inc, Albany Division	Albany
G2904	Health Research, Inc, Roswell Park Division	Buffalo
G2887XB	Helen Hayes Hospital	West Haverstraw
G2475XB	Highland Hospital of Rochester	Rochester
G0621	Hospital for Joint Diseases and Medical Center, Including the Research Institute for Skeletomuscular Diseases	New York
G0047	Hospital for Special Surgery	New York
G2920	ICD Rehabilitation and Research Center	New York
G1005XO	Jewish Board of Family and Children's Services, Inc	New York
G0369	Kingsbrook Jewish Medical Center and Isaac Albert Research Institute	Brooklyn
G2375	Long Island Jewish-Hillside Medical Center	New Hyde Park
G0397	Maimonides Medical Center	Brooklyn
G0086	Mary Imogene Bassett Hospital	Cooperstown
G0383XB	Memorial Hosp for Cancer and Allied Diseases	New York
G0059	Montefiore Hospital and Medical Center	New York
G0139	Mount Sinai School of Medicine of CUNY	New York
G2518XB	Nassau County Medical Center, Including Meadowbrook Medical Education and Research Foundation, Inc	East Meadow
G0173XM	New School for Social Research	New York
G0526XB	New York Blood Center, Inc	New York
G1370XB	New York City Department of Health	New York
G0765XM	New York, City Univ of	New York
G0765XM	New York, City Univ of, Baruch College	New York
G0765XM	New York, City Univ of, Bronx Cmty College	Bronx

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033076

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0765XM	New York, City Univ of, Brooklyn College	Brooklyn
G0765XM	New York, City Univ of, City College	New York
G0765XM	New York, City Univ of, Graduate School and University Center	New York
G0765XM	New York, City Univ of, Herbert H. Lehman College	Bronx
G0765XM	New York, City Univ of, Hunter College	New York
G0765XM	New York, City Univ of, John Jay College of Criminal Justice	New York
G0765XM	New York, City Univ of, Kingsborough Community College	Brooklyn
G0765XM	New York, City Univ of, Manhattan Cmty College	New York
G0765XM	New York, City Univ of, Medgar Evers College	Brooklyn
G0765XM	New York, City Univ of, New York City Community College	Brooklyn
G0765XM	New York, City Univ of, Queens College	Flushing
G0765XM	New York, City Univ of, Queensborough Community College	New York
G0765XM	New York, City Univ of, Research Foundation	New York
G0765XM	New York, City Univ of, College of Staten Island	Staten Island
G0765XM	New York, City Univ of, York College	Jamaica
G2887XB	New York Dept of Health and Regional Offices	Albany
G0208	New York Medical College-Flower and Fifth Avenue Hospitals, Metropolitan Hospital, and Bird S. Coler Memorial Hospital	New York
G0374XM	New York, State Univ of, at Albany	Albany
G0508	New York, State Univ of, at Binghamton	Binghamton
G0163	New York, State Univ of, at Buffalo	Buffalo
G0596	New York, State Univ of, at Stony Brook	Stony Brook
G0474	New York, State Univ of, College at Brockport	Brockport
G0506XM	New York, State Univ of, College at Buffalo	Buffalo
G0259XM	New York, State Univ of, College at Cortland	Cortland
G0386XM	New York, State Univ of, College at Oswego	Oswego
G0457	New York, State Univ of, College of Arts and Science at Geneseo	Geneseo

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033077

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0220	New York, State Univ of, College of Environmental Science and Forestry	Syracuse
G0305	New York, State Univ of, Downstate Medical Ctr	Brooklyn
G0127	New York, State Univ of, Upstate Medical Ctr	Syracuse
G0390XO	New York Univ, Exclusive of the Medical Ctr	New York
G0405	New York University Medical Center	New York
G0788	North Shore University Hospital	Manhasset
G2887XB	Oxford Home for Veterans and Their Dependents	Oxford
G0034	Presbyterian Hospital (Columbia Univ. Health Sciences)	New York
G2247	Public Health Research Institute of the City of New York, Inc	New York
G2375	Queens Hospital Center	Jamaica
G1001	Rensselaer Polytechnic Institute	Troy
G0624	Research Foundation for Mental Hygiene, Inc (NYS Office of Mental Health, NYS Office of Mental Retardation and Developmental Disabilities, NYS Division of Alcoholism and Substance Abuse - All Operating Components of the NYS Department of Mental Hygiene) Including	
	Capital District Psychiatric Center	Albany
	Long Island Research Institute	Central Islip
	NYS Institute for Basic Research in Mental Retardation	Staten Island
	New York State Psychiatric Institute	New York
	Research Institute on Alcoholism	Buffalo
	Rockland Research Institute	Orangeburg
	Special Projects Research Unit	Albany
G0172	Rochester, University of	Rochester
G0230	Rockefeller University	New York
G2036	Rockland County Health & Social Svcs Complex	Pomona
G0491	Roosevelt Hospital	New York
G2904	Roswell Park Memorial Institute	Buffalo
G0536XB	Sloan-Kettering Institute for Cancer Research	New York
G0076	St Luke's Hospital Center	New York
G2972XB	St Mary's Hospital	Rochester
G0376	St Vincent's Hosp and Medical Ctr of New York	New York

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033078

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0280XM	Syracuse University	Syracuse
G0373XM	Teachers College, Columbia University	New York
G2438XB	Trudeau Institute	Saranac Lake
G0010	USPHS Hospital, Staten Island	New York
G2045	Veterans Administration Hospital-Northport	Northport
G0002	Yeshiva Univ, Albert Einstein College of Med	Bronx
	NORTH CAROLINA	
G0191	Duke University Medical Center and Duke University Exclusive of the Medical Center	Durham
G2242	North Carolina A & T State University	Greensboro
G0285	North Carolina State University at Raleigh	Raleigh
G0177	North Carolina, Univ of, at Chapel Hill	Chapel Hill
G0242	Wake Forest Univ, Bowman Gray Sch of Medicine	Winston-Salem
G1087	Wake Forest Univ, Except School of Medicine	Winston-Salem
G0078	Western Carolina Center	Morganton
G0191	Whitehead Medical Research Institute	Durham
	OHIO	
G3143XB	Akron General Medical Center	Akron
G0485	Akron, University of	Akron
G0683	Battelle Columbus Laboratories of the Battelle Memorial Institute	Columbus
G2843XB	Cancer Center, Inc	Cleveland.
G1167	Case Western Reserve University	Cleveland
G0088	Children's Hospital Medical Center	Cincinnati
G0249	Children's Hospital Research Foundation, Inc	Columbus
G0667XM	Cincinnati, Univ of, Except Medical Center	Cincinnati
G0337	Cincinnati, Univ of, Medical Center, Including Colleges of Medicine, Nursing, and Health and Pharmacy	Cincinnati

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033079

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0502XB	Cleveland Clinic Foundation and Cleveland Clinic Educational Foundation	Cleveland
G0171	Cleveland Psychiatric Institute	Cleveland
G2678	Cox Heart Institute	Dayton
G2678	Fels Research Institute	Yellow Springs
G1936XB	Jewish Hospital of Cincinnati, Including the School of Nursing, Children's Psychiatric Center, and May Institute for Medical Research	Cincinnati
G0542	Kent State University	Kent
G1724	Medical College of Ohio at Toledo	Toledo
G0269XB	Mount Sinai Hospital of Cleveland	Cleveland
G0121	Ohio Agricultural Research & Development Ctr	Wooster
G0121	Ohio State University and Research Foundation	Columbus
G0662XB	St Luke's Hospital Association (United Methodist Church)	Cleveland
G0350XB	University Hospitals of Cleveland	Cleveland
G2678	Wright State University (All Components)	Dayton
G2907XM	Youngstown State University	Youngstown
	OKLAHOMA	
G0327	Oklahoma Medical Research Foundation, Inc	Oklahoma City
*G2402XO	Oklahoma, University of	Norman
G0241	Oklahoma, University of, Health Sciences Ctr	Oklahoma City
	OREGON	
G0134	Good Samaritan Hospital and Medical Center	Portland
G0214	Kaiser Foundation Hospital	Portland
G0043XB	Medical Research Foundation of Oregon and Oregon Regional Primate Research Center	Portland
G2399XM	Northwest Regional Educational Laboratory	Portland
G0505XM	Oregon Research Institute	Eugene
G0111XM	Oregon State University	Corvallis

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033080

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0288XM	Oregon, University of, Graduate School	Eugene
G2931	Oregon, University of, Health Sciences Center, Including Schools of Medicine, Dentistry, and Nursing	Portland
	PENNSYLVANIA	
G0125	Albert Einstein Medical Center, Northern Div	Philadelphia
G0952XB	Allegheny Health, Education and Research Corporation - Allegheny-Singer Research Corporation and Allegheny General Hospital	Pittsburgh
G0784XM	American Institutes for Research	Pittsburgh
G0338	Arthur P. Noyes Research Foundation	Norristown
G0436XM	Bucknell University	Lewisburg
G1218	Carnegie-Mellon University	Pittsburgh
G0129	Children's Hospital of Philadelphia (Joseph Stokes, Jr., Research Inst of)	Philadelphia
G0360	Children's Hospital of Pittsburgh	Pittsburgh
G0045	Fox Chase Cancer Center (Institute for Cancer Research and American Oncologic Hosp)	Philadelphia
G1556	Franklin Institute	Philadelphia
G0594	Geisinger Medical Center, Institute for Medical Education and Research	Danville
G0475	Hahnemann Medical College and Hospital	Philadelphia
G0936	H. K. Cooper Institute for Oral-Facial Anomalies and Communicative Disorders (Lancaster Cleft Palate Clinic)	Lancaster
G0273XB	Lankenau Hospital	Philadelphia
G0189XB	Magee-Womens Hospital	Pittsburgh
G1378	Marriage Council of Philadelphia, Inc (Reviewed by G0012)	Philadelphia
G2121XM	Marywood College	Scranton
G0057XB	Montefiore Hospital	Pittsburgh
G0338	Norristown State Hospital	Norristown
G0333	Pennsylvania Hospital	Philadelphia
G0222	Pennsylvania, Medical College of	Philadelphia
G0573	Pennsylvania State Univ & Commonwealth Camps	University Park
G1668	Pennsylvania State Univ, Milton S. Hershey Medical Center	Hershey

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033081

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0012	Pennsylvania, University of	Philadelphia
G1531	Philadelphia Department of Public Health	Philadelphia
G0324	Philadelphia Geriatric Center	Philadelphia
G0344	Philadelphia Psychiatric Center	Philadelphia
G0881	Philadelphia State Hospital	Philadelphia
G1532	Pittsburgh Child Guidance Center	Pittsburgh
G2929	Pittsburgh, University Health Center of	Pittsburgh
G0418	Pittsburgh, University of	Pittsburgh
G2200	Presbyterian-University Hospital	Pittsburgh
G0465	Presbyterian-Univ of Pennsylvania Medical Ctr	Philadelphia
G2264XM	Research for Better Schools, Inc	Philadelphia
G0795	St Joseph's Hospital	Lancaster
G2880	Temple Univ, Excluding the Health Sciences Ctr	Philadelphia
G2879	Temple University Health Sciences Center	Philadelphia
G0049	Thomas Jefferson Univ, All Components	Philadelphia
G0362XB	Wills Eye Hospital and Research Institute	Philadelphia
G0054XB	Wistar Institute	Philadelphia
	PUERTO RICO	
G1348XM	Catholic University of Puerto Rico	Ponce
G0256XB	Puerto Rico, Univ of, Medical Sciences Campus	San Juan Rio Piedras
	RHODE ISLAND	
G0467	Brown University	Providence
*G0318	Rhode Island Hospital	Providence
G2212XB	Roger Williams General Hospital	Providence
	SOUTH CAROLINA	
G2621	Clemson University	Clemson
G0533	South Carolina Department of Mental Health	Columbia
G0240	South Carolina, Medical University of	Charleston
*G0629XO	South Carolina, University of	Columbia

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033082

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	TENNESSEE	
G0490XM	George Peabody College for Teachers	Nashville
G0393	Meharry Medical College	Nashville
→ G1716	Oak Ridge Associated Universities	Oak Ridge
→ G1716	Oak Ridge National Laboratory	Oak Ridge
G0648	St Jude Children's Research Hospital	Memphis
G0170	Tennessee, University of, Center for the Health Sciences	Memphis
G0124	Tennessee, University of - Knoxville	Knoxville
G0401	Vanderbilt University	Nashville
	TEXAS	
G2255	Audie L. Murphy Veterans Administration Hospital	San Antonio
G0307	Baylor College of Medicine	Houston
G2255	Bexar County Hospital District	San Antonio
G0398XM	Houston, University of	Houston
*G2344XO	Southwest Educational Development Corporation (AKA Southwest Educational Development Lab)	Austin
G1045	Texas A & M University and Research Foundation, College Station Campus Only	College Station
G3027	Texas Department of Public Welfare	Austin
G0564	Texas Tech University	Lubbock
G3154	Texas Tech Univ School of Medicine at Lubbock (Including Academic Health Centers at El Paso and Amarillo)	Lubbock
*G1121XO	Texas, University of, at Arlington	Arlington
G0123	Texas, University of, at Austin	Austin
G0113	Texas, University of, Cancer Center (and its M.D. Anderson Hospital and Tumor Institute)	Houston
G2615	Texas, University of, Health Science Center at Dallas	Dallas
*G2760	Texas, University of, Health Science Center at Houston	Houston

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033083

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G2255	Texas, University of, Health Science Center at San Antonio, Including Medical School, Dental School, and Graduate School of Biomedical Sciences, Sch of Nursing, Sch of Allied Health Sciences, and Graduate School of Pharmacy	San Antonio
G0107	Texas, Univ of, Medical Branch at Galveston	Galveston
G0010	USPHS Hospital, Galveston	Galveston
	UTAH	
*G2426	Deseret Fdn for Medical Education & Research	Salt Lake City
G0462	Utah State University	Logan
G0235	Utah, University of	Salt Lake City
G0235	Utah, University of, Research Institute	Salt Lake City
G0235	Veterans Administration Hospital	Salt Lake City
	VERMONT	
G0194	Vermont, University of, and State Agricultural College	Burlington
G2335XB	Veterans Administration Ctr-White River Junction	White River Jct
	VIRGINIA	
G2684	Eastern Virginia Medical Authority and Eastern Virginia Medical School	Norfolk
G2275XM	Human Resources Research Organization	Alexandria
G0010	USPHS Hospital, Norfolk	Norfolk
G0239	Virginia Commonwealth University (All Schools and Divisions)	Richmond
G0306	Virginia, University of	Charlottesville

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033084

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	WASHINGTON	
G0522	Children's Orthopedic Hosp and Medical Ctr	Seattle
G2627XB	Fred Hutchinson Cancer Research Center	Seattle
G0029XB	Pacific Northwest Research Foundation	Seattle
G0913XB	Swedish Hospital Medical Center	Seattle
G0010	USPHS Hospital, Seattle	Seattle
*G0900	Virginia Mason Research Center, Including Mason Clinic and Virginia Mason Hospital	Seattle
G1717	Washington Department of Social and Health Services, All Components	Olympia
*G0105XO	Washington State University	Pullman
G0299	Washington, University of	Seattle
	WEST VIRGINIA	
G0431	West Virginia University	Morgantown
	WISCONSIN	
G0315	Central Wisconsin Colony and Training School	Madison
G2891XB	Columbia Hospital	Milwaukee
G0387XM	Marquette University	Milwaukee
G0763	Mendota Mental Health Institute	Madison
G3010XB	Mount Sinai Medical Center of Milwaukee	Milwaukee
G0503	Southern Wisconsin Center for the Developmentally Disabled	Union Grove
G3051	St Mary's Hospital	Milwaukee
G0077	Wisconsin, Medical College of, Inc	Milwaukee
G0319	Wisconsin, University of, Madison Campus	Madison
G2106XM	Wisconsin, University of, Parkside	Kenosha

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033085

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	BANGLADESH	
G3061	Cholera Research Laboratory	Dacca
	SWITZERLAND	
*G1137	World Health Organization	Geneva

TOTAL NUMBER OF INSTITUTIONS AND COMPONENTS WITH ACCEPTABLE GENERAL ASSURANCES — 551

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033086

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☐ FOLLOWUP ☐ REVISION

☐ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☐ RENEWAL ☐ CONTINUATION

APPLICATION IDENTIFICATION NUMBER *(If known)*

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of Public Law 93-348, as implemented by Part 46 of Title 45 of the Code of Federal Regulations, as amended, (45 CFR 46). Administration of the DHEW policy and regulation is the responsibility of the Office for Protection from Research Risks, National Institutes of Health, Bethesda, Md 20014.

1. TITLE OF PROPOSAL OR ACTIVITY

2. PRINCIPAL INVESTIGATOR/ACTIVITY DIRECTOR/FELLOW

3. DECLARATION THAT HUMAN SUBJECTS EITHER WOULD OR WOULD NOT BE INVOLVED

☐ A. NO INDIVIDUALS WHO MIGHT BE CONSIDERED HUMAN SUBJECTS, INCLUDING THOSE FROM WHOM ORGANS, TISSUES, FLUIDS, OR OTHER MATERIALS WOULD BE DERIVED, OR WHO COULD BE IDENTIFIED BY PERSONAL DATA, WOULD BE INVOLVED IN THE PROPOSED ACTIVITY. (IF NO HUMAN SUBJECTS WOULD BE INVOLVED, CHECK THIS BOX AND PROCEED TO ITEM 7. PROPOSALS DETERMINED BY THE AGENCY TO INVOLVE HUMAN SUBJECTS WILL BE RETURNED.)

☐ B. HUMAN SUBJECTS WOULD BE INVOLVED IN THE PROPOSED ACTIVITY AS EITHER: ☐ NONE OF THE FOLLOWING, OR INCLUDING: ☐ MINORS, ☐ FETUSES, ☐ ABORTUSES, ☐ PREGNANT WOMEN, ☐ PRISONERS, ☐ MENTALLY RETARDED, ☐ MENTALLY DISABLED. UNDER SECTION 6. COOPERATING INSTITUTIONS, ON REVERSE OF THIS FORM, GIVE NAME OF INSTITUTION AND NAME AND ADDRESS OF OFFICIAL(S) AUTHORIZING ACCESS TO ANY SUBJECTS IN FACILITIES NOT UNDER DIRECT CONTROL OF THE APPLICANT OR OFFERING INSTITUTION.

4. DECLARATION OF ASSURANCE STATUS/CERTIFICATION OF REVIEW

☐ A. THIS INSTITUTION HAS NOT PREVIOUSLY FILED AN ASSURANCE AND ASSURANCE IMPLEMENTING PROCEDURES FOR THE PROTECTION OF HUMAN SUBJECTS WITH THE DHEW THAT APPLIES TO THIS APPLICATION OR ACTIVITY. ASSURANCE IS HEREBY GIVEN THAT THIS INSTITUTION WILL COMPLY WITH REQUIREMENTS OF *DHEW Regulation 45 CFR 46*, THAT IT HAS ESTABLISHED AN INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS AND, WHEN REQUESTED, WILL SUBMIT TO DHEW DOCUMENTATION AND CERTIFICATION OF SUCH REVIEWS AND PROCEDURES AS MAY BE REQUIRED FOR IMPLEMENTATION OF THIS ASSURANCE FOR THE PROPOSED PROJECT OR ACTIVITY.

☐ B. THIS INSTITUTION HAS AN APPROVED GENERAL ASSURANCE (DHEW ASSURANCE NUMBER _____) OR AN ACTIVE SPECIAL ASSURANCE FOR THIS ONGOING ACTIVITY, ON FILE WITH DHEW. THE SIGNER CERTIFIES THAT ALL ACTIVITIES IN THIS APPLICATION PROPOSING TO INVOLVE HUMAN SUBJECTS HAVE BEEN REVIEWED AND APPROVED BY THIS INSTITUTION'S INSTITUTIONAL REVIEW BOARD IN A CONVENED MEETING ON THE DATE OF _____ IN ACCORDANCE WITH THE REQUIREMENTS OF THE *Code of Federal Regulations on Protection of Human Subjects (45 CFR 46)*. THIS CERTIFICATION INCLUDES, WHEN APPLICABLE, REQUIREMENTS FOR CERTIFYING FDA STATUS FOR EACH INVESTIGATIONAL NEW DRUG TO BE USED (SEE REVERSE SIDE OF THIS FORM).

THE INSTITUTIONAL REVIEW BOARD HAS DETERMINED, AND THE INSTITUTIONAL OFFICIAL SIGNING BELOW CONCURS THAT:

EITHER ☐ HUMAN SUBJECTS WILL NOT BE AT RISK; OR ☐ HUMAN SUBJECTS WILL BE AT RISK.

5. AND 6. SEE REVERSE SIDE

7. NAME AND ADDRESS OF INSTITUTION

8. TITLE OF INSTITUTIONAL OFFICIAL	TELEPHONE NUMBER
SIGNATURE OF INSTITUTIONAL OFFICIAL	DATE

HEW-596 (Rev. 4-75)

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO REQUESTING AGENCY.

THE ORIGINAL COLOR OF THIS FORM IS YELLOW

1033087

5. INVESTIGATIONAL NEW DRUGS - ADDITIONAL CERTIFICATION REQUIREMENT

SECTION 46.17 OF TITLE 45 OF THE Code of Federal Regulations states, "Where an organization is required to prepare or to submit a certification . . . and the proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 130.3(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received."

INVESTIGATIONAL NEW DRUG CERTIFICATION

TO CERTIFY COMPLIANCE WITH FDA REQUIREMENTS FOR PROPOSED USE OF INVESTIGATIONAL NEW DRUGS IN ADDITION TO CERTIFICATION OF INSTITUTIONAL REVIEW BOARD APPROVAL, THE FOLLOWING REPORT FORMAT SHOULD BE USED FOR EACH IND: (ATTACH ADDITIONAL IND CERTIFICATIONS AS NECESSARY).

- IND FORMS FILED: ☐ FDA 1571, ☐ FDA 1572, ☐ FDA 1573

- NAME OF IND AND SPONSOR _____

- DATE OF 30-DAY EXPIRATION OR FDA WAIVER
  (FUTURE DATE REQUIRES FOLLOWUP REPORT TO AGENCY) _____

- FDA RESTRICTION _____

- SIGNATURE OF INVESTIGATOR _____ DATE _____

6. COOPERATING INSTITUTIONS - ADDITIONAL REPORTING REQUIREMENT

SECTION 46.16 OF TITLE 45 OF THE *Code of Federal Regulations* IMPOSES SPECIAL REQUIREMENTS ON THE CONDUCT OF STUDIES OR ACTIVITIES IN WHICH THE GRANTEE OR PRIME CONTRACTOR OBTAINS ACCESS TO ALL OR SOME OF THE SUBJECTS THROUGH COOPERATING INSTITUTIONS NOT UNDER ITS CONTROL. IN ORDER THAT THE DHEW BE FULLY INFORMED, THE FOLLOWING REPORT IS REQUESTED WHEN APPLICABLE.

USE FOLLOWING REPORT FORMAT FOR EACH INSTITUTION OTHER THAN GRANTEE OR CONTRACTING INSTITUTION WITH RESPONSIBILITY FOR HUMAN SUBJECTS PARTICIPATING IN THIS ACTIVITY: (ATTACH ADDITIONAL REPORT SHEETS AS NECESSARY).

INSTITUTIONAL AUTHORIZATION FOR ACCESS TO SUBJECTS

- SUBJECTS: STATUS (WARDS, RESIDENTS, EMPLOYEES, PATIENTS, ETC.) _____

NUMBER _____ AGE RANGE _____

NAME OF OFFICIAL (PLEASE PRINT) _____

TITLE _____ TELEPHONE _____

NAME AND ADDRESS OF COOPERATING INSTITUTION _____

- OFFICIAL SIGNATURE _____

NOTES: *(e.g., report of modification in proposal as submitted to agency affecting human subjects involvement)*

1033088

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

JULY, 1979

William Calhoun, Ph.D.
Professor and Head
Department of Psychology
The University of Tennessee
Knoxville, TN 37916

Telephone: 974-2531

Howard Ronald Friedman, Ph.D.
Clinical Psychologist
The Regional Mental Health Center
240 W. Tyrone Road
Oak Ridge, TN 37830

Telephone: 482-1076

A. Seaton Garrett, Jr., M.D.
Medical Director
Oak Ridge National Laboratory
Building 4500 N
Oak Ridge, TN 37830

Telephone: 574-7431

Donald W. Goodwin, Ph.D.
Minister, United Church, Chapel-on-the-Hill
85 Kentucky Avenue
Oak Ridge, TN 37830

Telephone: 482-1016 (Office)
482-1850 (Home)

Martha S. Hansard, Ph.D.
Associate Section Leader for Computer Methodology and Systems, Epidemiology
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, TN 37830

Karl F. Hübner, M.D.
Chief, Outpatient Clinical Studies
Director, REAC/TS
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, TN 37830

Telephone: 576-3098

Melvin E. Koons, J.D.
Union Carbide Corporation Nuclear Division
P. O. Box M
Oak Ridge, TN 37830

Telephone: 576-1432

Robert Lange, M.D. (Chairman)
Director
The University of Tennessee Memorial Research Center
The University of Tennessee Center for the Health Sciences, Knoxville Units
1924 Alcoa Highway
Knoxville, TN 37920

Telephone: 971-3165

Steve Lawrence, B.S.
Manager for Administration
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, TN 37830

Telephone: 576-3303

Clarence C. Lushbaugh, M.D.
Chairman, Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, TN 37830

Telephone: 576-3090

1033089

L. Clifford McKee, Jr., M.D.
Metropolitan Nashville General
Hospital
72 Hermitage Avenue
Nashville, TN 37210

Telephone: FTS 8 852-5022
322-3355

Ruby Miller, B.S.
Public Relations Representative
Union Carbide Corporation -
Nuclear Division
Oak Ridge National Laboratory
P. O. Box X, Building 4500 N
Oak Ridge, TN 37830

Telephone: 574-4165

John B. Storer, M.D.
Director, Biology Division
Oak Ridge National Laboratory
Oak Ridge, TN 37830
(Y-12 Area, Building 9207)

Telephone: 574-0212

For information regarding Committee business, contact the Committee Secretary:

Dianne Gresham
Medical and Health Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, TN 37830

Telephone: 576-3098

1033090

FEDERAL REGISTERS marked with specific areas relating to Title 21.

1033091

policymaking employees and tenured employees at institutions of higher education were published in the Federal Register on December 12, 1978. Proposed interpretations concerning the prohibition of mandatory retirement up until age 70 may be expected in the near future. Also to conform with changes in ADEA coverage under the Fair Labor Standards Act Amendments of 1974 and the 1978 ADEA amendments, minor proposed revisions may be expected (early next year) in sections of these interpretations concerning the definitions of "employer" and discrimination within the age range covered under the Act.

Contact: Francis V. LaRuffa, Chief, Branch of Age Discrimination, Wage and Hour Division, U.S. Department of Labor, 200 Constitution Avenue, N.W., Room S3502, Washington, D.C. 20210 (202) 523-7640.

Regulatory Analysis: A regulatory analysis was not prepared.

Action: Responsibility transferred to the Equal Employment Opportunity Commission.

29 CFR Part 2520—Elimination of Form EBS-1.

A revision of certain reporting requirements will be proposed to eliminate the need for employee benefit plans to file a Plan Description Form EBS-1 with the Department.

Basis for Action: The revision is intended to eliminate duplicative reporting and reduce the paperwork burden imposed by ERISA.

Contact: Peter Straub, Pension and Welfare Benefit Programs, U.S. Department of Labor, 200 Constitution Avenue, N.W., Room N4472, Washington, D.C. 20210 (202) 523-8377.

Regulatory Analysis: A regulatory analysis was not required.

Action: A final regulation was published.

29 CFR 92.1-92.9—Labor Management Services Administration Regulations to be Issued Governing Employee Benefit Payments Under the Redwood National Park Expansion Act (Pub. L. 95-250)

These provisions will define the eligibility criteria which employees must meet in order to receive benefits under the Act.

Basis for action: These regulations were necessary to implement Section 102(b) and Sections 103(d)-103(i) of title I and all of title II of Pub. L. 95-250.

Contact: Ron Glass, Division of Employee Protections, Labor-Management Services Administration, U.S. Department of Labor, Room N5641, 200 Constitution Avenue, N.W.,

Regulatory Analysis: A regulatory analysis was not required.

Action: A final regulation was published.

30 CFR Part 46—State Grants Regulations

Basis for Action: To improve regulations implementing Sections 503 of FMSHA.

Contact: Frank A. White, Office of Standards, Regulations and Variances, Mine Safety and Health Administration, 4015 Wilson Boulevard, Arlington, Virginia 22203 (703) 235-1910.

Regulatory Analysis: A regulatory analysis was not required.

Action: A final regulation was published.

30 CFR Parts 55, 56, and 57—Miscellaneous Amendments Including Standards for Exposure to Radon Daughters (Part 57 only)

Basis for action: To implement improved safety and health standards under Section 301 of the Amendments Act.

Contact: Frank A. White, Office of Standards, Regulations and Variances, Mine Safety and Health Administration, 4015 Wilson Boulevard, Arlington, Virginia 22203 (703) 235-1910.

Regulatory Analysis: A regulatory analysis was not required.

Action: Final regulation was published.

C. The following officials shall serve on the Department of Labor's Regulatory Review Panel:

Chair: The Under Secretary of Labor.

Members:

The Solicitor of Labor;
The Assistant Secretary for Labor-Management Standards;
The Assistant Secretary for Employment Standards;
The Assistant Secretary for Policy Evaluation and Research;
The Asssitant Secretary for Employment and Training;
The Assistant Secretary for Occupational Safety and Health
The Assistant Secretary for Mine Safety and Health;
The Assistant Secretary for Administration and Management;
The Inspector General;
The Commissioner of Labor Statistics;
The Deputy Under Secretary for International Labor Affairs; and
The Deputy Under Secretary for Legislation and Intergovernmental Relations.

Executive Secretary: A designated

Signed this 22nd day of August, 1979 at Washington, D.C.

Ray Marshall,

Secretary of Labor.

[FR Doc. 79-26755 Filed 8-27-79; 8:45 am]

BILLING CODE 4510-23-M

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[21 CFR Parts 16, 56, 71, 171, 180, 310, 312, 314, 320, 330, 361, 430, 431, 601, 630, 1003, and 1010]

[Docket No. 77N-0350]

Protection of Human Subjects; Standards for Institutional Review Boards for Clinical Investigations; Waiver of Requirement

AGENCY: Food and Drug Administration.

ACTION: Waiver of Requirement.

SUMMARY: The Food and Drug Administration (FDA) is waiving the requirement for submitting a summary of the presentation as part of the written notice of participation for a public hearing on "Standards for Institutional Review Boards for Clinical Investigations" for the scheduled September 18, 1979 hearing in Bethesda, MD. The agency is also correcting the date for the San Francisco hearing by changing the date from October 2, 1979 to October 3, 1979.

DATES: Public hearings on September 18, October 3, and October 16, 1979. Written notices of participation required by September 4, September 18, and October 2, 1979.

ADDRESS: Written comments to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: John C. Petricciani, Bureau of Biologics (HFB-4), Food and Drug Administration, Department of Health, Education, and Welfare, 8800 Rockville Pike, Bethesda, MD 20205, 301-496-9320.

SUPPLEMENTARY INFORMATION: In the Federal Register of August 14, 1979 (44 FR 47699), FDA announced public hearings on proposed standards for institutional review boards (IRB's) for clinical investigations. One of these public hearings is scheduled for Bethesda, MD, on September 18, 1979.

Under the requirements of 21 CFR 15.21, a written notice of participation must be filed with the FDA Hearing Clerk. The written notice of participation requires the name, address, and telephone number of the

1033092

person desiring to make a statement, along with any business affiliation, a summary of the scope of the presentation with references to the appropriate subpart of the proposed regulations, and the approximate amount of time requested for the presentation. The written notices of participation were required to be submitted not later than September 4, 1979 for the Bethesda, MD, hearing.

The agency received telephoned comments from persons interested in participating in the September 18, 1979 hearing at Bethesda, MD, indicating that there is inadequate time to prepare and submit the required summary of the presentation by the September 4, 1979 deadline.

The agency agrees with these comments and is therefore waiving the requirement to submit a summary of the presentation for the September 18, 1979 hearing in Bethesda, MD, only. Because the San Francisco and Houston hearings are scheduled for October 3 and October 16, respectively, persons interested in participating in the other hearings have sufficient time to prepare a summary and will be required to submit this information with the notice of participation required for those hearings.

This action is not expected to have any adverse effect on the scheduled September 18, 1979 hearing at Bethesda, MD, for either the public or the agency.

The agency is also correcting the date for the San Francisco hearing specified in the August 14, 1979 Federal Register announcement. This announcement inadvertently identified the date for the San Francisco hearing as October 2, 1979. The correct date for this hearing is October 3, 1979.

Dated: August 23, 1979.

Joseph P. Hile,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 79-26785 Filed 8-24-79; 11:11 am]

BILLING CODE 4110-03-M

[21 CFR Part 74]

[Docket No. 77C-0276]

Listing of Color Additives Subject to Certification; D&C Orange No. 4

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) proposes to revise the specifications for D&C Orange No. 4 by adding a tolerance for 4,4'-(diazoamino)-dibenzenesulfonic acid. This revision is necessary because a tolerance for 4,4'-(diazoamino)-dibenzenesulfonic acid was inadvertently omitted in the listing regulation for D&C Orange No. 4.

DATE: Comments by October 29, 1979.

ADDRESS: Written comments to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Gerald L. McCowin, Bureau of Foods (HFF-334), Food and Drug Administration, Department of Health, Education, and Welfare, 200 C St. SW., Washington, DC 20204, 202-472-5740.

SUPPLEMENTARY INFORMATION: A regulation published in the Federal Register of September 30, 1977 (42 FR 52395) listed D&C Orange No. 4 for use in externally applied drugs and cosmetics (see §§ 74.1254 and 74.2254 (21 CFR 74.1254 and 74.2254)). A final rule published in the Federal Register of April 7, 1978 (43 FR 14641) confirmed the effective date of November 1, 1977 for the "permanent" listing of D&C Orange No. 4, and also revised the specifications for total color and the sum of volatile matter and chlorides and sulfates (as sodium salts) in response to two objections to the regulation. The revision became effective on April 7, 1978.

The agency has recently become aware that the specifications for D&C Orange No. 4 do not include a tolerance for 4,4'-(diazoamino)-dibenzenesulfonic acid (DAADBSA). A tolerance of not more than 0.1 percent DAADBSA was inadvertently omitted from the specifications when the final regulation was published in the Federal Register. FDA has determined, consistent with its policy on the certification of color additives, as well as with the requirement necessary to establish the safety of D&C Orange No. 4, that the tolerance of DAADBSA should be included as originally intended in the specifications for D&C Orange No. 4.

After reviewing the analytical data, FDA has concluded that a tolerance of not more than 0.1 percent for DAADBSA can be met when good manufacturing practices are employed in the production of D&C Orange No. 4.

FDA has carefully considered the environmental effects of the proposed regulation and, because the proposed action will not significantly affect the quality of the human environment, has concluded that an environmental impact statement is not required. A copy of the environmental impact assessment is on file with the Hearing Clerk, Food and Drug Administration.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 706(b), (c), and (d), 74 Stat. 399-403 as amended (21 U.S.C 376(b), (c), and (d))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1), it is proposed that Part 74 be amended in § 74.1254 by inserting, after the entry for "subsidiary colors" in the specifications in paragraph (b), a new entry to read as follows:

§ 74.1254 D&C Orange No. 4.

* * * * *

(b) * * *

4,4'-(diazoamino)-dibenzenesulfonic acid, not more than 0.1 percent.

* * * * *

Interested persons may, on or before October 29, 1979, submit to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857, written comments regarding this proposal. Four copies of all comments shall be submitted, except that individuals may submit single copies of comments. The comments are to be identified with the Hearing Clerk docket number found in brackets in the heading of this document. Received comments may be seen in the above office, between 9 a.m. and 4 p.m., Monday through Friday.

In accordance with Executive Order 12044, the economic effects of this proposal have been carefully analyzed, and it has been determined that the proposed rulemaking does not involve major economic consequences as defined by that order. A copy of the regulatory analysis assessment supporting this determination is on file with the Hearing Clerk, Food and Drug Administration.

Dated: August 17, 1979.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 79-26847 Filed 8-27-79; 8:45 am]

BILLING 4110-03-M

[21 CFR Part 184]

[Docket No. 78N-0369]

Whey, Whey Products, and Hydrogen Peroxide; Affirmation of Gras Status as Direct Human Food Ingredients; Extension of Comment Period

AGENCY: Food and Drug Administration.

ACTION: Extension of Comment Period.

SUMMARY: The agency extends the comment period on its proposal to affirm the generally recognized as safe (GRAS) status of whey and whey products as direct human food ingredients and hydrogen peroxide for use as an antimicrobial agent in cheesemaking and whey processing. This action is taken in response to a request for extension of the comment period.

1033093

disqualification, the Commissioner shall so notify other agencies in the Department of Health, Education, and Welfare that support research involving human subjects at the time of or after proposing disqualification of the board under § 56.204(a).

§ 56.215 Actions alternative or additional to disqualification.

Disqualification of an institutional review board under this subpart is independent of, and neither in lieu of nor a precondition to, other proceedings or actions authorized by the act. The Commissioner may, at any time, through the Department of Justice institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of, or after, disqualification. The Commissioner may also refer pertinent matters to another Federal, State, or local government agency for such action as that agency determines to be appropriate.

§ 56.219 Reinstatement of a disqualified institutional review board.

(a) An institutional review board that has been disqualified may be reinstated as eligible to review clinical investigations subject to requirements for prior submission to the Food and Drug Administration, or as acceptable to be the reviewer of clinical investigations to be submitted to the Food and Drug Administration, if the Commissioner determines, upon an evaluation of a written submission from the board, that the board has adequately assured that it will operate in compliance with the standards set forth in this part and other applicable regulations in this chapter, e.g., Parts 312 or 812.

(b) A disqualified board that wishes to be so reinstated shall present in writing to the Commissioner reasons why it believes it should be reinstated and a detailed description of the corrective actions it has taken or intends to take to assure that the acts or omissions that led to disqualification will not recur. The Commissioner may condition reinstatement upon the board's being found in compliance with the applicable regulations upon an inspection.

(c) If a board is reinstated, the Commissioner shall so notify the board and all persons who were notified under § 56.213 of the disqualification of the board. A determination that a board has been reinstated is disclosable to the public under Part 20 of this chapter.

PART 71—COLOR ADDITIVE PETITIONS

3. By amending Part 71:

a. In § 71.1 by adding new paragraph (i) to read as follows:

§ 71.1 Petitions.

* * * * *

(i) If clinical investigations involving human subjects are involved, petitions filed with the Commissioner under section 706(b) of the act shall include a statement regarding each such clinical investigation contained in the petition that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

b. In § 71.6 by adding a new sentence at the end of paragraph (b) to read as follows:

§ 71.6 Extension of time for studying petitions; substantive amendments; withdrawal of petitions without prejudice.

* * * * *

(b) * * * If clinical investigations involving human subjects are involved, additional information or data submitted in support of filed petitions shall include a statement regarding each such clinical investigation from which the information or data are derived, that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

SUBCHAPTER B—FOOD FOR HUMAN CONSUMPTION

PART 171—FOOD ADDITIVE PETITIONS

4. By amending Part 171:

a. In § 171.1 by adding new paragraph (m) to read as follows:

§ 171.1 Petitions.

* * * * *

(m) If clinical investigations involving human subjects are involved, petitions filed with the Commissioner under section 409(b) of the act shall include a statement regarding each such clinical investigation relied upon in the petition that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

b. In § 171.6 by adding a new sentence at the end of the paragraph to read as follows:

§ 171.6 Amendment of petition.

* * * If clinical investigations involving human subjects are involved, additional information and data submitted in support of filed petitions shall include a statement regarding each such clinical investigation from which the information or data are derived that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6) of this chapter.

PART 180—FOOD ADDITIVES PERMITTED IN FOOD ON AN INTERIM BASIS OR IN CONTACT WITH FOOD PENDING ADDITIONAL STUDY

Part 180 is amended in § 180.1 by adding a new paragraph (c)(6) to read as follows:

§ 180.1 General.

* * * * *

(c) * * *

(6) If clinical investigations involving human subjects are involved, such investigations filed with the Commissioner shall include, with respect to each investigation, either a statement that the investigation has been or will be conducted in compliance with the requirements for institutional review set forth in part 56 of this chapter; or a statement that the investigation is not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

SUBCHAPTER D—DRUGS FOR HUMAN USE

PART 310—NEW DRUGS

§ 310.3 [Amended]

5. By amending Part 310 in § 310.3 *Definitions and interpretations,* by deleting and reserving paragraph (j).

PART 312—NEW DRUGS FOR INVESTIGATIONAL USE

6. By amending Part 312 in § 312.1 by redesignating paragraphs (d)(11) and (d)(12) as (d)(12) and (d)(13) and adding a new paragraph (d)(11) to read as follows:

§ 312.1 Conditions for exemption of new drugs for investigational use.

* * * * *

(d) * * *

(11) The clinical investigations are not being conducted in compliance with the requirements regarding institutional

1033094

review set forth in this part or Part 56 of this chapter, or

* * * * *

PART 314—NEW DRUG APPLICATIONS

7. Part 314 is amended:

a. In § 314.1 by adding a new item 17 to Form FD–356H in paragraph (c)(2) and by redesignating paragraphs (f)(7) and (f)(8) as (f)(8) and (f)(9) and adding a new paragraph (f)(7) to read as follows:

§ 314.1 Applications.

* * * * *

(c) * * *

(2) * * *

Form FD–356H—Rev. 1974:

* * * * *

17. *Conduct of clinical investigations.* A statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

(f) * * *

(7) A statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements the institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

b. In § 314.8 by adding a new paragraph (n) to read as follows:

§ 314.8 Supplemental applications.

* * * * *

(n) A supplemental application that contains clinical investigations involving human subjects shall include a statement by the applicant regarding each such investigation that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

c. In § 314.9 by adding new paragraph (e) to read as follows:

§ 314.9 Insufficient information in application.

* * * * *

(e) The information contained in an application shall be considered insufficient to determine whether a drug is safe and effective for use unless the application includes a statement regarding each clincial investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

d. In § 314.12 by adding new paragraph (e) to read as follows:

§ 314.12 Untrue statements in application.

* * * * *

(e) Any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

e. In § 314.110 by adding new paragraph (a)(11) to read as follows:

§ 314.110 Reasons for refusing to file applications.

(a) * * *

(11) The applicant fails to include in the application a statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.26 of this chapter.

* * * * *

f. In § 314.111 by adding paragraph (a)(11) to read as follows:

§ 314.111 Refusal to approve the application.

(a) * * *

(11) Any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

* * * * *

g. In § 314.115 by adding new paragraph (c)(7) to read as follows:

§ 314.115 Withdrawal of approval of an application.

* * * * *

(c) * * *

(7) That any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

* * * * *

PART 320—BIOAVAILABILITY AND BIOEQUIVALENCE REQUIREMENTS

8. Part 320 is amended:

a. In § 320.31 by adding a new paragraph (f) to read as follows:

§ 320.31 Applicability of requirements regarding a "Notice of Claimed Investigational Exemption for a New Drug."

* * * * *

(f) An in vivo bioavailability study in humans shall be conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter, regardless of whether the study is conducted under a "Notice of Claimed Investigational Exemption for a New Drug."

b. In § 320.57 by adding a new paragraph (e) to read as follows:

§ 320.57 Requirements of the conduct of in vivo bioequivalence testing in humans.

* * * * *

(e) If a bioequivalence requirement provides for in vivo testing in humans, any person conducting such testing shall comply with the requirements of § 320.31.

PART 330—OVER-THE-COUNTER (OTC) HUMAN DRUGS WHICH ARE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED

9. Part 330 is amended in § 330.10 by adding new paragraph (e) to read as follows:

§ 330.10 Procedures for classifying OTC drugs as generally recognized as safe and effective and not misbranded, and for establishing monographs.

* * * * *

(e) *Institutional review.* Information and data submitted under this section after (insert effective date of this paragraph) shall include a statement regarding each clinical investigation involving human subjects, from which the information and data are derived, that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

PART 361—PRESCRIPTION DRUGS FOR HUMAN USE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED: DRUGS USED IN RESEARCH

10. Part 361 is amended in § 361.1 by revising paragraph (d)(9) to read as follows:

1033095

review set forth in this part or Part 56 of this chapter, or

* * * * *

PART 314—NEW DRUG APPLICATIONS

7. Part 314 is amended:

a. In § 314.1 by adding a new item 17 to Form FD–356H in paragraph (c)(2) and by redesignating paragraphs (f)(7) and (f)(8) as (f)(8) and (f)(9) and adding a new paragraph (f)(7) to read as follows:

§ 314.1 Applications.

* * * * *

(c) * * *

(2) * * *

Form FD–356H—Rev. 1974:

* * * * *

17. *Conduct of clinical investigations.* A statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

(f) * * *

(7) A statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements the institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

b. In § 314.8 by adding a new paragraph (n) to read as follows:

§ 314.8 Supplemental applications.

* * * * *

(n) A supplemental application that contains clinical investigations involving human subjects shall include a statement by the applicant regarding each such investigation that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

c. In § 314.9 by adding new paragraph (e) to read as follows:

§ 314.9 Insufficient information in application.

* * * * *

(e) The information contained in an application shall be considered insufficient to determine whether a drug is safe and effective for use unless the application includes a statement regarding each clincial investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

d. In § 314.12 by adding new paragraph (e) to read as follows:

§ 314.12 Untrue statements in application.

* * * * *

(e) Any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

e. In § 314.110 by adding new paragraph (a)(11) to read as follows:

§ 314.110 Reasons for refusing to file applications.

(a) * * *

(11) The applicant fails to include in the application a statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.26 of this chapter.

* * * * *

f. In § 314.111 by adding paragraph (a)(11) to read as follows:

§ 314.111 Refusal to approve the application.

(a) * * *

(11) Any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

* * * * *

g. In § 314.115 by adding new paragraph (c)(7) to read as follows:

§ 314.115 Withdrawal of approval of an application.

* * * * *

(c) * * *

(7) That any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

* * * * *

PART 320—BIOAVAILABILITY AND BIOEQUIVALENCE REQUIREMENTS

8. Part 320 is amended:

a. In § 320.31 by adding a new paragraph (f) to read as follows:

§ 320.31 Applicability of requirements regarding a "Notice of Claimed Investigational Exemption for a New Drug."

* * * * *

(f) An in vivo bioavailability study in humans shall be conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter, regardless of whether the study is conducted under a "Notice of Claimed Investigational Exemption for a New Drug."

b. In § 320.57 by adding a new paragraph (e) to read as follows:

§ 320.57 Requirements of the conduct of in vivo bioequivalence testing in humans.

* * * * *

(e) If a bioequivalence requirement provides for in vivo testing in humans, any person conducting such testing shall comply with the requirements of § 320.31.

PART 330—OVER-THE-COUNTER (OTC) HUMAN DRUGS WHICH ARE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED

9. Part 330 is amended in § 330.10 by adding new paragraph (e) to read as follows:

§ 330.10 Procedures for classifying OTC drugs as generally recognized as safe and effective and not misbranded, and for establishing monographs.

* * * * *

(e) *Institutional review.* Information and data submitted under this section after (insert effective date of this paragraph) shall include a statement regarding each clinical investigation involving human subjects, from which the information and data are derived, that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

PART 361—PRESCRIPTION DRUGS FOR HUMAN USE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED: DRUGS USED IN RESEARCH

10. Part 361 is amended in § 361.1 by revising paragraph (d)(9) to read as follows:

1033096

§ 361.1 Radioactive drugs for certain research uses.

* * * *

(d) * * *

(9) *Approval by an institutional review board.* The investigator shall obtain the review and approval of an institutional review board that conforms to the requirements for Part 56 of this chapter.

* * * * *

PART 430—ANTIBIOTIC DRUGS; GENERAL

11. Part 430 is amended in § 430.20 by adding new paragraph (g) to read as follows:

§ 430.20 Procedures for the issuance, amendment, or repeal of regulations.

* * * * *

(g) No regulation providing for the certification of an antibiotic drug for human use shall be issued or amended unless each clinical investigation in involving human subjects on which the issuance or amendment or the regulation is based was conducted in compliance with the requirements for institutional review set for the in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

ART 431—CERTIFICATION OF NTIBIOTIC DRUGS

12. Part 431 is amended in § 431.17 by adding a new paragraph (l) to read as follows:

§ 431.17 New antibiotic and antibiotic-containing products.

* * * * *

(l) A statement regarding each clinical investigation involving human subjects contained in the request that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

SUBCHAPTER F—BIOLOGICS

PART 601—LICENSING

13. Part 601 is amended:

a. In § 601.2 by revising paragraph (a) to read as follows:

§ 601.2 Applications for establishment and product licenses; procedures for filing.

(a) *General.* To obtain a license for any establishment or product, the manufacturer shall make application to the Director, Bureau of Biologics, on forms prescribed for such purposes, and the case of an application for a product license, shall submit data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed standards of safety, purity, and potency; with respect to each nonclinical laboratory study, either a statement that the study was conducted in compliance with the requirements set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a statement that describes in detail all differences between the practices used in the study and those required in the regulations; a statement regarding each clinical investigation involving human subjects contained in the application, that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter; a full description of manufacturing methods; data establishing stability of the product through the dating period; sample(s) representative of the product to be sold, bartered, or exchanged or offered, sent, carried or brought for sale, barter, or exchange; summaries of results of tests performed on the lot(s) represented by the submitted sample(s); and specimens of the labels, enclosures and containers proposed to be used for the product. An application for license shall not be considered as filed until all pertinent information and data have been received from the manufacturer by the Bureau of Biologics. In lieu of the procedures described in this paragraph, applications for radioactive biological products shall be handled as set forth in paragraph (b) of this section.

* * * * *

b. In § 601.25 by revising paragraph (h)(1) and adding a new paragraph (1) to read as follows:

§ 601.25 Review procedures to determine that licensed biological products are safe, effective, and not misbranded under prescribed, recommended, or suggested conditions of use.

* * * * *

(h) *Additional studies.* (1) Within 30 days following publication of the final order, each licensee for a biological product designated as requiring further study to justify continued marketing on an interim basis, pursuant to paragraph (f)(3) of this section, shall satisfy the Commissioner of Food and Drugs in writing that studies adequate and appropriate to resolve the questions raised about the product have been undertaken, or the Federal Government may undertake these studies. Any study involving a clinical investigation that involves human subjects shall be conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter, unless it is not subject to such requirements in accordance with § 56.6 of this chapter. The Commissioner may extend this 30-day period if necessary, either to review and act on proposed protocols or upon indication from the licensee that the studies will commence at a specified reasonable time. If no such commitment is made, or adequate and appropriate studies are not undertaken, the product licenses shall be revoked.

(j) [Reserved]

(k) [Reserved]

(l) *Institutional review.* Information and data submitted under this section after (insert effective date of this paragraph) shall include statements regarding each clinical investigation involving human subjects that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

b. By revising § 601.30 to read as follows:

§ 601.30 Licenses required; products for controlled investigation only.

Any biological or trivalent organic arsenical manufactured in any foreign country and intended for sale, barter or exchange shall be refused entry by collectors of customs unless manufactured in an establishment holding an unsuspended and unrevoked establishment license and license for the product. Unlicensed products that are not imported for sale, barter or exchange and that are intended solely for purposes of controlled investigation are admissible only if the investigation is conducted in accordance with section 505 of the Federal Food, Drug, and Cosmetic Act and the requirements set forth in Parts 56, 58, and 312 of this chapter.

PART 630—ADDITIONAL STANDARDS FOR VIRAL VACCINES

14. Part 630 is amended:

By revising the first sentence of § 630.11 to read as follows:

§ 630.11 Clinical trials to qualify for license.

To qualify for license, the antigenicity of the vaccine shall have been determined by clinical trials of adequate statistical design conducted in compliance with Part 56 of this chapter, unless exempted under § 56.6. * * *

1033097

10330980

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830

Medical and
Health Sciences
Division

(615) 576-3098

January 18, 1980

Roy Kinard, D.V.M.
Office for Protection
from Research Risks
Office of the Director
Department of Health, Education
and Welfare
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Kinard:

General Assurance G1716

Enclosed is a list of members of the ORAU/ORNL Committee on Human Studies. This list has been updated to show changes in our membership that have occurred from resignations, relocation to other areas, and replacements.

The information given is in accordance with a letter received from you on April 12, 1977. If further information is needed, please let us know.

Sincerely,

Dianne Gresham

Dianne Gresham
Secretary, Committee on Human Studies

dg

Enclosure

1033099

IRB MEMBER ROSTER

ORAU/ORNL Committee on Human Studies

January, 1980

Name of Institutional Officer (other than chairperson) to whom correspondence concerning Board affairs should be addressed: C. C. Lushbaugh, M.D.

Name:	William H. Calhoun
Earned degrees:	A.A., B.A., Ph.D.
Position or Occupation:	Professor & Head, Department of Psychology The University of Tennessee, Knoxville
Board certification, licenses, etc.:	
Relationship to institution:	Consultant
Representative capacity:	Clinical psychologist, community representative

Name:	Howard R. Friedman
Earned degrees:	B.B.A. and Ph.D.
Position or Occupation:	Chief Clinical Psychologist and Director Children and Youth Program Regional Mental Health Center Oak Ridge, TN and Adjunct Associate Professor, Department of Psychology, The University of Tennessee, Knoxville; Psychology Consultant, Campbell County Schools, TN
Board Certification, licenses, etc.:	Licensed Clinical Psychologist, Tennessee
Relationship to institution:	Consultant
Representative capacity:	Clinical psychologist, community representative

Name:	A. Seaton Garrett, Jr.
Earned degrees:	M.D.
Position or Occupation:	Medical Director, Oak Ridge National Laboratory, Union Carbide Corporation Nuclear Division, Oak Ridge, TN
Board certification, licenses, etc.:	Board Eligible Internal Medicine
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, practitioner

Name:	Donald W. Goodwin
Earned degrees:	B.D., Ph.D.
Position or Occupation:	Minister, United Church, Chapel-on-the-Hill Oak Ridge, TN
Board certification, licenses, etc.:	N/A
Relationship to institution:	Consultant
Representative capacity:	Ethicist, community representative

Name:	Martha S. Hansard
Earned degrees:	B.S., M.S. (2), Ph.D.
Position or Occupation:	Associate Section Leader for Computer Methodology and Systems in Epidemiology and Scientist, Medical and Health Sciences Division, ORAU
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORAU
Representative capacity:	Administrator, community representative

Name:	Karl F. Hübner
Earned degrees:	M.D.
Position or Occupation:	Director, Outpatient Nuclear Medicine, Medical and Health Sciences Division, ORAU, and Director, Radiation Emergency Assistance Center/Training Site (REAC/TS), ORAU
Board certification, licenses, etc.:	Certified nuclear medicine; Licensed in Tennessee
Relationship to institution:	Employee of ORAU
Representative capacity:	Investigator, administrator, practitioner

Name:	Melvin E. Koons
Earned degrees:	B.A., J.D.
Position or Occupation:	Purchasing Agent, Union Carbide Corporation Nuclear Division Lawyer
Board certification, licenses, etc.:	Licensed in North Dakota and Tennessee
Relationship to institution:	Employee of UCCND (ORNL)
Representative capacity:	Lawyer

Name:	Robert Lange (Chairman of Committee)
Earned degrees:	B.A., M.D.
Position or Occupation:	~~Research~~ Professor; ~~Director~~, ~~The University of Tennessee Memorial Research Center~~ (Chairman)
Board certification, licenses, etc.:	Licensed Tennessee, Minnesota, Missouri, and Georgia: Certified internal medicine
Relationship to institution:	Consultant
Representative capacity:	Administrator, practitioner

Name:	Steve Lawrence
Earned degrees:	B.S. M.S.
Position or Occupation:	Manager for Administration, ORAU
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORAU
Representative capacity:	Administrator, ethicist, community representative

Name:	Clarence C. Lushbaugh
Earned degrees:	B.S., Ph.D., M.D.
Position or Occupation:	Chairman, Medical and Health Sciences Division, ORAU
Board certification, licenses, etc.:	Certified pathology; licensed Tennessee
Relationship to institution:	Employee of ORAU
Representative capacity:	Investigator, administrator, practitioner
Name:	L. Clifford McKee
Earned degrees:	B.A., M.D.
Position or Occupation:	Associate Professor of Medicine, Department of Medicine, Vanderbilt University
Board certification, licenses, etc.:	Certified internal medicine; licensed Tennessee
Relationship to institution:	Consultant
Representative capacity:	Administrator, practitioner
Name:	Ruby L. Anderson Miller
Earned degrees:	B.S.
Position or Occupation:	Public Relations Representative, Union Carbide Corporation Nuclear Division, ORNL
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, community representative
Name:	John B. Storer
Earned degrees:	M.D.
Position or Occupation:	Director, Biology Division, ORNL
Board certification, licenses, etc.:	None
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, investigator,
Name:	Dianne Gresham
	Secretary to the ORAU/ORNL Committee on Human Studies
	Non-voting member

1033102

Oak Ridge Associated Universities (ORAU)
Oak Ridge National Laboratory (ORNL)

HSC 2/4/80

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

See page 19

February 1, 1980

61ST CUMULATIVE LIST 1980

OF INSTITUTIONS WHICH HAVE ESTABLISHED

GENERAL ASSURANCES

OF COMPLIANCE WITH HEW REGULATIONS ON

PROTECTION OF HUMAN SUBJECTS

1. INCOMING PROPOSALS - GRANTS OR CONTRACTS

a. If the professional review of a proposal indicates that the project *does not involve* human subjects (box on signature page of application or box 3A of HEW-596), as defined in 45 CFR 46, the application can be processed without further regard to the question of institutional assurances.

b. If the professional review of a proposal indicates that the project *does involve* human subjects (box on signature page of application or box 3B of HEW-596), the next step is to determine whether the institution has checked either box 4A or 4B.

- If 4A is checked, this means that the applicant institution does *not have* an approved assurance on file but will supply documentation and certification of review when requested. This action is initiated by the OPRR, OD, NIH; Westwood Bldg., Room 303; Bethesda, Maryland 20205; upon receipt of a copy of the proposal and summary statement from the *operating agency* immediately following an initial review.

- If 4B is checked, this means that the applicant institution has an approved general assurance on file. The fill-in spaces in this paragraph indicate the HEW general assurance "G" number for the institution as presented in the "Cumulative Listing" and the date when the proposal was certified.

1033103

c. Draft requests for proposals (RFPs or RFAs) should be reviewed to determine whether performance will involve human subjects at risk. If these will be involved, the RFP should include the "Notice to Offerors" required by 41 CFR 3-4.5504(a). Offerings and proposals submitted in response to the RFP should be handled as in 1.b. above.

d. Operating agencies may define "submission date" to fit administrative requirements. It is suggested that sole source responses to RFPs should be considered to be submitted as of the closing date of the RFP and should then be handled as in 1.b. above.

e. Competitive responses to RFPs should be considered to be submitted as of the date of submission of the best and final offer, after establishing the zone of consideration or source selection, and should then proceed as in 1.b. above.

2. SUBMISSION OF CERTIFICATIONS - Whenever possible, the review and approval by Institutional Review Boards should occur prior to submission of the application or proposal and a certification to that effect should be included in or with the application or proposal itself, preferably on form HEW-596 (Rev. 4/75). Under no circumstances will the review of an application by the Department of Health, Education, and Welfare be completed until certification is received. The point at which review will be deferred or terminated is left to the operating agency involved.

Institutions having on file with HEW an approved general assurance must submit certification within 30 days of the receipt of a written request thereof; and in any event *within 60 days* after the deadline or submission date for which the application or proposal was submitted.

Institutions not having on file an approved general assurance will indicate their status by checking box 4A on form HEW-596 accompanying the proposal *and when requested must submit the required assurances of compliance and certification of the review and approval* of the application or proposal by its Institutional Review Board within 30 days of the receipt of a written request from the Office for Protection from Research Risks (OPRR).

3. RESTRICTION CODES are presented as a suffix to the general assurance "G" number. This change conforms with Section 474.(a) of the Public Health Service Act, which specifically applies to both *biomedical* and *behavioral* research and with the derivative HEW regulations.

A restriction usually indicates that additional expertise in the Institutional Review Board membership is necessary for particular activities requiring certification.

An XM suffix indicates that the IRB has no or insufficient medical members. A proposed activity requiring medical expertise to assess risks, benefits, and the adequacy of safeguards cannot be certified under an XM restriction.

An XB suffix indicates that the IRB has no or insufficient members expert in the behavioral sciences. A proposed activity requiring behavioral expertise for assessing risks, benefits, and the adequacy of safeguards cannot be certified under an XB restriction.

An XO suffix indicates a restriction that uniquely applies to the institution under conditions of the general assurance agreement [call (301) 496-7041 for details].

When a proposal to be submitted to HEW comes within the scope of an XM or XB restriction, either biomedical or behavioral, the IRB reviewing the proposal must include additional voting members whose qualifications offset the restriction. Their names and qualifications should be reported immediately to OPRR and a statement added under "Notes" on the HEW-596 form certifying IRB review and approval that the additional professionally qualified members have been reported to OPRR. Proposals that come within the certification restrictions that are not preceded or accompanied by appropriate compensating reviewers will be deferred for rereview and recertification.

4. QUESTIONS with regard to the status of Special or General Assurances of Compliance may be directed to:

Assurance Management Desk (Patricia McGuire) (301) 496-7041

5. CONSULTATION for Special and General Assurances:

Roy Kinard, D.V.M. (301) 496-7041

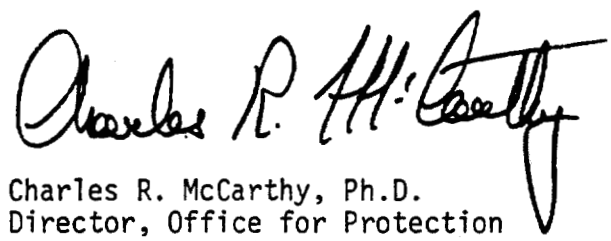
J. R. Marches, Ph.D. (301) 496-7041

6. FORMS

Bulk orders for additional copies of HEW 596 should be addressed to:

Office Service Section
Division of Research Grants
National Institutes of Health
Westwood Building, Room A-17
Bethesda, Maryland 20205

Single copies of HEW 596 can be obtained from OPRR or by duplicating the back pages of this listing.



Charles R. McCarthy, Ph.D.
Director, Office for Protection
from Research Risks
Office of the Director
National Institutes of Health

1033106

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	ALABAMA	
G0198	Alabama, University of, Birmingham	Birmingham
G0610	Alabama, University of	University
G2522	South Alabama, University of, Including the Medical Center	Mobile
G0055	Tuskegee Institute	Tuskegee Inst
	ARIZONA	
G0799XM	Arizona State University	Tempe
G0026	Arizona, University of	Tucson
G1287XB	St. Joseph's Hospital and Medical Center, Including Barrow Neurological Institute	Phoenix
	ARKANSAS	
*G0336	Arkansas, University of, Medical Center	Little Rock
	CALIFORNIA	
G0784XM	American Institutes for Research	Palo Alto
G0144	California Institute of Technology	Pasadena
G0261	California State Health and Welfare Agency Department of Health Services Department of Mental Health Department of Developmental Services Department of Social Services Department of Alcohol and Drug Abuse Office of Statewide Health Planning and Development	Sacramento
G2354XM	California State University, Dominguez Hills	Carson
G0278	California, University of, Berkeley	Berkeley
G0195	California, University of, Davis	Davis
G0380	California, University of, Irvine	Irvine
G0238	California, University of, Los Angeles	Los Angeles
G0193	California, University of, Riverside	Riverside
G0389	California, University of, San Diego	La Jolla
G0155	California, University of, San Francisco	San Francisco
G0282	California, University of, Santa Barbara	Santa Barbara

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033107

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0205XM	California, University of, Santa Cruz	Santa Cruz
G0234	Cedars-Sinai Medical Center	Los Angeles
*G2564	Charles R. Drew Postgraduate Medical School	Los Angeles
G0135	Childrens Hospital of Los Angeles	Los Angeles
G0287XB	Children's Hospital of San Francisco	San Francisco
G0009	City of Hope National Medical Center	Duarte
G0432	Institute for Medical Research	San Jose
G2169XM	Institute for Research in Social Behavior	Oakland
*G2400	Institute of Medical Sciences	San Francisco
*G2367	John Wesley County Hospital Attending Staff Association	Los Angeles
G0214	Kaiser Foundation Research Institute, a Division of Kaiser Foundation Hospitals, Kaiser Foundation Hospitals in Northern California, Southern California, Oregon, and Hawaii	Oakland
G0278	Lawrence Berkeley Laboratory University of California	Berkeley
G0226	Loma Linda University	Loma Linda
G0226	Loma Linda University (La Sierra Campus)	Riverside
G0359XB	Los Angeles County Harbor General Hospital, Professional Staff Association of	Torrance
*G0213	Los Angeles County Hospital-University of Southern California Medical Center, Professional Staff Association of	Los Angeles
*G2564	Martin Luther King, Jr. General Hospital and Its Staff Association Foundation	Los Angeles
*G0367XO	Mental Research Institute	Palo Alto
G0145	Mount Zion Hospital and Medical Center	San Francisco
G2961	Northern California Cancer Program	Palo Alto
*G2400	Pacific, Univ of, School of Dentistry	San Francisco
*G2400	Pacific, Univ of, School of Medical Sciences	San Francisco
G0082XB	Palo Alto Medical Research Foundation	Palo Alto
*G2400	Presbyterian Hospital of the Pacific Medical Center, Inc	San Francisco
G0067	Rancho Los Amigos Hospital and Its Professional Staff Association	Downey
G1416	Rand Corporation	Santa Monica
*G1096	Salk Institute	San Diego
G0420	San Diego State University	San Diego
G0420	San Diego State University Foundation	San Diego

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033108

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0729XM	San Francisco State University	San Francisco
G1472XM	Scientific Analysis Corporation (Including the Institute for Scientific Analysis and Performance Sites in Berkeley, Los Angeles, and San Diego)	San Francisco
G0108	Scripps Clinic and Research Foundation	La Jolla
*G0122	Southern California, University of	Los Angeles
G0378	SRI International	Menlo Park
G0011	Stanford University	Stanford
G0010	USPHS Hospital, San Francisco	San Francisco
G1620	Veterans Administration Hospital-Long Beach	Long Beach
G1796	Veterans Administration Hospital-Sepulveda	Sepulveda
G1658XB	Veterans Administration Wadsworth Medical Center	Los Angeles
G1591XM	Wright Institute	Berkeley
	COLORADO	
G0845	Children's Hospital of Denver	Denver
G2823XB	Colorado Regional Cancer Center, Inc	Denver
G1144	Colorado State University	Fort Collins
G0455XM	Colorado, University of	Boulder
G0268	Colorado, University of, Medical Center	Denver
G0277XM	Denver, University of (Colorado Seminary)	Denver
G0267	National Asthma Center	Denver
G0068	National Jewish Hospital and Research Center	Denver
	CONNECTICUT	
G0672XB	Connecticut State Department of Health	Hartford
G0039	Connecticut, University of	Storrs
G1966	Connecticut, University of, Health Center	Farmington Hartford
G1533	Connecticut Valley Hospital	Middletown
G0331XB	Hartford Hospital	Hartford
G0007	Institute of Living	Hartford
G0003	John B. Pierce Fdn of Connecticut, Inc	New Haven
G0821	Saint Francis Hospital	Hartford
G2895	Waterbury Hospital Health Center	Waterbury
*G0243	Yale University	New Haven

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033109

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	DELAWARE	
G0148	Delaware Division of Mental Health of the Department of Health and Social Services	New Castle
G0013	Delaware, University of	Newark
G2480	Wilmington Medical Center, Inc	Wilmington
	DISTRICT OF COLUMBIA	
G0784XM	American Institutes for Research	Washington
G1398XB	American National Red Cross	Washington
G1674XM	Bureau of Social Science Research, Inc	Washington
G0365XM	Catholic University of America	Washington
G0042	Children's Hospital of D.C., Research Foundation of	Washington
G1249	Gallaudet College	Washington
G0294	George Washington University	Washington
G0228	Georgetown University	Washington
G0841	Howard University	Washington
G1989	National Academy of Sciences, Including National Academy of Engineering, Institute of Medicine, and National Research Council	Washington
G1036XM	National Children's Center, Inc	Washington
G3045XO	Veterans Administration Central Office (NCI-VA COOP CANCER THERAPY PROJECTS ONLY)	Washington
G0180XB	Washington Hospital Center	Washington
	FLORIDA	
G2905	Florida State Department of Health and Rehabilitative Services	Tallahassee
G0119	Florida State University	Tallahassee
G0382	Florida, University of	Gainesville
G0840XB	Miami Heart Institute	Miami Beach
G0301	Miami, University of	Coral Gables
G0301	Miami, University of	Miami
G0275	Mt Sinai Medical Center of Greater Miami	Miami Beach
G2321	Papanicolaou Cancer Research Institute	Miami
G1065	South Florida, University of	Fort Myers St Petersburg Sarasota Tampa

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033110

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	GEORGIA	
*G0138	Emory Univ Division of Basic Health Sciences	Atlanta
G0622	Emory Univ Graduate Sch of Arts and Sciences	Atlanta
*G0138	Emory Univ Nell Hodgson Woodruff School of Nursing	Atlanta
G0595	Emory Univ School of Dentistry	Atlanta
*G0138	Emory Univ School of Medicine	Atlanta
G0197	Georgia Dept of Human Resources, All Units	Atlanta
G0520	Georgia Institute of Technology, Including its Engineering Experiment Station, and its Georgia Tech Research Institute	Atlanta
G0151	Georgia, Medical College of	Augusta
G0248	Georgia, University of, and its Research Fdn	Athens
*G1467	Grady Memorial Hospital	Atlanta
	HAWAII	
G0104	Hawaii, University of (Including the Entire System and the Research Corporation)	Honolulu
G0214	Kaiser Foundation Hospital	Honolulu
	IDAHO	
G0218XM	Idaho, University of	Moscow
*G1869	Mountain States Tumor Institute	Boise
	ILLINOIS	
G0395	American Dental Assn and ADA Health Fdn	Chicago
G0332XM	Anna Mental Health and Developmental Center	Anna
G1626	Chicago, University of (Division of Biological Sciences and Pritzker School of Medicine, Division of Social Sciences, School of Social Service Administration, and Related Units)	Chicago
G0114	Children's Memorial Hospital	Chicago
G0430	Downey Veterans Administration Hospital	Downey
G0182	Evanston Hospital	Evanston
G0430	Health Sciences, Univ of/Chicago Medical Sch	Chicago

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033111

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0053	Hektoen Institute for Medical Research	Chicago
G2959	Illinois Cancer Council	Chicago
G1561	Illinois State Psychiatric Institute	Chicago
G0345	Illinois, University of, at Chicago Circle	Chicago
G0291	Illinois, University of, Medical Center Campus, Including Rockford School of Medicine, and Peoria School of Medicine	Chicago
G0102	Illinois, Univ of, and all components at Urbana-Champaign	Urbana
G1373XM	Lincoln Developmental Center	Lincoln
G2369	Loyola University Medical Center	Maywood
G0095	Michael Reese Hospital and Medical Center	Chicago
G2763	Mount Sinai Hospital Medical Center of Chicago	Chicago
G0518XM	Northern Illinois University	DeKalb
G0190	Northwestern Memorial Hospital	Chicago
G0190	Northwestern University	Chicago
G0190	Northwestern University	Evanston
G0190	Rehabilitation Institute of Chicago	Chicago
G0175	Rush-Presbyterian-St Luke's Medical Center	Chicago
G0309	Southern Illinois University	Carbondale
G2606	Southern Illinois University	Edwardsville
G0309	Southern Illinois Univ School of Medicine	Springfield
G0190	VA Lakeside Hospital of Chicago	Chicago
G1970XM	Western Illinois University	Macomb

INDIANA

G0314XM	DePauw University	Greencastle
G0945	Fort Wayne State Hosp and Training Center	Ft Wayne
G0185	Indiana Univ and Indiana Univ Foundation	Bloomington Indianapolis
G0185	Indiana University (Law School)	Indianapolis
G0185	Indiana Univ-Purdue Univ (Medical Facility)	Indianapolis
G0185	Indiana University Regional Campuses at Fort Wayne, Gary, Kokomo, New Albany, Richmond, and South Bend	
G1397	Indianapolis Center for Advanced Research	Indianapolis
G0883	Larue D. Carter Memorial Hospital	Indianapolis
G1697	Marion County Assn for Retarded Citizens, Inc	Indianapolis

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033112

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G1246XB	Methodist Hospital of Indiana, Inc	Indianapolis
G1119XM	Notre Dame, University of	Notre Dame
G0131	Purdue Univ and Purdue Research Foundation	West Lafayette
	IOWA	
*G0343XO	Iowa State Univ of Science and Technology	Ames
G0209	Iowa, University of	Iowa City
*G0856XO	Woodward State Hospital-School	Woodward
	KANSAS	
G0038	Kansas State University	Manhattan
*G0157XO	Kansas, University of - Lawrence Campus	Lawrence
G0229	Kansas, University of, Medical Center College of Health Sciences and Hospital	Kansas City
G0081	Menninger Foundation	Topeka
	KENTUCKY	
G0223	Kentucky, Univ of, and the Research Foundation	Lexington
G0527	Louisville, University of, and Louisville, University of, Foundation, Inc; Except Schools of Med and Dent	Louisville
G0023	Louisville, University of, Schools of Medicine and Dentistry	Louisville
G0223	Veterans Administration Hospital	Lexington
	LOUISIANA	
G0442	Alton Ochsner Medical Foundation	New Orleans
*G0262XO	Louisiana State Univ and A & M College System	Baton Rouge
*G2428XO	Louisiana State Univ in Baton Rouge	Baton Rouge
*G2485	Louisiana State Univ Medical Center	New Orleans
G0137XM	Pinecrest State School	Pineville
G0018	Tulane Medical Center	New Orleans
G2386	Tulane University Except Medical Center	New Orleans

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033113

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0010	USPHS Hospital (National Leprosarium)	Carville
G0010	USPHS Hospital, New Orleans	New Orleans
	MAINE	
G3007	Eastern Maine Medical Center	Bangor
G0513	Maine Medical Center	Portland
	MARYLAND	
G0402	Baltimore City Hospitals	Baltimore
G0010	Division of Hospitals and Clinics, BMS, DHEW (Includes 9 USPHS Hospitals and 26 Outpatient Clinics)	West Hyattsville
G3109XB	Frederick Cancer Research Center	Frederick
G0186	Friends Medical Science Research Center, Inc	Baltimore
G0640	Institute for Behavioral Research, Inc	Silver Spring
G2857	John F. Kennedy Institute for Handicapped Children	Baltimore
G0352	Johns Hopkins Univ Faculty of Arts and Sciences	Baltimore
G0274	Johns Hopkins Univ School of Hygiene and Public Health	Baltimore
G0174	Johns Hopkins Univ School of Medicine and Johns Hopkins Hospital	Baltimore
G0326	Maryland, Univ of, at Baltimore	Baltimore
G0296	Maryland, Univ of, at College Park	College Park
G0400	Sinai Hospital of Baltimore, Inc	Baltimore
G0010	USPHS Hospital, Baltimore	Baltimore
	MASSACHUSETTS	
G3270	Affiliated Hospitals Center, Inc. (Formerly listed as the Boston Hospital for Women, Peter Bent Brigham Hospital, and Robert Bent Brigham Hospital)	Boston
G0784XM	American Institutes for Research	Cambridge
G0286	Beth Israel Hospital	Boston

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033114

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0554	Boston City Hospital	Boston
G0554	Boston Department of Health and Hospitals	Boston
G0554	Boston Division of Community Health Services	Boston
G0783	Boston Mental Health Foundation, Inc	Boston
G0783	Boston State Hospital	Boston
G0322XM	Boston Univ, Charles River Campus	Boston
G0550	Boston Univ Medical Center	Boston
G0550	Boston Univ School of Graduate Dentistry	Boston
G0550	Boston Univ School of Medicine	Boston
G0132XM	Brandeis University	Waltham
G2396XB	Center for Blood Research, Inc	Boston
G0406	Children's Hospital Medical Center	Boston
G0117XM	Clark University	Worcester
G0098	Danvers State Hospital	Hathorne
G2042	Eunice Kennedy Shriver Center	Waltham
G0410XB	Eye Research Institute of Retina Foundation	Boston
G0412XB	Forsyth Dental Center	Boston
G2397	Harvard Medical Sch and Sch of Dental Medicine	Boston
G2238	Harvard Univ, Faculty of Arts and Sciences	Cambridge
G2494XM	Harvard Univ, Graduate School of Education	Cambridge
G2398	Harvard Univ, School of Public Health	Boston
G2573	Harvard Univ, University Health Services	Cambridge
G0791	Joslin Diabetes Foundation, Inc	Boston
G0087XB	Lahey Clinic Foundation, Inc	Boston
G0449XB	Lemuel Shattuck Hospital	Jamaica Plain
G0554	Long Island Chronic Disease Hospital	Boston Harbor
G2304XO	Mass Developmental Disabilities Council	Boston
G0212XB	Massachusetts Eye and Ear Infirmary	Boston
G0167	Massachusetts General Hospital	Boston
G0097	Massachusetts Institute of Technology	Cambridge
G0597	Massachusetts Mental Health Center	Boston
G0597	Massachusetts Mental Health Research Corp	Boston
G0147	Massachusetts, University of - Amherst	Amherst
G2736	Massachusetts, University of, Medical School	Worcester
G0554	Mattapan Chronic Disease Hospital	Mattapan
G0576	McLean Hospital	Belmont
G3123	Mount Auburn Hospital	Cambridge
G0494XB	New England Deaconess Hospital	Boston
G0133	New England Medical Center Hospital	Boston
G3064	North Charles Mental Health Research & Training Foundation, Inc	Cambridge

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033115

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0297	Northeastern University	Boston
G3018XB	Pondville Hospital	Walpole(Norfolk)
G2515XM	Research Institute for Educational Problems	Cambridge
G0771	Sidney Farber Cancer Institute, Inc	Boston
G0351XB	St Margaret's Hospital for Women	Boston
G0554	Trustees of Health & Hosps, City of Boston, Inc	Boston
G2107	Tufts-New England Medical Center	Boston
G2379	Tufts University - Boston	Boston
*G0266XO	Tufts University - Medford	Medford
G0550	University Hospital, Inc	Boston
G0010	USPHS Hospital, Boston	Boston
G2042	Walter E. Fernald State School	Belmont
G0085	Worcester Foundation for Experimental Biology	Shrewsbury
	MICHIGAN	
G0363	Child Research Center of Michigan	Detroit
G0363	Children's Hospital of Michigan	Detroit
G0497XM	Detroit, University of	Detroit
G0357	Edsel B. Ford Institute for Medical Research	Detroit
G0357	Henry Ford Hospital	Detroit
G0101	Lafayette Clinic	Detroit
G0656XB	Michigan Cancer Foundation	Detroit
G0615	Michigan Department of Public Health	Lansing
G0384	Michigan State University	East Lansing
G0295	Michigan, University of	Ann Arbor
G0295	Michigan, University of	Dearborn
G0295	Michigan, University of	Flint
G1009XM	Oakland University	Rochester
G0008	Sinai Hospital of Detroit	Detroit
G2483	Veterans Administration Medical Center-Ann Arbor	Ann Arbor
G0354	Wayne State University	Detroit
G0720	Western Michigan University	Kalamazoo
	MINNESOTA	
G0065	Hennepin County Medical Center	Minneapolis
G0041	Mayo Foundation	Rochester
G0065	Minneapolis Medical Research Foundation, Inc	Minneapolis

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

103116

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0463	Minnesota, University of	Austin
G0463	Minnesota, University of	Duluth
G0463	Minnesota, University of	Minneapolis
G0463	Minnesota, University of	Morris
G0463	Minnesota, University of	St Paul
G0463	Minnesota, University of, Technical College	Crookston
G0463	Minnesota, University of, Technical College	Waseca
	MISSISSIPPI	
G0561XM	Mississippi, University of (Main Campus)	University
G0366	Mississippi, University of, Medical Center	Jackson
G0366	Veterans Administration Center	Jackson
	MISSOURI	
G2791XM	American Nurses' Association, Inc	Kansas City
G0298XB	Cancer Research Center	Columbia
G0298XB	Ellis Fischel State Cancer Hospital	Columbia
G0424	Jewish Hospital of St Louis	St Louis
G0320XB	Kirksville College of Osteopathic Medicine	Kirksville
G2936XB	Missouri Cancer Programs	Columbia
G0292	Missouri, University of	Columbia
G0292	Missouri, University of	Kansas City
G0292	Missouri, University of	Rolla
G0292	Missouri, University of	St Louis
G0356	St Louis University	St Louis
*G2056	Veterans Administration Med Ctr - Kansas City	Kansas City
G0279XM	Washington University (Excluding Schools of Medicine and Dentistry)	St Louis
G2351	Washington University School of Medicine	St Louis
	NEBRASKA	
G1120	Creighton University	Omaha
G3112	Father Flanagan's Boys' Home	Boys Town
G0407	Nebraska, Univ of, Including the Medical Ctr	Omaha
G0407	Nebraska, Univ of, Including the State Univ of Nebraska	Lincoln

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033117

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	NEVADA	
G0762	Nevada, University of, Reno Campus (includes all components of the University, Reno Campus)	Reno
	NEW HAMPSHIRE	
G0427XM	Dartmouth College Faculty of Arts & Sciences	Hanover
G0227	Dartmouth Medical School	Hanover
	NEW JERSEY	
G0349	College of Medicine and Dentistry of New Jersey	Newark
G0349	CMDNJ-New Jersey Dental School	Newark
G0349	CMDNJ-New Jersey Medical School	Newark
G0349	CMDNJ-New Jersey School of Osteopathic Medicine	Piscataway
G0349	CMDNJ-Rutgers Medical School	Piscataway
G0981XM	Educational Testing Service	Princeton
G0492XB	Institute for Medical Research	Camden
G0837	Newark Beth Israel Medical Center	Newark
G0570XM	Princeton University	Princeton
G0349	Rutgers Medical School	Piscataway
G0300	Rutgers, The State Univ of New Jersey	Camden
G0300	Rutgers, The State Univ of New Jersey	New Brunswick
G0300	Rutgers, The State Univ of New Jersey	Newark
	NEW MEXICO	
*G0472	New Mexico, University of	Albuquerque
*G0353	New Mexico, University of, Health Sciences Group-School of Medicine, Colleges of Pharmacy and Nursing	Albuquerque
	NEW YORK	
G0217	Albany Medical College of Union University	Albany
G2129	American Health Foundation	New York
G1064XB	Associated Universities, Inc, Including Brookhaven National Laboratory	Upton

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033118

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G2116XM	Barnard College	New York
G0341	Beth Israel Medical Center	New York
G1831XM	Center for Policy Research, Inc	New York
G2277XM	Child Welfare League of America, Inc	New York
G0381	Children's Hospital of Buffalo	Buffalo
G0437XM	Columbia Univ, Except Health Sciences Division	New York
G0034	Columbia Univ Health Sciences and Presbyterian Hospital	New York
G0063XM	Cornell Univ, Except Medical College	Ithaca
G0245	Cornell University Medical College	New York
G0109XO	Eastman Dental Center	Rochester
G2912	Genesee Hospital	Rochester
G2887XB	Health Research, Inc, Albany Division	Albany
G2904	Health Research, Inc, Roswell Park Division	Buffalo
G2887XB	Helen Hayes Hospital	West Haverstraw
G2475XB	Highland Hospital of Rochester	Rochester
G0621	Hospital for Joint Diseases and Medical Center, Including the Research Institute for Skeletomuscular Diseases	New York
G0047	Hospital for Special Surgery	New York
G2920	ICD Rehabilitation and Research Center	New York
G1005XO	Jewish Board of Family and Children's Services, Inc	New York
G0369	Kingsbrook Jewish Medical Center and Isaac Albert Research Institute	Brooklyn
G2375	Long Island Jewish-Hillside Medical Center	New Hyde Park
G0397	Maimonides Medical Center	Brooklyn
G0086XB	Mary Imogene Bassett Hospital	Cooperstown
G0383XB	Memorial Hosp for Cancer and Allied Diseases	New York
G0059	Montefiore Hospital and Medical Center	New York
G0139	Mount Sinai School of Medicine of CUNY	New York
G2518XB	Nassau County Medical Center, Including Meadowbrook Medical Education and Research Foundation, Inc	East Meadow
G0173XM	New School for Social Research	New York
G0526XB	New York Blood Center, Inc	New York
G1370	New York City Department of Health	New York
G0765XM	New York, City Univ of	New York
G0765XM	New York, City Univ of, Baruch College	New York
G0765XM	New York, City Univ of, Bronx Cmty College	Bronx
G0765XM	New York, City Univ of, Brooklyn College	Brooklyn

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033119

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0765XM	New York, City Univ of, City College	New York
G0765XM	New York, City Univ of, Graduate School and University Center	New York
G0765XM	New York, City Univ of, Herbert H. Lehman College	Bronx
G0765XM	New York, City Univ of, Hunter College	New York
G0765XM	New York, City Univ of, John Jay College of Criminal Justice	New York
G0765XM	New York, City Univ of, Kingsborough Community College	Brooklyn
G0765XM	New York, City Univ of, Manhattan Cmty College	New York
G0765XM	New York, City Univ of, Medgar Evers College	Brooklyn
G0765XM	New York, City Univ of, New York City Community College	Brooklyn
G0765XM	New York, City Univ of, Queens College	Flushing
G0765XM	New York, City Univ of, Queensborough Community College	New York
G0765XM	New York, City Univ of, Research Foundation	New York
G0765XM	New York, City Univ of, College of Staten Island	Staten Island
G0765XM	New York, City Univ of, York College	Jamaica
G2887XB	New York Dept of Health and Regional Offices	Albany
G0208	New York Medical College-Flower and Fifth Avenue Hospitals, Metropolitan Hospital, Bird S. Coler Memorial Hospital, and Lincoln Medical and Mental Health Center, Bronx	Valhalla
G0374XM	New York, State Univ of, at Albany	Albany
G0508	New York, State Univ of, at Binghamton	Binghamton
G0163	New York, State Univ of, at Buffalo	Buffalo
G0596	New York, State Univ of, at Stony Brook	Stony Brook
G0474	New York, State Univ of, College at Brockport	Brockport
G0506XM	New York, State Univ of, College at Buffalo	Buffalo
G0259XM	New York, State Univ of, College at Cortland	Cortland
G0386XM	New York, State Univ of, College at Oswego	Oswego
G0457	New York, State Univ of, College of Arts and Science at Geneseo	Geneseo
G0220	New York, State Univ of, College of Environmental Science and Forestry	Syracuse
G0305	New York, State Univ of, Downstate Medical Ctr	Brooklyn
G0127	New York, State Univ of, Upstate Medical Ctr	Syracuse
G0390XO	New York Univ, Exclusive of the Medical Ctr	New York

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0405	New York University Medical Center	New York
G0788	North Shore University Hospital	Manhasset
G2887XB	Oxford Home for Veterans and Their Dependents	Oxford
G0034	Presbyterian Hospital (Columbia Univ. Health Sciences)	New York
G2247	Public Health Research Institute of the City of New York, Inc	New York
G2375	Queens Hospital Center	Jamaica
G1001	Rensselaer Polytechnic Institute	Troy
G0624	Research Foundation for Mental Hygiene, Inc (NYS Office of Mental Health, NYS Office of Mental Retardation and Developmental Disabilities, NYS Division of Alcoholism and Substance Abuse - All Operating Components of the NYS Department of Mental Hygiene) Including	
	Capital District Psychiatric Center	Albany
	Long Island Research Institute	Central Islip
	NYS Institute for Basic Research in Mental Retardation	Staten Island
	New York State Psychiatric Institute	New York
	Research Institute on Alcoholism	Buffalo
	Rockland Research Institute	Orangeburg
	Special Projects Research Unit	Albany
G0172	Rochester, University of	Rochester
G0230	Rockefeller University	New York
G2036	Rockland County Health & Social Svcs Complex	Pomona
G0491	Roosevelt Hospital	New York
G2904	Roswell Park Memorial Institute	Buffalo
G0536XB	Sloan-Kettering Institute for Cancer Research	New York
G0076	St Luke's Hospital Center	New York
G2972XB	St Mary's Hospital	Rochester
G0376	St Vincent's Hosp and Medical Ctr of New York	New York
G0280XM	Syracuse University	Syracuse
G0373XM	Teachers College, Columbia University	New York
G2438XB	Trudeau Institute	Saranac Lake
G0010	USPHS Hospital, Staten Island	New York
G2045	Veterans Administration Hospital-Northport	Northport
G0002	Yeshiva Univ, Albert Einstein College of Med	Bronx

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033121

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	NORTH CAROLINA	
G0191	Duke University Medical Center and Duke University Exclusive of the Medical Center	Durham
G2242	North Carolina A & T State University	Greensboro
G0285	North Carolina State University at Raleigh	Raleigh
G0177	North Carolina, Univ of, at Chapel Hill	Chapel Hill
G0242	Wake Forest Univ, Bowman Gray Sch of Medicine	Winston-Salem
G1087	Wake Forest Univ, Except School of Medicine	Winston-Salem
G0078XM	Western Carolina Center	Morganton
G0191	Whitehead Medical Research Institute	Durham
	OHIO	
G3143XB	Akron General Medical Center	Akron
G0485	Akron, University of	Akron
G0683	Battelle Columbus Laboratories of the Battelle Memorial Institute	Columbus
G2843XB	Cancer Center, Inc	Cleveland
G1167	Case Western Reserve University	Cleveland
G0088	Children's Hospital Medical Center	Cincinnati
G0249	Children's Hospital Research Foundation, Inc	Columbus
G0667XM	Cincinnati, Univ of, Except Medical Center	Cincinnati
G0337	Cincinnati, Univ of, Medical Center, Including Colleges of Medicine, Nursing, and Health and Pharmacy	Cincinnati
G0502XB	Cleveland Clinic Foundation and Cleveland Clinic Educational Foundation	Cleveland
G0171	Cleveland Psychiatric Institute	Cleveland
G2678	Cox Heart Institute	Dayton
G2678	Fels Research Institute	Yellow Springs
G1936XB	Jewish Hospital of Cincinnati, Including the School of Nursing, Children's Psychiatric Center, and May Institute for Medical Research	Cincinnati
G0542	Kent State University	Kent
G1724	Medical College of Ohio at Toledo	Toledo
G0269XB	Mount Sinai Hospital of Cleveland	Cleveland
G0121	Ohio Agricultural Research & Development Ctr	Wooster

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033122

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0121	Ohio State University and Research Foundation	Columbus
G0662	St Luke's Hospital Association (United Methodist Church)	Cleveland
G0350XB	University Hospitals of Cleveland	Cleveland
G2678	Wright State University (All Components)	Dayton
G2907XM	Youngstown State University	Youngstown
	OKLAHOMA	
G0327	Oklahoma Medical Research Foundation, Inc	Oklahoma City
*G2402XO	Oklahoma, University of	Norman
G0241	Oklahoma, University of, Health Sciences Ctr	Oklahoma City
	OREGON	
G0134	Good Samaritan Hospital and Medical Center	Portland
G0214	Kaiser Foundation Hospital	Portland
G0043XB	Medical Research Foundation of Oregon and Oregon Regional Primate Research Center	Portland
G2399XM	Northwest Regional Educational Laboratory	Portland
G0505XM	Oregon Research Institute	Eugene
G0111XM	Oregon State University	Corvallis
G0288XM	Oregon, University of	Eugene
G2931	Oregon, University of, Health Sciences Center, Including Schools of Medicine, Dentistry, and Nursing	Portland
	PENNSYLVANIA	
G0125	Albert Einstein Medical Center, Northern Div	Philadelphia
G0952XB	Allegheny Health, Education and Research Corporation - Allegheny-Singer Research Corporation and Allegheny General Hospital	Pittsburgh
G0784XM	American Institutes for Research	Pittsburgh
G0338	Arthur P. Noyes Research Foundation	Norristown
G0436XM	Bucknell University	Lewisburg
G1218	Carnegie-Mellon University	Pittsburgh
G0129	Children's Hospital of Philadelphia (Joseph Stokes, Jr., Research Inst of)	Philadelphia

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033123

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0360	Children's Hospital of Pittsburgh	Pittsburgh
G0045	Fox Chase Cancer Center (Institute for Cancer Research and American Oncologic Hosp)	Philadelphia
G1556	Franklin Institute	Philadelphia
G0594	Geisinger Medical Center; Institute for Medical Education and Research	Danville
G0475	Hahnemann Medical College and Hospital	Philadelphia
G0936	H. K. Cooper Institute for Oral-Facial Anomalies and Communicative Disorders (Lancaster Cleft Palate Clinic)	Lancaster
G0273XB	Lankenau Hospital	Philadelphia
G0189XB	Magee-Womens Hospital	Pittsburgh
G1378	Marriage Council of Philadelphia, Inc (Reviewed by G0012)	Philadelphia
G2121XM	Marywood College	Scranton
G0057XB	Montefiore Hospital	Pittsburgh
G0338	Norristown State Hospital	Norristown
G0333	Pennsylvania Hospital	Philadelphia
G0222	Pennsylvania, Medical College of	Philadelphia
G0573	Pennsylvania State Univ & Commonwealth Camps	University Park
G1668	Pennsylvania State Univ, Milton S. Hershey Medical Center	Hershey
G0012	Pennsylvania, University of	Philadelphia
G1531	Philadelphia Department of Public Health	Philadelphia
G0324	Philadelphia Geriatric Center	Philadelphia
G0344	Philadelphia Psychiatric Center	Philadelphia
G0881	Philadelphia State Hospital	Philadelphia
G1532	Pittsburgh Child Guidance Center	Pittsburgh
G2929	Pittsburgh, University Health Center of	Pittsburgh
G0418	Pittsburgh, University of	Pittsburgh
G2200	Presbyterian-University Hospital	Pittsburgh
G0465	Presbyterian-Univ of Pennsylvania Medical Ctr	Philadelphia
G2264XM	Research for Better Schools, Inc	Philadelphia
G0795	St Joseph's Hospital	Lancaster
G2880	Temple Univ, Excluding the Health Sciences Ctr	Philadelphia
G2879	Temple University Health Sciences Center	Philadelphia
G0049	Thomas Jefferson Univ, All Components	Philadelphia
G0362XB	Wills Eye Hospital and Research Institute	Philadelphia
G0054XB	Wistar Institute	Philadelphia

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033124

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	PUERTO RICO	
G1348XM	Catholic University of Puerto Rico	Ponce
G0256XB	Puerto Rico, Univ of, Medical Sciences Campus	San Juan Rio Piedras
	RHODE ISLAND	
G0467	Brown University	Providence
*G0318	Rhode Island Hospital	Providence
G1252	Rhode Island, University of	Kingston
G2212XB	Roger Williams General Hospital	Providence
	SOUTH CAROLINA	
G2621	Clemson University	Clemson
G0533	South Carolina Department of Mental Health	Columbia
G0240	South Carolina, Medical University of	Charleston
G0629XM	South Carolina, University of	Columbia
	TENNESSEE	
G2869	East Tennessee State University	Johnson City
G0490XM	George Peabody College for Teachers	Nashville
G0393	Meharry Medical College	Nashville
G1716	Oak Ridge Associated Universities	Oak Ridge
G1716	Oak Ridge National Laboratory	Oak Ridge
G0648	St Jude Children's Research Hospital	Memphis
G0170	Tennessee, University of, Center for the Health Sciences	Memphis
G0124	Tennessee, University of - Knoxville	Knoxville
G0401	Vanderbilt University	Nashville
	TEXAS	
G2255	Audie L. Murphy Veterans Administration Hospital	San Antonio
G0307	Baylor College of Medicine	Houston

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G2255	Bexar County Hospital District	San Antonio
G0398XM	Houston, University of	Houston
*G2344XO	Southwest Educational Development Corporation (AKA Southwest Educational Development Lab)	Austin
G1045	Texas A & M University and Research Foundation, College Station Campus Only	College Station
G3027	Texas Department of Public Welfare	Austin
G0564	Texas Tech University	Lubbock
G3154	Texas Tech Univ School of Medicine at Lubbock(Including Academic Health Centers at El Paso and Amarillo)	Lubbock
*G1121XO	Texas, University of, at Arlington	Arlington
G0123	Texas, University of, at Austin	Austin
G1815	Texas, University of, at Dallas	Richardson
G0113	Texas, University of, Cancer Center (and its M.D. Anderson Hospital and Tumor Institute)	Houston
G2615	Texas, University of, Health Science Center at Dallas	Dallas
G2760	Texas, University of, Health Science Center at Houston	Houston
G2255	Texas, University of, Health Science Center at San Antonio, Including Medical School, Dental School, and Graduate School of Biomedical Sciences, Sch of Nursing, Sch of Allied Health Sciences, and Graduate School of Pharmacy	San Antonio
G0107	Texas, Univ of, Medical Branch at Galveston	Galveston
G0010	USPHS Hospital, Galveston	Galveston
	UTAH	
G2426	LDS Hospital	Salt Lake City
G2426	LDS Hospital - Deseret Foundation	Salt Lake City
G0462	Utah State University	Logan
G0235	Utah, University of	Salt Lake City
G0235	Utah, University of, Research Institute	Salt Lake City
G0235	Veterans Administration Hospital	Salt Lake City

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033126

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
	VERMONT	
G0194	Vermont, University of, and State Agricultural College	Burlington
G2335XB	Veterans Administration Ctr-White River Junction	White River Jct
	VIRGINIA	
G2684	Eastern Virginia Medical Authority and Eastern Virginia Medical School	Norfolk
G2275XM	Human Resources Research Organization	Alexandria
G0010	USPHS Hospital, Norfolk	Norfolk
G0239	Virginia Commonwealth University (All Schools and Divisions)	Richmond
G0306	Virginia, University of	Charlottesville
	WASHINGTON	
G0522	Children's Orthopedic Hosp and Medical Ctr	Seattle
G2627XB	Fred Hutchinson Cancer Research Center	Seattle
G0029XB	Pacific Northwest Research Foundation	Seattle
G0913XB	Swedish Hospital Medical Center	Seattle
G0010	USPHS Hospital, Seattle	Seattle
*G0900	Virginia Mason Research Center, Including Mason Clinic and Virginia Mason Hospital	Seattle
G1717	Washington Department of Social and Health Services, All Components	Olympia
G0105	Washington State University	Pullman
G0299	Washington, University of	Seattle
	WEST VIRGINIA	
G0431	West Virginia University	Morgantown
	WISCONSIN	
G0315	Central Wisconsin Colony and Training School	Madison
G2891XB	Columbia Hospital	Milwaukee

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033127

GENERAL ASSURANCE NUMBER	INSTITUTION	CITY
G0387XM	Marquette University	Milwaukee
G0763	Mendota Mental Health Institute	Madison
G3010XB	Mount Sinai Medical Center of Milwaukee	Milwaukee
G0503	Southern Wisconsin Center for the Developmentally Disabled	Union Grove
G3051	St Mary's Hospital	Milwaukee
G0077	Wisconsin, Medical College of, Inc	Milwaukee
G0319	Wisconsin, University of, Madison Campus	Madison
G2106XM	Wisconsin, University of, Parkside	Kenosha
	BANGLADESH	
G3061	International Centre for Diarrheal Disease Research, Bangladesh	Dacca
	SWITZERLAND	
*G1137	World Health Organization	Geneva

TOTAL NUMBER OF INSTITUTIONS AND COMPONENTS WITH ACCEPTABLE GENERAL ASSURANCES -- 564

RESTRICTION CODE
XM -- No Medical or IND Studies
XB -- No Behavioral Studies
XO -- Other Restriction (Call 301-496-7005)
* -- Final Acceptance of Revisions Pending

1033128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☐ FOLLOWUP ☐ REVISION

☐ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☐ RENEWAL ☐ CONTINUATION

APPLICATION IDENTIFICATION NUMBER *(If known)*

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of Public Law 93-348, as implemented by Part 46 of Title 45 of the Code of Federal Regulations, as amended, (45 CFR 46). Administration of the DHEW policy and regulation is the responsibility of the Office for Protection from Research Risks, National Institutes of Health, Bethesda, Md 20014.

1. TITLE OF PROPOSAL OR ACTIVITY

2. PRINCIPAL INVESTIGATOR/ACTIVITY DIRECTOR/FELLOW

3. DECLARATION THAT HUMAN SUBJECTS EITHER WOULD OR WOULD NOT BE INVOLVED

☐ A. NO INDIVIDUALS WHO MIGHT BE CONSIDERED HUMAN SUBJECTS, INCLUDING THOSE FROM WHOM ORGANS, TISSUES, FLUIDS, OR OTHER MATERIALS WOULD BE DERIVED, OR WHO COULD BE IDENTIFIED BY PERSONAL DATA, WOULD BE INVOLVED IN THE PROPOSED ACTIVITY. (IF NO HUMAN SUBJECTS WOULD BE INVOLVED, CHECK THIS BOX AND PROCEED TO ITEM 7. PROPOSALS DETERMINED BY THE AGENCY TO INVOLVE HUMAN SUBJECTS WILL BE RETURNED.)

☐ B. HUMAN SUBJECTS WOULD BE INVOLVED IN THE PROPOSED ACTIVITY AS EITHER: ☐ NONE OF THE FOLLOWING, OR INCLUDING: ☐ MINORS, ☐ FETUSES, ☐ ABORTUSES, ☐ PREGNANT WOMEN, ☐ PRISONERS, ☐ MENTALLY RETARDED, ☐ MENTALLY DISABLED. UNDER SECTION 6. COOPERATING INSTITUTIONS, ON REVERSE OF THIS FORM, GIVE NAME OF INSTITUTION AND NAME AND ADDRESS OF OFFICIAL(S) AUTHORIZING ACCESS TO ANY SUBJECTS IN FACILITIES NOT UNDER DIRECT CONTROL OF THE APPLICANT OR OFFERING INSTITUTION.

DECLARATION OF ASSURANCE STATUS/CERTIFICATION OF REVIEW

☐ A. THIS INSTITUTION HAS NOT PREVIOUSLY FILED AN ASSURANCE AND ASSURANCE IMPLEMENTING PROCEDURES FOR THE PROTECTION OF HUMAN SUBJECTS WITH THE DHEW THAT APPLIES TO THIS APPLICATION OR ACTIVITY. ASSURANCE IS HEREBY GIVEN THAT THIS INSTITUTION WILL COMPLY WITH REQUIREMENTS OF *DHEW Regulation 45 CFR 46*, THAT IT HAS ESTABLISHED AN INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS AND, WHEN REQUESTED, WILL SUBMIT TO DHEW DOCUMENTATION AND CERTIFICATION OF SUCH REVIEWS AND PROCEDURES AS MAY BE REQUIRED FOR IMPLEMENTATION OF THIS ASSURANCE FOR THE PROPOSED PROJECT OR ACTIVITY.

☐ B. THIS INSTITUTION HAS AN APPROVED GENERAL ASSURANCE (DHEW ASSURANCE NUMBER _____) OR AN ACTIVE SPECIAL ASSURANCE FOR THIS ONGOING ACTIVITY, ON FILE WITH DHEW. THE SIGNER CERTIFIES THAT ALL ACTIVITIES IN THIS APPLICATION PROPOSING TO INVOLVE HUMAN SUBJECTS HAVE BEEN REVIEWED AND APPROVED BY THIS INSTITUTION'S INSTITUTIONAL REVIEW BOARD IN A CONVENED MEETING ON THE DATE OF _____ IN ACCORDANCE WITH THE REQUIREMENTS OF THE *Code of Federal Regulations on Protection of Human Subjects (45 CFR 46)*. THIS CERTIFICATION INCLUDES, WHEN APPLICABLE, REQUIREMENTS FOR CERTIFYING FDA STATUS FOR EACH INVESTIGATIONAL NEW DRUG TO BE USED (SEE REVERSE SIDE OF THIS FORM).

THE INSTITUTIONAL REVIEW BOARD HAS DETERMINED, AND THE INSTITUTIONAL OFFICIAL SIGNING BELOW CONCURS THAT:

EITHER ☐ HUMAN SUBJECTS WILL NOT BE AT RISK; OR ☐ HUMAN SUBJECTS WILL BE AT RISK.

5. AND 6. SEE REVERSE SIDE

7. NAME AND ADDRESS OF INSTITUTION

8. TITLE OF INSTITUTIONAL OFFICIAL	TELEPHONE NUMBER
SIGNATURE OF INSTITUTIONAL OFFICIAL	DATE

-596 (Rev. 4-75)

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO REQUESTING AGENCY.

THE ORIGINAL COLOR OF THIS FORM IS YELLOW

1033129

5. INVESTIGATIONAL NEW DRUGS - ADDITIONAL CERTIFICATION REQUIREMENT

SECTION 46.17 OF TITLE 45 OF THE Code of Federal Regulations states, "Where an organization is required to prepare or to submit a certification . . . and the proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 130.3(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received."

INVESTIGATIONAL NEW DRUG CERTIFICATION

TO CERTIFY COMPLIANCE WITH FDA REQUIREMENTS FOR PROPOSED USE OF INVESTIGATIONAL NEW DRUGS IN ADDITION TO CERTIFICATION OF INSTITUTIONAL REVIEW BOARD APPROVAL, THE FOLLOWING REPORT FORMAT SHOULD BE USED FOR EACH IND: (ATTACH ADDITIONAL IND CERTIFICATIONS AS NECESSARY).

- IND FORMS FILED: ☐ FDA 1571, ☐ FDA 1572, ☐ FDA 1573

- NAME OF IND AND SPONSOR _____

- DATE OF 30-DAY EXPIRATION OR FDA WAIVER
  (FUTURE DATE REQUIRES FOLLOWUP REPORT TO AGENCY) _____

- FDA RESTRICTION _____

- SIGNATURE OF INVESTIGATOR _____ DATE _____

6. COOPERATING INSTITUTIONS - ADDITIONAL REPORTING REQUIREMENT

SECTION 46.16 OF TITLE 45 OF THE *Code of Federal Regulations* IMPOSES SPECIAL REQUIREMENTS ON THE CONDUCT OF STUDIES OR ACTIVITIES IN WHICH THE GRANTEE OR PRIME CONTRACTOR OBTAINS ACCESS TO ALL OR SOME OF THE SUBJECTS THROUGH COOPERATING INSTITUTIONS NOT UNDER ITS CONTROL. IN ORDER THAT THE DHEW BE FULLY INFORMED, THE FOLLOWING REPORT IS REQUESTED WHEN APPLICABLE.

USE FOLLOWING REPORT FORMAT FOR EACH INSTITUTION OTHER THAN GRANTEE OR CONTRACTING INSTITUTION WITH RESPONSIBILITY FOR HUMAN SUBJECTS PARTICIPATING IN THIS ACTIVITY: (ATTACH ADDITIONAL REPORT SHEETS AS NECESSARY).

INSTITUTIONAL AUTHORIZATION FOR ACCESS TO SUBJECTS

- SUBJECTS: STATUS (WARDS, RESIDENTS, EMPLOYEES, PATIENTS, ETC.) _____

NUMBER _____ AGE RANGE _____

NAME OF OFFICIAL (PLEASE PRINT) _____

TITLE _____ TELEPHONE _____

NAME AND ADDRESS OF COOPERATING INSTITUTION _____

- OFFICIAL SIGNATURE _____

NOTES: *(e.g., report of modification in proposal as submitted to agency affecting human subjects involvement)*

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20205

General Assurance G1716

February 5, 1980

Dianne Gresham
Secretary, Committee on Human
Studies
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Ms. Gresham:

Thanks for your letter of January 18 and the new roster of your human subjects review board. The membership is acceptable and the roster is on file as an amendment to your general assurance G1716.

Sincerely yours,

Roy Kinard

Roy Kinard, D.V.M.
Office for Protection
from Research Risks
Office of the Director

1033131

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

1. DISTRICT ADDRESS
297 Plus Park Blvd.
Nashville, TN. 37217

TO

2. NAME AND TITLE OF INDIVIDUAL
Dr. Karl F. Hubner, Chief of Out-Patient Nuclear Medicine

3. DATE
5-30-80

4. FIRM NAME
Oak Ridge Associated Universities

5. HOUR
9:10 a.m.
p.m.

6. NUMBER AND STREET
Medical & Health Sciences Div. - E. Vance Rd.

7. CITY AND STATE
Oak Ridge, TN.

8. ZIP CODE
37830

Notice of Inspection is hereby given pursuant to Section 704(a) & (e) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374(a) & (e)] [1] and/or Part F or G, Title III of the Public Health Service Act [42 U.S.C. 262-264] [2]

9. SIGNATURE *(Food and Drug Administration Employee(s))*
Norman T. Miller

10. TYPE OR PRINT NAME AND TITLE *(FDA Employee(s))*
Invest. Aide
Norman T. Miller

[1]Applicable portions of Section 704 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374] are quoted below:

Sec. 704. (a) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and written notice to the owner, operator, or agent in charge, are authorized (1) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. In the case of any factory, warehouse, establishment, or consulting laboratory in which prescription drugs are manufactured, processed, packed, or held, inspection shall extend to all things therein *(including records, files, papers, processes, controls, and facilities)* bearing on whether prescription drugs which are adulterated or misbranded within the meaning of this Act, or which many not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Act, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of this Act. No inspection authorized for prescription drugs by the preceding sentence shall extend to financial data, sales data other than shipment data, pricing data, personnel data *(other than data as to qualifications of technical and professional personnel performing functions subject to this Act)*, and research data *(other than data, relating to new drugs and antibiotic drugs and devices and, subject to reporting and inspection under regulations lawfully issued pursuant to section 505(i) or (j), section 507(d) or (g), section 519, or 520(g), and data relating to other drugs or devices which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505(j))*. A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.

Sec. 704(e) Every person required under section 519 or 520(g) to maintain records and every person who is in charge or custody of such records shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and to copy and verify, such records.

[2]Applicable sections of Parts F and G of Title III Public Health Service Act [42 U.S.C. 262-264] are quoted below:

Part F - Licensing - Biological Products and Clinical Laboratories and ******

Sec. 351(c) "Any officer, agent, or employee of the Department of Health, Education, and Welfare, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation of any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product or other product aforesaid for sale, barter or exchange in the District of Columbia, or to be sent, carried, or brought from any State or possession into any other State or posession or into any foreign country, or from any foreign country into any State or possession."

Part F — ******Control of Radiation.

Sec. 360 A(a) "If the Secretary finds for good cause that the methods, tests, or programs related to electronic product radiation safey in a particular factory, warehouse, or establishment in which electronic products are manufactured or held, may not be adequate or reliable, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are thereafter authorized (1) to enter, at reasonable times any area in such factory, warehouse, or establishment in which the manufacturer's tests *(or testing programs)* required by section 358(h) are carried out, and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, the facilities and procedures within such area which are related to electronic product radiation safety. Each such inspection shall be commenced and completed with reasonable promptness. In addition to other grounds upon which good cause may be found for purposes of this subsection, good cause will be considered to exist in any case where the manufacturer has introduced into commerce any electronic product which does not comply with an applicable standard prescribed under this subpart and with respect to which no exemption from the notification requirements has been granted by the Secretary under section 359(a)(2) or 359(e)."

(b) "Every manufacturer of electronic products shall establish and maintain such records *(including testing records)*, make such reports, and provide such information, as the Secretary may reasonably require to enable him to determine whether such manufacturer has acted or is acting in compliance with this subpart and standards prescribed pursuant to this subpart and shall, upon request of an officer or employee duly designated by the Secretary, permit such officer or employee to inspect appropriate books, papers, records, and documents relevant to determining whether such manufacturer has acted or is acting in compliance with standards prescribed pursuant to section 359(a)."

.....

(f) "The Secretary may by regulation (1) require dealers and distributors of electronic products, to which there are applicable standards prescribed under this subpart and the retail prices of which is not less than $50, to furnish manufacturers of such products such information as may be necessary to identify and locate, for purposes of section 359, the first purchasers of such products for purposes other than resale, and (2) require manufacturers to preserve such information. Any regulation establishing a requirement pursuant to clause (1) of the preceding

1033132

sentence shall (A) authorize such dealers and distributors to elect, in lieu of immediately furnishing such information to the manufacturer to hold and preserve such information until advised by the manufacturer or Secretary that such information is needed by the manufacturer for purposes of section 359, and (B) provide that the dealer or distributor shall, upon making such election, give prompt notice of such election *(together with information identifying the notifier and the product)* to the manufacturer and shall, when advised by the manufacturer or Secretary, of the need therefor for the purposes of Section 359, immediately furnish the manufacturer with the required information. If a dealer or distributor discontinues the dealing in or distribution of electronic products, he shall turn the information over to the manufacturer. Any manufacturer receiving information pursuant to this subsection concerning first purchasers of products for purposes other than resale shall treat it as confidential and may use it only if necessary for the purposes of notifying persons pursuant to section 359(a)."

Sec. 360 B.(a) It shall be unlawful —

(1) ***

(2) ***

(3) "for any person to fail or to refuse to establish or maintain records required by this subpart or to permit access by the Secretary or any of his duly authorized representatives to, or the copying of, such records, or to permit entry or inspection, as required or pursuant to section 360A."

***

Part G — Quarantine and Inspection

Sec. 361(a) "The Surgeon General, with the approval of the Secretary is authorized to make and enforce such regulations as in his judgement are necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or posession into any other State or posession. For purposes of carrying out and enforcing such regulations, the Surgeon General may provide for such inspection, fumigation, disinfection, sanitation, pest extermination, destruction of animals or articles found to be so infected or contaminated as to be sources of dangerous infection to human beings, and other measures, as in his judgement *may be necessary.*"

Human Studies

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

Rec. 10-6-80

OCT 1 - 1980

Clarence C. Lushbaugh, M.D.
Director
Medical and Health Sciences Division
Oak Ridge Associated Universities
East Vance Road, P.O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Lushbaugh:

On May 30 and June 3, 1980, Mr. Norman T. Miller from the Food and Drug Administration met with Dr. Hubner and Ms. Gresham to review your institutional procedures for the protection of human subjects. This procedural review visit was a routine revisit following the one made on July 27, 1977. Following the earlier visit, a letter was sent to Dr. Lange. In this letter we made several suggestions for improving your procedures and records.

On December 21, 1977, you wrote us accepting the recommendations made in our letter. On February 15, 1978 we acknowledged your assurances and expressed appreciation for your courtesy and cooperation.

In reviewing the report of the recent visit, we find that your procedures appear to be generally in compliance with FDA regulations and to be in accord with commonly accepted committee practices. Mr. Miller discussed with Dr. Hubner the need to update your 1977 written guidelines to make them correspond with current committee procedures and the advisability of documenting in the meeting minutes the departure of the clinical investigator from the room when his study is being discussed and voted upon. Dr. Hubner agreed to both of these suggestions. You may want to wait to revise your written guidelines until later this year. We anticipate that both DHHS and FDA proposed regulations on IRBs will be made final and published at that time.

Careful committee evaluation of informed consent procedures is an important aspect of the protection of subjects involved in research activities. The committee should consider not only the elements of informed consent but also the circumstances under which consent is obtained as well as the ability of the subject to comprehend the language used. The consent forms that accompanied Mr. Miller's report were technical in language and lacked certain information which we believe most subjects would want to have. Specifically, in the consent form entitled

1033134

"(COPD and Sarcoidosis)" for Dr. Hubner's study with ^{68}Ga-Microspheres, the overall radiation dose is not given, nor is there an explanation that multiple doses are to be administered. The information which is given with regard to the radiation dose is vague and we believe uninformative.

In addition, the last paragraph of this form refers to the fact that the subject has been "...fully informed of the possible risks...." When the elements of informed consent are not fully explained in writing to the subject, the investigator should submit a written narrative of the full information to be presented orally to the subject for the committee's review. This should be done, for example, when oral consent or an abbreviated written consent with oral augmentation is used. Only by reviewing such a narrative can the committee be assured that all pertinent information is provided to the subject. In addition, if a copy of the narrative is provided to the subject, misunderstandings between the investigator and subject may be avoided.

If you wish to discuss the procedural review at your institution or other aspects of institutional review procedures, we invite you to contact us.

We appreciate the cooperation shown our staff during the procedural review.

Sincerely yours, & with personal greetings -

Frances O. Kelsey

Frances O. Kelsey, Ph.D., ~~M.D.~~
Director
Division of Scientific Investigations
Bureau of Drugs

cc:
Dr. Karl F. Hubner, Chief
Out-Patient Nuclear Medicine
Oak Ridge Associated Universities

1033135

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
(615) 576-3098

Medical and
Health Sciences
Division

October 25, 1980

Roy Kinard, D.V.M.
Office for Protection from Research Risks
Office of the Director
Department of Health, Education and Welfare
National Institutes of Health
Bethesda, MD 20014

Dear Dr. Kinard:

General Assurance G1716

At the last meeting of the Committee on Human Studies on April 18, 1980, the Committee confirmed its membership, its responsibilities, and its functions.

A "Suggested Checklist for Use by Institutions in Evaluating Their Procedures for the Protection of Human Subjects" distributed by FDA on September 5, 1978, was utilized in reviewing the ORAU/ ORNL Committee on Human Studies Guidelines in January-February, 1980. The guidelines were found to be in agreement with the FDA Checklist, and this report was distributed to the Committee members.

The Committee membership has not changed since the last report sent to you on January 18, 1980. The Committee meets again this month and any changes in membership will be reported to your office promptly.

Sincerely,

Dianne Gresham

Dianne Gresham
Secretary, Committee on Human Studies

dg

1033136

1981

1033137

ORAU/ORNL COMMITTEE ON HUMAN STUDIES MEMBERS

1967 - Present

G. A. Andrews, M.D.
E. Balish, Ph.D.
A. B. Brill, M.D.
*W. Calhoun, Ph.D.
~~(R. J. Cloutier)~~
C. L. Edwards, M.D.
*H. R. Friedman, Ph.D.
*S. A. Fry, M.B., Ch.B.
*A. S. Garrett, M.D.
*D. W. Goodwin, Ph.D.
R. O. Goh, M.D.
*R. Griesemer, Ph.D., D.V.M.
*M. S. Hansard, Ph.D.
~~(H. Harmon)~~
R. Heyssel, M.D.
*K. F. Hübner, M.D.
R. M. Kniseley, M.D.
*M. E. Koons, J.D.
*R. D. Lange, M.D.
*S. Lawrence
S. Lawyer, J.D.
T. A. Lincoln, M.D.
*C. C. Lushbaugh, M.D.
*L. C. McKee, M.D.
*R. Miller
B. M. Nelson, M.D.
*J. B. Storer, M. D.
E. Tompkins
J. B. Woods, M.D.

*Current Membership

2/23/81

1033138

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20205

March 12, 1981

General Assurance G1716

Rec 3-16-81

Dr. Clarence C. Lushbaugh
Director
Medical and Health Sciences Division
Oak Ridge Associated Universities
East Vance Road, P. O. Box 117
Oak Ridge, Tennessee 37830

Dear Dr. Lushbaugh:

The FDA sent us a copy of a letter of October 1, 1980 to you describing certain problems of compliance with human subjects regulations. We assume that these problems have been attended to and that your review procedures are now in compliance. But we just want to let you know that we are aware of the problems and to remind you that we will be glad to advise or answer questions pertaining to compliance, especially with the HEW regulations 45 CFR 46 covering grants and contracts.

Sincerely yours,

Roy Kinard

Roy Kinard, D.V.M.
Office for Protection
from Research Risks
Office of the Director

cc: Human Studies Committee File
Dr. Hüner

1033139

ORAU/ORNL Committee on Human Studies

IMPLEMENTING GUIDELINES FOR RESEARCH ON HUMAN SUBJECTS

(In Compliance with DHEW and ERDA Regulations on Protection of Human Subjects)

(March 1977)

A. Basic Principles (See Definitions, Annex 1.)

The Committee on Human Studies for Oak Ridge Associated Universities and Oak Ridge National Laboratory has officially adopted the code of ethics adopted by the World Medical Association, known as the Declaration of Helsinki. It accepts as amplification of this document the statement of the British Medical Research Council. The guiding principles of operation of this Committee are, however, those set forth in detail by DHEW in Federal Register, March 13, 1975, Vol. 40, No. 50, Part II, Protection of Human Subjects, Technical Amendments, pp. 11854-11858, and by ERDA in an August 17, 1976 document titled "Protection of Human Subjects Proposed Regulations" (10 CFR Part 705) as amended in 10 CFR, Part 745 (FR 41, November 30, 1976, pp. 52434-52438). (See Annex Items 2 and 3.) Wherever these guidelines appear to differ substantively from those in the Federal Register, those in the Federal Register should be understood to be dominant and to be followed.

B. Committee Membership and Structure

The Committee shall consist of persons of either sex and any race with varying backgrounds, training, vocation and community interests who, while cognizant of the research goals and programs of the two sponsoring institutions (ORNL and ORAU), are sufficiently qualified to safeguard the rights and welfare of human subjects and review the relative merit of human studies in respect to any risks involved. The Committee will be composed of at least two lay persons, two research scientists and two clinicians. Two of the medical professionals, however, must be from institutions other than ORNL or ORAU, the institutions from which will emanate applications for permission to conduct a particular human study. Because of the dual sponsorship of this Committee, the Medical Director of the Health Division, ORNL; Director of Biology Division, ORNL; and the Chairman of the Medical and Health Sciences Division of ORAU shall be members of the Committee. The Directors of the two sponsoring institutions (ORAU and ORNL) shall designate to these divisional directors the responsibility for seeing that their respective staffs comply with HEW and ERDA regulations for the protection of human subjects. The Chairman and Secretary of the Committee shall be elected at one (January) of two annual meetings of the Committee. A person nominated for Committee membership by a member of the Committee or a sponsoring institution shall be made a member only with the concurrence of the other Committee members. Because of the complexity of modern laws and regulations protecting human rights, governing contractural obligations and guiding the use of government funds and facilities for research, at least one member will be a lawyer cognizant of the Federal Regulations. A lawyer consultant will be

1033140

agreed upon and will be readily available to counsel the Committee if the Committee membership does not include a lawyer member. Similarly, if the membership does not contain a minister or a psychologist (or psychiatrist), some person with a related vocation who is interested in protecting persons from emotional and psychologic trauma must be available to the Committee for consultation on individual projects whether or not psychologic stress or risk is obviously involved. (See Annex 4, 5, and 6.)

C. Procedures for Carrying out Initial and Continuing Review of Applications and Projects

1. Initial Review

All applications for support of research, training, demonstration or general research support projects, including those of fellows and trainees, which involve the use of human subjects, must be presented to and approved by the Committee on Human Studies, prior to submission for funding, and with the identical experimental design used for grant submission or ERDA "189" proposals. Regardless of the nature or degree of risk anticipated, the application must be presented in writing on the proper form (Annex 7). The application should not contain extraneous material; that is, the investigator should not submit a copy of an IND or ERDA-189 as a substitute for the form specified. The applicant must be prepared to discuss in person before the Committee detailed information on the following points:

a. The possible risk to the rights and welfare of human subjects, including the rights of privacy, freedom from harassment and confidentiality of data. A description of the provisions made to minimize these risks must also be presented.

b. Methods used to acquire informed consent. The form on which it is obtained and the risk described. Special emphasis shall be placed on the appropriateness of a consent form to the particular situation inherent in the study plan in question (Annex 8).

c. The relative risks of the project as compared to the probable benefits to the subjects and to society. For each application, the Committee will document whether or not physical or psychological risks are likely to ensue as a result of the proposed research study, and further, that such potential risks have been evaluated in respect to the subject and his rights, needs and benefits. In addition, informed consent documents must be submitted to and approved by the Committee for each study so that members can be ensured that each human subject will receive candid explanations of specific procedures and their purposes, of attendant specific discomforts and risks, and possible benefits, if any. In addition, the Committee must be satisfied in

each study evaluation that the subjects will be instructed that they are free to withdraw their consent to participate and to discontinue their participation in the proposed project at any time without prejudice to them. No informed consent form will be considered acceptable if it contains any exculpatory clauses or attempts in any way to absolve the Principal Investigator's responsibility for the health (physical or mental) and welfare of the human subjects to be involved.

Specific deficiencies in a proposal will be identified by the Committee in writing for the proposer and also directed to the attention of that Committee member (the Director of the Health or Biology Division, ORNL, or Chairman of the Medical and Health Sciences Division, ORAU) who also has the responsibility designated to him by the Director of his sponsoring institution (either ORNL or ORAU) to obtain staff compliance with DHEW and ERDA Regulations and Guidelines for Protection of Human Subjects. Such a statement of deficiency by the Committee will be understood to require (1) delay in submission of the proposed grant or contract application to HEW or ERDA, and (2) resubmission for Committee approval before the project proposals are allowed to go forward in the funding process. A statement of approval by the Committee will be accompanied by HEW-596 (Annex 9) for the institutional director's signature for simultaneous submission with an NIH, NSF or ERDA grant proposal.

A member of the Committee who is from the institution (ORNL or ORAU), from which the research proposal is being submitted, will be expected to attend the Committee only for his information, and will have no persuasive or voting powers concerning the acceptability of that proposal and its level of compliance with HEW and ERDA guidelines.

Approval of a proposal for a study involving human subjects shall be formalized only after a majority of the qualified (see paragraph above) Committee members have had a chance to review the written proposal, discuss it with the other members of the Committee, obtain adequate answers from the author to their questions, and reach complete agreement of acceptability. No proposal will be approved to which any Committee member objects on the basis of consideration of the physical or mental welfare of any human subject. In special cases where a Committee member cannot attend, his comment and vote can be obtained by mail.

The Committee's findings will be transmitted in writing to the appropriate officer of the laboratory proposing the research and to the applicant. Release of funds shall be controlled by the guidelines to HEW-596 (Annex 9). The applicant's administrative superior shall maintain continuing review of the project activities. If a responsible investigator plans a change in study protocol, he must submit the proposed changes to the Committee for approval before putting them into practice.

D. Procedures of the Committee to Provide Advice and Counsel to Investigators

On request, senior investigators will appear before the Committee at its called meetings to answer any questions concerning a proposal. The question and replies will form part of the official minutes of the Committee and will be distributed to the concerned staff members, together with recorded actions of the Committee on a Review and Action Form (Annex 10).

Committee Meetings

The Committee will meet at least twice a year. The first meeting of the year will be early in January, if possible, to meet the following administrative needs:

1. Election of Chairperson and Secretary,

2. Reelection of members and replacement of those members no longer able to serve,

3. Report of the Secretary on the previous year's Committee activities and on the number of approved studies that are still active and therefore require critical review in the new year. Establishment of the calendar for scheduled review of continuing projects, documented by an annual status report that reports any emergent problems and indicates the need for changes in research protocols or forms for obtaining informed consent.

The second biannual meeting will address any problems in these administrative areas that have risen since the first meeting.

Other meetings will be called to meet the scheduled annual critical reviews, and as needed, to consider a specific new proposal(s) involving humans as subjects where HEW, ERDA, NSF or other governmental funding agencies have fixed deadlines which the research applicant is trying to meet. In special cases where time is short, and particularly where the defined risk to the human subject is a commonly accepted one (i.e., a physical examination by a licensed physician) and does not require discussion with the project proposer, the appropriate members of the Committee (Annex 6) may be polled by phone by the Secretary under the Chairman's direction after the members have had a chance to review the proposal sent to them by mail.

E. Requirements for Reporting any Emergent Problems or Proposed Precedural Changes to the Committee

All senior investigators with proposed or active projects will receive notice of Committee meetings and will appear before the Committee in person. At this time they shall present in writing any proposed changes in procedures and shall describe any new risks and benefits, and any methods for safeguarding patients' rights and procedures for informed consent in advance of instituting these changes.

All investigators with active research programs involving human subjects that have been approved by the Committee must be kept aware of the need for an immediate report to the Committee secretary, Chairperson, or institutional representatives of emergent problems bearing on the heatlth and welfare of human subjects and of needs for protocol modifications, restrictions or termination.

F. Procedures to Maintain an Active and Effective Committee

1. The chairman will ensure an active Committee by calling, in addition to the regular Annual Meeting, at least one additional meeting each year.

2. The members will be enjoined to assess every ongoing project as well as new proposals.

3. Extramural Committee members will be paid a consultant's fee, providing they are able to accept it, and travel expenses.

4. Full Committee Minutes will be distributed promptly to all members in draft form for corrections and review, so that the opinions and actions can be recorded accurately.

5. On a regular basis, at least annually, at some full Divisional professional staff meeting, the respective institutional representative will explain this program for protection of human subjects to his staff and reinforce the importance to his division of his staff following the HEW and ERDA Regulations and Guidelines on the use of human subjects in research.

G. Location of Records

The records of this Committee will be kept in the office of the Executive Secretary and will be available to the Committee, staff, and government auditors on demand.

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830
(615) 576-3098

Medical and
Health Sciences
Division

March 20, 1981

Roy Kinard, D.V.M.
Office of Protection from
Research Risks
Office of the Director
Department of Health and Human Services
Public Health Service
National Institutes of Health
Bethesda, Maryland 20205

Dear Dr. Kinard:

General Assurance G1716

I am responding to your letter to Dr. C. C. Lushbaugh dated March 12, 1981. You refer to an FDA investigation of our internal review board, the ORAU/ORNL Committee on Human Studies, which took place on May 30 and June 3, 1980. At that time the investigator, Mr. Norman Miller, stated the need to update the 1977 written guidelines.

In response to that suggestion our internal review board on October 30, 1980, appointed a a subcommittee chaired by Mel Koons, an attorney, to revise the guidelines and update all consent forms for ongoing proposals. Dr. Lee Washburn, a research scientist for ORAU, also attended the Workshop on IRB Compliance Activities in Washington, D.C. on November 7, 1980, and reported to Mr. Koons the discussions that took place at this meeting. Mr. Koons has also recieved the printed notes published from the November 7 meeting and copies of the Federal Register dated January 27, 1981. The subcommittee is currently working to revise the guidelines using all of this material as a reference. As soon as the Committee has approved the new guidelines a copy will be sent to your office.

Enclosed is a current list of our membership showing changes made since January, 1980. Please note that the Committee has two new members, Drs. Shirley A. Fry of ORAU and Richard A. Griesemer of ORNL. The attached block diagram illustrates the structure of the Committee and the relationship of the members to the Committee.

1033145

We will continue to keep you informed of Committee actions and appreciate very much your offer of assistance in keeping abreast of changing regulations for the protection of human subjects in research projects. Please let us know if you need further information.

Sincerely,

Dianne Gresham

Dianne Gresham, Secretary
ORAU/ORNL Committee on Human Studies

dg

Enclosures

1033146

General Assurance G1716

IRB MEMBER ROSTER

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

MARCH, 1981

Name of Institutional Officer (other than chairperson) to whom correspondence concerning Board affairs should be addressed: C. C. Lushbaugh, M.D.

Name:	William H. Calhoun
Earned degrees:	A.A., B.A., Ph.D.
Position or Occupation:	Professor & Head, Department of Psychology The University of Tennessee, Knoxville Units
Board certification, licenses, etc:	
Relationship to institution:	Consultant
Representative capacity:	Clinical psychologist, community representative

Name:	Howard R. Friedman
Earned degrees:	B.B.A. and Ph.D.
Position or occupation:	Chief Clinical Psychologist and Director Children and Youth Program Regional Mental Health Center Oak Ridge, TN and Adjunct Associate Professor, Department of Psychology, The University of Tennessee, Knoxville; Psychology Consultant, Campbell County Schools, TN
Board certification, licenses, etc.:	Licensed Clinical Psychologist, TN
Relationship to institution:	Consultant
Representative capacity:	Clinical psychologist, community representative

Name:	Shirley A. Fry
Earned degrees:	M.B., Ch.B.
Position or occupation:	Clinician, Radiation Emergency Assistance Center/Training Site, ORAU
Board certification, licenses, etc.:	E.C.F.M.G. Certification, Chicago, IL
Relationship to institution:	Employee of ORAU
Representative capacity:	Investigator, practitioner

1033147

Name:	A. Seaton Garrett, Jr.
Earned degrees:	M.D.
Position or occupation:	Medical Director, Oak Ridge National Laboratory, Union Carbide Corporation, Nuclear Division, Oak Ridge, TN
Board certification, license, etc.:	Board Eligible Internal Medicine
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, practitioner

Name:	Donald W. Goodwin
Earned degrees:	B.D., Ph.D.
Position or occupation:	Minister, United Church, Chapel-on-the Hill, Oak Ridge, TN
Board certification, licenses, etc.:	N/A
Relationship to institution:	Consultant
Representative capacity:	Ethicist, community representative

Name:	Richard A. Griesemer
Earned degrees:	D.V.M., Ph.D.
Board certification:	Diplomate, American College of Veterinary Pathologists
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, investigator

Name:	Martha S. Hansard
Earned degrees:	B.S., M.S. (2), Ph.D.
Position or occupation:	Associate Section Leader for Computer Methodology and Systems in Epidemiology and Scientist, Medical and Health Sciences Division, ORAU
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORAU
Representative capacity:	Administrator, community representative

Name:	Karl F. Hubner
Earned degrees:	M.D.
Position or occupation:	Director, Outpatient Nuclear Medicine, Medical and Health Sciences Division, ORAU, and Director, Radiation Emergency Assistance Center/ Training Site (REAC/TS), ORAU
Board certification, licenses, etc.;	Certified nuclear medicine; licensed in TN
Relationship to institution:	Employee of ORAU
Representative capacity:	Investigator, administrator, practitioner

1033148

Name:	Melvin E. Koons
Earned degrees:	B.A., J.D.
Position or occupation:	Purchasing Agent, Union Carbide Corporation Nuclear Division; Lawyer
Board certification, licenses, etc.:	Licensed in North Dakota and Tennessee
Relationship to institution:	Employee of UCCND (ORNL)
Representative capacity:	Lawyer

Name:	Robert Lange (Chairman of Committee)
Earned degrees:	B.A., M.D.
Position or occupation:	Professor and Chairman, Department of Medical Biology The University of Tennessee Center for the Health Sciences, Knoxville Units
Board certification, licenses, etc.:	Licensed Tennessee, Minnesota, Missouri, and Georgia: Certified internal medicine
Relationship to institution:	Consultant
Representative capacity:	Administrator, practitioner

Name:	Steve Lawrence
Earned degrees:	B.S.
Position or occupation:	Assistant Director Administration, ORAU
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORAU
Representative capacity:	Administrator, ethicist, community representative

Name:	Clarence C. Lushbaugh
Earned degrees:	B.S., Ph.D., M.D.
Position or occupation:	Chairman, Medical and Health Sciences Division, ORAU
Board certification, licenses, etc.;	Certified pathology; licensed Tennessee
Relationship to institution:	Employee of ORAU
Representative capacity:	Investigator, administrator practitioner

Name:	L. Clifford McKee
Earned degrees:	B.A., M.D.
Position or occupation:	Associate Professor of Medicine, Department of Medicine, Vanderbilt University
Board certification, licenses, etc.:	Certified internal medicine; licensed Tennessee
Relationship to institution:	Consultant
Representative capacity:	Administrator, practitioner

Name:	Ruby L. Anderson Miller
Earned degrees:	B.S.
Position or occupation:	Public Relations Representative, Union Carbide Corporation Nuclear Division, ORGDP
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORGDP
Representative capacity:	Administrator, community representative

Name:	John B. Storer
Earned degrees:	M.D.
Position or occupation:	Senior research investigator
Board certification, licenses, etc.:	None
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, investigator

Name:	Dianne Gresham Secretary to the ORAU/ORNL Committee on Human Studies Non-voting member

- - - - - -

Oak Ridge Associated Universities (ORAU)
Oak Ridge National Laboratory (ORNL)

1033150

Annex 4

General Assurance G1716

IRB MEMBER ROSTER

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

OCTOBER, 1981

Name of Institutional Officer (other than chairperson) to whom correspondence concerning Board affairs should be addressed: C. C. Lushbaugh, M.D.

Name:	William H. Calhoun
Earned degrees:	A.A., B.A., Ph.D.
Position or Occupation:	Professor & Head, Department of Psychology The University of Tennessee, Knoxville Units
Board certification, licenses, etc:	
Relationship to institution:	Consultant
Representative capacity:	Clinical psychologist, community representative

Name:	Howard R. Friedman
Earned degrees:	B.B.A. and Ph.D.
Position or occupation:	Chief Clinical Psychologist and Director Children and Youth Program Regional Mental Health Center Oak Ridge, TN and Adjunct Associate Professor, Department of Psychology, The University of Tennessee, Knoxville; Psychology Consultant, Campbell County Schools, TN
Board certification, licenses, etc.:	Licensed Clinical Psychologist, TN
Relationship to institution:	Consultant
Representative capacity:	Clinical psychologist, community representative

Name:	Shirley A. Fry
Earned degrees:	M.B., Ch.B.
Position or occupation:	Clinician, Radiation Emergency Assistance Center/Training Site, ORAU
Board certification, licenses, etc.:	E.C.F.M.G. Certification, Chicago, IL
Relationship to institution:	Employee of ORAU
Representative capacity:	Investigator, practitioner

1033151

Name:	A. Seaton Garrett, Jr.
Earned degrees:	M.D.
Position or occupation:	Medical Director, Oak Ridge National Laboratory, Union Carbide Corporation, Nuclear Division, Oak Ridge, TN
Board certification, license, etc.:	Board Eligible Internal Medicine
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, practitioner

Name:	Donald W. Goodwin
Earned degrees:	B.D., Ph.D.
Position or occupation:	Minister, United Church, Chapel-on-the Hill, Oak Ridge, TN
Board certification, licenses, etc.:	N/A
Relationship to institution:	Consultant
Representative capacity:	Ethicist, community representative

Name:	Richard A. Griesemer
Earned degrees:	D.V.M., Ph.D.
Board certification:	Diplomate, American College of Veterinary Pathologists
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, investigator

Name:	Karl F. Hubner
Earned degrees:	M.D.
Position or occupation:	Director, Outpatient Nuclear Medicine, Medical and Health Sciences Division, ORAU, and Director, Radiation Emergency Assistance Center/ Training Site (REAC/TS), ORAU
Board certification, licenses, etc.;	Certified nuclear medicine; licensed in TN
Relationship to institution:	Employee of ORAU
Representative capacity:	Investigator, administrator, practitioner

Name:	Melvin E. Koons
Earned degrees:	B.A., J.D.
Position or occupation:	Purchasing Agent, Union Carbide Corporation Nuclear Division; Lawyer
Board certification, licenses, etc.:	Licensed in North Dakota and Tennessee
Relationship to institution:	Employee of UCCND (ORNL)
Representative capacity:	Lawyer

1033152

Name:	Robert Lange (Chairman of Committee)
Earned degrees:	B.A., M.D.
Position or occupation:	Professor and Chairman, Department of Medical Biology The University of Tennessee Center for the Health Sciences, Knoxville Units
Board certification, licenses, etc.:	Licensed Tennessee, Minnesota, Missouri, and Georgia: Certified internal medicine
Relationship to institution:	Consultant
Representative capacity:	Administrator, practitioner

Name:	Steve Lawrence
Earned degrees:	B.S.
Position or occupation:	Assistant Director Administration, ORAU
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORAU
Representative capacity:	Administrator, ethicist, community representative

Name:	Clarence C. Lushbaugh
Earned degrees:	B.S., Ph.D., M.D.
Position or occupation:	Chairman, Medical and Health Sciences Division, ORAU
Board certification, licenses, etc.;	Certified pathology; licensed Tennessee
Relationship to institution:	Employee of ORAU
Representative capacity:	Investigator, administrator practitioner

Name:	L. Clifford McKee
Earned degrees:	B.A., M.D.
Position or occupation:	Associate Professor of Medicine, Department of Medicine, Vanderbilt University
Board certification, licenses, etc.:	Certified internal medicine; licensed Tennessee
Relationship to institution:	Consultant
Representative capacity:	Administrator, practitioner

Name:	Ruby L. Anderson Miller
Earned degrees:	B.S.
Position or occupation:	Associate Director of Public Relations, Union Carbide Corporation Nuclear Division, ORGDP
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORGDP
Representative capacity:	Administrator, community representative

Name:	John B. Storer
Earned degrees:	M.D.
Position or occupation:	Senior research investigator
Board certification, licenses, etc.:	None
Relationship to institution:	Employee of ORNL
Representative capacity:	Administrator, investigator

Name:	Martha L. Wray
Earned degrees:	B.S., M.S.
Position or occupation:	Group Leader for Computer Methodology and Systems in Epidemiology, Medical and Health Sciences Division, ORAU
Board certification, licenses, etc.:	N/A
Relationship to institution:	Employee of ORAU
Representative capacity:	Administrator, community representative

Name:	Dianne Gresham Secretary to the ORAU/ORNL Committee on Human Studies Non-voting member

Oak Ridge Associated Universities (ORAU)
Oak Ridge National Laboratory (ORNL)

1033154

Annex 5 Summarized
Committee Assignments

Committee Members and Their Responsible Area

*0 William H. Calhoun, Ph.D., Univ. of TN, Clinical Psychologist
*0 Howard R. Friedman, Ph.D., Regional Mental Health Center, Clinical Psychologist
W Shirley A. Fry, M.B., Ch.B., ORAU, Clinician
A. Seaton Garrett, Jr., M.D., ORNL, Occupational Medicine
*0 Donald W. Goodwin, Ph.D., United Church, Oak Ridge, Minister
*00 Richard A. Griesemer, D.V.M., Ph.D., ORNL, Official Representative
*W Martha L. Wray, M.S., ORAU, Epidemiology
Karl F. Hübner, M.D., ORAU, Clinical Research
* Melvin E. Koons, J.D., UCCND, Lawyer
0 Robert Lange, M.D., Univ. of TN, Chairman, Extramural Representative
* Steve Lawrence, B.S., ORAU, Administrator
00 Clarence C. Lushbaugh, M.D., Ph.D., ORAU, Official Representative
0 L. Clifford McKee, M.D., Vanderbilt University, Extramural Representative
*W Ruby L. Miller, B.S., UCCND, Extramural Representative
John B. Storer, M.D., ORNL, Clinical Research

Dianne Gresham, Committee Secretary, Non-Voting Member

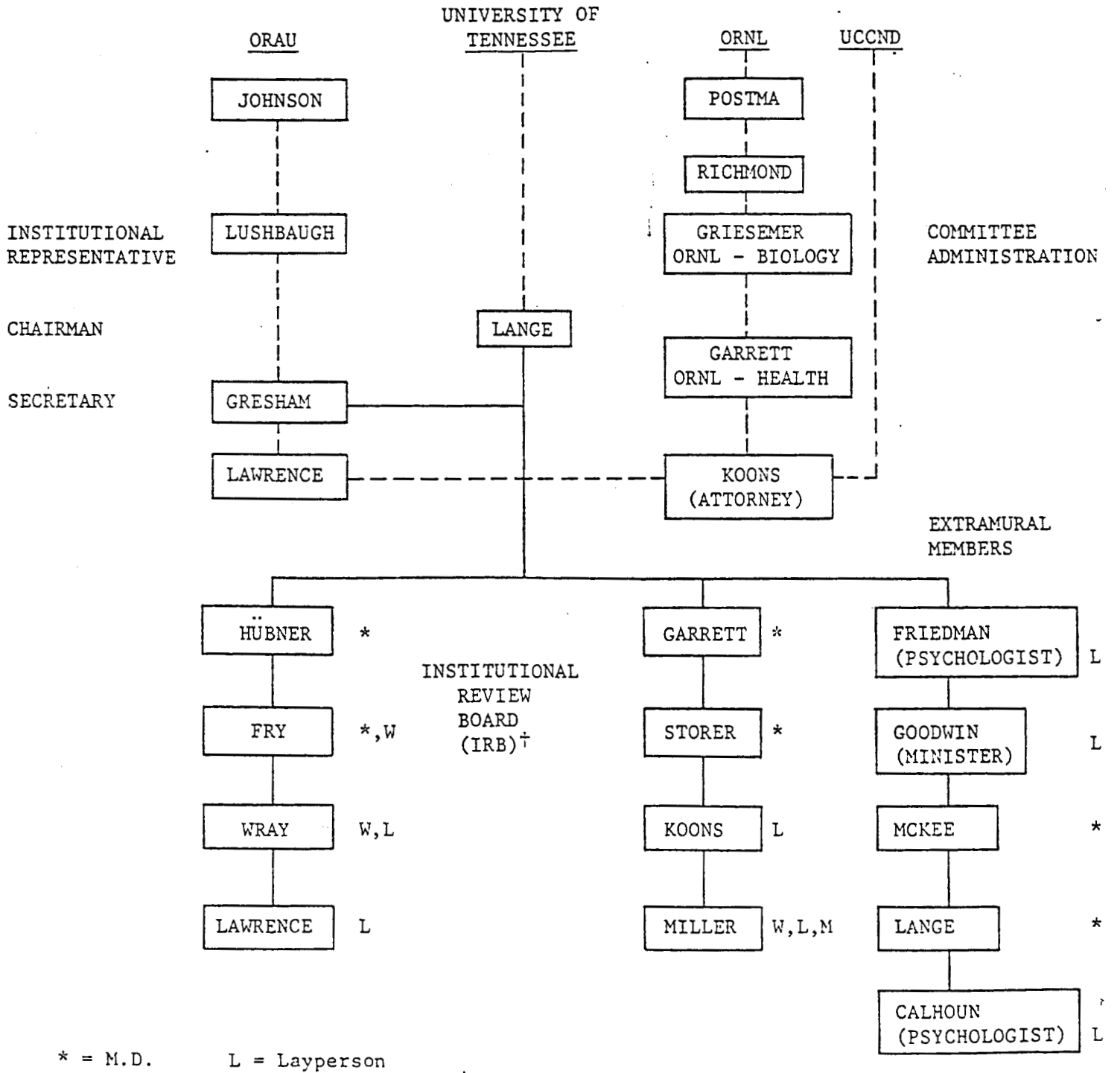
---

0 - Extramural member
00 - Institutional representative
* - Non-M.D. member
W - Woman member

1033155

Block diagram of the bi-institutional Committee structure, administration, lines of authority and present membership and functional identities.

BLOCK DIAGRAM OF ADMINISTRATIVE AND MEMBERSHIP STRUCTURE OF ORAU/ORNL COMMITTEE ON HUMAN STUDIES



* = M.D. L = Layperson
W = Woman M = Minority

†ON ORNL PROPOSALS, ORNL AFFILIATES DO NOT VOTE; ON ORAU PROPOSALS, ORAU AFFILIATES DO NOT VOTE; EXTRAMURAL MEMBERS VOTE ON ALL PROPOSALS.

†VOTING MEMBERS

1033156

1982

1033157

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

Implementing Guidelines for Research on Human Subjects

(April 1982)

A. Basic Principles (See Definitions, Annex 1)

1. The Committee on Human Studies for Oak Ridge Associated Universities and Oak Ridge National Laboratory has officially adopted the code of ethics adopted at the 29th World Medical Assembly held in Tokyo, Japan in 1975. The guiding principles of operation of this Committee are the same as those published in the Federal Register from time to time, by the Food and Drug Administration (FDA), and Departments of Health and Human Services (HHS) and Energy (DOE).

2. The Committee adopts the concept of obtaining informed consent from all who participate in research programs and requires that such consent contain the basic elements hereinafter described.

B. Committee Membership and Structure

The Committee shall consist of persons of both sexes and any race with varying backgrounds, training, vocation, and community interests who, while cognizant of the research goals and programs of the two sponsoring institutions (ORNL and ORAU), are sufficiently qualified to safeguard the rights and welfare of human subjects and review the relative merit of human studies in respect to any risks involved. The Committee will be composed of at least two lay persons, two research scientists and two clinicians. Two of the medical professionals, however, must be from institutions other than ORNL or ORAU, the institutions from which will emanate applications for permission to conduct a particular human study. Because of the dual sponsorship of this Committee, the Medical Director of the Health Division, ORNL; Director of Biology Division, ORNL; and the Chairman of the Medical and Health Sciences Division of ORAU shall be members of the Committee. The Directors of the two sponsoring institutions (ORAU and ORNL) shall designate to these divisional directors the responsibility for seeing that their respective staffs comply with applicable regulations for the protection of human subjects. The Chairman and Secretary of the Committee shall be elected at the annual meeting of the Committee. A person nominated for Committee membership by a member of the Committee or a sponsoring institution shall be made a member only with the concurrence of the other Committee members. Because of the complexity of modern laws and regulations protecting human rights, governing contractural obligations and guiding the use of government funds and facilities for research, at least one member will be a lawyer cognizant of the Federal Regulations. A lawyer consultant will be agreed upon and will be readily available to counsel the Committee if the Committee membership does not include a lawyer member. Similarly, if the membership does not contain a minister or a psychologist (or psychiatrist), some person with a related vocation who is interested in protecting persons from emotional and psychologic trauma

1033158

must be available to the Committee for consultation on individual projects whether or not psychologic stress or risk is obviously involved. (See Annex 4, 5, and 6).

C. Procedures for Carrying Out Initial and Continuing Review of Applications and Projects

1. Initial Review

All applications for support of research, training, demonstration, or general research support projects, including those of fellows and trainees, which involve the use of human subjects, must be presented to and approved by the Committee on Human Studies, prior to initiation of the project. Regardless of the nature or degree of risk anticipated, the application must be presented in writing on the proper form (Annex 7). The application should not contain extraneous material; that is, the investigator should not submit a copy of the funding proposal as a substitute for the form specified. The applicant must be prepared to discuss in person before the Committee detailed information on the following points:

a. The possible risk to the rights and welfare of human subjects, including the rights of privacy, freedom from harassment and confidentiality of data. A description of the provisions made to minimize these risks must also be presented.

b. Methods used to acquire informed consent. The form on which it is obtained and risk described. Special emphasis shall be placed on the appropriateness of a consent form to the particular situation inherent in the study plan in question (Annex 8).

c. The relative risks of the project as compared to the probable benefits to the subjects and to society. For each application, the Committee will document whether or not physical or psychological risks are likely to ensue as a result of the proposed research study, and further, that such potential risks have been evaluated in respect to the subject and his rights, needs, and benefits. In addition, informed consent documents must be submitted to and approved by the Committee for each study so that members can be ensured that each human subject will receive candid explanations of specific procedures and their purposes, of attendant specific discomforts and risks, and possible benefits, if any. In addition, the Committee must be satisfied in each study evaluation that the subjects will be instructed that they are free to withdraw their consent to participate and to discontinue their participation in the proposed project at any time without prejudice to them. No informed consent form will be considered acceptable if it contains any exculpatory clauses or attempts in any way to absolve the Principal Investigator's responsibility for the health (physical or mental) and welfare of the human subjects to be involved.

1033159

d. Specific deficiencies in a proposal will be identified by the Committee in writing for the proposer and also directed to the attention of that Committee member (the Director of the Health or Biology Division, ORNL, or Chairman of the Medical and Health Sciences Division, ORAU) who also has the responsibility designated to him by the Director of his sponsoring institution (either ORNL or ORAU) to obtain staff compliance with appropriate Federal Regulations and Guidelines for Protection of Human Subjects. Such a statement of deficiency by the Committee will be understood to require (1) delay in submission of the proposed grant or contract application, and (2) resubmission for Committee approval before the project proposals are allowed to go forward in the funding process. A statement of approval by the Committee will be accomplished by appropriate Federal forms for the institutional director's signature for simultaneous submission with the funding proposal.

e. A member of the Committee who is from the institution (ORNL or ORAU), from which the research proposal is being submitted, will be expected to attend the Committee only for his information, and will have no persuasive or voting powers concerning the acceptability of that proposal and its level of compliance with Federal guidelines.

2. Approval and Continuing Review

a. Approval of a proposal for a study involving human subjects shall be formalized only after a majority of the qualified (see paragraph above) Committee members have had a chance to review the written proposal; discuss it with the other members of the Committee; obtain answers from the author, if desired, to their questions; and vote unanimously to accept.

b. The Committee's findings will be transmitted in writing to the appropriate officer or the laboratory proposing the research and to the applicant The applicant's administrative superior shall maintain continuing review of the project activities. If a responsible investigator plans a change in study protocol, he must submit the proposed changes to the Committee for approval before putting them into practice.

D. Procedures of the Committee to Provide Advice and Counsel to Investigators

On request, senior investigators will appear before the Committee at its called meetings to answer any questions concerning a proposal. The question and replies will form part of the official minutes of the Committee and will be distributed to the concerned staff members, together with recorded actions of the Committee on a Review and Action Form (Annex 10).

E. Committee Members

The Committee will meet as often as necessary but no less than twice per calendar year. At the first meeting of the year, the following actions will be taken:

1. Election of Chairperson and Secretary

2. Reelection of members and replacement of those members no longer able to serve

3. Report of the Secretary on the previous year's Committee activities and on the number of approved studies that are still active and, therefore, require critical review in the new year. Establishment of the calendar for scheduled review of continuing projects, documented by an annual status report that reports any emergent problems and indicates the need for changes in research protocols or forms for obtaining informed consent.

4. The second biannual meeting will address any problems in these administrative areas that have risen since the first meeting.

5. Other meetings will be called to meet the scheduled annual critical reviews, and as needed, to consider a specific new proposal(s) involving humans as subjects where governmental funding agencies have fixed deadlines which the research applicant is trying to meet.

F. Expedited Review Procedures for Certain Kinds of Research Involving No More Than Minimal Risk and for Minor Changes in Approved Research

1. The Food and Drug Administration has established, and published in the Federal Register, a list of categories of research that may be reviewed by the Committee through an expedited review procedure. The list will be amended, as appropriate, through periodic republication in the Federal Register. A current list will be kept on file in the Secretary's office at ORAU.

2. The Committee may review some or all of the research appearing on the list through an expedited review procedure, if the research involves no more than minimal risk. The Committee may also use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Under an expedited review procedure, the review may be carried out by the Committee chairperson or by one or more experienced reviewers designated by the chairperson from among members of the Committee. In reviewing the research, the reviewers may exercise all of the authorities of the Committee except that if the reviewers do not approve the research, it must be referred to the full Committee for consideration. A research activity may be disapproved only after review by the full Committee.

3. The chairperson shall cause the secretary to send to each Committee member copies of each procedure approved through the expedited review procedure.

G. Requirements for Reporting Any Emergent Problems or Proposed Procedural Changes to the Committee

1. All senior investigators with proposed or active projects will receive notice of Committee meetings and, if requested, will appear before the Committee in person. At this time they shall present in writing any proposed changes in procedures and shall describe any new risks and benefits, and any methods for safeguarding patients' rights and procedures for informed consent in advance of instituting these changes.

2. All investigators with active research programs involving human subjects that have been approved by the Committee will be informed (a) of the need for an immediate report to the Committee secretary, Chairperson, and institutional representatives of emergent problems bearing on the health and welfare of human subjects and (b) that the Committee must approve all protocol modificatios, restrictions, or terminations.

H. Procedures to Maintain an Active and Effective Committee

1. The chairman will ensure an active Committee by calling, in addition to the regular meetings, such special meetings as required.

2. The member will be enjoined to assess every ongoing project as well as new proposals.

3. Extramural Committee members will be paid a consultant's fee, providing they are able to accept it, and travel expenses.

4. Full Committee Minutes will be distributed promptly to all members in draft form for corrections and review, so that the opinions and actions can be recorded accurately.

5. On a regular basis, at least annually, the respective institutional representative will explain this program for protection of human subjects to appropriate staff and reinforce the importance of following the Regulations and Guidelines on the use of human subjects in research.

I. Committee Records

1. The records of this Committee will be kept in the office of the Executive Secretary of the Committee at ORAU and will be available to the Committee, staff, and government auditors on demand. The records shall include the following:

   a. Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

b. Minutes of Committee meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the Committee; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

c. Records of continuing review activities.

d. Copies of all correspondence between the Committee and the investigators.

e. A list of Committee members identified by name; earned degrees, representative capacity, indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to Committee deliberations; and any employment or other relationship between each member and the institution; for example, full-time employee, part-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.

f. The Committee's written procedures.

g. Statements of significant new findings provided to subjects, as required by the Committee.

2. The above records shall be retained for at least three years after completion of the research, and the records shall be accessible for inspecting and copying by authorized representatives of sponsoring Federal agencies at reasonable times and in a reasonable manner.

ANNEX 1

DEFINITIONS

1. Clinical Investigation: Any experiment that involves a "test article," one or more human subjects, or both, and that is either subject to prior submission to a Federal regulatory agency or the results of which are intended to later support an application to a Federal agency for a research or marketing permit.

2. Test Article. Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug and Cosmetic Act, as amended, sections 351, 354-360F of the Public Health Service Act, as amended and Section 105(a) of the Energy Reorganization Act of 1974, as amended.

3. Human Subject. (a) An individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A subject may be either a healthy individual or a patient; or, (b) an individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the person or (2) identifiable information.

4. Institution. Either Oak Ridge Associated Universities (ORAU) or Oak Ridge National Laboratory (ORNL).

5. Institutional Review Board (IRB). As used herein the term means the ORAU/ORNL Committee on Human Studies; the group formally designated by the Institutions to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects in order to assure the protection of their rights and welfare.

6. Investigator. An individual who actually conducts a clinical investigation or who is the responsible leader of an investigation conducted by a team.

7. Minimal Risk. The risks of harm that are anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

8. Sponsor. The institution that initiates a clinical investigation to be conducted by one or more of its investigators.

9. Quorum. A majority of the Committee eligible to vote on a given proposal.

1033164

Alternate Language for 2. "Approval and Continuing Review" Procedure

Except when an expedited review procedure is used, the Committee shall review each research proposal at convened meetings at which a majority of the members are present, including at least one member whose primary concerns are in non-scientific areas. In order for each proposal to be approved, it shall receive the approval of a majority of those eligible to vote.

1033165

COMMITTEE ON HUMAN STUDIES MEMBERS AND AREAS OF RESPONSIBILITY

DECEMBER, 1982

*0 Calhoun, William H., Ph.D., University of Tennessee, Psychologist

* Flatt, Kenneth, B.S., ORAU, Administrator

*0 Friedman, Howard R., Ph.D., Regional Mental Health Center, Clinical Psychologist

W Fry, Shirley A., M.B., B.Ch. (MPH), ORAU, Clinician

Garrett, A. Seaton, Jr., M.D., ORNL, Occupational Medicine

*0 Goodwin, Donald W., Ph.D., United Church, Oak Ridge, Minister

*00 Griesemer, Richard A., D.V.M., Ph.D., ORNL, Official Representative

Hübner, Karl F., M.D., ORAU, Clinical Research

* Koons, Melvin E., J.D., ORFMA, Attorney

0 Lange, Robert, M.D., University of Tennessee, Chairman, Extramural Representative

00 Lushbaugh, C. C., Ph.D., M.D., ORAU, Official Representative

0 McKee, L. Clifford, M.D., Vanderbilt University, Extramural Representative

*W Miller, Ruby L., B.S., APR, UCCND, Extramural Representative

Storer, John B., M.D., ORNL, Clinical Research

*W Wray, Martha, B.S., M.D., ORAU, Systems Analyst, Epidemiology Group

Dianne Gresham, Committee Secretary, Non-Voting Member

---

0 Extramural member
00 Institutional representative
* Non-M.D. member
W Woman member

1033166

1990

1033167

MEMORANDUM

TO: Members of the ORAU/ORNL Committee on Human Studies

FROM: Karl F. Hubner, M.D. KFH
Chairman

RE: FDA Audit of the Committee's Actions

DATE: January 17, 1990

Mr. Ed Maticha of the FDA audited procedures and records of the ORAU/ORNL Human Use Committee on 10-17-89. Subsequent to the audit, I met with Mr. Maticha on 10-23-89. At that meeting, Mr. Maticha shared with me his observations of the Committee's activities and procedures and pointed out several deficiencies. His written report or copies thereof are attached.

Mr. Maticha's observations were as follows:

1) Expedited review is sometimes used to approve studies not appropriate for expedited review.

2) Studies or amendments are sometimes approved by mail vote, rather than at a convened meeting.

3) Written progress reports are not always on file with the IRB. Minutes of meetings also do not always show all active studies reviewed annually.

4) Minutes of meetings do not show numbers of members voting for, against, or abstaining from a vote. The 5-86 minutes did not say which studies received continuing review.

5) Consent forms approved did not always have all required elements of informed consent. For Study #70, the original application on file lacked a consent form, and records do not show that anyone reviewed a change to the consent form for Study #70 (the change was an improvement).

I should like to comment on each of these points.

I asked Mr. Maticha to give me specific examples of projects that were proved by expedited review. He indicated that two of Dr. James Crook's proposals on treating patients with hypertension were protocols that should not have been approved by expedited review. Those proposals had been approved by other IRB's, and since there was no change in protocol, we felt the protocol did not require whole committee review. However, the inspector indicated that even though projects and protocols had been approved by the IRB's of other institutions, such proposals still have to be reviewed (full

review) by the review board of the investigator's institution. This was unknown to me.

In regard to the second issue, mail vote, he indicated that only approval by expedited review can be given by mail. He also indicated that proposals can be reviewed by conference call with possible taping of the conversation and deliberations and a summary statement of these discussions to be added as minutes to the Committee's files. The FDA wants documentation of discussions and would like to see the interaction between the various committee members.

In regard to item #3, Mr. Maticha indicated that the progress reports submitted to our Committee are incomplete and there has not been a progress report on the DTPA projects. He emphasized that the FDA guidelines require continuing review on ongoing studies. He pointed specifically to Proposals #48C (1986) and #73 (1986). I told the inspector that his observations were not correct in this regard. I showed him the list of active studies that were reviewed at the 1989 mid-year committee meeting in Oak Ridge. This list shows all active on-going proposals and also contains progress reports and future plans regarding the activity status of those proposals. He was not aware of this list and acknowledged that our investigators have in fact been in compliance with the FDA guidelines. He did indicate, however, that each proposal and each progress report should be specifically mentioned in the minutes.

Item #4, incomplete voting records. Mr. Maticha emphasized that the minutes should show the numbers of members voting for, against or abstaining from a vote. My response was that proposals submitted to ORAU/ORNL Human Use Committee for consideration are only approved by unanimous vote. I also explained to him that a quorum for our Committee is simple majority, and also indicated that the investigators do not vote on their own proposals. He suggested that we should review the guidelines of the Committee, reevaluation the membership of the Committee, change the wording on the membership chart, and document the voting procedure. I also told him that we do keep all voting sheets on file.

The last item #5), requirements for a consent form, involves study protocol Nos. 70 and 75. Study #75 is a protocol on the use of nephedipine. This is Dr. Crook's proposal. The reviewer's criticism was that the side effects were not adequately described. Also, the alternative treatments and conventional treatment were not spelled out for lay persons. He said there were three or four versions of the consent form. Mr. Koons had approved the last version, which was, however, subsequently changed by Dr. Crook. In regard to Project #75, the consent form does not describe alternative treatment, confidentiality, or indicate a contact person in case of questions or problems. Also, there is no statement regarding voluntary participation and the freedom to withdraw from the study. He also indicated that another institution's IRB had disapproved that consent form. Even though the changes made by Dr. Crook were an improvement, these changes

should have been reported to the Committee and approved by the Committee prior to implementation. I indicated to Mr. Maticha that we will make a special effort to document our voting procedures, improve consent forms and improve record keeping as well.

He indicated to me that this initial listing of observations during his review is not an official report. An official report is supposed to follow shortly. So far, I have not received an official report.

1993

1033171

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

Building 31
Room 5B-63
301/496-7005

Rec 6/25/93 M50
2:20 P.M. mail

June 10, 1993

Dr. Jon M. Veigel
President
Oak Ridge Associated Universities
PO Box 117
Oak Ridge, Tennessee 37831-0117

Re: Assurance Number M-1394

Dear Dr. Veigel:

The Department of Health and Human Services (HHS) has approved the renewal of your Multiple Project Assurance dated April 19, 1993 submitted by your institution in compliance with the requirements for the protection of human subjects (45 CFR 46).

Your new Assurance became effective on May 1, 1993 and retains the same identification number of M-1394. The approval period is for five years. Therefore, it will expire on April 30, 1998 and a new Assurance is to be negotiated with the Office for Protection from Research Risks (OPRR) prior to that date. Please reference your Multiple Project Assurance number with all future correspondence to this office.

Your Institutional Review Board (IRB) has been assigned identification number 01. This IRB number, along with your Assurance number, will be required in certain forms (e.g., PHS-2590) and other correspondence.

The Assurance defines the relationship of your institution to HHS since it sets out your responsibilities and the procedures that will be used by your institution to protect human subjects. Among the most important elements of the Assurance are the reporting requirements to this office and your agreement to disseminate the content of this Assurance to those individuals at your institution who are in any way associated with human subject research.

1033172

A copy of the approved Assurance is enclosed, as is a blank format sheet to facilitate the future reporting of changes in your IRB membership.

If I can be of further help, please contact me.

Sincerely,

Katherine Duncan, M.D.
Adjunct Medical Officer
Division of Human Subject Protections
Office for Protection from Research Risks

Enclosures

cc: Kamal Mittal, Ph.D.

KD/sb

1033173

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117
President's Office

Multiple Project Assurance of Compliance with DHHS Regulations for Protection of Human Research Subjects

Oak Ridge Associated Universities and Oak Ridge National Laboratory, hereinafter known as the "institution" (see Appendix A), hereby gives assurance, as specified below, that it will comply with the Department of Health and Human Services (DHHS) regulations for the protection of human research subjects, 45 CFR Part 46, as amended to include provisions of the Federal Policy for the Protection of Human Subjects (56FR28003) as Subpart A, and as may be further amended during the approval period for this Assurance.

PART 1 - PRINCIPLES, POLICIES, AND APPLICABILITY

I. Ethical Principles

A. This institution is guided by the ethical principles regarding all research involving humans as subjects, as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (entitled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research [the "Belmont Report"]), regardless of whether the research is subject to Federal regulation or with whom conducted or source of support (i.e., sponsorship).

B. All institutional and non-institutional performance sites for this institution, domestic or foreign, will be obligated by this institution to conform to ethical principles which are at least equivalent to those of this institution, as cited in the previous paragraph or as may be determined by the DHHS Secretary.

II. Institutional Policy

A. All requirements of Title 45, Part 46, of the Code of Federal Regulations (45 CFR 46) will be met for all applicable DHHS-supported research, and all other human subject research regardless of sponsorship[1], except as otherwise noted in this Assurance. Federal (all departments and agencies bound by the Federal Policy) funds for which this Assurance applies may not be expended for research involving human subjects unless the requirements of this Assurance have been satisfied.

---

[1] Note to Preparers: Compliance with 45 CFR 46 regardless of sponsorship is a choice elected by most institutions for internal consistency of operations. Election will require compliance with all requirements of 45 CFR 46 (Subparts A through D) and acceptance by other Federal departments and agencies without the need for preparing separate and additional Assurances.

B. Except for those categories specifically exempted or waived under Section 101(b)(1-6) or 101(i), all research covered by this Assurance will be reviewed and approved by an Institutional Review Board (IRB) which has been established under a Multiple Project Assurance (MPA) with OPRR (see Part 1, II, G). The involvement of human subjects in research covered by this Assurance will not be permitted until an appropriate IRB has reviewed and approved the research protocol and informed consent has been obtained from the subject or the subject's legal representative (see Sections 111, 116, and 117).

C. This institution assures that before human subjects are involved in nonexempt research covered by this Assurance, the IRB(s) will give proper consideration to:

1. the risks to the subjects,
2. the anticipated benefits to the subjects and others,
3. the importance of the knowledge that may reasonably be expected to result, and
4. the informed consent process to be employed.

D. Certification of IRB review and approval for all Federally-sponsored research involving human subjects will be submitted to the Office of Research Administration (ORA) for forwarding to the appropriate Federal department or agency. Compliance will occur within the time and in the manner prescribed for forwarding certifications of IRB review to DHHS or other Federal departments or agencies for which this Assurance applies. As required under Section 119, the IRB will review and recommend approval for involvement of human subjects in Federal research activities for which there was no prior intent for such involvement, but will not permit such involvement until certification of the IRB's review and approval is received by the appropriate Federal department or agency.

E. Institutions that are not direct signatories to this Assurance are not authorized to cite this Assurance. This institution will ensure that such other institutions and investigators not bound by the provisions of this Assurance for DHHS-sponsored research will satisfactorily assure compliance with 45 CFR 46, as required (see Part 2, I, D and II, K), as a prior condition for involvement in human subject research which is under the auspices of this institution (see Part 1, III, A). Institutions that have entered into an Inter-Institutional Amendment (IIA) to this Assurance must submit a Single Project Assurance (SPA) to the Office for Protection from Research Risks (OPRR) of DHHS for DHHS-sponsored research, on request, when that research is not conducted under the auspices of a signatory institution to this Assurance.

F. This institution will ensure that any of its affilates materially engaged in the conduct of nonfederally sponsored research involving human subjects will possess mechanisms to protect human research subjects that are at least equivalent to those procedures provided for in the ethical principles to which this institution is committed (see Part 1, I).

1033175

G. This institution will comply with the requirements set forth in Section 114 of the regulations regarding cooperative research projects. When research covered by this Assurance is conducted at or in cooperation with another entity, all provisions of this Assurance remain in effect for that research. This institution may accept, for the purpose of meeting the IRB review requirements, the review of an IRB established under another DHHS MPA. Such acceptance must be (a) in writing, (b) approved and signed by an official of this institution's Office of Research Administration(s), and (c) approved and signed by correlative officials of each of the other cooperating institutions. A copy of the signed understanding will serve as an addendum to this Assurance and will be forwarded to the OPRR of DHHS by the ORA(s).

H. This institution will exercise appropriate administrative overview to insure that the institution's policies and procedures designed for protecting the rights and welfare of human subjects are being effectively applied in compliance with this Assurance.

III. Applicability

A. Except for research in which the only involvement of humans is in one or more of the categories exempted or waived under Section 101(b)(1-6) or 101(i), this Assurance applies to all research involving human subjects, and all other activities which even in part involve such research, regardless of sponsorship(1), if one or more of the following apply:

1. the research is sponsored by this institution, or
2. the research is conducted by or under the direction of any employee or agent of this institution in connection with his or her institutional responsibilities, or
3. the research is conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, or
4. the research involves the use of this institution's non-public information to identify or contact human research subjects or prospective subjects.

B. All human subject research which is exempt under Section 101(b)(1-6) or 101(i) will be conducted in accordance with: (1) the Belmont Report, (2) this institution's administrative procedures to ensure valid claims of exemption, and (3) orderly accounting for such activities.

C. Components of this institution are bound by the provisions of this Assurance. Those components which can be expected to participate in human subject research sponsored by DHHS or other Federal departments or agencies for which this Assurance will apply are identified in Appendix A. Appendix A will be revised as changes occur and revisions forwarded to OPRR.

D. This Assurance must be accepted by other Federal departments or agencies that are bound by the Federal Policy for the Protection of

Human Subjects when appropriate for the research in question and therefore applies to all human subject research so sponsored. Research that is neither conducted nor supported by a Federal department or agency but is subject to regulation as defined in Section 102(e) must be reviewed and approved, in compliance with Sections 101, 102, and 107 through 117.

1033177

PART 2 - RESPONSIBILITIES[2]

I. Institution

A. This institution acknowledges that it bears full responsibility for the performance of all research involving human subjects, covered by this Assurance, including complying with Federal, state, or local laws as they may relate to such research.

B. This institution will require appropriate additional safeguards in research that involves: (1) fetuses, pregnant women, or human ova in vitro fertilization (see 45 CFR 46 Subpart B), (2) prisoners (see 45 CFR 46 Subpart C), (3) children (see 45 CFR 46 Subpart D), (4) the cognitively impaired, or (5) other potentially vulnerable groups.

C. This institution, including all its named components (see Appendix A), acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects of research covered by this Assurance.

D. This institution is responsible for acquiring appropriate Assurances or Amendments, when requested, and certifications of IRB review and approval for federally sponsored research from all its standing affiliates (see Appendix B) and Assurances or Agreements for all others, domestic or foreign, which may otherwise become affiliated on a limited basis in such research.

E. This institution is responsible for ensuring that no affiliates cooperating in the conduct of federally sponsored research for which this Assurance applies do so without an appropriate assurance of compliance and satisfaction of IRB certification requirements.

F. In accordance with the compositional requirements of Section 107, this institution has established the IRB(s) listed in the attached roster(s) (see Appendix C). Certain research supported by the U.S. Department of Education will be reviewed in accordance with the requirements of Title 34 CFR Parts 350 and 356 which require that the IRB(s) include one person who is primarily concerned with the welfare of handicapped children or mentally disturbed persons.

G. This institution will provide both meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

H. This institution recognizes that involvement in research activities of any OPRR-recognized Cooperative Protocol Research Programs will involve additional reporting and recordkeeping requirements related

---

[2] Note to Preparers: This Part contains several administrative provisions that may be handled differently from one institution to another. Discretionary changes are expected. Please remember to highlight any changes to help speed review and approval.

to human subject protections.

I. This institution is responsible for ensuring that it and all its affiliates comply fully with all applicable Federal policies and guidelines, including those concerning notification of seropositivity, counseling, and safeguarding confidentiality where research activities directly or indirectly involve the study of human immunodeficiency virus (HIV).

II. Office of Research Administration (ORA) **[complete for each ORA if more than one signatory institution and two or more ORAs]**

A. The ORA(s) will receive from investigators, through their supervisors, all research protocols which involve human subjects, keep investigators informed of decisions and administrative processing, and return all disapproved protocols to them. The office of the Director of the ORAU serves in the capacity of the ORA for ORAU.

B. The ORA(s) is responsible for reviewing the preliminary determinations of exemption by investigators and supervisors and for making the final determination based on Section 101 of the regulations. Notice of concurrence for all exempt research will be promptly conveyed in writing to the investigator. All nonexempt research will be forwarded to the appropriate IRB.

C. The ORA(s) will make the preliminary determination of eligibility for expedited review procedures (see Section 110). Expedited review of research activities will not be permitted where full board review is required (e.g., provision of emergency medical care which also constitutes the conduct of more than minimal risk research).

D. The ORA(s) will review all research (whether exempt or not) and decide whether the institution will permit the research. If approved by the IRB, but not permitted by the ORA, the ORA will promptly convey notice to the investigator and the IRB Chair. Neither the ORA nor any other office of the institution may approve a research activity that has been disapproved by the appropriate IRB.

E. The ORA(s) will forward certification of IRB approval of proposed research to the appropriate Federal department or agency only after all IRB-required modifications have been incorporated to the satisfaction of the IRB.

F. The ORA(s) will designate procedures for the retention of signed consent documents for at least three years past completion of the research activity.

G. The ORA(s) will maintain and arrange access for inspection of IRB records as provided for in Section 115.

H. The ORA(s) is responsible for ensuring constructive communication among the research administrators, department heads, research

1033179

investigators, clinical care staff, human subjects, and institutional officials as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.

I. The ORA(s) will arrange for and document in its records that each individual who conducts or reviews human subject research has first been provided with a copy of this Assurance, as well as with ready access to copies of 45 CFR 46, regulations of other Federal departments or agencies as may apply, the Belmont Report, and all other pertinent Federal policies and guidelines related to the involvement of human subjects in research.

J. The ORA(s) will report promptly to the IRB(s), appropriate institutional officials, the Office for Protection from Research Risks (OPRR), and any other sponsoring Federal department or agency head:

1. any injuries to human subjects or other unanticipated problems involving risks to subjects or others,
2. any serious or continuing noncompliance with the regulations or requirements of the IRB, and
3. any suspension or termination of IRB approval for research.

K. The ORA(s) will ensure (a) solicitation, receipt, and management of <u>all</u> assurances of compliance (whatever the appropriate format), and certifications of IRB review (where appropriate) for all affiliates to this institution (including those listed in Appendix B), and (b) subsequent submission of these documents to the proper authorities as a condition for involvement in human subject research activities sponsored by DHHS or any other Federal department or agency for which this Assurance applies.

L. The ORA will ensure that all affiliated performance sites that are not otherwise required to submit assurances of compliance with Federal regulations for the protection of research subjects at least document mechanisms to implement the equivalent of ethical principles to which this institution is committed (see Part 1, I).

M. When an IRB of this institution accepts responsibility for review of research which is subject to this Assurance and conducted by any independent investigator who is not otherwise subject to the provisions of this Assurance, the ORA will obtain and retain an Noninstitutional Investigator Agreement (NIA) to document the investigator's commitment to abide: (1) by the same requirements for the protection of human research subjects as does this institution(s) and (2) the determinations of the IRB(s).

N. The ORA(s) assumes responsibility for ensuring conformance with special reporting requirements for any OPRR-recognized Cooperative Protocol Research Programs in which the signatory institution(s) participate(s).

O. The ORA(s) will be responsible for procedural and recordkeeping

1033180

audits not less than once every year for the purpose of detecting, correcting, and reporting (as required) administrative and/or material breaches in uniformly protecting the rights and welfare of human subjects as required at least by the regulations and as may otherwise be additionally required by this institution(s).

P. The ORA(s) will ensure compliance with the requirements set forth in this Assurance and Section 114 regarding cooperative research projects. In particular, where the IRB of another institution with a DHHS MPA is relied upon, the ORA(s) will ensure documentation of this reliance will be (a) in writing, (b) approved and signed by the ORA(s), (c) approved and signed by the correlative officials of each of the other cooperating institutions, and (d) retained by the ORA for at least three years past completion of the related research project. Where an agreement between MPA IRBs is planned, the ORA(s) will forward a copy of the required signed understanding to OPRR for inclusion in this Assurance as an addendum.

III. Institutional Review Board (IRB)

A. The IRB(s) will review, and have the authority to approve, require modification in, or disapprove all research activities, including proposed changes in previously approved human subject research. For approved research, the IRB will determine which activities require continuing review more frequently than every twelve months or need verification that no changes have occurred if there was a previous IRB review and approval.

B. IRB decisions and requirements for modifications will be promptly conveyed to investigators and the ORA, in writing. Written notification of decisions to disapprove will be accompanied by reasons for the decision with provision of an opportunity for reply by the investigator, in person or in writing.

C. Initial and continuing convened IRB reviews and approvals will occur in compliance with 45 CFR 46 and provisions of this Assurance for each project unless properly found to be exempt (Section 101[b] and [i]) by the Office of Research Administration. Continuing reviews will be preceded by IRB receipt of appropriate progress reports from the investigator, including available study-wide findings.

D. The IRB(s) will observe the quorum requirements of Section 108(b). This institution's IRB(s) has effective knowledge of subject populations, institutional constraints, differing legal requirements, and other factors which can foreseeably contribute to a determination of risks and benefits to subjects and subjects' informed consent and can properly judge the adequacy of information to be presented to subjects in accordance with requirements of Sections 103(d), 107(a), 111, and 116.

E. The IRB(s) will determine, in accordance with the criteria found at 45 CFR 46.111 and Federal policies and guidelines for involvement of human subjects in HIV research, that protections for human research subjects are adequate.

F. The IRB(s) will ensure that legally effective informed consent will be obtained and documented in a manner that meets the requirements of Sections 116 and 117. The IRB will have the authority to observe or have a third party observe the consent process.

G. Where appropriate, the IRB(s) will determine that adequate additional protections are ensured for fetuses, pregnant women, prisoners, and children, as required by Subparts B, C, and D of 45 CFR 46. The IRB(s) will notify OPRR promptly when IRB membership(s) is modified to satisfy requirements of 45 CFR 46.304 and when the IRB fulfills its duties under 45 CFR 46.305(c).

H. Scheduled meetings of the IRB(s) for review of each research activity will occur not less than every 12 months and may be more frequent, if required by the IRB on the basis of degree of risk to subjects. The IRB may be called into an interim review session by the Chairperson at the request of any IRB member or institutional official to consider any matter concerned with the rights and welfare of any subject.

I. The IRB(s) will prepare and maintain adequate documentation of its activities in accordance with Section 46.115 and in conformance with Office of Research Administration requirements.

J. The IRB(s) will forward to the Office of Research Administration any significant or material finding or action, at least to include the following:

1. injuries or any other unanticipated problems involving risks to subjects or others,
2. any serious or continuing noncompliance with the regulations or requirements of the IRB, and
3. any suspension or termination of IRB approval.

K. In accordance with Section 109, the IRB(s) will have the authority to suspend or terminate previously approved research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.

L. The IRB(s) for this institution will ensure effective input (consultants or voting or nonvoting members) for all initial and continuing reviews conducted on behalf of performance sites where there will be human research subjects. IRB minutes will document attendance of those other than regular voting members. The IRB list(s) in Appendix C includes those who are identified as knowledgeable about any affiliate institution having entered into an Inter-Institutional Amendment or other Assurance when relying on one or more of the IRBs of this institution.

M. The IRB(s) will act with reasonable dispatch, upon request, to provide full board review of protocols of OPRR-recognized Cooperative Protocol Research Programs (CPRP). The IRB will not employ expedited review procedures for CPRP protocols when they are to be entered into for the purpose of research. Although emergency medical care based on such protocols is permitted without prior IRB

approval, patients receiving emergency care under these conditions will not be counted as research subjects and resultant data will not be used for research purposes.

N. Certifications of IRB review and approval will be forwarded through the ORA to the appropriate Federal department or agency for research sponsored by such departments or agencies.

IV. Research Investigator

A. Research investigators acknowledge and accept their responsibility for protecting the rights and welfare of human research subjects and for complying with all applicable provisions of this Assurance.

B. Research investigators who intend to involve human research subjects will not make the final determination of exemption from applicable Federal regulations or provisions of this Assurance.

C. Research investigators are responsible for providing a copy of the IRB-approved and signed informed consent document to each subject at the time of consent, unless the IRB has specifically waived this requirement. All signed consent documents are to be retained in a manner approved by the Office of Research Administration.

D. Research investigators will promptly report proposed changes in previously approved human subject research activities to the IRB. The proposed changes will not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects.

E. Research investigators are responsible for reporting progress of approved research to the Office of Research Administration, as often as and in the manner prescribed by the approving IRB on the basis of risks to subjects, but no less than once per year.

F. Research investigators will promptly report to the IRB any injuries or other unanticipated problems involving risks to subjects and others.

G. No research investigator who is obligated by the provisions of this Assurance, any associated Inter-Institutional Amendment, or Noninstitutional Investigator Agreement will seek to obtain research credit for, or use data from, patient interventions that constitute the provision of emergency medical care without prior IRB approval. A physician may provide emergency medical care to a patient without prior IRB review and approval, to the extent permitted by law (see Section 116[f]). However, such activities will not be counted as research nor the data used in support of research.

H. Research investigators will advise the IRB, Office of Research Administration and the appropriate officials of other institutions of the intent to admit human subjects who are involved in research protocols for which this Assurance or any related Inter-Institutional Amendment or Noninstitutional Investigator Agreement

1033183

applies. When such admission is planned or a frequent occurrence, those institutions must possess an applicable OPRR-approved Assurance prior to involvement of such persons as human subjects in those research protocols.

V. Affiliated Institutions and Investigators

A. Each affiliate to this institution that is involved in DHHS-sponsored research activities must provide to the Office of Research Administration an appropriate written assurance of compliance with the Belmont Report and 45 CFR 46 (or equivalent protections if a foreign site).

B. Each affiliate institution must respond to a request by the Office of Research Administration of this institution for an Inter-Institutional Amendment or for a Single Project Assurance (standard or modified), when and as appropriate, whichever is most suited to the circumstances.

C. Each non-institutional affiliate (e.g., a private practice physician not otherwise an employee of this institution or who otherwise would not ordinarily be bound by the provisions of this Assurance) who is involved in human subject research of this institution must respond to a request by the Office of Research Administration of this institution for an Noninstitutional Investigator Agreement when required.

D. Performance sites that are not legally inseparable components of this institution (whether an institutional or non-institutional affiliate) are not authorized to cite this Assurance.

PART 3 - SIGNATURES

I. Institutional Endorsement(s)

The officials signing below assure that any research activity conducted, supported, or otherwise subject to DHHS or other Federal departments or agencies that are authorized to rely on this Assurance (Parts 1, 2, 3 and Appendices) or any other sources provided for in this Assurance, will be reviewed and approved by the appropriate IRB(s) in accordance with the requirements of all applicable Subparts of Part 46, Title 45 of the Code of Federal Regulations, with this Assurance, and the stipulations of the IRB(s).

A. Primary Signatory Institution (if any)

1. AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: for Jon T Thomas Date: 4/19/93
Name: for Dr. Jon M. Veigel
Title: President
Institution and Oak Ridge Associated Universities
Address: P.O. Box 117
Oak Ridge, Tennessee 37831-0117

Phone: 615/576-3300

2. PRIMARY CONTACT (If same, write "SAME")

Signature: [signature] Date: 4/19/93
Name: J. Glenn Davis, M.D., M.P.H.
Title: Vice President and Director, Medical Sciences Division
Institution and
Address: Oak Ridge Associates Universities
Address: P.O. Box 117
Oak Ridge, Tennessee 37831-0117

Phone: 615/576-3090

. Other Signatory Institutions **[complete as many times as needed]**

1. AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: David E Reichle Date:

Name: David Reichle, Ph.D.

Title: Associate Director, for Environmental, Life and Social Sciences

Institution and Address: Oak Ridge National Laboratory
P.O. Box 2008
Oak Ridge, Tennessee 37831

Phone: 615/574-4333

2. PRIMARY CONTACT (If same write "SAME")

Signature: Barry A. Berven for Russ Knapp Date: 4/20/93

Name: Russ Knapp, Ph.D.
Title: Group Leader, Health Safety Research Division
Institution and Address: Oak Ridge National Laboratory
P.O. Box 2008
Oak Ridge, Tennessee 37831

Phone: 615/574-6225

****

FOR DHHS USE ONLY

II. Office for Protection from Research Risks (DHHS) Approval

A. DHHS RECOMMENDING OFFICIAL

Signature: Katherine Duncan Date: 4/21/93

Name: Katherine Duncan, M.D.
Title: Adjunct Medical Officer
Address: Division of Human Subject Protections
Office for Protection from Research Risks (OPRR)
9000 Rockville Pike
Building 31 Room 5B-59
Bethesda, MD 20892
Phone: (301) 496-7005

EFFECTIVE DATE OF ASSURANCE: 5/1/93

EXPIRATION DATE OF ASSURANCE: 4/30/98

1033186

B. DHHS APPROVING OFFICIAL

Signature: Clifford C. Scharke Date: 6.3.93

Name: Clifford C. Scharke, D.M.D., M.P.H.
Title: Chief, Assurance Branch
Address: Division of Human Subject Protections
Office for Protection from Research Risks (OPRR)
9000 Rockville Pike
Building 31 Room 5B-59
Bethesda, MD 20892
Phone: (301) 496-7041

1033187

APPENDICES

1033188

Oak Ridge Associated Universities' components:

1. Medical Sciences Division

2. Training and Management Systems Division

3. Science/Engineering Education Division

4. Energy/Environment Systems Division

1033189

Oak Ridge National Laboratory operated by Martin Marietta Energy Systems.

1033190

APPENDIX C
Resubmit as Changes Occur]

IRB NO: M1394-01
ASSURANCE NO: 1394
DATE: April 16, 1993

INSTITUTIONAL REVIEW BOARD (IRB) MEMBERSHIP(1)

NAME(S) OF SIGNATORY INSTITUTION(S) Oak Ridge Associated Universities' Medical Sciences Division and Oak Ridge National Laboratory

SCOPE: [e.g., oncology]

Member Name First	Middle	Last	Highest Degrees Earned	Primary Scientific or Nonscientific Specialty	Affiliation with Institution(s)(2) (Yes/No; If Yes, which one(s)	Address and Phone Number For Chairperson Only
*William	H.	Calhoun	Ph.D.	Clinical Psychology	UT	Dr. William H. Calhoun University of Tennessee Department of Psychology Knoxville, TN 37919 615/974-3423
J.	Glenn	Davis	M.D.; M.P.H.	Preventive Medicine/ Aerospace Medicine	ORAU	
Ella		Dubose	MBA	Administrative Support	ORNL	
Fun	H.	Fong	M.D.	Emergency/Radiation Medicine	ORAU	
RJ	Michael	Fry	M.D.	Radiation Research	ORNL	
Shirley	A.	Fry	M.D.	Epidemiology	ORAU	
Howard		Friedman	Ph.D.	Psychology	ORNL	IRB Chair Signature:
Seaton		Garrett	M.D.	Occupational Medicine	ORNL	Restrictions Codes are presented as suffix to the Multiple Project Assurance "M" number. A restriction is based on the composition of the IRB(s) and indicates that additional expertise on the IRB os necessary for particular activities.
Robert		Hall	M.D.	Internal Medicine	UT	
Karl	F.	Hübner	M.D.	Nuclear Medicine	UT	An XM suffix indicates an insufficient number of medical members (Minimum 2).
Mel		Koons	J.D.	Attorney	No	
Russ		Knapp	Ph.D.	Nuclear Medicine	ORNL	An XB indicates that the IRB has an insufficient number of behavioral science experts (Minimal number is 2).
Ten-ching		Lee	Ph.D.	Biochemistry	ORAU	When an application or proposal comes within the scope of a restricted IRB, the IRB must add additional members to offset the restriction. Their names and qualifications must be reported to and approved by OPRR prior to the award funds.
Helen		Vodopick	M.D.	Oncology	No	
Marta	V.	Rivera	B.A.	Applied Administration	ORAU	

* DENOTES CHAIRPERSON
** DENOTES ALTERNATES (IF ANY, DENOTE MEMBER FOR WHOM ALTERNATE WILL SERVE
NV DENOTES NON-VOTING MEMBERS

NOTES
(1) EACH SIGNATORY INSTITUTION MUST CONTRIBUTE ONE OR MORE VOTING MEMBERS TO THE IRB UPON WHICH IT RELIES FOR REVIEWS. EACH AFFILIATE INSTITUTION MUST BE REPRESENTED BY AT LEAST ONE OR MORE IDENTIFIED CONSULTANTS OR NONVOTING MEMBERS TO THE RELIED UPON IRB WHO ARE KNOWLEDGEABLE ABOUT THE AFFILIATE'S SITUATION.
(2) AFFILIATION MAY TAKE THE FORM OF FULL OR PART-TIME EMPLOYMENT, MEMBER OF GOVERNING PANEL OR BOARD, STOCKHOLDER, OR PAID OR UNPAID CONSULTANT (FOR PURPOSES OTHER THAN IRB FUNCTIONS).

0031191

1994

1033192

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

January 1994

Edward D. Aebischer
Oak Ridge National Laboratory
P.O. Box 2008
Oak Ridge, TN 37831-6276

105 MIT
MS 6496

Telephone: 574-7717

William H. Calhoun, Ph.D. (Chairman)
Professor and Head
Department of Psychology
University of Tennessee
307 Austin Peay Hall
Knoxville, TN 37996-0900

Telephone: 974-3423 (w)
Home Address: 7204 Wellington Drive
Knoxville, Tn 37919
Telephone: 558-0136 (h)

J. Glenn Davis, M.D.[1]
Vice President and Chairman,
Medical Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, TN 37831

Telephone: 576-3090

Ella R. Dubose, M.S.
Oak Ridge National Laboratory
Bldg 3025
MS 6033

Telephone: 576-1865

---

[1] Institutional Representative

1033193

Howard R. Friedman, Ph.D.
Y-12 Bldg 9706-2
MS 8103

Telephone: 574-1578

R.J. Michael Fry, M.D.
209 Briarcliff Avenue
Oak Ridge, TN 37830

Telephone: 483-3211

Shirley A. Fry, M.B., B.Ch.; MPH
Assistant Director
Medical Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, TN 37830

Telephone: 576-3480

A. Seaton Garrett, Jr., M.D.
Medical Director
Oak Ridge National Laboratory
Building 4500-N, Rm. K-122
Oak Ridge, TN 37830
MS 6220

Telephone: 574-7431

Robert E. Hall, M.D.
University of Tennessee Medical Center
Department of Medicine
Box U-114
1924 Alcoa Highway
Knoxville, TN 37920

544-9160
SS# 021-36-6208

1033194

Karl F. Hübner, M.D.
Director of Research
Department of Radiology
University of Tennessee Medical
Center at Knoxville
1924 Alcoa Highway
Knoxville, TN 37920

Telephone: 544-9662

F.F. Russell Knapp, Ph.D.
Oak Ridge National Laboratory
Bldg 3047
MS 6022

Telephone: 574-6225

Melvin E. Koons, J.D.
Energy Education Division/
Tennessee Innovation Center, Inc.
1055 Commerce Park Drive
Oak Ridge, TN 37831

Telephone: 482-2440
FAX: 483-0941

Ten-ching Lee, Ph.D.
ORAU MSD

Telephone: 576-3123

Jean McGinnis, Ph.D.
Oak Ridge National Laboratory
4500-ON
I206
MS 6253

Telephone: 574-4334

1033195

Helen Vodopick, M. D.
Oak Ridge Medical Clinic, P.C.
170 W. Tennessee Avenue
Oak Ridge, TN 37830

Telephone: 483-7411

For information regarding Committee business, contact the Committee Secretary:

Marta V. Rivera, B.A.
Medical Sciences Division
Oak Ridge Associated Universities
P. O. Box 117
Oak Ridge, TN 37831

Telephone: 576-3480

1033196