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ARGONNE NATIONAL LABORATORY
P. O. Box 5207
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June 12, 1947

Dr. Robert S. Stone
c/o Atomic Energy Commission
1901 Constitution Avenue, N.W.
Washington, D. C.

BEST COPY AVAILABLE

Dear Dr. Stone:

As agreed upon at the meeting at Site B, Argonne National Laboratory on June 4, I am sending you this brief report on the organization of the health and biological program at the Laboratory, on our responsibilities in this field as I see them, on the basic philosophy behind our biological research operations, the program organization of the biological research division by "discipline," a list of current research problems, and a brief statement of the research program for the medical, health physics, and biological research divisions.

As you remember, the demand for the health and biological research program originated with the theoretical physicists in the winter of 1941-42. As they became convinced that the chain reaction would be successful, they were deeply concerned over the obvious radioactive hazards involved in such an operation when carried on at the essential high power levels. As a result the Laboratory organized a health division, and the present medical, health physics and biological research divisions represent the evolution of this over-all program during the past five years.

The health problems in the routine operations of the Laboratory are obvious but vital. In addition to the customary medical problems of employment, routine and severance health examinations and the normal first aid and employee health service activities, there are the whole field of new problems superposed due to the fact that almost all phases of the Laboratory operation involve radioactive materials or radiation sources. These radiations run the gamut from the softest of x-rays to the hardest of gammas, and they include beta and alpha emitters and both slow and fast neutrons. The rules for one species of radioactive material may differ widely from another of similar radioactive character because of vital metabolic differences. The hazard situation is one of tremendous complexity but the health services must be prepared to guard against damage from any or all of them and must be prepared to act swiftly in case an accident does occur. Even the normal health services reflect this situation since physical examinations must evaluate susceptibility to possible radiation damage and must establish a clear record against which future claims of such damage can be judged. Every request for medical attention must be considered from the radiation hazard view-

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point. Each cut and abrasion must be checked for possible contamination. Each headache must be assessed for possible radiation overexposure. The health services are inextricably and inevitably woven into a variety of personnel policy decisions. Vacations, insurance, hazard pay, to mention three, rest directly upon the health service organizations in the long run.

Any laboratory operating in the field of radioactivity, chain reacting piles or high energy accelerators will sooner or later face liabilities of disastrous magnitude unless it maintains a health service organization of the highest calibre.

It was decided early in the development of the health protection program at the Laboratory that the health organization should be a fact finding and advisory unit, not an enforcement or police group. Enforcement must lie directly with the top laboratory administration. As a result of this policy the advice and assistance of the health organizations are sought by the laboratory personnel.

The health protection organization is divided into a medical and a health physics division, corresponding to the medical and biochemical phases of the work and to its purely physical aspects. The medical division makes all blood urine and fecal analyses. These analyses form a continuing record of the blood picture of the body content of toxic materials (such as plutonium, uranium, beryllium, etc.) and of liver and kidney function for each individual exposed to radiation or toxic materials. A hand study record is also kept on each person exposed to radiation, the capillary and finger print ridge picture furnishing a sensitive test of radiation damage. This division is also responsible for the medical examinations and for the employee health service. Finally, but by no means least, it is the responsibility of the medical division, in consultation with the health physics and the biological research divisions, to establish the code of "permissible" levels for radiation exposure, for "permissible" body content of radioactive or toxic materials, and the associated "permissible" levels of of airborne hazardous materials, surface contaminations, etc.

The health physics division maintains the personnel radiation meter and film badge records, thus giving a continuous radiation exposure history of each laboratory employee exposed to radiation hazard. They also maintain the hand and foot count record and supervise laundry monitoring, receiving and shipment of radioactive materials, etc. They maintain a continuous monitoring service in all active areas, marking all contaminated areas and mapping these for the advice of the occupants of the area and for the record. Air is monitored for its radioactive content and "hot" experiments are monitored for over-all "permissible" level and for stray radiation. Such monitoring is imperative in experimental work with ten curie sources or above and with beams of radiation

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from a pile. This group is also responsible for general radiation hazard safety in all laboratory operations including apparatus design and building design and alteration. Finally, they are responsible for approval of all radiation monitoring and survey equipment.

In the case of both divisions, the routine operations continually present new demands. The medical division is engaged in a continuous research program of development of more sensitive biochemical assay or methods of assay for new substances. They also continue a search for new indicators of incipient radiation damage more sensitive than those presently available and test such new methods against the radiation histories. The health physics division is continually faced with the need for the development of new instruments. They also are faced with many new problems in determining the actual dosage received by the tissue due to radioactive material in the tissue itself. In some cases this can be computed with fair satisfaction, in others it will have to be solved as a research problem.

In attempting to discharge the above duties it immediately became apparent at the outset that the data and understanding of the phenomena needed to make more than hopeful guesses was lacking. During the ensuing five years much has been learned and in some cases fairly intelligent decisions replace earlier guesses. The field is still, however, largely unexplored and only vaguely understood in unrelated spots. Operating health safety demands, continuing vigorous research and hope for therapy in the case of accident or war lies almost entirely in such a well conceived and vigorously prosecuted research program.

As I see it our research responsibilities in biology are as follows. They can be summed up tersely as a responsibility to understand the interaction of "radiation" in all its forms with living systems. Only in this way can we meet the problems intelligently which face us even in an industrial peace time development and which become staggering in a war time situation. As for me, the condition of my personal conscience and the equanimity with which I personally will be able to face public opinion should a cataclysm fall upon us will be directly proportional to the strength and vigor of the effort we expend on this research.

I feel no responsibility for pushing ahead general biological research using tracers - interest, yes but responsibility, no. It is our responsibility to make such tracers available and to determine the hazards present in their use. I am willing to help this over-all program by making techniques and instruments available and by furnishing some limited training. Beyond this, I personally would not be willing to go for our task as I see it is already too great and unknowably urgent.

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The problems we must face are those of acute exposure, those of the long term effects of both acute and chronic exposure as possible limiting factors in the peace time industrial program and finally, those associated with the military aspects of "atomic" energy.

The problem of acute exposure to total body radiation and to a few fission products has been solved during the past five years fairly satisfactorily from the statistical viewpoint of establishing "permissible" levels. Even certain phases of the action of such an acute dose have been clarified (such as the bleeding incident to such an exposure). For many radioactive substances, however, we are not yet in the clear on acute "permissible" level. As for an understanding that would make a conceivable therapy possible, that remains in the future.

The study of the long term effects has been under way for about three years but actually is only at its beginning. These studies must be pushed ahead. "Permissible" levels for short term safety may yield long term disaster.

These programs involve a great mass of empirical experimentation for "permissible" levels can not await possible complete understanding of the interaction of radiation and living systems. They must be done with statistically significant numbers of animals and they must be done with many varieties of animals for the results to be statistically valid and for species specificity to be sufficiently clear to permit extrapolation to the human.

Such empirical experiments will not give the understanding of the phenomena which is needed. This must be gotten from fundamental investigations. These, too, need vigorous attack. The two approaches are complementary. Each serves as a guide for the other; each supplies the other with a testing ground for the validity of new interpretations of results obtained.

In the case of the military implications it seems to me that we are under a deep responsibility to supply facts and perhaps ideas. A Nobel Prize winner in genetics was recently quoted in the newspapers as saying that if any considerable number of atomic bombs were used in a war the amount of residual radioactivity spread world wide in the atmosphere would be sufficient to produce enough recessive mutations in the human race to produce its effective destruction in fifty generations. What he really said, I do not know but this will be the public belief. If the time comes when an atom bomb attack by us is imperative we must know whether this is true or false and if true we must have a method ready to eliminate a wide spread distribution of such residual activities.

Similar answers are needed in connection with radiological warfare. The biologists have laid a fair ground work for such answers in the last four years and have given the subject considerable study, but much remains to be done.

The logical answer to the prosecution of a total war seems to me to be biological warfare not "atom bombs." Here, again, however, radiobiology may furnish a key to the production of many new BW agents. This should be explored particularly from the point of view of the possibilities of the use of pile irradiation in this connection.

The program in biological research at the Argonne National Laboratory is based on this view of our responsibilities. It has been my feeling that the investigations outlined were too important to trust to some outside agency's possible continuing interest as a guarantee of vitally needed knowledge. In addition I believe a completely integrated program is essential at some one or more locations. The phenomena are complex and truly comparable results by differing disciplines are hard to obtain. It has been a basic point of philosophy of the biology division that when an animal experiment is set up it is established and scheduled for all of the disciplines. Each obtains its results on the same group of animals so that their results are completely comparable. Another point of basic philosophy argues for an integrated program, that is that in each discipline the results obtained should be gotten on a strictly quantitative - or as nearly a true quantitative basis as possible. This has called and is calling for an extensive development of new and highly sensitive techniques and instruments. Many of these advances in techniques and instruments can be shared; others can be modified for use from one discipline to another. The efficiency of having a qualified group engaged in this type of developmental work with all of the disciplines in mind is much greater than where such work is done for but one or two special fields.

Organization of Biological Division by Disciplines

1. Biophysics Studies of the pathogenesis of very early manifestations of radiation damage of animal or plant cells call for the application of sensitive and quantitative physical and physico-chemical methods of investigation.

It may be presumed that minute and subtle changes occur in the physical and physico-chemical constituents of cells following exposure. These are not detectable with the ordinary methods of measurement currently employed.

It will be the concern of this group to pursue investigations of this type, including studies on animal and plant cells; e.g., studies of changes in permeability, electrical potentials, submicroscopic cellular constituents, to mention just a few.

Consequently, the development and standardization of new instruments and the improvement of existing types will constitute a considerable portion of the activities of this group.

2. Biochemistry and Physical Chemistry The interpretation of any alteration produced in a living organism by ionizing radiation ultimately demands an explanation in biochemical terms. No methods of reversing these alterations can be rationally developed unless these biochemical explanations are available.

Studies of the general metabolism of injected and ingested radioactive elements are of importance, for closely related to this are problems of accelerating excretion of these materials once they have gained entrance into the organism either by inhalation, ingestion, or wound contamination.

The program must also include extensive studies on the chemical consequences or irradiation of biological systems, including in vivo and in vitro exposures and studies of the effects on metabolism, enzymes, proteins, and nucleic acids. The profound effects on growth and reproduction of cells that are observed following irradiation must in the last analysis be referable to chemical disturbances initiated at the time of exposure. It is probable that sensitivity of cells to irradiation is also in large part due to the presence or absence of peculiarly sensitive metabolic or rather chemical moieties.

Chemical studies using radioactive and non-radioactive tracers form another very important part of these investigations.

3. Physiology Extensive and careful studies of physiologic abnormalities induced by external irradiation are essential for an intelligent interpretation of the complex picture of radiation disease and complementary to the studies performed by other groups.

The conventional types of physical and chemical measurements available to physiologists are of great help for a better understanding of the pathologic physiology of the acute, sub-acute, and chronic phases of radiation injury.

The investigation of cardiac and circulatory function, liver and kidney function, blood, urine and feces chemistry are examples of modes of inquiry. The dependence of certain types of injury upon dose and intensity are problems which need elucidation and interpretation in physiological terms. Successful therapeutic measures to be taken in case of accidents will largely depend upon progress made in this field.

4. Experimental Pathology As a first approximation for the determination of toxicity and "tolerance levels" of radioactive materials and external irradiation for humans, studies will be continued on mammals. Acute and chronic toxicity studies of this kind are limited in scope; they include the assembling of data such as survival, haematological effects, organ-specific alterations, and eventually tumor induction.

Such investigations in order to be of significance from a toxicological point of view must necessarily be carried out on statistically significant numbers of animals and for the correct interpretation in terms of human "tolerance", on different animal species. Results obtained in this way raise numerous questions as to the pathogenesis of certain lesions and they stimulate investigative work concerning certain isolated phenomena observed in the course of such studies. They provide a valuable background for research directly applicable to the problems of health protection in the case of many new health hazards, which might otherwise not be noticed.

The work on the hemorrhagic factor or factors in radiation sickness, for instance, is an important aspect of the work in this group. It is conceivable that the successful elucidation of those mechanisms might materially brighten our prospects for an effective therapy of this phase of radiation disease.

Experiments on various bacteriological and immunological aspects are also of considerable importance in view of the profound alterations in the hematopoietic system (leucopenia) produced by irradiation and the relationship of this system to resistance to bacterial infection and hence to survival.

5. <u>Histology and Cytology</u> Histological and cytological methods are indispensable tools for the recognition of damage produced by many injurious agents and it is desirable that various abnormalities produced by irradiation be studied by many of the well-known standard histologic staining techniques and that these be combined and broadened by the application of the more recently developed and established cytochemical procedures.

It is the objective of these investigations to advance from mere description of abnormalities to the interpretation of such abnormalities by developing this mode of approach and by combining it with other methods of inquiry; e.g., electron-microscopy, phase-contrast microscopy, ultraviolet absorption and spectrophotometry, tissue culture and motion-picture photography, and radioautography.

Studies carried out in this way will help to bridge the gap that now exists between descriptive morphology on the one hand and physiology and chemistry on the other.

6. <u>Cellular Biology (Microbiology and Genetics)</u> When reduced to fundamentals, inquiry into the changes in animals caused by irradiation becomes inquiry into changes brought about in the individual cell. Extension, then, of radiobiological investigations to the cellular level may hasten our understanding of what happens to the more complex biological systems when irradiated. Such studies may conveniently be carried out with the free-living unicellular and simpler multicellular organisms, for they offer some advantages not obtained in other more complex animals. In the case of many of them, relatively rigid control of nutritive and other environmental conditions is possible, and rather precise knowledge of many of the physiological responses to environmental change is available.

Accordingly, it is planned to study the effects of irradiation on microorganisms. These studies will be directed toward recognition and measurement of physiological effects, immediate and delayed, of various kinds of radiations emanating from within and without the organism. These responses include, among other, changes in permeability, mineral metabolism, respiratory activities and growth characteristics.

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It is altogether conceivable that many important physiological changes observed after irradiation are due primarily to small changes in the genetic complex of the cell. Therefore, the cellular studies will include consideration of genetic effects produced by irradiation. Of special importance will be the general problem of resolution of purely cytoplasmic and primarily nuclear effects and the extent to which these are interrelated.

7. Hematology It is well known that the hematopoietic system is one of the most vulnerable to radiation. The reasons for this are wholly obscure. The study of the effects of irradiation on the hematopoietic system and of the mechanisms involved in these effects will be continued vigorously. It is probable that imaginative research carried out in this field may well help to provide an understanding of some of these mechanisms, for the cells of no other organ are as easily accessible for study and few cells can as profitably be subjected to various cytochemical, physiological, or biochemical methods of investigation as the cells of the blood.

Furthermore, hematological observations are indispensable adjuncts in any study of acute or chronic chemical and radioactive toxicity and a strong hematological service group will have to be maintained for this purpose alone.

8. Training Personnel temporarily at the Laboratory as well as new members of the staff will be trained in tracer and radiobiological research methods and in other research techniques peculiar to the Laboratory's biological investigations.

Current Research Problems

Medical Division

1. Bio-assay for Plutonium and other Radioactive Materials This program was originally developed because of the necessity for information about the quantity of plutonium fixed in the bodies of workers with that material. Only with such estimates is it possible to adequately protect the worker from the chronic effects of exposure to radiation by removal from further exposure. This program is now largely out of the development stage and has been for some time applied to the bio-assay of our exposed individuals.

If other radioactive substances of comparable hazard come into use in the Laboratory, methods for their detection with suitable sensitivity will have to be devised for the reason given above. The materials which, it can be predicted, will have to be investigated in the future are thorium, uranium^{233} and beryllium. (It is recognized that this latter substance is not a radioactive hazard, however, it is a comparatively new substance from the Laboratory and industrial points of view and requires much investigation before its hazard to humans is accurately assessed.)

Inherent in this program is the determination of the excretion rate of these materials since this factor must be known in any estimation of the amount fixed in the body. Work with lower mammals is useful in a preliminary approximation of the chronic excretion rate in humans, however, as with plutonium, it is essential to actually determine the excretion rate in humans. In consequence, work in patients with other radio-isotopes will have to be undertaken from time to time in the future.

2. Wound Therapy A major concern at this and other installations has been the possibility of contamination of wounds with radioactive materials. The possibility of introduction of harmful or fatal amounts into the body by this means with damage to the individual involved, has been a possibility of grave concern to the Health Divisions of the various installations. Consequently, a program here has been undertaken to assess the likelihood of wound contamination, to determine the means of wound decontamination and to determine the best means for the treatment of wounds contaminated with radioactive materials. This program, to date, has been carried out on a small scale due to lack of suitable personnel and space. However, it has been determined in a preliminary way that in the case of plutonium (here, our most serious hazard) it is bound with extraordinary rapidity to the surface of the wound so that it cannot be washed out of the wound with any useable agent yet tested, and that fifty per cent transport to the rest of the body (liver and bones) takes place in approximately 24 hours. Consequently, it would appear that the wound problem is a serious one and deserves further investigation. Also, the problem should be extended to the investigation of other radioactive isotopes, particularly uranium^{233} and some of the representative isotopes produced in the pile or in fission.

3. Biochemical Investigations Pradtically speaking, at the present time our only means for the evaluation of damage due to radiations or the deposition of radioactive materials in the body is through blood count determinations. It has been recognized for many years that these determinations are at once non-specific and insensitive. Consequently, the then Metallurgical Laboratory felt that it was necessary to search for other biochemical reactions occurring in the body of the irradiated person which would be more sensitive and more specific. The biochemical group has concerned itself with a search for these tests. To date none has appeared which offers great promise. However, because of the seriousness of the problem we have felt that the search should continue and that all promising leads should be investigated.

Since other toxic, non-radioactive materials are handled by the Laboratory such as beryllium, and since the clinical problem involved is not well understood it is felt that the work of this group could legitimately be extended to the search for biochemical alterations following exposure to these materials. In consequence, work along these lines has been done and it is expected will continue in the future.

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4. Skin Studies The problem of detecting early damage to the skin is at the present time an unsolved problem. The current clinical criteria serve, essentially, only to detect damage after it is well established and probably irreversible. Consequently, a program looking for more sensitive criteria of damage to the skin was undertaken at this Laboratory. In brief, the criteria which were felt to be of promise and which have been investigated were:

1) Alterations in the finger ridge patterns, and

2) alterations in the capillary patterns of the nail folds.

This program has been carried on for the past three years and will be carried on in the future, according to present plans.

Health-Physics Division

1. Continuous Air Monitoring System One of the most acute immediate problems. This comprises a complete system for continuously sampling laboratory air to detect and continuously indicate the level of long-lived isotope, for instance Pu, concentration above the natural activity due to the daughters of radon and thoron. These naturally occurring short-lived elements make the problem quite difficult since their concentration may readily be ten or more times that of the long-lived element sought. Work has been started in collaboration with Shonka and Bradley in the Instrument Division.

2. Quartz-fiber Electrometers and Electroscopes Many improvements are possible and certain types of instruments are acutely needed to which these devices, which are and can be the most reliable of all, are directly applicable as the simplest and most economical solution. This includes fast neutrons for which we as yet have no really satisfactory instrument, slow neutrons, and beta rays. For the latter the immediate solution is evident, but the working models are not complete, including detachable small chambers for monitoring fingers.

A portable Lindeman electrometer with about one volt sensitivity without a power pack using a single small battery or electrets is a solution for the problems encountered in many types of portable instruments. Work is proceeding on these devices in the Shop and Instrument Division.

3. Condenser Ion Chambers Improvements in the Ryerson Pocket Meters are now being made which will stop discharges due to dropping or shock. The development of small condenser chambers for finger or local monitoring is under consideration.

4. Film Monitoring An investigation of special compound filters for film badges to remove the remaining error due to the wave-length dependence of film used in personnel badges which are under re-design. Part of this investigation is under way.

5. Slow Neutrons Measurements at Site A in a wide thermal beam with synthetic "tissue wall" ion chambers in order to determine accurately the slow neutron flux for permissible level or tolerance. This figure is at present under considerable controversy but can be largely settled by these measurements in collaboration with Dr. G. Failla.

6. Fast Neutrons Development of a suitable pressure ion chamber for use with quartz-fiber electroscopes to read in terms of rem or total "damage." This work is partially complete but awaits personnel and facilities.

7. Tissue Dose Measurements The use of plastics as a tissue substitute incorporating various radioactive materials, the hot plastic to be measured in an extrapolation chamber. From these data tissue doses may be calculated for even the most complicated decay schemes and film calibrated so that film radio-autographs may be interpreted in roentgens.

8. Breath or Expired Air Measurements (a) A method for measurement of the ionization of expired air to determine the lung concentration of an individual "infected" with an alpha emitter. (b) A simple, quick, reliable system for measuring the breath radon content.

9. An ultrasensitive pressure ion chamber arrangement to assay total body content of a gamma ray emitter.

Biology Division

Withrow Plant cell (corn) - electrical potentials; cell surface changes (permeability, changes in fibre structure, cell distrotion); temperatures. (Preceded by development of new techniques). Instrument development imperative.

Barron Effects of irradiation on enzyme systems.

Norris Carbon-14 toxicity - metabolism - permissible level? Distribution of Sr-89 and Ra. Effect of previous irradiation on metabolism of Fission Products.

Schubert Mechanisms of elimination of radio elements. Methods of treatment - (accidents).

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Patt Alteration of organ function by radiation. Cardiovascular, kidney, liver, endocrine, skin. Effect of temperature on effect of irradiation.

Brues - Lisco - Allen - (Burrows) Chronic toxicity (tumor incidence, anaemia, leukemia). Sr-89, Pu-239, Y-91, P-32, (C-14) for statistical evaluation of delayed response and investigations of pathogenesis of these abnormalities. Studies of quantitative relationship between dose, character of action, time of appearance (for possible extrapolation from animal to man). For comparative purposes total body x-radiation is being investigated.

Bloom - McLean Bone metabolism - histological and tracer studies

Rhoades (Bloom) Local effects of Pu-239 introduced under skin - how does radioactivity change response to local inflammation (Y-91 and Ra - alpha vs. beta control). Proposed cytochemical techniques (demonstration of enzyme activity (phosphatase nucleic acid stains).

Powers Irradiation genetics - paramaecium - nucleic acid (P-32 tracer studies,) metabolism, growth characteristics - tissue culture studies.

Jacobson Methods of increasing radio resistance to irradiation of cells normally very sensitive - participation in other experiments.

Program for 1948

Medical Division

1. Employees Health Service is responsible for the performance of the routine physical and x-ray examinations on all individuals employed by the Project. These are done at intervals designated by the Director of the Division. In addition, all occupational illnesses or injuries are treated by this organization. In addition, it has been the policy of the Laboratory to see all illnesses, regardless of their probable origin, on Project personnel. This policy must be continued since new or unsuspected occupational illnesses can only be discovered if the worker feels free to visit the Employees Health Service for any disability. At present the Employees Health Service is staffed by part-time physicians through an arrangement with the University of Chicago. It is recommended by this office that a full time staff be hired for the Argonne National Laboratory during the above fiscal year. This recommendation is made because it is felt that the move to the new site will probably take place during the fiscal year 1948-49. It would be well to have our own full time staff trained and operating smoothly before that move.

2. Laboratory Studies (a) Clinical The clinical laboratory will continue the routine and special blood and urine examinations on Project personnel. In addition, they will cooperate in certain animal work undertaken by the Medical Division. (b) Experimental Experimental investigations leading to new methods for the evaluation of biological change in persons working with radioactive materials will be continued.

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3. Biochemical Studies (a) Development and routine application of methods for looking for heavy metals and other special project materials in biological specimens obtained from Project personnel or in persons being studied clinically. (b) Investigations concerned with the improvement of existing methods of routine determination and the development of new methods of determining excretion levels of other toxic materials. Among the new materials which will be investigated during the year 1947-48 under discussion will be thorium and certain of the relatively long-lived beta active radioactive isotopes.

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Proposed work includes: a systematic study of the effects of radiation on the endocrine system, the output of the heart after irradiation, and the effects on it of therapeutic agents, etc.

2. Effects of irradiation on the structure and functions of the blood and of the defenses against infection.

The radiation sensitivity of blood cells has been carefully investigated, as well as the end products of pigment metabolism from red blood cell destruction. The present work is directed toward a study of the responses of blood cells under stress, which appears to show the unexpected result that cells under stress are less sensitive to radiation than the same cells in the normal state. Problems to be investigated further in the near future include the relative responses of cells subjected to external and (localized) internal irradiation, the meaning of the successive crises and recoveries in blood cell response, and the blood response of cold-blooded animals. The relation of the blood changes to susceptibility to infection will also be made the subject of study.

3. Acute toxic effects of external radiation and absorbed radioactive substances: Their mechanism, prevention and treatment.

In addition to the problems discussed elsewhere, studies on the possible role of histamine and other substances from tissue are being continued to settle the question of general tissue breakdown as a factor in the radiation response.

4. Response to various types of radiation of blood cells, cultured tissue cells, and single-celled organisms.

Attempts are being made to verify delayed death of irradiated cells in culture and to compare blood and tissue cell responses. The possible fixation of C-14 in tissue under varying conditions of growth is being studied. Investigation of the genetic changes which occur in unicellular organisms, in relation to the type of radiation and specific ionization is underway.

Plans for future work include a detailed study of the nature and sequence of changes which occur in isolated cells of higher animals, observed microscopically, chemically, and by means of the electron microscope.

5. Chronic effects of radiation and radioactive materials in animals.

Work in this category has been in progress for about three years; in addition to information about fission products and plutonium, some studies have been made on the effects of these elements on growth and of growth on the response of these elements. New and important knowledge has been obtained about actions of radium, although this element has been the subject of considerable study in the past.

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Further work will include: statistical studies of shortening of the life-span of external radiation, with particular attention to causes of death; and studies over larger periods of time, with larger animals, and with new radioactive hazardous materials.

The hypotheses of accelerated ageing following radiation, and of the absence of a true threshold for chronic radiation effects, are still being tested and will condition much of the future work.

6. Mode of action of radiation in the production of cancer.

The chronic radiation experiments have been conceived and set up in such a way as to determine what quantitative laws govern the development of tumors. It is observed that the minimum latent period for cancer development by all forms of radiation is larger than with chemical carcinogens. This suggests intermediate factors, and there will be sought in changes in cell chemistry on cell surfaces. Since the length of latency suggests the possibility of intermediate stages, certain of these might be inhibited or abolished after irradiation. Investigation of the effect of temperature on carcinogenesis has been begun, using amphibians.

7. Response to different types of radiation of various organs and tissues.

Studies of liver, kidney, and cardiovascular physiology were done during the war and the endocrine system is now under study. The question of the role of the adrenal cortex in radiation sickness is still in need of considerable study, and this is being undertaken. This field of work will probably prove to be of considerable importance in the therapy of radiation sickness, from both external and internal radiation.

Studies are also being pursued on plant cells and tissues. At present, the effect of radiation on electrophysiological properties of cell surfaces are under study. Surface phenomena are in many cases appropriately studied in plant material, and it is thought that cell surfaces may be especially vulnerable to radiation damage because of the orientation of polar graphs on surfaces.

8. Studies on chemical effects of radiation which are basic to its biological action.

The effects of uranium and of various forms of radiation on enzymes, proteins, and biochemical properties of yeasts and bacterium have been described in our reports. A long term well organized study of the effects of radiation on substances such as enzymes, proteins and nucleic acids, has been planned, and it is intended that correlation with known chemical effects of radiation should be made where possible.

9. Absorption, deposition and elimination of radioactive elements from the body.

These studies were a major part of the wartime effort of the

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Metallurgical Laboratory. As a result it has been possible in many cases to make reasonably good predictions regarding the acute and chronic effects of fission products.

These studies are to be continued in coordination with toxicity studies. The reasons for the unexpectedly high toxicity of plutonium are being sought in its rather specialized distribution in tissues, and may serve as a guide to toxicity of other alpha-ray emitting elements.

The elimination of absorbed radioactive materials is of particular importance, since their absorption may not always be effectively prevented. The displacement of plutonium on other heavy elements was described by Schubert; this should be further investigated from the standpoing of developing practical means for the use of this principle, and studies are also proposed on methods for the removal of radioactive strontium and rare earths and radium.

10. Design and standardization of instruments to carry out the foregoing.

This is a field which will always play an important part in the pursuit of biophysical studies as outlined above. Almost all of the fields of work included here involve the use of highly spedialized apparatus, much of which must be developed.

Norman Hilberry

Norman Hilberry
Associate Director
ARGONNE NATIONAL LABORATORY

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Probably Declassified

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Report of the
23-24 January 1947 Meeting
of the
INTERIM MEDICAL COMMITTEE
U. S. ATOMIC ENERGY COMMISSION

by
Stafford L. Warren, M. D.
Chairman, Interim Medical Advisory Board

Members Attending:

Dr. R. S. Stone
Dr. G. Failla
Dr. John Wirth
Dr. H. L. Friedell
Dr. R. E. Zirkle
Dr. J. Sterner
Dr. A. H. Dowdy
Dr. A. M. Brues
Dr. Louis Hempelmann
Dr. J. G. Hamilton
Dr. A. Hollendaer
Dr. S. T. Cantril
Dr. J. Svirbely
Dr. L. Donaldson
Dr. James Nolan
Dr. B. L. Vosburgh
Dr. B. S. Wolf
Dr. K. Z. Morgan

Downgraded to Unclassified per authority M. F. Moore Dtd Feb 7, 1964

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Report of the 23-24 January 1947
Interim Medical Committ
United States Atomic Ener

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9, 1946
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1. Review and Scope of the Medical Re

A. Since the inception of the
research program aimed at the diag Here
to the development of atomic energy
include those injurious effects produc r-
body exposure to radiations emitted by va t
during the experimental or processing operat
toxicity or localized radiation from such mater
body.

Considerable preliminary or pilot experimental an
information has been obtained by this research program durin
three years. Of necessity, many fields were completely neglect
injurious effects following single exposures to large amounts of r
tion have been determined experimentally; some of the changes followin
prolonged chronic radiation exposure have been surveyed; the biological effects which follow the introduction of various toxic and radioactive materials into the body have been partially demonstrated. Such pilot studies have been useful in the estimation of maximum allowable exposure levels of radiation or toxic materials to which personnel can be safely exposed for a period of time, and the control of such hazards by the prevention of such exposures. Such standards were designed for war time expediency and are not necessarily applicable to peace time.

While the above information has been extremely useful in this work, it immediately becomes obvious that many critical problems of far reaching scope remain to be solved. Information concerning the method of production of these injurious effects in body tissues is almost completely lacking. No methods are available which might stop or delay the development of radiation injuries. No therapeutic measures are at hand to use following accidental injury due to radiation or radioactive materials. Such problems relate to the fundamental nature of living matter and demand the careful and continued attention of competently trained scientists.

B. The following list indicates briefly the survey of the general studies on radiation effects.

The known radiations encountered in nuclear fission, as well as those encountered from naturally radioactive substances divide themselves into the following types: alpha rays, beta rays, gamma rays and neutrons. The literature on the biological effects of x-rays and gamma rays is voluminous and a good deal of background information was obtained from this source. On the other hand, very little had been written about the biological effects of alpha rays, beta rays and neutrons. It became necessary, therefore, to initiate studies to cope with the unique and pressing problems as rapidly as possible.

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The report of the Medical Advisory Committee to the Director of the Medical Division of Manhattan Engineer District of September 9, 1946 contained the following summary of the problems and the methods of approach being used up to the present,

1. The Physical Measurement of Radiation of Various Types. Here it was and still is necessary to develop better methods of accurately measuring and standardizing the dosage of radiation in two vitally important areas (1) the measurement of the extent of any radiation which might be found in an industrial area and (2) in the biological experimentation.

2. The Biologic Effects of Radiation. Because of the known deleterious effect of radiation on the animal organism, it becomes necessary to determine the effect of controlled dosages of the various types of radiation on various animal and plant species, including marine life. Such observations can be used in the control of possible human exposure and have practical use in medico-legal problems arising from contamination by effluents.

Some of the types of biological effects it is possible to study are given below. Only pilot studies have been done on most of these effects.

a. The survival time or percentage reduction in normal life span of different animal and plant species following a given dose.

b. The genetic effects of radiation as manifested in the development of abnormal individuals from changes in the heredity mechanism.

c. Histopathological changes as demonstrated by abnormal changes in the makeup of the various body tissues.

d. Physiological changes produced by the alteration of the normal functioning of living tissues following irradiation.

e. Biochemical and enzymatic disturbances which are the potential sources of these physiological abnormalties.

3. Methods for the Detection of Minimal Radiation Damage are being developed directly from experiments of the above types and are applied to the study of the human individual. These include studies on:

a. Biochemical and enzymatic changes which may be detected and which, if measurable, can be corrected before irreversible damage has taken place. Examples of such changes would be effects on the metabolism of coproporphyrins, excretion of abnormal substances in the urine, and the like.

b. It has been known that radiation depresses the function of the hematopoietic system (bone marrow, lymph nodes, etc.) and detailed study is indicated to detect early changes under controlled dose radiation with all blood elements under continuous observation.

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c. The production of anatomical changes such as epilation, skin erythema, and alterations in the integrity of the skin and the like, must likewise be studied under controlled dosage.

4. Methods for the Prevention of Radiation Injuries. These include:

a. Methods of physical detection of external radiation by the development of sensitive direct reading instruments capable of the detection of amounts of radiation well below those necessary for demonstrable injury to the animal or human subjects.

b. Methods for the determination of harmful amounts of radioactive dusts and gases in air, in water and in body tissues. Many radioactive materials are deposited in the body, like radium, and in such locations produce injury to tissue, particularly the bone marrow. Methods based on the determination of dangerous amounts of these substances by examination of the excreta and direct measurements of the body itself are first developed in animals and then applied to human beings.

5. Protective Measures. Studies on (1) the efficiency of shielding against radioactive materials (2) the efficiency of exhaust and ventilating systems against dangerous amounts of dusts (3) the development of protective clothing and devices and (4) the development of remote control processing methods have been extremely important in the Manhattan District protection program to date and will continue to be fundamental to the development of a safe atomic power program.

6. The possible treatment of radiation injury deserves extensive study with high priority. Experimental replacement of the damaged hematopoietic elements destroyed by severe radiation exposure offers one possibility. Detection and neutralization of hypothetical but unknown toxic substances produced by radiation is another possibility. This difficult and fundamental problem deserves consistent and detailed study.

All the above studies are of necessity done with alpha, beta and gamma rays and neutrons of varying intensity, singly and in various combinations. Also, the effects of acute and chronic exposure must be determined separately because of their dissimilarity.

C. The following list indicates briefly the study of the hazards due to special materials. For brevity, it is preferable to discuss the potential toxicity of special materials by first indicating the types of studies to be carried out, and then by listing those materials on which studies have been made or on which studies are necessary.

1. First, an actual determination of the toxicity of a substance must be made, measuring how poisonous it is, both in acute and in chronic exposures. The amounts administered are decreased until asymptomatic levels are found. In this way, toxic levels may be avoided in laboratory and plant environments. Some pilot work in this direction has been completed for a few compounds of uranium, plutonium and certain special oils.

a. The mode of entrance into the body (ingestion, inhalation or skin absorption) must be studied as different manifestations and degrees of toxicity may be produced by each route employed. Storage in and excretion from the body must be studied in chronic experiments at various levels of exposure.

b. A careful analysis must be made as to the character of the biological changes; specifically, production of physiological, histopathological and biochemical and genetic evidences of damage. Some progress has been made here.

c. The nature of these injuries and the mechanism by which they occur must likewise be studied. This affords information as to the necessary protective measures, and indicated therapy after exposure. Very little has been attempted here except in one or two instances.

2. Preventative measures require study.

a. The comparative effectiveness of physical methods for the removal of hazardous dusts; namely, the reduction in skin contact and prevention of ingestion, must be measured. Methods for accurate estimation of such hazards must be developed and used. The efficiency of certain protective chemicals, ointments, etc., must be studied. Only pilot studies have been done here.

b. Protective devices such as portable respirators and clothing must be tested for those hazardous substances against which they will be used. No practical mask, military or otherwise, which will protect against some of the worst hazards has been found yet.

c. Finally, appropriate investigation must be made of those therapeutic measures to be used in the treatment of both acute and chronic toxicity states.

3. Completion of the various phases of the program outlined above would provide complete information as to those medical aspects which must be taken into account in the protection of the worker, as well as treatment of injury should it occur. The following is a nearly complete list of the substances on which studies of this type are necessary:

a. Uranium and its compounds.

(1) Uranium metal and its chemical compounds: oxides, nitrate, chlorides, bromide, tetra and hexafluoride, sodium and ammonium diuranates. Some pilot studies have been completed.

(2) Uranium chain of heavy metals:

Uranium X^1
Uranium X^2
Radium
Polonium

Relatively little has been accomplished here.

(3) Fission products of cleavage of U-235 and plutonium. Very meagre pilot studies have been done here.

(4) Artificial isotopes of uranium - 232, 234, etc. Almost nothing has been done here.

b. Thorium and its chain, almost unknown.

c. Plutonium - some pilot work.

d. Special accessory materials - pilot work only.

(1) Fluorocarbons

(2) Fluorine

(3) Beryllium

(4) Others

D. Production Hazards. The results of the laboratory studies made on the materials discussed above are applied to the prevention and control of industrial hazards which arise in the large manufacturing areas where these materials are used in large amounts. These are illustrated by the following:

1. In the Electromagnetic and Diffusion Methods for the isolation of uranium 235, the major hazards are from the uranium compounds, the concentration of uranium X1 and X2, and the special accessory materials and by-products formed in the process of manufacture.

2. In the graphite pile where plutonium (239) is produced on a large scale, the hazards are from the alpha, beta dn gamma rays, neutrons, the plutonium metal and its compounds, the various radioactive fission products resulting from the pile operation.

3. The chemical isolation of polonium following its formation in the pile incorporates hazards from alpha radiation following absorption into the body.

4. Chemical purification process in making uranium metal results in hazards from alpha, beta and gamma radiation and the chemical toxicity of the uranium of other products used.

5. Study of the medical aspects of plant programs aside from the determination of the effect of radiation and chemical toxicity, include additional information obtained from plant investigations as from:

a. Clinical survey of all exposed personnel.

b. Monitoring of hazards by special instruments and methods.

c. Surveys of new types of graphite piles and production equipment.

E. Hazards of Atomic Catastrophe in Production Areas.

1. Immediate effects:

a. - Radiation. The radiation occurring at the time of the explosion coupled with blast and heat causes biological effects which may differ from those occurring following other acute known effects from gamma and neutron radiation, and demand study. Some pilot work and observation of the Japanese indicate that this may be so.

b. Blast. The total blast energy of atomic explosion is very great and may have totally different types of shock waves, recoil waves from ordinary explosives and unique biological effects may be produced. Some pilot work has been done.

c. Actinic Radiation. The intense burns from actinic type of radiation have not been studied. This also includes the combination effect of all three items in this group: blast, radiation and heat.

2. Delayed Effects.

a. Protective devices. Study of methods of protection against the radioactivity deposited at the time of blast.

b. Decontamination. Methods of decontamination of soil and the like must be worked out for cleaning up active areas. Some experience is available on this from New Mexico and the ships from Bikini which is applicable.

c. Investigative equipment. Special equipment must be developed and tested for use in investigating bombed areas.

d. Study of casualty effects. Field study of fission clouds, possible injury to water supply, soil and the like, human damage by population surveys.

e. Study of treatment of all immediate effects such as radiation, heat and blast.

F. Preparation of pertinent information in proper form for use by catastrophe units in production areas.

II. Current Medical Research Program.

A. To permit continuity, it is recommended the current program be continued during 1947-1948. The current program is reviewed by topics under the following list of the participating organizations:

Argonne National Laboratory
University of Rochester
University of California at Berkeley

[redacted]

Columbia University
University of Washington
Monsanto Chemical Co. (Clinton Lab) USPHS
Monsanto Chemical Co. (Dayton)
Los Alamos
Western Reserve University
University of California at Los Angeles
University of Tennessee
University of Virginia

Brookhaven and other future laboratories are not included.

B. Future expansion of the medical and biological research program on a long term contract basis (5 years or more) is necessary in order to secure information of a more fundamental character which is necessary in order to cope with the special hazards of atomic energy development. Also it is imperative to open new fields of application for the products of atomic energy in biology and medicine. The Committee feels that such expansion can best be planned and put into effect after the establishment of a Medical-Biological Division. (See Appendix A). After the Regional Laboratories are well organized, the obvious usefulness of isotopes in a wide application to biological research will offer so many tremendous opportunities that developments in this field are assured.

C. Specific Projects: (in brief, topical outline)

1. Argonne National Laboratory - Dr. Austin M. Brues, Director.

a. The physiological picture of animals exposed to acute and chronic irradiation.

b. The effects of irradiation on the structure and functions of the blood and on the hematological defenses against infection.

c. The acute toxic effects of external radiation and absorbed radioactive substances: their mechanism of injury; prevention of possible damage and treatment of already injured individuals.

d. The abnormal responses of blood cells, cultured tissue cells and single celled organisms to various types of radiation.

e. The chronic effects of radiation and radioactive materials in animals.

f. The mode of action of radiation in the production of cancer.

g. The response to different types of radiation of the various organs and tissues, including tumors.

h. Studies on the chemical effects of radiation which are fundamental to its biological response.

[redacted]

[redacted]

i. The absorption, deposition and elimination of radioactive elements from the body.

j. The design and standardization of instruments to carry out the foregoing.

2. University of Rochester - Dr. Andrew H. Dowdy, Director.

a. Radiation and Radiology Section:

(1) Instrument design, measurement standardization, industrial monitoring.

(2) Biological effect of tracer amounts of polonium, radium and uranium in human and animal subjects. Application of tracer experiments to serve other parts of the project.

(3) Physiological effects of exposure to acute and chronic radiation including the radio-isotopes; search for therapeutic methods of value.

(4) Development of possible chemical techniques or methods of detection of radiation damage, and the mechanism by which such effects are produced.

(5) By means of spectroscopic methods, to study the distribution of uranium and other heavy metals of importance in animal tissue; a search for possible clues as to the method of bony deposition of radioactive materials.

(6) Study of the time intensity factor in radiation, and development of methods of producing instantaneous exposure to radiation (A bomb effect).

(7) Study of the metabolism of plutonium, polonium, radium, etc., in human subjects.

b. Pharmacology:

(1) Study of the inhalation toxicity of various uranium, beryllium and thorium compounds. Studies in the mechanism of production of inhalation toxicity.

(2) By chemical techniques, studies of the mechanism of uranium fixation in bones, uranium complex formation, methods of excretion of uranium.

(3) Acute toxicity effects of uranium, beryllium and thorium compounds by ingestion.

(4) Pathological effects of uranium, beryllium and thorium poisoning, and mechanism by which produced.

(5) Physiological effects of uranium, beryllium and thorium poisoning.

(6) Special toxicity studies.

(7) Certification of respiratory protective devices.

c. Experimental Surgery.

(1) Clinical, hematological and pathological effects of acute lethal radiation.

(2) Methods of bone marrow transplantation.

(3) Studies in bone marrow reserve and radiation effect.

(4) Tissue culture studies related to bone marrow production.

(5) Effect of folic acid and rutin on marrow regeneration.

(6) Studies of metabolism of iodine by thyroid.

d. Experimental Hematology.

(1) Comparative study of blood histamine after radiation and hematological effects in cells.

(2) Studies of life cycle of blood platelets.

(3) Studies on life cycle of leukocytes.

(4) Studies on marrow reserves after radiation.

(5) Evaluation of coagulation defects following irradiation.

(6) Techniques for early detection of hematological changes resulting from ionizing radiation.

e. Genetics.

(1) Continuation of studies of effect of chronic radiation on mice.

(2) Continuation of studies on effect of acute and chronic radiation (x-ray) on D rosophilia.

(3) Histogenetics.

f. Training personnel in all above sections.

3. University of California at Berkeley.

a. Dr. Joseph Hamilton's program.

(1) Metabolism of fission products, radium, actinium, protoactinium, uranium, neptunium, plutonium, americium and curium in animals and man.

(2) Metabolism of possibly hazardous artificially induced radioactive elements from plant construction materials such as chromium, nickel, etc.

(3) Metabolism of beryllium.

(4) Development of methods of treatment of poisoning from fissionable elements, notably plutonium and uranium 233 and from the long lived fission products.

(5) Behaviour of fission products and fissionable elements in soils and plants.

(6) Study of alpha particle irradiation and the thyroid gland in animals and man by Asticine (Element 85).

(7) Development of methods for decontamination of radioactive ships from Operation Crossroads.

(8) The execution of certain radio chemical analyses for Operation Crossroads and training of Army and Navy personnel.

(9) A study of the metabolism of elements chemically similar to the fissionable elements and the fission products.

b. Dr. John H. Lawrence's program.

(1) Biological effects of fission products.

(2) A search for uranium compounds that will localize in organs other than the liver and spleen.

(3) Biological effects of the disintegration products of boron and lithium following neutron irradiation.

(4) Genetics of the carcinogenic effect of beta rays.

(5) Physiological chemistry of the biological action of radiations.

(6) Changes in water balance following radiation injury.

the Columbia River and the possible contamination of sea water (including Bikini). The work under this contract involves studies of the following nature:

(1) Acute and chronic effects of external radiation on fishes.

(2) Breeding studies on salmon and trout following irradiation.

(3) Studies of the effects of the Hanford effluent on salmon and trout.

(4) Effects of internally deposited radioactive materials on aquatic organisms.

(5) Field studies on the effect of possible Hanford pollution on aquatic life in the Columbia River.

(6) Studies on the transfer of radioactive materials in "food chains", starting with the simpler biological forms (i.e. plankton) and following the distribution and fate of such materials as these contaminated animalcules are successively eaten and metabolized by higher forms (fishes, etc.).

(7) Feeding experiments using radioactive materials in the foods.

6. Hanford Engineer Works (Research Project) - Dr. Simeon T. Cantril, Director.

a. Health physics research and development in radiation monitoring, instrumentation.

b. Training of technicians and other personnel in problems of radiation protection.

c. Applied biologic research relative to phases of radiation hazard peculiar to Hanford Engineer Works operations and waste disposal:

(1) Soil, water and air contamination by radioactive materials

(2) Studies under controlled conditions of the effects of radioactive materials on domestic animals.

(3) Studies under controlled conditions of the effects of radioactive materials on vegetation.

(4) Fish Studies: (In collaboration with University of Washington, project listed previously.)

(a) Effects of waste effluent on salmon and trout.

(b) Effects of internally deposited radioactive materials.

(c) Field studies on possible pollution of Columbia River and fish by Hanford waste.

(d) Plankton experiments - absorption studies.

7. Monsanto and U. S. Public Health Service, Clinton Laboratories - Dr. Alexander Hollander, Director.

a. Studies of the biological effects of slow and fast neutrons, beta and gamma radiation are in progress as a follow-up of previously reported work.

b. Effects of plutonium on bone healing is being studied.

c. The parabiotic twin technique is being used to study the indirect effects of radiation.

d. A concentrated attack is being made on radiation effects on the rate of mitosis, chromosome breaks and exchanges, gene mutations and the general genetical makeup of the cell, including cytoplasmic factors.

e. Tracer experiments of a number of metabolic systems have been initiated using various micro-organisms.

f. Effects of radiation on cell constituents, proteins, nucleic acids and enzymes are being studied by modern physical-chemical tools, (including isotopes.)

g. Radiation effects are being investigated on blood constituents and blood forming organs as well as on the nervous system.

h. Cooperative research arrangements are being made with the Universities of Tennessee, Vanderbilt University, Washington University, University of Pennsylvania, John Hopkins University and Carnegie Institution.

i. Close cooperation with the National Institute of Health and the National Cancer Institute has been set up.

j. Instrumentation of radiation monitoring developed by health physics will be continued.

k. Health physics research is to be extended.

l. A training program.

8. Monsanto Chemical Co. (Dayton) - Dr. James Svirbely, Director.

a. Biological effects of chronic and acute exposures to polonium and polonium compounds by various modes of administration to determine the maximum permissible levels for human exposure. Tracer experiments may be indicated for clinical investigation. Mechanism of action, correlation of excretion levels with visceral content and genetic effects will be studied.

b. Maximum permissible levels for alpha radiation in individual viscera, especially the kidney. This is a specific phase of the first problem.

c. Study of maximum permissible levels for polonium to use in safe waste disposal.

d. Correlation of excretion levels and exposure in production personnel.

e. Study of prophylaxis and therapy of the toxic effects of polonium.

f. Biologic effects and methods of measurement for protection against radiation from special neutron sources prepared at Dayton.

g. Development of continuous monitoring equipment and other types.

h. Studies of the prevention of contamination and on decontamination.

9. Western Reserve University - Dr. Hymer L. Friedell, Director.

a. Studies on toxicity of thorium.

(1) Biological effects.

(a) Study of biological effects of soluble thorium compounds, lethal effects, weight changes, histopathologic, hematologic and biochemical changes.

(b) Study of biological effects of insoluble thorium compounds as in a(1) above, but also includes radiation effects.

(2) Distribution studies.

(a) Study of thorium distribution in tissues by chemical assay.

(b) Study of distribution by tracer technique.

(3) Biochemical studies.

(a) Transport of thorium across gastro-intestinal and respiratory epithelium.

(b) Mode of transfer of thorium in blood and tissues.

(c) Manner and characteristics of thorium deposition in tissue.

(d) Review of enzyme systems affected and enzyme inhibition.

b. Study of radiation effects of internally distributed radioactive elements.

(1) "Summation" studies of several radioactive elements of widely varying specific ionization.

(a) Study of beta emitters lodging in specific tissues (bone, kidney, thyroid, etc.).

(b) Study of alpha emitters lodging in specific tissues (bone, kidney, thyroid, etc.).

(c) Comparison and summation of alpha and beta emitters having approximately similar deposition in tissue.

c. Synthesis of compounds into which radioactive elements may be introduced.

(1) Comparison of radiation effects of various beta emitters alternately introduced into the same compound.

(2) Comparison of radiation effects of beta and alpha emitters (wide divergence of specific ionization) alternately and concomitantly introduced into the body.

d. Study of the distribution of the above noted radioactive compounds.

(1) By assay of radioactivity in tissues.

(2) By radioautographs of tissues and similar suitable means.

10. Los Alamos - Dr. Louis Hempelmann, Director.

a. Plant hazard research.

(1) Development of method for the determination of minute amounts of plutonium in the excreta and body tissues of humans and animals.

(2) Determination of the fraction of injected plutonium excreted per day by humans and animals. (In collaboration with the University of Rochester).

(3) Metabolism of plutonium in animals.

(4) Hematological studies in laboratory personnel exposed chronically to small repeated doses of radiation and radioactive material and accidentally exposed to large doses of radiation.

(5) Development of instruments to measure radiation.

(6) Development of safe techniques for plant operation.

(7) Clinical studies on acute radiation disease.

b. Proposed fundamental and applied research program.

(1) The fundamental studies on the acute effects of radiation.

(2) Treatment of acute radiation disease.

(3) Methods of detecting early radiation injury.

(4) Continued studies of the metabolism of plutonium, U-235 and other radioactive materials.

(5) Detection of accumulated plutonium in the lungs.

(6) Biochemical studies of nucleoprotein and the effect of radiation of the fundamental physiology of the cell. (In collaboration with Washington University, St. Louis, Mo.).

(7) Detailed study of absorption of plutonium from contaminated surfaces and wounds.

(8) Any special problems arising from new operating hazards on this project.

11. University of California at Los Angeles - Dr. Stafford L. Warren, Director.

a. The mechanism of blood vessel injury by radiation.

b. Bone marrow injury by radiation, its repair and treatment.

c. Mechanism of "metal" deposition in bone and mechanism of removal from bone.

d. Protein degradation following radiation and chemical injury.

12. Contracts approved by the Interim Medical Committee and awaiting U. S. Atomic Energy Commission approval:

a. University of Virginia - Dr. Alfred Chanutin, Director.

(1) Study of the effects of various types of radiation (alpha, beta, gamma and neutrons) on the circulating blood proteins by electrophorosis and protein fractionization technique. To determine whether means of early detection of radiation damage can be accomplished in this way.

b. University of Tennessee - Dr. Henry Wills, Director.

(1) Study of the mechanism of toxic effects of uranium and other heavy metal compounds on the kidney. This is a continuation of Dr. Wills' work with the Rochester Manhattan Project during the war and contributes to that general study.

D. Estimated total Health-Safety research budgets for fiscal year 1946-1947 and 1947-1948.

1.

Contractor	Fiscal Year 1946-1947	Fiscal Year 1947-1948	Probable Local Budget
Los Alamos	$ 100,000.	$ 200,000.	$ 500,000.
Univ of Rochester	1,200,000.	1,300,000.	1,800,000.
UofC at Berkeley			
Program II 3a	100,000.	125,000.)	
II 3b	115,000.	200,000.)	400,000.
II 3c	20,000.	35,000.)	
Clinton Lab	180,000.	500,000.	500,000.
Monsanto (Dayton)	40,000.	225,000.	200,000.
Hanford	200,000.	500,000.	500,000.
Western Reserve	100,000.	155,000.	200,000.
U of Washington	28,000.	100,000.	150,000.
Columbia University	100,000.	100,000.	100,000.
Argonne	1,200,000.	1,400,000.	1,500,000.
~~Brookhaven~~		[illegible]	500,000.
~~U of Virginia~~	~~25,000.~~	~~50,000.~~	50,000.
~~U of Tennessee~~	~~16,000.~~	~~16,000.~~	16,000.
UofC at Los Angeles	100,000.	200,000.	200,000.
~~Western Regional~~		[illegible]	500,000.
Total Medical-Biological	$3,524,000.	$5,906,000.	$7,116,000.
Health-Physics	500,000.	1,000,000.	1,300,000.
Training	(?) 50,000.	5,000,000.	1,750,000.
Field Survey & Service Research	(?) 3,000,000.	2,000,000.	3,000,000.
Estimated Grand Total	$7,074,000.	$13,906,000.	$13,166,000.

Note: See D2 for estimated totals of Regional Laboratories including budgets for research in the participating universities. Only those currently active are shown.

[redacted]

2. Eventual Health-Safety research budgets, 1949-50. Estimated annual budget for research. Does not include monitoring or clinical services which are charged to operating budgets. Each Regional Laboratory budget represents the totals of the local research and those of the participating universities.

Regional Laboratory	Training	Biological-Medical	Health-Physics	Field Survey and Service Research
Argonne	$500,000.	$4,000,000.	$ 250,000.	$ 100,000.
Brookhaven	500,000.	4,000,000.	250,000.	1,425,000.
Clinton Lab	250,000.	1,000,000.	250,000.	200,000.
Hanford	100,000.	1,000,000.	100,000.	50,000.
Los Alamos	200,000.	750,000.	250,000.	25,000.
Western	200,000.	1,000,000.	200,000.	100,000.
Total	$1,750,000.	$11,750,000.	$1,300,000.	$2,000,000.
Grand Total				$16,800,000.

This total should be equivalent to approximately 20-25% of the total research effort of the U. S. Atomic Energy Commission.

3. Example of estimated Medical Research Budget for a Regional Laboratory. 1949-50.

Brookhaven	Training	Medical-Biological	Health-Physics	Field Survey and Services
Local	$ 100,000.	$1,000,000.	$ 50,000.	$ 50,000.
Rochester	175,000.	900,000.	25,000.	700,000.
Columbia	25,000.	200,000.	25,000.	50,000.
Cornell	25,000.	200,000.		
Harvard	50,000.	200,000.	25,000.	
Yale	25,000.	200,000.		
M.I.T.	50,000.	200,000.	50,000.	50,000.
Princeton	25,000.	50,000.		
Brown		50,000.		*
Others	25,000.	1,000,000.	25,000.	500,000.
Total	$ 500,000.	$4,000,000.	$ 200,000.	$1,425,000**

*May be directed into new or above affiliated group as need arises for investigation of certain problems.

**This total is large because this area carries the major industrial and production activities.

III. Health-Physics.

A. Health-Physics is the name applied to a newly developed and highly specialized branch of Radiology. The principal function of Health-Physics has been to make a study of radiation problems and to devise means of preventing radiation damage. The records obtained by this group are of medico-legal importance. The manpower shortage in this field is acute.

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In general there are two principal sections in each health-physics division:

1. Research and development in instrumentation and energy levels.

2. Service under operating conditions in the plant.

B. The duties of the service section of health-physics are:

1. Personnel monitoring the measurement and recording of the daily radiation dosage received by each person.

2. Instrument service.

a. The calibration and maintainance of the varied and numerous instruments employed.

3. Building surveys. A daily measurement and recording of working areas.

4. Off-area surveys. An approved monitoring of the radiation level in the air and water discharged from the plants so that it presents no hazard to neighboring communities. The cost of the service sections of health-physics should be borne by each plant as an operating cost. Only the costs of the research and development sections are indicated in Section II D1 and 2.

C. The problems of the research and development sections of the health-physics divisions have been quite varied and perhaps can be indicated best by the following list which presents a few typical examples:

1. Instrument development.

a. Personnel monitoring instruments such as pocket meters and film badges have been developed but still need improvement.

b. Many problems were encountered in the development and production of fairly suitable portable and fixed meters to measure the alpha, beta, gamma, thermal neutron and fast neutron exposures received by personnel under varying situations.

c. Survey meters of all types, especially electrostatic and electronic instruments were developed and produced. These need considerable improvement, particularly for alpha and neutron measurements.

2. Special measurement of energies to which personnel is exposed.

a. Relative to instruments:

[redacted]

[redacted]

(1) Test meters for energy dependence and saturation effects.

(2) Develop photographic film monitoring techniques.

(3) Develop an instrument to measure fast neutrons in the presence of gamma rays.

(4) Devise methods of measuring plutonium in air in the presence of other alpha emitting substances.

(5) Develop continuous air monitoring instruments to measure alpha, beta and gamma radioactive gas and suspended dust in the air.

(6) Develop automatic hand counters, area radiation warning instruments, automatic water activity counters, etc.

b. Applied physics measurements.

(1) Develop remote control operations for working with radioisotopes.

(2) Make a study of various types of shielding, radiation shipping containers, etc.

(3) Develop methods of determining the amount of plutonium, polonium, uranium, etc., that are fixed in the body.

(4) Develop methods of estimating excessive radiation exposures from the amount of radioactive sodium and potassium in the blood.

(5) Measure the efficiency of masks, respirators, gloves, and clothing in preventing body radiation exposure.

(6) Develop and operate methods of decontamination.

(7) Study new methods of radioactive waste disposal.

(8) Help in the design of new buildings to minimize radiation exposure.

c. Physics research.

(1) Carry out "sky-shine" experiments.

(2) Study effects of high energy radiation on tissue.

(3) Study radiation scattering in shields and in tissue.

(4) Determine value of n/r, etc.

[redacted]

d. Theoretical.

(1) Make numerous tolerance calculations to determine radiation hazards presented by external and internal exposure.

(2) Calculate radiation from extended sources.

(3) Set up radiation protection tables, rules, regulations, etc.

e. Educational program.

(1) Train health physicists for other atomic energy sites, for those universities and laboratories that have radiation problems, as well as for the Army and Navy.

(2) Consult with numerous individuals and committees on radiation problems.

(3) Help outside organizations to check their laboratories and operations for radiation hazards.

(4) Train chemists, physicists, etc, who are not health physicists but who need a proper respect for radiation problems.

(5) Operate health-physics training programs. This is urgently needed. None are available now.

D. The table in Section II D1 and 2 gives an indication of the present and future total manpower and total expenditures of health-physics. Past annual costs have been quite large but are not available.

IV. Training program.

A. One of the most serious difficulties impeding the immediate progress of the general program designed to safeguard civilian and industrial personnel against the deleterious effects of the products of nuclear energy and the promotion of the beneficial utilization of such products is the lack of a sufficient number of well-trained personnel. Such a situation has arisen from the combination of a hiatus in basic science training during the war and the uniqueness of the problems confronting the Atomic Energy Commission.

It is recommended that an extensive training program be sponsored by the Atomic Energy Commission to facilitate the training of suitable personnel in the various branches of atomic energy. As a result of the crowding of the universities, some building program will probably be necessary. Such a program should embody the following objectives:

1. To increase the usefulness of present project personnel, academic seminars should be instituted and in certain instances, attendance of courses in the basic sciences of physiology, histology, biology, physics, bio-physics, chemistry, etc, should be required as a part of their regular scheduled duties.

[redacted]

2. To acquaint trained project and non-project personnel with new or special techniques relating to present and future programs of the Atomic Energy Commission. Average time one month.

3. To train a backlog of technical and professional personnel in the medical, biological, industrial hygiene and health-physics aspects of atomic energy.

The objective would be to accept well qualified doctors of philosophy, physicians and technicians for a training period of not less than one year in the special branches of bio-physics, biology, isotope techniques, toxicology, health-physics, related industrial hygiene and the various technical procedures pertaining to the enumerated subjects.

In order to provide an additional backlog of trained personnel for the future and to promote cordial public relations, facilities and fellowships should be established to encourage suitable post graduate candidates to elect major subjects for their degrees in those fields pertaining to atomic energy. This aspect of the program envisions a training period of one to four years, depending upon the prior qualifications of the candidate.

B. It is recommended that a committee be appointed by the Atomic Energy Commission for the development of an integrated training program for the education of scientific workers in the correlation of atomic energy with the national sciences, biology and medicine.

V. Recommendations on Organization.

A. Administrative creation of a new division of Health-Safety.

1. The responsibility for the health and safety of personnel employed by the Atomic Energy Commission in the conduct of their program extends throughout the entire program. Many of the hazards are not well understood. Frequently new research findings or new production procedures bring to light entirely new problems with unknown hazards and unpredictable safeguards.

2. Careful health and safety planning is necessary in anticipation of predicted hazards. Such planning must be in step with the plans of the four statutory divisions of the Atomic Energy Commission. Biological experimental work is slow, difficult and time consuming. Anticipatory planning and conduct of large scale biological work is mandatory so that results may be available as soon as possible before any exposure of personnel occurs. Thus a large effort, equivalent to perhaps 20-25% of the total research appropriation should be put into a health-safety program.

B. Health-Safety Advisory Board.

1. It is recommended that a Health-Safety Advisory Committee be formed by administrative action consisting of nine members, three to be

[redacted]

[redacted]

appointed for two years, three to be appointed for four years and three to be appointed for six years. This Committee should parallel the statutory General Advisory Committee to the Atomic Energy Committee and should be appointed by the Atomic Energy Committee to advise it in matters relating to medical, biological, industrial hygiene, health-physics and related research problems. It is further recommended that the Health-Safety Advisory Committee recommend the appointment of appropriate advisory sub-committees.

2. The following list of fourteen names is recommended for consideration in making the appointments on the Health-Safety Advisory Board to the Atomic Energy Commission:

a. Medical:

Dr. Joseph Aub, M.D. - Harvard (Consultant to Manhattan)
Dr. Hymer L. Friedell, M.D. - Western Reserve University (Manhattan)
Dr. Robert S. Stone, M.D. - University of California at Berkeley (Manhattan)
Dr. Stafford L. Warren, M.D. - University of California at Los Angeles (Manhattan)

b. Biological:

Dr. Austin M. Brues - Argonne Nat'l. Laboratory
Dr. Joseph G. Hamilton, M.D. - University of California at Berkeley
Dr. M. H. Jacobs, Ph.D. - University of Penn. (non-Manhattan)
Dr. Hans Muller, Ph.D. - Indiana University (non-Manhattan)

c. Industrial:

Dr. Simeon T. Cantril, M.D. - Hanford (Manhattan)
Dr. Andrew H. Dowdy, M.D. - University of Rochester (Manhattan)
Dr. James Sterner, M.D. - Eastman Kodak Co. (Manhatten)

d. Health Physics:

Dr. G. Failla, Ph.D. - Columbia University
Dr. K. Z. Morgan, Ph.D. - Clinton Laboratory
Dr. H. M. Parker, Ph.D. - Hanford

Note: In this Committee, there is no representative from Los Alamos (Dr. Louis Hempelmann); Brookhaven (unappointed); U.S.P.H.S. (Dr. E. Williams); Army (Colonel James P. Cooney) Navy (Captain George Lyon) nor the small university contractors (no recommendation).

C. It is recommended that a Division of Health Safety be created by administrative action and that its responsibilities and authority be on a par with the four statutory Divisions of Production, Research, Engineering and Military Applications.

[redacted]

The interim period has placed a severe strain on the current health safety program as a result of personnel losses and the critical nature of its function and responsibilities has suddenly increased with the reactivation of the Atomic Energy Commission Research Program.

D. It is recommended that the Director of the Division of Health-Safety be appointed as soon as possible and that he hold the degree of Doctor of Medicine and that if possible, he be familiar with some large portion of the Manhattan District medical program in order to stabilize the future of the current program.

The following list of suitable candidates have been selected and proposed in the order named by this Committee for consideration as the Director of Health-Safety. These men have had extensive executive experience with the Manhattan Project and are Doctors of Medicine except for Dr. Zirkle who was included in the secret balloting of the Committee, and because of his records, warrants consideration for this post.

Name	Age	Title	Background
Dowdy, Andrew H.	42	Prof of Radiology, U of R	Research in medicine, radiology and chemotherapy; cancer and radioisotopes. Clinicla training and teaching in Radiology. Director Rochester Manhattan Project.
Cantril, Simeon T.	40	Consultant in Radiology, Hanford Project. Radiology, private practice.	Clinical and research experience in radiology and cancer. Former medical director, Hanford Engineer Works.
Stone, Robert S.	51	Professor of Radiology, U of California	Clinical and teaching experience in radiology research with isotopes and cancer. Director of Health-Safety program, Metallurgical Project, Manhattan Dist.
Firth, John	(?)40	Principal Investigator, National Institute of Health Baltimore, Md.	Cancer research, clinical service, Clinton Laboratories.
Hamilton, Joseph G.	39	Ass't Professor of Medicine & Radiology, Univ of California.	Clinical and teaching experience, biological and medical applications of nuclear physics; radiochemist.

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Name	Age	Title	Background
Hempelmann, Louis	37	Medical Research Director, Los Alamos Project	Experience in research in biophysics and chemistry and large scale radiological safety at Alamogordo and Bikini.
Brues, Austin M.	40	Ass't. Professor Medicine, Univ. of Chicago	Research in cancer and shock and isotopes. Clinical and teaching training in Internal Med.
Sterner, James	42	Director, Industrial medicine Eastman Kodak Co.	Experimental and clinical problems in industrial hygiene and toxicology. Instructor in medicine, Medical Director for electromagnetic process at Oak Ridge.
Zirkle, Raymond E.	42	Director of Biophysics Institute Univ. of Chicago	Research in experimental biology, radiology and teaching.
Wolf, Bernard S.	35	Probable Medical Director, Brookhaven	Clinical experience in radiology and surgery. Board of Radiology member. Previously a member of Medical Section, Manhatten.
Brundage, Birchard M. (Major, AUS)	36	Chief, Medical Division, Manhattan Dist.	Clinical training and Industrial Medicine.

Other Doctors of Medicine of high caliber with executive experience who either work or are still associated with the Project, are listed in alphabetical order by the Chairmen for consideration. They all have considerable knowledge of the overall program:

Dr. John Ferry - Whiting, Indiana
Dr. Hymer Friedell - Western Reserve Univ., Cleveland
Dr. Joe Howland (Maj, AUS) University of Rochester
Dr. Leon Jacobson - University of Chicago
Dr. Adolph Kammer - Schenley Distributors, N. Y. C.
Dr. J. J. Nickson - Argonne National Laboratory
Dr. James Nolan - Geo. Washington Univ., St. Louis, Mo.
Dr. C. J. Watson - Minneapolis, Minnesota.

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The following are listed for consideration because of their knowledge of the field of radiology research and cancer, but have no knowledge of the project:

Dr. C. P. Rhoades, Memorial Hospital, New York City.
Dr. Shields Warren, Harvard University.
Dr. Robert Newall, Stanford University.
Dr. John H. Lawrence, University of California.

There are undoubtedly others.

E. The Interim Medical Committee was unable to finish its consideration of other committees within the two days of conferences. In view of the importance of making decisions promptly so that a working force may start in the near future, the Chairman has taken the option of interpreting the partially expressed intent of the Committee and offers the following organization and names for consideration by the Commission, Mr. Wilson and the new Director of Health-Safety as a stop-gap for the period until July 1, 1947. More mature consideration, in the meantime, by the Director of Health-Safety and the Medical Advisory Committee can make the proper realignments with the assistance of experienced advice from appropriate subcommittees formed from the membership of such bodies as the National Academy of Science, The Committee on Growth of the National Research Council, the United States Public Health Service, the various foundations and other appropriate agencies.

The following list of names is submitted for consideration. It was the intention of the Interim Committee to include as many institutions and as many fields of related endeavor as possible. There is no intention of rating the persons named and no attempt was made to segregate as to specialty or institution. It should also be understood that this list of 100 is by no means a complete coverage of the field but is a working nucleus.

Name	Location	Specialty
Dr. C. P. Rhoads	Memorial Hosp. (Cornell)	Cancer Research
Dr. Robert S. Newell	Stanford University	Radiology
Dr. Frank B. Jewett	Pres. Nat'l. Acad. Sc.	Physics
Dr. Wm. J. Robbins	NYC Botanical Gardens	Botany
Dr. Eugene P. Pendergrass	Univ. of Pa.	Radiology
Dr. Perrin Long	John Hopkins Univ.	Chemotherapy
Dr. Raymond E. Zirkle	Univ. of Chicago	Radiobiology
Dr. Paul Neal	Nat'l. Inst. Health, USPHS	Indus. Hygiene
Dr. Geo. P. Berry	Univ. of Rochester	Bacteriology
Dr. Paul Aebersold	Oak Ridge	Biophysics
Dr. Waldo Cohn	Clinton Lab.	Radiochemistry
Dr. H. L. Friedell	Western Reserve	Radiology
Dr. Louis Hempelmann	Los Alamos	Radiobiology
Dr. Wm. F. Bale	Univ. of Rochester	Biophysics
Dr. J. G. Hamilton	Univ. of California	Radiobiology
Dr. Andrew H. Dowdy	Univ. of Rochester	Radiology
Dr. G. Failla	Columbia University	Biophysics
Dr. Paul Hahn	Vanderbilt University	Physiology
Dr. J. C. Aub	Harvard	Indus. Medicine

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Name	Location	Specialty
Dr. James Nolan	Washington University	Obs and Gyn
Dr. K. S. Cole	Univ. of Chicago	Biophysics
Dr. R. S. Stone	Univ. of California	Radiology
Dr. A. M. Bruss	Univ. of Chicago	Medicine
Dr. David Rittenberg	Columbia University	Chemistry
Dr. E. W. Sinott	Yale University	Botany
Dr. Louis Flexner	Carnegie Institute	Anatomy
Dr. H. S. N. Greene	Yale University	Pathology
Dr. J. W. Fertig	Columbia University	Biostatistics
Dr. A. J. Riker	Wisconsin University	Botany
Dr. W. R. Earle	U.S.P.H.S.	Cytology
Dr. Sewall Wright	Chicago University	Zoology
Dr. Wright Langham	Los Alamos	Biophysics
Dr. A. P. Krueger	Univ. of California	Bacteriology
Dr. W. C. Rose	Univ. of Illinois	Biochemistry
Dr. Lauren Donaldson	Univ. of Washington	Zoology
Dr. L. Carmichael	Tufts University	Psychology
Dr. T. M. Rivers	Rockefeller Foundation	Virus Research
Dr. Kurt Stern	Univ of Rochester	Genetics
Dr. L. H. Snyder	Ohio State University	Genetics
Dr. E. W. Goodpasture	Vanderbilt University	Pathology
Dr. E. N. Harvey	Princeton University	Physiology
Dr. Wm S. McCann	Univ. of Rochester	Medicine
Dr. V. C. Twitty	Stanford University	Zoology
Dr. E. V. Cowdry	Barnard Free Skin & Cancer Hospital	Cytology
Dr. Francis O. Schmitt	M.I.T.	Zoology
Dr. D. B. Phemister	Univ. of Chicago	Surgery
Dr. Frank Fremont-Smith	Josiah-Macy Foundation	Psychiatry
Dr. Harold Hodge	Univ. of Rochester	Pharmacology
Dr. Gerhardt Dessauer	General Electric Co.	Biophysics
Dr. Karl Voegtlin	Nat'l Institute of Health	Toxicology
Dr. Wallace O. Fenn	Univ. of Rochester	Physiology
Dr. Phillip Drinker	Harvard University	Physiology
Dr. Howard Haggard	Yale University	Industrial Hygiene
Dr. Robert A. Kehoe	Univ. of Cincinnati	Industrial Medicine
Dr. James Sterner	Eastman Kodak Co.	Industrial Medicine
Dr. Donald D. Irish	Dow Chemical Co.	Industrial Toxicology
Dr. Geo H. Whipple	Univ. of Rochester	Pathology
Dr. H. T. Karsner	Western Reserve	Pathology
Dr. Shields Warren	Harvard University	Pathology
Dr. S. Bayne Jones	Yale University	Bacteriology
Dr. Peyton Rous	Rockefeller Institute	Cancer
Dr. M. C. Winternitz	Yale University	Pathology
Dr. Willard Allen	Washington University	Obs and Endrocrinology
Dr. M. B. Visscher	Univ. of Minnesota	Physiology
Dr. E. M. K. Geiling	Univ. of Chicago	Physiological Chem.
Dr. Andrew C. Ivy	Northwestern	Physiology
Dr. L. T. Fairhall	U.S.P.H.S.	Indus. Toxicology

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Name	Location	Specialty
Dr. Adolph Kammer	Schlenley Corp.	Indus. Medicine
Dr. H. H. Schrenk	U.S. Bureau of Mines	Toxicology
Dr. W. F. VonOettingen	U.S.P.H.S.	Toxicology
Dr. A. J. Lehman	U.S. Food & Drug	Indus. Toxicology
Dr. Alfred Blalock	Johns Hopkins	Surgery
Dr. J. J. Morton	Univ. of Rochester	Surgery
Dr. Conrad Elvehjem	Univ. of Wisconsin	Physiol. Chemistry
Dr. R. R. Sayers	U.S. Bureau of Mines	Indus. Toxicology
Dr. Alton Ochsner	Tulane University	Surgery
Dr. J. L. Bollman	Mayo Foundation	Physiology
Dr. H. W. Smith	New York University	Physiology
Dr. A. D. Welch	Western Reserve Univ.	Pharmacology
Dr. W. D. McNider	Univ. of No. Carolina	Pathology
Dr. S. C. Madden	Emory University	Pathology
Dr. J. S. Lawrence	Univ. of Rochester	Medicine
Dr. V. du Vigneaud	Cornell University	Biochemistry
Dr. Geo. W. Corner	Carnegie Institute	Anatomy
Dr. C. F. Kettering	General Motors Corp.	Research
Dr. J. W. Howland	Univ. of Rochester	Med. and Biophysics
Dr. Wm. Gehrman	DuPont Co.	Indus. Medicine
Dr. D. D. Van Slyke	Rockefeller Inst.	Biochemistry
Dr. L. A. Maynard	Cornell University	Biochemistry
Dr. Wm. A. Noyes	Univ. of Rochester	Chemistry
Dr. Joseph Treon	Univ. of Cincinnati	Indus. Toxicology
Dr. H. B. Van Dyke	Rutgers University	Pharmacology
Dr. H. S. Gasser	Rockefeller Institute	Physiology
Dr. F. A. Bryan	Univ. of Rochester	Indus. Medicine
Dr. Carl F. Cori	Washington University	Biochemistry
Dr. Charles G. King	Nutrition Found. Corp.	Nutrition
Dr. H. W. Beams	Univ. of Iowa	Zoology
Dr. Rene DuBos	Rockefeller Institute	Bacteriology
Dr. Anton Carlson	Univ. of Chicago	Physiology
Dr. George Beadle	Calif. Inst. Tech.	Biology

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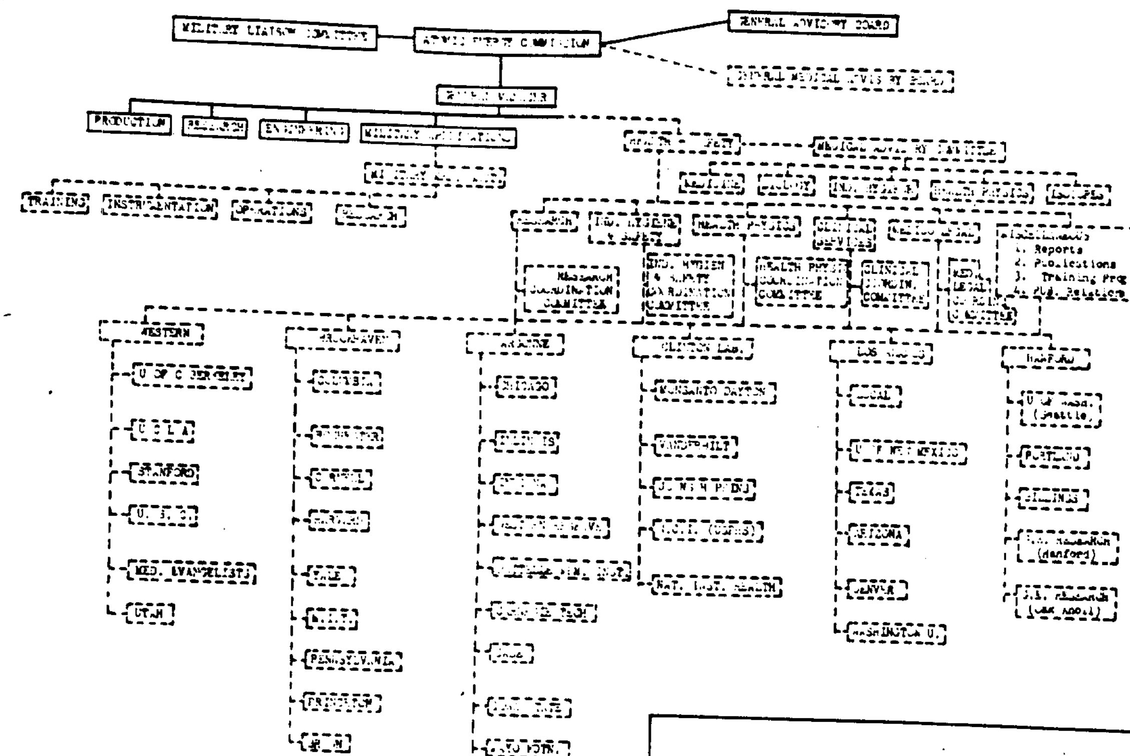

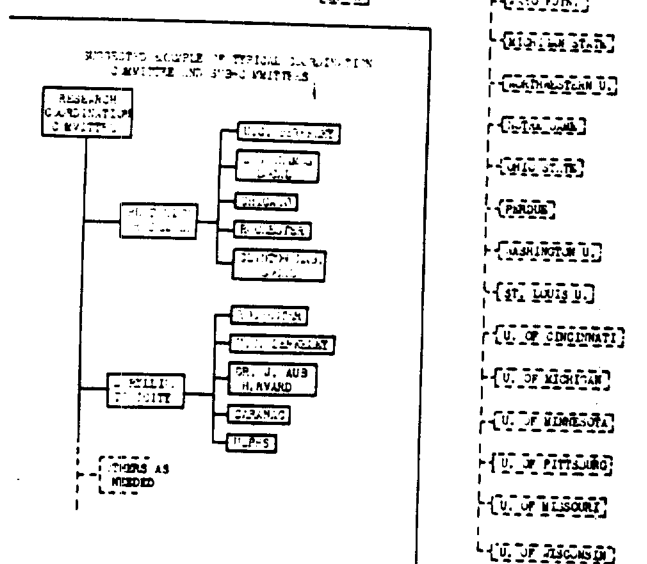

1. The suggested personnel for the General Medical Advisory Board appears on page 24 of the report of the 23-24 January 1947 meeting of the Interim Medical Committee of the United States Atomic Energy Commission.

2. The list of names suggested for the position of Director of the Division of Health-Safety appears on page 25 of the 23-24 January 1947 meeting of the Interim Medical Committee of the United States Atomic Energy Commission.

3. The suggested personnel for the Medical Advisory Committee and its sub-committees of Medicine, Biology, Industrial Hygiene, Health Physics and Isotopes are listed on pages 26 thru 27 of the 23-24 January 1947 meeting of the Interim Medical Committee of the United States Atomic Energy Commission.

4. It is suggested that the Military Medical Section under the division of Military Application have members representing all armed services.

5. The Coordination Committees shown under Research, Industrial Hygiene & Safety, Health Physics, Clinical Services and Medico-legal should each be composed of the 6 regional Directors or their authorized representatives plus 3 outside competent men. The personnel of the necessary sub-committees under each of these Coordination Committees should be proposed by the Coordination Committee as conditions warrant, and be representative of major topics under research for proper horizontal evaluation.

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APPENDIX A

AGENDA FOR MEDICAL COMMITTEE FOR ATOMIC RESEARCH

JANUARY 23, 24, 1947

I. Review and approval of past program. (Medical summary 1943-46 to be reviewed and approved if possible).

II. Scope of Research Program 1946-47. (Appendix A)

(University of Chicago) Argonne National Laboratories
University of Rochester
University of California
Hamilton
Stone
Columbia University
University of Washington, Seattle
Monsanto Chemical Corp. (Clinton Laboratories) USPHS
Monsanto Chemical Corporation (Dayton)
Los Alamos Western Reserve University

Contracts Awaiting Approval:

University of Virginia
University of Tennessee

III. Recommendations for Future Research Policy

A. Scope of fundamental work (that approved in September meeting) (Appendix A)
B. Human Testing with special materials

IV. Organization of Medical Responsibilities

A. Advisory Committees

1. Advisory Committee on Medical Research and application (Tolerances, Standards and Hazard Interpretations in addition to research programs).
2. Advisory Committee on Industrial Medicine and Toxicology.
3. Advisory Committee on Health Physics.

B. Recommendation for the continuation of operation of the Medical Division at the present level with the available reduced force now in that office as well as salary schedule.

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APPENDIX A (Cont'd.)

C. Training Program

1. Statement of the urgent need for qualified trained physicians.
2. Source of physicians.
   A.S.T.P.
   Civilian
3. Recommendations for specific training program.

V. Recommendations for Medical Director and Delineation of Responsibilities.

VI. Representation on Advisory Board to Atomic Energy Commission

VII. Release of Information

Recommendation for a mass meeting of all present and former Atomic Energy Commission medical researchers, at which time a program (4 days) would present accurate information on all medical aspects related to atomic energy then available for security clearance. This meeting would be open to scientific personnel in all parts of the country. The following suggestions are pertinent:

A. Approximately 6-8 months preparation would be required.
B. A central location should be selected to insure a maximum attendance.
C. Abstracts of the program should be circulated at least one month prior to the date of the meeting (similar to that procedure used by the Federated Societies of Physiology, Biochemistry, etc.) These abstracts should be approved by a previously selected editorial board before release.
D. Consideration should be given toward the founding of a new scientific society whose major interest would be based on problems of radiobiology as related to medical interest. The Journal of Radiobiology now being launched could well be made the official journal of this society.

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APPENDIX A (Cont'd.)

pes of study include I General Studies in Radiation including (1) physical asurement of radiation, (2) biological effects of radiation (3) methods of tection of minimal radiation damages and (4) methods for the prevention of diation injuries. II Hazards due to special Materials (for non-radioactive, dioactive and fission materials) (1) degree of toxicity (2) preventative asures. III Special Production Hazards and IV Hazards of Military Uses.

rgonne National Laboratories (University of Chicago)

1. General physiological picture of acute and chronic radiation.
2. Radiation effect on blood clotting, lymphocyte distribution and spread of infection.
3. Toxic effects of external radiation and absorbed radioactivity.
4. Response of blood cells to various types of radiation.
5. Chronic effects of radiation and radioactive materials in animals.
6. Mode of action of radiation in carcinogenesis.
7. Chemical and physiological basis of radiation effects.
8. Metabolism of radioactive elements.
9. Instrument standardization, design, etc.

niversity of Rochester

adiation and Radiology Section

1. Instrument design, measurement standardization, industrial monitoring.
2. Biological effect of tracer amounts of polonium, radium and uranium in human and animal subjects. Application of tracer experiments to serve other parts of the project.
3. Physiological effects of exposure to acute and chronic radiations including radio isotopes; search for therapeutic methods of value.
4. Development of possible chemical technique or methods of detection of radiation damage and the mechanism by which such effects are produced.
5. By means of spectroscopic methods to study distribution of uranium and other heavy metals of importance in animal tissue; search for possible clues as to the method of bony deposition of radioactive materials.
6. Study of the time intensity factor in radiation and development of methods of producing instantaneous exposure to radiation (A bomb effect).
7. Study of the metabolism of plutonium, polonium, radium, etc., in human subjects.

Pharmacology

1. Study of the inhalation toxicity of various uranium, beryllium and thorium compounds. Studies in the mechanism of production of inhalation toxicity.

APPENDIX A (Cont'd.)

2. By chemical technique, studies of the mechanism of uranium fixation in bones, uranium complex function, methods of excretion of uranium.
3. Toxicity of uranium, beryllium and thorium compounds by ingestion.
4. Pathological effects of uranium, beryllium and thorium poisoning and mechanism by which produced.
5. Physiological effects of uranium, beryllium and thorium poisoning.

<u>Experimental Surgery</u>

1. Clinical, hematological and pathological effects of acute lethal radiation.
2. Methods of bone marrow transplantation.
3. Studies in bone marrow reserve and radiation effect.
4. Tissue culture studies related to bone marrow production.
5. Effect of folic acid and rutin on marrow regeneration.
6. Studies in metabolism of iodine by thyroid (15%).

<u>Experimental Hematology</u>.

1. Comparative study of blood histamine and hematological effects in cells.
2. Studies on life cycle of blood platelets.
3. Studies on life cycle of WBC leukocytes.
4. Studies on marrow reserves after radiation.
5. Evaluation of coagulation defects following irradiation.
6. Techniques for early detection of hematological changes resulting from ionizing radiation.

<u>Genetics</u>

1. Continuation of studies of effect of chronic radiation on mice.
2. Continuation of studies on effect of acute and chronic radiation (X-ray) on Drosophilia.
3. Histogenetics.

<u>University of California</u>

1. Studies of the metabolism of plutonium, uranium and fission products in rats and men.
2. Fission product tracer studies.
3. Metabolism of radium, actinium, americium and curium in animals and men.
4. Studies (pilot) on possibly hazardous artificially induced radioactive elements, i.e. chromium, nickel, etc.
5. Beryllium tracer studies.
6. Treatment of plutonium poisoning.

APPENDIX A (Cont'd.)

7. Behavior of fission products in soils.
8. Biological effects of fission recoils.
9. Search for other U compounds which will localize in organs other than liver and spleen (15%).
10. Biological effect of disintegration products of boron and lithium of the neutron irradiation (15%).
11. Study of element 85 in the thyroid (15%).
12. Training of Crossroads personnel.
13. Studies in whole body radiation of human subjects.
14. Studies on metabolism of radioactive iodine in animals and man.

<u>Columbia University</u>

1. Studies on the measurement of fast neutrons for biological dosage.
2. Development of a method of measuring neutron dose by chemical means.
3. Measurement of radioactive isotopes for biological and medical application.
4. Correlation of tissue doses and biological effects produced by external irradiation and by radioactive isotopes internally administered.
5. Exploratory biological experiments to extend use of radio-active isotopes as tracers on therapeutic agents (15%).
6. Studies of the fundamental biological action of ionizing radiation.
7. Measurement of the radiation of radioactive isotopes to provide data for the protection of personnel and films in transit.

<u>University of Washington</u> (Seattle)

1. Acute and chronic effects of external radiation on fishes.
2. Breeding studies on salmon following radiation.
3. Studies on the effects of Hanford effluent on salmon and trout.
4. Effect of internally deposited radioactive materials on fishes.
5. Field studies on the effect of possible Hanford pollution on fish life of the Columbia River.
6. Plankton experiments - effect of radiation on higher forms (new).
7. Feeding experiment on deposited radioactive materials (new).

<u>Monsanto Chemical Corp</u>. (Clinton Laboratories) USPHS

1. Continuation of studies on the biological effect of slow fast and thermal neutrons on rats and mice.
2. Continuation on studies on the comparative biological effect of penetrating radiation.
3. The effect of internally deposited plutonium on bone healing.
4. Cytological program on the biological effect of radiation on simple cells and tissue.
5. Instrumentation and techniques of radiation monitoring.

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APPENDIX A (Cont'd.)

onsanto Chemical Co. (Dayton) New program being organized.

1. Biological effects following chronic exposure of animals to polonium by inhalation and parenteral administration.
2. Correlation between chronic exposure of workers and polonium excretion rate.
3. Mechanism of action of polonium toxicity.
4. Development of special health physics technique for specific use in polonium purification.

Los Alamos

1. Fundamental studies on the effect of acute radiation exposure.
2. Treatment of acute radiation disease.
3. Methods of detecting early radiation changes.
4. Metabolism of plutonium, U^{235} and other radioactive materials.
5. Detection of accumulated plutonium in the lungs.
6. Biochemical studies of nucleoproteins and the effect of radiation on the fundamental physiology of the cell.
7. Detailed study of absorption of plutonium from contaminated wounds.
8. Any special problems arising from medical hazards peculiar to this project.

Western Reserve University

1. Investigation of the toxic effects of thorium and its isotopes.
2. Comparative studies on the biological effect of external radiation and that from internally deposited radioactive materials.
3. Use of radioactive isotopes in fundamental biological research.

These general titles are given inasmuch as a program has not been actively formulated.

Contracts Awaiting Approval:

University of Virginia - Dr. Alfred Chanutin

Study of the effects of various types of radiation (alpha, beta, gamma & neutrons) on the circulating blood proteins by electrophorosis and protein fractionization technique. To determine whether means of early detection of radiation damage can be accomplished in this way.

University of Tennessee - Dr. Henry Wills

Study of the mechanism of toxic effects of uranium and other heavy metal compounds on the kidney. This is a continuation of Dr. Wills' work with the Rochester Manhattan Project during the war and contributes to that general study.

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APPENDIX A (Cont'd.)

University of California, Los Angeles - Dr. Stafford L. Warren

1. The mechanism of blood vessel injury by radiation.
2. Bone marrow injury by radiation, its repair and treatment.
3. Mechanism of "metal" deposition in bone and mechanism of removal from bone.
4. Protein degradation following radiation and chemical injury.

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APPENDIX A (Cont'd.)

I General Studies of Radiation

The radiations encountered in nuclear fission as well as those encountered from naturally radioactive substances divide themselves into the following types: Alpha rays, beta rays, gamma rays and neutrons. Information available from the literature on previous studies indicates a rather extensive knowledge of the biological effects of X-rays and gamma rays and very little information on alpha and beta rays and neutrons.

The programs were and are organized using the following basic outline:

A. The Physical Measurement of Radiation of various types - Here it is necessary to develop methods of accurately measuring and standardizing the dosage of radiation to be used in the biological experimentation and measurement of the extent of any hazardous radiation which might be found in a plant area.

B. The Biologic Effects of Radiation. Because of the known deleterious effect of radiation on the animal organism, it becomes necessary to determine the effect of controlled dosages of the various types of radiation on various animal species, so that such observations can be used in the control of possible human exposure.

The types of biological effect possible to study are:

(1) The Survival Time or percentage that the effect of a given dose will reduce the normal life span of different animal species.

(2) The Genetic Effects of radiation as manifested in the development of abnormal individual types from changes in the hereditary mechanism.

(3) Histopathological Changes as demonstrated by abnormal changes in the make-up of the various body tissues.

(4) Physiological Changes produced by the alteration of the normal functioning of animal tissues following radiation.

(5) Biochemical and Enzymatic disturbances which are the potential source of these physiological abnormalities.

APPENDIX A (Cont'd.)

C. Methods for the Detection of Minimal Radiation Damage are developed directly from observation of the above types and are applied to study of the human individual or worker. These include studies on:

(1) Biochemical and Enzymatic Changes which may be detected and which, if measurable, can be corrected before irreversible damage has taken place. Examples of such change would be effects on the metabolism of coproporphyrins, excretion of abnormal substances in the urine and the like.

(2) It has been known that radiation depresses the function of the hematopoetic system and detailed study is indicated to detect early changes under controlled dose radiation with all blood elements under continuous observation.

(3) The Production of Anatomical Changes such as epilation, skin erythema, and alterations in the integrity of the skin and the like must likewise be studied under controlled dosage.

D. Studies are likewise indicated on methods for the prevention of radiation injuries. These include:

(1) Methods of physical detection of external radiation by the development of sensitive direct reading instruments capable of the detection of amounts of radiation well below those necessary for demonstrable injury to the animal subjects.

(2) Methods for the determination of harmful amounts of radioactive dusts and gases in air, in water and the like. Many radioactive materials like radium are deposited in the body and in such locations produce injury to tissue. Methods based on the determination of dangerous amounts of these substances by examination of the excreta and direct measurements of the body itself are necessary.

E. Protective Measures. Studies on the efficiency of shielding against radioactive materials, the efficiency of exhaust and ventilating systems against dangerous amounts of dusts, the development of protective clothing and devices, and the development of remote control processing methods have been extremely important in the Manhattan District protection program to date and will continue into the future.

F. The possible therapeusis of radiation damage by the use of replacement therapy for the damaged bodily elements, as well as the reduction in the exposure following deposition of radioactive materials in the body deserves considerable study. Replacement of the damaged hematopoetic elements destroyed by severe radiation exposure offers one possibility; detection and neutralization of unknown toxic substances produced by radiation and other such difficult problems deserve consistent and detailed study.

~~S E C R E T~~

APPENDIX A (Cont'd.)

All the above studies are necessary on alpha, beta and gamma rays and neutrons of varying intensity. In addition, the radiation from the radioactive substances to be discussed has likewise to be considered. Also, the effects of acute and chronic exposure must be determined because of their dissimilarity.

II Hazards Due to Special Materials

For brevity it is preferable to discuss the potential toxicity of special materials by first indicating the type of study to be carried out, followed by the presentation of these materials on which studies have been necessary.

A. First, an actual determination of the toxicity of a substance must be made indicating how poisonous it may be in both acute and chronic exposure. In this way the toxic levels may be avoided in laboratory and plant environments.

(1) The mode of entrance into the body by ingestion, inhalation and skin absorption must be studied as different manifestations and degrees of toxicity may be produced by each route employed.

(2) A careful analysis must be made as to the character of the biological changes with the production of physiological, histopathological and biochemical evidences of damage incurred.

(3) The nature of these injuries and the mechanism by which they occur must likewise be studied inasmuch as this affords information as to the necessary protection and indicated therapy after exposure.

B. Preventative measures require study.

(1) The effectiveness of physical methods for the removal of hazardous dusts, reduction in skin contact and prevention of ingestion must be measured, and methods for accurate determination of such hazards must be developed and used. The use of certain chemicals, ointments, and the like as protective measures must be studied as to their efficiency.

(2) Protective devices such as respirators and clothing must be tested on required substances against which they will be used.

(3) Finally, appropriate investigation of therapeutic measures to be used in the treatment of both acute and chronic poisoning states should they occur in industrial exposure must be made.

Completion of all phases of the above program on a variety of substances provides complete information as to the medical aspects necessary to be considered in protection of the worker, prevention of injury and treatment of injury should it occur.

APPENDIX A (Cont'd.)

C. Substances on which studies of this type are necessary are:

(1) Uranium and its compounds

a. Uranium metal and its chemical compounds, oxide, nitrate, chloride, bromide, tetra and hexa-fluoride, sodium and ammonium sulfates.

b. Uranium chain of heavy metals

Uranium X1
Uranium X2
Radium
Polonium

c. Fission products of cleavage of U-235 and plutonium.

d. Artificial isotopes of uranium - 232, 234, etc.

(2) Thorium and its chain

(3) Plutonium

(4) Special Accessory Materials

a. Fluorocarbons
b. Fluorine
c. Beryllium
d. Others

III Production Hazards

The results of studies made on the materials discussed above are applied for the prevention and control of industrial hazards arising in the large manufacturing areas where these materials are used in large amounts.

A. In the Electromagnetic and Diffusion Methods for the isolation of uranium 235 the major hazards are from the uranium compounds, the concentration of uranium X1 and X2, and the special accessory materials and by-products formed in the process of manufacture.

B. In the graphite pile where plutonium (239) is produced on a large scale, the hazards are from the alpha, beta and gamma rays, neutrons, the plutonium metal and its compounds, the various radioactive fission products resulting from the pile operation.

C. The chemical isolation of polonium following its formation in the pile incorporates hazards from alpha radiation following absorption into the body.

APPENDIX A (Cont'd.)

D. Study of the medical aspects of plant programs aside from the [...]ination of the effect of radiation and chemical toxicity, include ad[...]onal information obtained from plant investigations as from:

(1) Clinical survey of all exposed personnel.

(2) Monitoring of hazards by special instruments and methods.

(3) Surveys of new types of graphite piles and production equipment.

IV **Hazards of Atomic Catastrophe in Production Areas.**

A. **Immediate Effects**

(1) **Radiation** - the radiation occurring at the time of the explosion coupled with blast and heat causes biological effects which may differ from those occurring following other acute known effects from gamma and neutron radiation, and demand study.

(2) **Blast** - the blast of atomic explosion is so intense and may have totally different types of shock waves, recoil waves with other unique biological effects which should be investigated.

(3) **Heat** - The intense burns from actinic type of radiation have not been studied. This also includes the combination effect of all three items in this group: blast, radiation and heat.

(B) **Delayed Effects**

(1) **Protective Devices** - study of methods of protection against the radioactivity deposited at the time of blast.

(2) **Decontamination** - methods of decontamination of soil and the like must be worked out for cleaning up active areas.

(3) **Investigative Equipment** - special equipment must be developed and tested for use in investigating bombed areas.

(4) **Study of casualty effects** - field study of fission clouds, possible injury to water supply, soil and the like, human damage by population surveys.

APPENDIX A (Cont'd.)

(5) Study of treatment of all immediate effects such as radiation, heat and blast.

(6) Preparation of pertinent information in proper form for use by catastrophe units in production areas.