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REPOSITORY Oak Ridge Institute for Science and Education, Medical Sciences Division

COLLECTION California Committee of Human Studies

BOX No. _____

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Ident. No. ORNL-14

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date: 04/22/85

Principal Investigators: Charles S. Dudney, Ph.D.
Thomas G. Matthews, Ph.D.

Co-Investigators: William G. Dreibelbis, C.I.H
Alan R. Hawthorne, Ph.D.

Title of Project: Indoor Air Quality Study in 60 Houses in the Tennessee Valley

I. OBJECTIVES OF STUDY:

The Health and Safety Research Division of Oak Ridge National Laboratory will be conducting a study of indoor air quality in 60 houses in the Tennessee Valley under the sponsorship of several federal agencies.

There will be two major operational elements of this study. One will be the collection of data from all of the houses in the study and will emphasize use of relatively small, passive sampling devices that can be analyzed to yield information on time-weighted average levels of chemical or naturally occurring radioactive species in the homes. The other major element will be the collection of data in six of the 60 homes and will emphasize the use of more elaborate sampling devices for one-week intervals in the summer and winter quarters. The six-home subset will be limited to houses in the area surrounding Oak Ridge.

The objective of one aspect of the study, applicable to all of the houses and defined by the TVA-supported IAG (#40-1459-84) which funds the major part of this study, is to determine the mean and standard deviation of the levels of radon and radon progeny in 60 selected homes during a one-year interval. Exposure to the short-lived radioactive progeny of radon has been associated with increased incidence of lung cancer among various uranium-mining populations. Various products from the phosphate-mining operations in central Florida have been shown to emanate radon at rates

which are higher than normal background emanation rates. Between the mid-1930's and the mid-1970's the fertilizer research program at Muscle Shoals, AL, processed large quantities of Florida ore and sold some of the resulting slag to local concrete block manufacturers. Some of those blocks were sold to general contractors who incorporated the blocks into detached single-family dwellings with basements. Only basement homes made from blocks that are free of such phosphate slag will be included in this study in order to obtain an estimate of background levels in homes. Air exchange will be measured in all 60 houses.

The objectives of other aspects of the study include: (1) determination of time-weighted average levels of NO2 and formaldehyde in all 60 homes for one week in each of the four calendar quarters, (2) detailed time-dependent, multi-location measurements of particulate material, nitrogen oxides, formaldehyde, and air exchange rate in 6 local homes, and (3) analysis of occasional samples of room air for organic chemicals in selected homes. Indoor exposures to combustion-related species have been associated with respiratory illnesses in epidemiological studies and laboratory rats exposed to formaldehyde have exhibited elevated rates of nasal tumors. Indoor air quality has been shown to be a complex phenomenon that depends on many temporal and spatial factors, including air exchange rates, temperature, humidity, occupant behavior, consumer products, building materials, construction practices, and architectural style. Additional information on exposures from the indoor environment is required to adequately assess the impact of indoor air quality on human health.

II. METHODS:

A. All Houses

For the major element of the study that applies to all of the houses, the following experimental methods will be used:

1. Radon

Once each quarter track etch detectors will be placed in the houses. A track etch detector is about the size and mass of a paper cup. There is a filter across the opening to prevent the entry of particles on which most of the radon progeny reside. Inside is a plastic detector. Subsequent radioactive decays within the chamber give rise to tracks that are detected during analysis. The density of tracks is proportional to the time-weighted average radon concentration.

Once each quarter each home will be visited by a specially equipped van. Samples of the air will be analyzed by high resolution alpha spectroscopy to determine radon levels.

2. Radon Progeny

For one week each quarter a radon progeny integrating sampling unit, known as a MOD, will be installed and operated in each house. A MOD is a box about the size of a table radio and requires 60 Hz 120 VAC for operation. The device pumps air (~0.1L/min) through a filter behind which is a TLD chip to detect radioactive decay events. Since radon passes through the filter only decay events from progeny on particulate material are detected.

During visits by the specially equipped van, levels of the progeny will be measured using alpha spectroscopy.

3. Air Exchange

In each house, sources of perflourocarbon gases will be installed. Two different kinds of sources will be installed, with one kind on the upper level and another kind on the lower level. For one week each quarter, passive samplers will be installed in several locations in each house and subsequently analyzed to estimate time-weighted average air exchange rates. This method was developed by Dietz and Cote (1982) and has been extensively used to measure air exchange rates in homes.

4. Formaldehyde

For one week in the summer and winter quarters, commercially available passive monitors will be installed in each house. The monitors will be manufactured and analyzed by either Air Quality Research, DuPont or Crystal Diagnostics.

5. Nitrogen Dioxide

For two weeks each quarter, passive samplers will be installed in each house. The samplers consist of a plastic tube, open at one end with fibers impregnated with triethanolamine inside near the other end. Laboratory analysis of the fibers yields an estimate of time-weighted average levels of nitrogen dioxide. These samplers have been extensively used in homes (Palmes et al., 1977; Palmes et al., 1979).

6. House Characteristics

Photographs will be taken of the houses and the sampling locations. Information will be collected concerning house characteristics, including age, size, layout, insulation materials, and combustion sources.

B. Six-House Detailed Study

In six of the study houses, the following experimental methods will be used in addition to those previously listed:

1. Radon

Wrenn chambers may be used indoors to continuously monitor radon concentrations. This instrument provides hourly concentrations of radon in the room air.

2. Air Exchange.

Continuous measurements of the air infiltration rate will be performed using tracer gas decay measurements. Freon 12 will be injected into the indoor atmosphere; its decaying concentration will be monitored as a function of time with a Miran infrared absorption spectrometer. This instrument will be located outside the home in an instrumented van with an air sampling tube running indoors. The concentration of the tracer gas will be microprocessor controlled in a range of approximately 1-10 ppm. When the concentration reaches 1 ppm, the control unit will open a valve to a small tank of freon located inside the home. The valve will subsequently be closed as the Freon concentration approaches 10 ppm. Fans will be used during and after freon injection to mix the gas throughout the home.

3. Formaldehyde

Continuous formaldehyde vapor concentration measurements will be performed indoors using a CEA Instrument Inc. Analyzer. This instrument will be located in an instrumented van outside the home with an air sampling tube running indoors.

4. Nitrogen Oxides, Nitrogen Dioxide

Total nitrogen oxides and specifically nitrogen dioxide will be monitored continuously using a Monitor Labs, Inc., nitrogen oxides analyzer. This instrument will be located in an instrumented van outside of the home with an air sampling tube running indoors

5. Carbon Monoxide

A Interscan electrochemical analyzer will be used to perform continuous measurements of carbon monoxide indoors. This instrument will be located in an instrumented van outside of the home with an air sampling tube running indoors.

6. Carbon Dioxide

A Miran Infrared absoprtion spectrometer will be used to continuously monitor indoor concentrations of carbon dioxide. This instrument will be located in an instrumented van outside of the home with an air sampling tube running indoors.

7. Particulates

Particulates will be sampled and/or monitored with the following instrumentation located indoors: a California Measurements, Inc., ten stage cascade impactor, a GCA Corporation Miniram aerosol monitor, and a Harvard-developed air sampling unit.

8. Organic Vapors

Volatile organic vapors will be collected on solid sorbent (eg., Tenax) traps for subsequent laboratory analysis. Spot sampling will be performed with a Photovac portable gas chromatograph.

9. Air Face Velocity

The velocity with which air moves indoors will be continuously monitored using hot-wire anemometers located indoors.

III. POSSIBLE HAZARDS AND THEIR EVALUATION:

A. Chemicals introduced into the houses.

A variety of fluorine-containing compounds will be used for air exchange measurements. The names of these compounds, their associated TLVs, and information on toxic levels are:

Name	TLV	Toxicity
Dichlorodifluoromethane (Freon 12)	4,950 mg/m3	200,000 ppm/30 min TClo inhal/human
Perfluoromethylcyclohexane (PMCH)	NA	825 ppm/14 hr. TClo inhal/rat
Perfluorodimethylcyclohexane(PDCH)	NA	100 ppm/14 hr. TClo inhal/rat/guinea pig

Appendix A provides copies of the entries for these chemicals from the latest issue of the NIOSH Registry of Toxic Effects of Chemicals.

Under normal operation, the microprocessor-controlled, Freon injection system will limit Freon concentrations to approximately 10 ppm, which is one percent of the Occupational Safety and Health Administration threshold limit value (TLV) for eight hours of exposure to Freon. The air inside the homes would be mixed during and after Freon injection to prevent abnormally high concentrations from developing near the injection point. The source of Freon will be limited such that total system failure, in which all the Freon was released, would result in concentrations less than 3,000 mg/m^3 ($\sim$60% of TLV) for a very tight (i.e., zero air exchange) house having 750 square feet of floor space and 8 foot ceilings. For houses that are either larger or leakier the levels would be less.

In all 60 houses, the perfluorocarbons tracers will be released passively from pellets. The rate of release is less than 1 mg/day for each pellet and three pellets for each tracer will be used in each house. For a house having 750 square feet of floor space and 8-foot ceilings with an air exchange rate greater than 0.2 h^{-1} then the levels of PMCH and of PDCH would be less than 0.00123 mg/m^3 (less than 0.0001 ppm).

B. Electrical Hazards

All electrical power cords will be routinely inspected before each use for worn insulation or other evidence of excessive wear.

MODs will be installed for one week each quarter. These devices are fused to prevent overheating. They will be installed in a manner so that they are unlikely to be knocked over.

The instrumented van containing instruments and chemicals used for measurement in the six houses will be secured to prevent unauthorized entry. Overload protection for AC power to the trailer will be provided. Groundfault interruptors will prevent accidental grounding of AC power to the metal chassis of the van.

C. Trip Hazards

All cords and sampling lines passing through the living area will be taped in place to prevent tripping.

IV. RADIOISOTOPES AND NEW DRUGS

None will be used.

V. RESPONSIBILITY OF PRINCIPAL INVESTIGATORS

Volunteers will be sought for participation in this study. Prior to the initial visits to potential homes, a principal investigator or one of the co-investigators will discuss with the homeowner the nature, purpose, and extent of the study. These discussions will emphasize in lay terms the potential intrusions and hazards that will affect the home environment. Appendix B provides a copy of the draft homeowner's agreement that all potential participants must read and sign before even preliminary measurements for study qualification will be made.

Safety will be considered during the house selection process. For example, homes with young children will be excluded unless the homeowner feels certain that the children will not be left unattended with the sampling equipment and the investigators feel that the homeowner will responsibly oversee any resident children.

The principal investigators will follow the procedures of the Committee on Human Studies in obtaining "informed consent" from each of the subjects in the study. The investigators recognize that they retain the primary responsibility for safe-guarding the interests of the participants in the study. Any significant changes in the study protocols or the development of any unexpected risks will be brought to the attention of the Committee on Human Studies.

Starting Date: June 1, 1985

Signatures: Charles S. Dudney — Principal Investigator

Alan Hawthorne — Principal Investigator

William G. Dauchelle — Co-Investigator

Thomas G. Walters — Co-Investigator

DIVISION REVIEW:

The application described above has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Official signing for the institution:

Signature Stephen V. Kaye, Ph.D.

Title Division Director, Health & Safety Research Division

Institution Oak Ridge National Laboratory

Date April 17, 1985

APPENDIX A

REFERENCES

Ditez, R. N., and Cate, E. A.; Environmental International 8:419-33; 1982.

Palmes, E. D., Tomczyck, C., and March, A. W.; Atmospheric Environment 71:869-72; 1977.

Palmes, E. D., Tomczyck, C., and March, A. W.; J. Air Pollution Control Assoc. 29(4):392-3; 1979.

APPENDIX A

eye-rbt 17500 mg/m3/10M TXCYAC 6,173,76
TXDS: ihl-hmn TCLo:900 ppm 17-I TFX CNS ARHYAL 43,1123,68
ihl-hmn TCLo:300 ppm/8H TFX BLD SCIEAS 176,293,72
orl-rat LD50:167 mg/kg DCWSD* 1/26/76
ihl-rat LC50:80000 mg/m3/30M FAVUAI 7,35,75
ihl-rat TCLo:500 ppm 6H 2Y TFX LIA TXAPA9 48,A185,79
ihl-mus LC50:14400 ppm/2H NIIRBZ 191,1,49
ipr-mus LD50:1500 mg/kg TXAPA9 9,139,66
scu-mus LD50:6450 mg/kg TXAPA9 4,354,62
orl-dog LDLo:3000 mg/kg QJPPAL 7,205,34
ihl-dog LCLo:14100 ppm/7H NIIRBZ 191,1,49
ipr-dog LDLo:950 mg/kg TXAPA9 10,119,67
scu-dog LDLo:2700 mg/kg QJPPAL 7,205,34
ivn-dog LDLo:200 mg/kg QJPPAL 7,205,34
ihl-cat LCLo:43000 mg/m3/4.5H ANBAAM 116,331,36
orl-rbt LDLo:1500 mg/kg HBTXAC 1,94,56
scu-rbt LDLo:2700 mg/kg QJPPAL 7,205,34
ihl-gpg LCLo:5000 ppm/2H FLCRAP 1,197,67
AQTX: AQUATIC TOXICITY RATING: TLm96:1000-100 ppm WQCHM* 3,-,74
REVIEW: CARCINOGENIC DETERMINATION:INDEFINITE IARC** 20,449,79
REVIEW: THRESHOLD LIMIT VALUE-air:100 ppm DTLVS* 4,275,80
REVIEW: TOXICOLOGY REVIEW FAZMAE 18,365,74
REVIEW: TOXICOLOGY REVIEW 272TAP 3,94,A9
REGS: OSHA STANDARD-air:TWA 500 ppm;Ceil 1000,Pk 2000/5M/2H (SCP-J) FEREAC 39,23540,74
DOT-ORM-A, LABEL:NONE FEREAC 41,57018,76
CRIT DOC: OCCUPATIONAL EXPOSURE TO METHYLENE CHLORIDE recm std-air:TWA 75 ppm,Pk 500 ppm/15M NTIS**
STATUS: CURRENTLY TESTED BY NTP FOR CARCINOGENESIS BY STANDARD BIOASSAY PROTOCOL AS OF SEPT 1980
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 1 127, VOL 3 S329
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8100000 METHANE, DICHLOROBIS(METHYLSULFONYL)-
UPDT:8007 CAS: 2244-16-8 MW: 241.11 MOLFM: C3-H6-Cl2-O4-S2
SYN: BISMETHYLSULFONYLCHLOROMETHANE * DICHLOROBIS(METHYLSULFONYL)METHANE
TXDS: ivn-mus LD50:42 mg/kg CSLNX* NX#09537

PA8200000 METHANE, DICHLORODIFLUORO-
UPDT:8007 CAS: 75-71-8 MW: 120.91 MOLFM: C-Cl2-F2
SYN: ALGOFRENE TYPE 2 * F 12 * FC 12 * ARCTON 6 * DICHLORODIFLUOROMETHANE * DICHLORODIFLUOROMETHANE (DOT) * DIFLUORODICHLOROMETHANE * DWUCHLORODWUFLUOROMETAN (Polish) * ELECTRO-CF 12 * FLUOROCARBON-12 * FREON 12 * ESKIMON 12 * FREON F-12 * FRIGEN 12 * GENETRON 12 * HALON * ISCEON 122 * ISOTRON 12 * LEDON 12 * PROPELLANT 12 * REFRIGERANT 12 * UCON 12
TXDS: ihl-hmn TCLo:200000 ppm/30M TFX:EYE JETOAS 9,385,76
ihl-hmn TCLo:200000 ppm/30M TFX:CNS JETOAS 9,385,76
ihl-rat LC50:80 pph/30M JETOAS 9,385,76
ihl-mus LC50:76 pph/30M JETOAS 9,385,76
ihl-rbt LC50:80 pph/30M JETOAS 9,385,76
ihl-gpg LC50:80 pph/30M JETOAS 9,385,76
AQTX: AQUATIC TOXICITY RATING: TLm96:over 1000 ppm WQCHM* 3,-,74
REVIEW: THRESHOLD LIMIT VALUE-air:1000 ppm DTLVS* 4,128,80
REVIEW: TOXICOLOGY REVIEW FAZMAE 18,365,74
REVIEW: TOXICOLOGY REVIEW NYSJAM 74(11),1939,74
REGS: OSHA STANDARD-air:TWA 1000 ppm (SCP-H) FEREAC 39,23540,74
DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS FEREAC 41,57018,76
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S111
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8220000 METHANE, DICHLORODIFLUORO- mixed with CHLORODIFLUOROMETHANE
UPDT:7905 CAS: 70231-20-0
SYN: DICHLORODIFLUOROMETHANE-MONOCHLORODIFLUOROMETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS FEREAC 41,57018,76

PA8250000 METHANE, DICHLORODIFLUORO- mixed with DICHLOROTETRAFLUOROETHANE
UPDT:7901 CAS: 57107-42-9
SYN: DICHLORODIFLUOROMETHANE-DICHLOROTETRAFLUOROETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS FEREAC 41,57018,76

PA8260000 METHANE, DICHLORODIFLUORO- mixed with 1,1-DIFLUOROETHANE
UPDT:7901 CAS: 25573-41-3
SYN: DICHLORODIFLUOROMETHANE and DIFLUOROETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS FEREAC 41,57018,76

PA8275000 METHANE, DICHLORODIFLUORO- mixed with FLUOROTRICHLOROMETHANE
UPDT:7907
SYN: DICHLORODIFLUOROMETHANE-TRICHLOROMONOFLUOROMETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS FEREAC 41,57018,76

PA8278000 METHANE, DICHLORODIFLUORO-, mixed with TRICHLOROFLUOROMETHANE (1:1)
UPDT:7903 MW: 258.27 MOLFM: C-Cl3-F .C-Cl2-F2
SYN: DICHLOROFLUOROMETHANE-TRICHLOROFLUOROMETHANE (DOT)
TXDS: ihl-rat LC50:20 ppm/30M JETOAS 9,385,76
ihl-mus LC50:72 ppm/30M JETOAS 9,385,76
ihl-gpg LC50:50 ppm/30M JETOAS 9,385,76

PA8278500 METHANE, DICHLORODIFLUORO- and METHANE, FLUOROTRICHLORO- mixed with CHLORODIFLUOROMETHANE
UPDT:7905
SYN: DICHLORODIFLUOROMETHANE-TRICHLOROMONOFLUOROMETHANE-MONOCHLORODIFLUOROMETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS FEREAC 41,57018,76

PA8280000 METHANE, DICHLORODIFLUORO- mixed with TRICHLOROTRIFLUOROETHANE
UPDT:7901
SYN: DICHLORODIFLUOROMETHANE-TRICHLOROTRIFLUOROETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS FEREAC 41,57018,76

PA8300000 METHANE, DICHLORODINITRO-
UPDT:7902 CAS: 1587-41-3 MW: 174.93 MOLFM: C-Cl2-N2-O4
SYN: DICHLORODINITROMETHANE
TXDS: ipr-mam LDLo:500 mg/kg COREAF 171,1396,20
ipr-mus LD50:20 mg/kg KHFZAN 10(6),53,76

PA8400000 METHANE, DICHLOROFLUORO-
UPDT:7908 CAS: 75-43-4 MW: 102.92 MOLFM: C-H-Cl2-F
SYN: ALGOFENE TYPE 5 * ARCTON 7 * DICHLOROFLUOROMETHANE * DICHLOROMONOFLUOROMETHANE * DWUCHLOROFLUOROMETAN (Polish) * FLUORODICHLOROMETHANE * FREON 21 * GENETRON 21
TXDS: ihl-gpg LCLo:10 ppm/1H FLCRAP 1,197,67
REVIEW: THRESHOLD LIMIT VALUE-air:10 ppm DTLVS* 4,132,80
REVIEW: TOXICOLOGY REVIEW FAZMAE 18,365,74
REGS: OSHA STANDARD-air:TWA 1000 ppm (SCP-H) FEREAC 39,23540,74
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S109
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8430000 METHANE, DICUMENYL-
UPDT:7908 CAS: 2344-92-3 MW: 332.43 MOLFM: C19-H24
SYN: DICUMENYLMETHANE * DIM (Fujimori)
TXDS: orl-mus LDLo:15 gm/kg IPAVAL 6,73,64
ihl-mus LCLo:122 mg/m3 IPAVAL 6,73,64
scu-mus LDLo:19 gm/kg IPKVAL 6,73,64
METHANE, DICYANO- see: OO1150000

PA8500000 METHANE, DIETHOXY-
UPDT:7908 CAS: 462-95-3 MW: 104.17 MOLFM: C5-H12-O2
SYN: ETHYLAL
TXDS: orl-rbt LD50:2604 mg/kg PSEBAA 29,730,32
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8575000 METHANE, DIIODO-
UPDT:7908 CAS: 75-11-6 MW: 267.83 MOLFM: C-H2-I2
SYN: DIIODOMETHANE * METHYLENE IODIDE
TXDS: scu-mus LD50:830 mg/kg TXAPA9 4,354,62
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8750000 METHANE, DIMETHOXY-
UPDT:8007 CAS: 109-87-5 MW: 76.11 MOLFM: C3-H8-O2
SYN: ANESTHENYL * DIMETHOXYMETHANE * FORMAL * FORMALDEHYDE DIMETHYLACETAL * METHYLAL * METHYLENE DIMETHYL ETHER * METHYLAL (DOT) * METYLAL (Polish)
TXDS: ihl-rat LC50:15000 ppm NPIRI* 1,73,74
orl-rbt LD50:5708 mg/kg PSEBAA 29,730,32
scu-gpg LDLo:3013 mg/kg BJIMAG 8,279,51
REVIEW: THRESHOLD LIMIT VALUE-air:1000 ppm DTLVS* 4,262,80
REGS: OSHA STANDARD-air:TWA 1000 ppm (SCP-F) FEREAC 39,23540,74
DOT-FLAMMABLE LIQUID, LABEL:FLAMMABLE LIQUID FEREAC 41,57018,76
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S71
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8800000 METHANE, DINITROFLUORO-
UPDT:7912 CAS: 7187-87-8 MW: 124.04 MOLFM: C-H-F-N2-O4
SYN: DINITROFLUOROMETHANE
TXDS: ipr-mus LD50:24 mg/kg KHFZAN 10(6),53,76

METHANEDIOL, DIACETATE see: AI9075000

PA8825000 METHANEDIOL, DIMETHANESULFONATE
UPDT:8011 CAS: 126-72-9 MW: 204.23 MOLFM: C3-H8-O6-S2
SYN: METHANESULFONIC ACID, METHYLENE ESTER * METHYLENE BIS(METHANESULFONATE) * METHYLENE DIMETHANESULFONATE
MTDS: dnd-rat-ipr 10 mg/kg CBINAB 3,149,71
dlt-rat-ipr 15 mg/kg CCPTAY 13,639,76
msc-mus:lym 50 umol/L MUREAV 25,107,74
TXDS: ipr-rat TDLo:15 mg/kg/(13D preg) TFX:TER JRPHA4 17,325,68

PA8990000 METHANE, DIPHENYL-
UPDT:7908 CAS: 101-81-5 MW: 168.25 MOLFM: C13-H12
SYN: BENZENE, BENZYL- * BENZYLBENZENE * DIPHENYLMETHANE * DITAN * DITANE * TOLUENE, alpha-PHENYL-
TXDS: orl-rat LDLo:5000 mg/kg AMIHAB 19,403,59
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

METHANEDITHIOL, S,S-DIESTER with O,O-DIETHYL PHOSPHORODITHIOATE see: TE4550000
METHANE (DOT) see: PA1490000
METHANE, ETHOXY see: KO0260000
METHANE, FLUOROTRICHLORO- see: FI6125000

PA9100000 METHANE, FLUOROTRICHLORO- with NITROMETHANE (99.7:0.3)
DEF Contains 0.3% NITROMETHANE in addition to FREON-11 (TOXAG 18,363,71)
UPDT:7901
SYN: FREON-11 S
TXDS: ipr-mus LD50:2799 mg/kg TOXAG 13(2),363,71

PA9200000 METHANE, FLUOROTRINITRO-
UPDT:7902 CAS: 1840-42-2 MW: 169.04 MOLFM: C-F-N3-O6
SYN: FLUOROTRINITROMETHANE
TXDS: ipr-mus LD50:57300 ug/kg KHFZAN 10(6),53,76
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

METHANE, (2-HYDROXYETHOXY)METHOXY- see: KL6475000
METHANE, HYDROXYIMINOBIS(2-METHYLCYCLOPROPYL)- see: GZ3015000

PA9450000 METHANE, IODO-
UPDT:8007 CAS: 74-88-4 MW: 141.94 MOLFM: C-H3-I
SYN: HALON 10001 * IODOMETANO (Italian) * IODOMETHANE * IODURE DE METHYLE (French) * JOD-METHAN (German) * JODOMETHAAN (Dutch) * METHYL IODIDE * METHYLJODID (German) * METYLJODIDE (Dutch) * METYLU JODEK (Polish) * MONOIODURO DI METILE (Italian)
MTDS: mmo-sat 2 uL/plate JNCIAM 62,873,79
mmo-sat 2 uL/plate JNCIAM 62,873,79
dnr-esc 10 ug/disc JNCIAM 62,873,79
mrc-smc 1000 ppm JNCIAM 62,901,79
mma-mus:lym 50 mg/L/4H MUREAV 59,61,79
msc-mus:lym 15 mg/L/2H MUREAV 59,61,79
IPDS: skn-hmn 1 gm/10M MLD BJIMAG 7,122,50
skn-rat 1 gm/30M MLD BJIMAG 7,122,50
TXDS: orl-rat LDLo:150 mg/kg BJIMAG 7,122,50
ihl-rat LCLo:3790 ppm/15M AMLER** No.23,50
skn-rat LDLo:800 mg/kg KODAK* ,,,71
scu-rat LDLo:150 mg/kg BJIMAG 7,122,50
scu-rat TDLo:50mg/kg TFX:ETA ZEKBAI 74,241,70
ihl-mus LCLo:5000 mg/m3/1H BJIMAG 7,122,50
ipr-mus TDLo:44 mg/kg/8W-I TFX:NEO CNREA8 35,1411,75
scu-mus LD50:110 mg/kg TXAPA9 4,354,62
REVIEW: CARCINOGENIC DETERMINATION-ANIMAL POSITIVE IARC** 15,245,77
REVIEW: THRESHOLD LIMIT VALUE-air:2 ppm (skin) DTLVS* 4,281,80
REVIEW: TOXICOLOGY REVIEW 272TAP 3,95,69
REGS: OSHA STANDARD-air:TWA 5 ppm (skin) (SCP-H) FEREAC 39,23540,74
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S98
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA9500000 METHANE, IODOTRINITRO-
UPDT:7902 CAS: 6070-06-5 MW: 278.94 MOLFM: C-I-N3-O6
SYN: IODOTRINITROMETHANE
TXDS: ipr-mus LD50:20 mg/kg KHFZAN 10(6),53,76

PA9540000 METHANE, ISOCYANATO- mixed with DICHLOROPROPANES or DICHLOROPROPENES (1:4)
UPDT:7901 CAS: 8006-01-1
SYN: DD-162 * TRAPEX * VORLEX
TXDS: orl-rat LD50:305 mg/kg GUCHAZ 6,532,73

PA9675000 METHANE, ISOTHIOCYANATO-
UPDT:7905 CAS: 556-61-6 MW: 73.12 MOLFM: C2-H3-N-S
SYN: (R)-ISOTHIOCYANATE DE METHYLE (French) * ISOTHIOCYANATOMETHANE * ISOTHIOCYANIC ACID, METHYL ESTER * ISOTIOCIANATO DI METILE (Italian) * METHYLISOTHIOCYANAT (Dutch) * METYLU IZOTIOCYJANIAN (Polish) * METHYL ISOTHIOCYANATE * METHYL MUSTARD OIL * METHYLSENFOEL (German) * MIC * MIT * MITC * MORTON EP-1616 * TRAPEX * TRAPEXIDE * VORLEX * VORTEX * WM 32
TXDS: orl-rat LD50:97 mg/kg ASCHAN 32,183,59

TOXICITY DATA HAS NOT BEEN EVALUATED.
OMISSION OF A SUBSTANCE OR NOTATION DOES NOT IMPLY ANY BELIEF FROM REGULATORY RESPONSIBILITY.

STATUS: REPORTED IN EPA TSCA INVENTORY, 1980
CYCLOHEXANE delta 1,2,3,4,5,6-HEXACHLORO- see: GV4550000

GV4900000 CYCLOHEXANE, 1,2,3,4,5,6-HEXACHLORO-, gamma-isomer
UPDT:8011 CAS: 58-89-9 MW: 290.82 MOLFM: C6-H6-Cl6
SYN: AALINDAN * ABLINE * ai-RINOL G 20 * AGROCIDE * AGROCIDE 2 * AGROCIDE 6G * AGROCIDE 7 * AGROCIDE 18 * AGROCIDE WP * AGRO-KEND * AMEISENMITTEL MERCK * AMEISENMITTEL SCHERING * APARASIN * APHTHIRIA * APLIDAL * ARPOLA * BAN * BENEXANE * BENTOX 10 * BENZENE HEXACHLORIDE gamma-isomer * gamma-BENZENE HEXACHLORIDE * BERGE * BHC * gamma-BHC * CELANEX * CHLORESENE * CODELINDANE * DBH * DETMOL EXTRAKT * DETOX 25 * DEVORAN * DOL GRANULE * DRILL TOX SPECIAL ACTION * ENT 7796 * ENTOMOZAN * ERADAMA * FORLIN * GALLOGAMA * GAMALID * GAMAPHEX * GAMMAHEXA * GAMMAHEXANE * GAMMALIN * GAMMALIN 20 * GAMMATOX * GAMMEX * GAMMEXANE * GAMMOPAZ * GERANE * HCCH * HCH * gamma-HCH * HECTOTOX * HEXA * HEXACHLORAN * gamma-HEXACHLORAN * HEXACHLORANE * gamma-HEXACHLORANE * gamma-HEXACHLOROBENZENE * 1-alpha 2-alpha,3-beta * alpha,5-alpha,6-beta-HEXACHLOROCYCLOHEXANE * gamma-HEXACHLOROCYCLOHEXANE * 1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE, gamma-ISOMER * gamma-1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE * HEXATOX * HEXAVERM * HERCIDE * HEXICIDE * HGI * HOSTEX * HYXIT * ISOTOX * JACUTIN * KOKOTINE * KWELL * LENDINE * LENTOX * LICENAL * LINDATOX * LINDAGAM * LINDAGRAIN * LINDAGRANOX * LINDANE * LINDANE (DOT) * gamma-LINDANE * LINDAPOUDRE * LINDATOX * LINDOSEP * LINTOX * LOREXANE * MERBOL 69 * MSZYCOL * NCI-C00204 * NEO-SCABICIDOL * NEXEN FB * NERIT * NEXIT-STARK * NEXOL-E * NICOCHLORAN * NOVIGAM * OMNITOX * OVADZIAK * OWADZIAK * PEDRACZAK * PFLANZOL * QUELLADA * SANG gamma * SILVANOL * SPRITZ-RAPIDIN * SPRUEHPFLANZOL * STREUNEX * TAP 85 * TRI-6 * VITON
MTDS: cyt-hum:fbr 63 mg/L/48H MUREAV 48,337,77
TXDS: orl-chd LDLo:180 mg/kg CMEPP** -,1,56
orl-chd TDLo:111 mg/kg TFX:SYS AEHLAU 25,374,72
orl-rat LD50:76 mg/kg SPEADM 74-1,-,74
skn-rat LD50:500 mg/kg WRPCA2 9,119,70
ipr-rat LDLo:35 mg/kg AEPPAE 212,463,51
orl-mus LD50:86 mg/kg FEPRA7 6,366,47
orl-mus TDLo:25 gm/kg/73W-C TFX:NEO FCTXAV 11,413,73
ipr-mus LDLo:75 mg/kg TXAPA9 23,208,72
orl-dog LD50:40 mg/kg SPEADM 74-1,-,74
ivn-dog LDLo:8 mg/kg TIEUA7 5,61,50
orl-rbt LD50:60 mg/kg JHEMA2 77,115,78
skn-rbt LD50:50 mg/kg ARDOAQ 16,3,52
ivn-rbt LDLo:4500 ug/kg JPETAB 92,140,48
orl-gpg LD50:177 mg/kg FEPRA7 6,306,47
orl-ham LD50:360 mg/kg JETOAS 7,159,74
orl-bwd LDLo:100 mg/kg TIEUA7 5,61,50
ims-bwd LDLo:26 mg/kg TIEUA7 5,61,50
AQTX: AQUATIC TOXICITY RATING: TLm96:under 1 ppm WQCHM* 3,-,74
REVIEW: CARCINOGENIC DETERMINATION:ANIMAL POSITIVE IARC** 20,195,79
REVIEW: CARCINOGENIC DETERMINATION:INDEFINITE IARC** 5,47,74
REVIEW: THRESHOLD LIMIT VALUE-air:0.5 mg/m3 (skin) DTLVS* 4,246,80
REVIEW: TOXICOLOGY REVIEW CNDOAB 10(3),43,75
REVIEW: TOXICOLOGY REVIEW RREVAH 56,107,75
REVIEW: TOXICOLOGY REVIEW PMDCAY 10,85,74
REVIEW: TOXICOLOGY REVIEW DTTIAF 80(20),485,73
REVIEW: TOXICOLOGY REVIEW ARDEAC 113(3),353,77
REVIEW: TOXICOLOGY REVIEW CTOXAO 13,231,78
REGS: OSHA STANDARD-air:TWA 500 ug/m3 (skin) (SCP-T) FEREAC 39,23540,74
DOT-ORM-A LABEL:NONE FEREAC 41,57018,76
STATUS: NCI CARCINOGENESIS BIOASSAY COMPLETED;RESULTS NEGATIVE (NCITR* NCI-CG-TR-14,77)
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 3 S290
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV4950000 CYCLOHEXANE, 1,2,3,4,5,6-HEXACHLORO-, (mixed isomers)
DEF:Technical BHC contains about 64% alpha, 10% beta, 13% gamma, 9% delta and 1% epsilonisomers of 1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE (IARC** 5,47,74)
UPDT:8011 CAS: 608-73-1 MW: 290.82 MOLFM: C6-H6-Cl6
SYN: BENZAHEX * BENZENEHEXACHLORIDE, mixed isomers * BENZEX * DOL * DOLMIX * FBHC * FHCH * 1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE (mixture of isomers) * HEXAFOR * HEXYCLAN * KOTOL * SOPROCIDE * TECHNICAL BHC * TECHNICAL HCH
TXDS: orl-mus TDLo:13 gm/kg/24W-C TFX:NEO GANNA2 62,431,71
REVIEW: CARCINOGENIC DETERMINATION:ANIMAL POSITIVE IARC** 20,195,79
REVIEW: CARCINOGENIC DETERMINATION:ANIMAL POSITIVE IARC** 5,47,74
CYCLOHEXANE, 1,2,3,4,5,6-HEXACHLORO-, trans- see: GV4375000

GV4990000 CYCLOHEXANE, HEXADECAFLUORODIMETHYL-
UPDT:7901 CAS: 26637-68-3 MW: 400.08 MOLFM: C8-F16
SYN: FORESHOT
TXDS: ihl-rat LCLo:100 ppm/14H 11FYAN 3,78,63
ihl-mus LCLo:500 ppm/14H 11FYAN 3,78,63
ihl-gpg LCLo:100 ppm/14H 11FYAN 3,78,63

GV5000000 CYCLOHEXANE, 1,2,3,4,5,6-HEXAKIS(2-CYANOETHOXY)-
UPDT:7901 CAS: 3055-84-3 MW: 458.60 MOLFM: C24-H30-N6-O6
SYN: 1,2,3,4,5,6-HEXAKIS(2-CYANOETHOXY)-CYCLOHEXANE
TXDS: ivn-mus LD50:180 mg/kg CSLNX* NX#02704
CYCLOHEXANE, 5-ISOCYANATO-1-(ISOCYANATOMETHYL)-1,3,3-TRIMETHYL- (9CI) see: NQ5460000

GV5030000 CYCLOHEXANE, ISOPROPYL-
UPDT:7903 CAS: 696-29-7 MW: 126.27 MOLFM: C9-H18
SYN: ISOPROPYLCYCLOHEXANE
AQTX: AQUATIC TOXICITY RATING: TLm96:1000-100 ppm WQCHM* 2,-,74
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980
delta(1)sup 1,alpha(1-CYCLOHEXANEMALONONITRILE see: OO3735250
CYCLOHEXANEMETHANAMINE see: GV6129000

GV5075000 CYCLOHEXANEMETHANOL
UPDT:7908 CAS: 100-49-2 MW: 114.21 MOLFM: C7-H14-O
SYN: BENZYL ALCOHOL, HEXAHYDRO- * CYCLOHEXANECARBINOL * CYCLOHEXYLCARBINOL * CYCLOHEXYLMETHANOL * HEXAHYDROBENZYL ALCOHOL * HYDROXYMETHYLCYCLOHEXANE * METHANOL, CYCLOHEXYL- * USAF DO-49
TXDS: ipr-mus LD50:250 mg/kg NTIS** AD277-689
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980
CYCLOHEXANEMETHANOL, alpha-(2-BROMOETHENYL)- see: UK5080000
CYCLOHEXANEMETHANOL, alpha-(2-CHLOROETHENYL)- see: UK5085000
CYCLOHEXANEMETHANOL, alpha-ETHYNYL- see: UK5090000

GV5200000 CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, ACETATE
UPDT:8010 MW: 166.22 MOLFM: C11-H18-O2
SYN: ACETIC ACID, 1-CYCLOHEXYL-2-PROPYN-1-YL ESTER
TXDS: orl-mus LD50:1200 mg/kg ARZNAD 7,85,57
CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, BENZOATE see: DG5775100
CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, BUTYRATE see: ES8935000
CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, CARBANILATE see: FQ6676000
CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, PROPIONATE see: UF0655000

GV5425000 CYCLOHEXANEMETHANOL, 4-HYDROXY-alpha-(ISOPROPYLAMINOMETHYL)-
UPDT:7901 CAS: 63960-63-2 MW: 201.35 MOLFM: C11-H23-N-O2
SYN: ETHANOL, 2-(ISOPROPYLAMINO)-1-(4-HYDROXYCYCLOHEXYL)- * WIN 3529
TXDS: ivn-mus LD50:460 mg/kg JPETAB 106,341,52

GV5600000 CYCLOHEXANEMETHANOL, 4-HYDROXY-alpha-(METHYLAMINOMETHYL)-
UPDT:7901 CAS: 61779-96-3 MW: 173.29 MOLFM: C9-H19-N-O2
SYN: ETHANOL, 2-(METHYLAMINO)-1-(4-HYDROXYCYCLOHEXYL)- * N-METHYL 2-(4-HYDROXYCYCLOHEXYL)ETHANOLAMINE * WIN 3580
TXDS: ipr-mus LD50:620 mg/kg JPETAB 103,341,52
ivn-mus LD50:295 mg/kg JPETAB 103,341,52

GV5950000 CYCLOHEXANEMETHANOL, alpha-(METHYLAMINOMETHYL)-
UPDT:7901 CAS: 21615-49-2 MW: 157.29 MOLFM: C9-H19-N-O
SYN: ETHANOL, 2-(METHYLAMINO)-1-CYCLOHEXYL- * alpha-[METHYLAMINOMETHYL)CYCLOHEXANEMETHANOL- * N-METHYL 2-CYCLOHEXYLETHANOLAMINE * WIN 3581
TXDS: ivn-mus LD50:37 mg/kg JPETAB 103,341,52
ipr-mus LD50:240 mg/kg JPETAB 103,341,52
CYCLOHEXANEMETHANOL, alpha-PHENYL- see: PC1935000

GV5965000 CYCLOHEXANEMETHANOL, 1-PHENYL-
UPDT:8007 MW: 190.31 MOLFM: C13-H18-O
SYN: 1-PHENYL CYCLOHEXANEMETHANOL
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#07313

GV6125000 CYCLOHEXANE, METHYL-
UPDT:7908 CAS: 108-87-2 MW: 98.21 MOLFM: C7-H14
SYN: CYCLOHEXYLMETHANE * HEXAHYDROTOLUENE * METHYLCYCLOHEXANE * METHYLCYCLOHEXANE (DOT) * METYLOCYKLOHEKSAN (Polish) * SERICINE B * TOLUENE HEXAHYDRIDE * TOLUENE, HEXAHYDRO-
TXDS: orl-rbt LDLo:4000 mg/kg JINTAB 25,299,43
REVIEW: THRESHOLD LIMIT VALUE-air:400 ppm DTLVS* 4,271,80
REVIEW: TOXICOLOGY REVIEW 27ZTAP 3,69,69
REGS: OSHA STANDARD-air:TWA 500 ppm (SCP-G) FEREAC 39,23540,74
DOT-FLAMMABLE LIQUID, LABEL:FLAMMABLE LIQUID FEREAC 41,57018,76
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S94
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV6128000 CYCLOHEXANEMETHYLAMINE
UPDT:8011 CAS: 3218-02-8 MW: 113.23 MOLFM: C7-H15-N
SYN: (AMINOMETHYL)CYCLOHEXANE * CYCLOHEXANEMETHANAMINE * CYCLOHEXYLMETHANAMINE * CYCLOHEXYLMETHYLAMINE
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#10002
CYCLOHEXANEMETHYLAMINE, N,N'-(1,4-BICYCLO(2.2.2)OCTYLENEDIMETHYLENE)BIS-, DIHYDROCHLORIDE see: DI7920000

GV6133000 CYCLOHEXANEMETHYLAMINE, N-(2-CHLOROETHYL)-N-ETHYL-PHENYL-, HYDROCHLORIDE
UPDT:8007 MW: 316.35 MOLFM: C17-H26-Cl-N .Cl-H
SYN: N-(2-CHLOROETHYL) N ETHYL-1-PHENYLCYCLOHEXANEMETHYLAMINE * 1-PHENYL-1-[N-(2-CHLOROETHYL)-N-ETHYLAMINOMETHYL]CYCLOHEXANE, HYDROCHLORIDE
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#07516

GV6135000 CYCLOHEXANEMETHYLAMINE, 2-CHLORO-2-(m-METHOXYPHENYL)-
UPDT:7902 CAS: 73806-39-9 MW: 239.84 MOLFM: C16-H22-Cl-N-O
SYN: 2-CHLORO-2-(m-METHOXYPHENYL)CYCLOHEXANEMETHYLAMINE
TXDS: orl-mus LD50:390 mg/kg ARZNAD 28,107,78
CYCLOHEXANEMETHYLAMINE, N,N'-(1,4-CYCLOHEXENYLENE)BIS-, DIACETATE see: GW2545000
CYCLOHEXANEMETHYLAMINE, N,N'-(1,4-CYCLOHEXYLENEDIMETHYLENE)DI-, DIHYDROCHLORIDE, (E)- see: GU7047000
CYCLOHEXANEMETHYLAMINE, N,N'-(1,4-CYCLOHEXYLENEDIMETHYLENE)DI-, DIHYDROCHLORIDE, (Z)- see: GU7049000

GV6150000 CYCLOHEXANEMETHYLAMINE, N,N-DIMETHYL-2-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 73806-39-0 MW: 247.42 MOLFM: C16-H25-N-O
SYN: N,N-DIMETHYL-2-(m-METHOXYPHENYL)CYCLOHEXANEMETHYLAMINE
TXDS: orl-mus LD50:214 mg/kg ARZNAD 28,107,78
CYCLOHEXANEMETHYLAMINE, N-(2-HYDROXYETHYL)-N-ETHYL-1-PHENYL- see: KL0560000

GV6300000 CYCLOHEXANEMETHYLAMINE, N-METHYL-
UPDT:7901 CAS: 75756-29-0 MW: 127.26 MOLFM: C8-H17-N
SYN: N-METHYL-N-(CYCLOHEXYLMETHYL) AMINE
TXDS: orl-rat LDLo:1410 mg/kg AIHAAP 30,470,69
skn-rbt LD50:630 mg/kg AIHAAP 30,470,69

GV6400000 CYCLOHEXANEMETHYLAMINE, 1-PHENYL-
UPDT:8007 MW: 189.33 MOLFM: C13-H19-N
SYN: 1-PHENYLCYCLOHEXANEMETHYLAMINE
TXDS: ivn-mus LD50:18 mg/kg CSLNX* NX#07506
CYCLOHEXANE, 1-METHYL-a-AMINOETHYLTHIOAZO- see: KH2540000

GV6670000 CYCLOHEXANE, 1,1,2,2,3,4,4,5,6-NONAFLUORO-
UPDT:7901 CAS: 22150-51-2 MW: 246.09 MOLFM: C6-H3-F9
SYN: 1H,2H,4H-NONAFLUOROCYCLOHEXANE
TXDS: ihl-mus LCLo:17000 ppm/10M ANASAB 16,3,61

GV6678000 CYCLOHEXANE, PIPERIDINOMETHYL-
UPDT:7901 CAS: 5005-72-1 MW: 181.36 MOLFM: C12-H23-N
SYN: PMC
TXDS: orl-mus LD50:160 mg/kg AIPTAK 167,273,67
ipr-mus LD50:55 mg/kg AIPTAK 167,273,67
ivn-mus LD50:20 mg/kg AIPTAK 167,273,67

GV6680000 CYCLOHEXANE, PIPERIDINOMETHYL-, CAMPHOSULFATE SALT
UPDT:7901 CAS: 62916-34-1 MW: 413.75 MOLFM: C12-H23-N .C10-H16-O4-S
SYN: PIPERIDINOMETHYLCYCLOHEXANE, CAMPHOSULFATE * SD 210-37
TXDS: orl-mus LD50:370 mg/kg AIPTAK 167,273,67
ipr-mus LD50:370 mg/kg AIPTAK 167,273,67
ivn-mus LD50:41 mg/kg AIPTAK 167,273,67

GV6690000 CYCLOHEXANE, PIPERIDINOMETHYL-, HYDROCHLORIDE
UPDT:7901 CAS: 5005-71-0 MW: 217.82 MOLFM: C12-H23-N .Cl-H
SYN: PIPERIDINOMETHYLCYCLOHEXANE CHLORHYDRATE SALT * SD 210-32
TXDS: orl-mus LD50:205 mg/kg AIPTAK 167,273,67
ipr-mus LD50:65 mg/kg AIPTAK 167,273,67
ivn-mus LD50:25 mg/kg AIPTAK 167,273,67

GV6735000 CYCLOHEXANEPROPIONIC ACID, ALLYL ESTER
UPDT:7908 CAS: 2705-87-5 MW: 196.32 MOLFM: C12-H20-O2
SYN: ALLYL CYCLOHEXANEPROPIONATE * 3-ALLYLCYCLOHEXYL PROPIONATE * ALLYL HEXAHYDROPHENYLPROPIONATE * CYCLOHEXANOL 3-ALLYL-, PROPIONATE
TXDS: orl-rat LD50:565 mg/kg FCTXAV 2,327,64
orl-rbt LD50:300 mg/kg FCTXAV 2,327,64
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV6760000 CYCLOHEXANEPROPIONIC ACID, alpha-CYCLOPENTYL-, 2-(DIETHYLAMINO)ETHYL ESTER, HYDROCHLORIDE
UPDT:7901 CAS: 6729-03-5 MW: 260.04 MOLFM: C20-H37-N-O2 .Cl-H
SYN: alpha-CYCLOPENTYLCYCLOHEXANEPROPIONIC ACID 2-(DIETHYLAMINO)ETHYL ESTER HYDROCHLORIDE
TXDS: ipr-mus LD50:220 mg/kg JACSAT 69,1849,47

GV6825000 CYCLOHEXANEPROPYLAMINE, N,N-DIMETHYL-gamma-PHENYL-, HYDROCHLORIDE
UPDT:7901 CAS: 15826-61-6 MW: 281.91 MOLFM: C17-H27-N .Cl-H
SYN: N,N-DIMETHYL-3-CYCLOHEXYL-3-PHENYL PROPYLAMINE HYDROCHLORIDE * GAMFEXINE HYDROCHLORIDE * WIN 1544
TXDS: orl-hmn TDLo:5 mg/kg TFX:PSY CTCEA9 9,549,67
CYCLOHEXANESPIRO-5'-HYDANTOIN see: HM2460000

GV6950000 CYCLOHEXANEVALERIC ACID
UPDT:[illegible] CAS: 7[illegible]-49-8 MW: 179.26 MOLFM: C6-H13-N-O2 S
SYN: CYCLAMATE * CYCLOHEXANESULFAMIC ACID * CYCLOHEXYLAMIDOSULPHONIC ACID * CYCLOHEXYLAMINE-N-SULFONIC ACID * CYCLOHEXYLSULPHAMIC ACID * N-CYCLOHEXYLSULPHONIC ACID * HEXAMIC ACID * SUCARYL * SUCARYL ACID * SULFAMIC ACID, CYCLOHEXYL (9CI)
TXDS: orl-man TDLo:27 gm/kg/78W-C TFX:ETA JOURAA 118,258,77

ivn-mus LD50:180 mg/kg CSLNX* NX#01774
REVIEW: CARCINOGENIC DETERMINATION:NO DATA IARC** 22,55,80
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

CYCLOHEXANESULFAMIC ACID, BARIUM SALT
[illegible] CAS: 66401-66-9
orl-rat LDLo:250 mg/kg NCNSA8 5,40,53
CYCLOHEXANESULFAMIC ACID, CALCIUM SALT (2:1) see: GV7100000

GV7100000 CYCLOHEXANESULFAMIC ACID, CALCIUM SALT (2:1)
UPDT:8009 CAS: 139-06-0 MW: 376.55 MOLFM: C12-H24-N2-O6-S2-Ca
SYN: CALCIUM CYCLAMATE * CALCIUM CYCLOHEXANESULFAMATE * CALCIUM CYCLOHEXANE SULPHAMATE * CALCIUM CYCLOHEXYLSULFAMATE * CALCIUM CYCLOHEXYLSULPHAMATE * CYCLAMATE, CALCIUM SALT * CYCLAMATE CALCIUM * CYCLOHEXANESULFAMIC ACID, CALCIUM SALT * CYCLAN * CYCLOHEXYLSULPHAMIC ACID, CALCIUM SALT * CYLAN * DIETIC * SALZIUMZYKLAMAT (German) * SUCARYL CALCIUM

MTDS: cyt-hmn:leu 250 mg/L	SCIEAS 164,568,69
cyt-ham:fbr 10 mg/L	MUREAV 39,1,76
cyt-ham:lng 100 mg/L	HLREAY 70,271,72
cyt-grb-ipr 150 mg/kg	CNJGAB 13,189,71
TXDS: orl-rat LDLo:10 mg/kg	CLDND*
orl-rat TDLo:3465 gm/kg/88W-C TFX:NEO	JNCIAM 49,751,72
scu-rat TDLo:45 gm/kg/66W-I TFX:ETA	FCTXAV 9,463,71
ivn-rat LDLo:3500 ug/kg	CLDND*
orl-mus LDLo:10 mg/kg	CLDND*
ivn-mus LDLo:3500 ug/kg	CLDND*
REVIEW: CARCINOGENIC DETERMINATION:ANIMAL POSITIVE	IARC** 22,55,80
REVIEW: TOXICOLOGY REVIEW	MUREAV 39,1,76
REVIEW: TOXICOLOGY REVIEW	WMWOA4 121,515,71
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980	

GV7175000 CYCLOHEXANESULFAMIC ACID, CALCIUM SALT, DIHYDRATE
UPDT:7901 CAS: 5897-16-3 MW: 422.62 MOLFM: C12-H24-N2-O6-S2 .2H2-O .Ca

TXDS: scu-rat LD50:100 mg/kg	FAONAU 44A,83,67

GV7350000 CYCLOHEXANESULFAMIC ACID, MONOSODIUM SALT
UPDT:8012 CAS: 139-05-9 MW: 165.18 MOLFM: C6-H12-N-O3-S .Na
SYN: ASSUGRIN * ASSUGRIN FLUSSIG * ASSUGRIN VOLLSUSS * ASUCRYL * CYCLAMATE * CYCLAMATE SODIUM * CYCLAMATE, SODIUM SALT * CYCLOHEXANESULFAMIC ACID, MONOSODIUM SALT * CYCLOHEXYLSULPHAMATE SODIUM * CYCLOHEXYLSULPHAMIC ACID, MONOSODIUM SALT * DULZOR-ETAS * HACHI SUGAR * IDIOSYC * NATREEN * NATRIUMCYKLAMAT (German) * SODIUM CYCLAMATE * SODIUM CYCLOHEXANESULFAMATE * SODIUM CYCLOHEXANESULPHAMATE * SODIUM CYCLOHEXYL SULFAMATE * SODIUM CYCLOHEXYL AMIDOSULPHATE * SODIUM CYCLOHEXYL SULPHAMATE * SODIUM CYCLOHEXYLSULPHAMIDATE * SODIUM SUCARYL * SUCARYL SODIUM * SUCCARIL * SUCROSA * SUCRUN 7 * SUESSETT * SUESTAMIN * SUGARIN * SUGARON

MTDS: cyt-lmn:leu 10 umol/L/5H	MUREAV 39,1,76
cyt-hmn:fbr 500 mg/L	ACYTAN 16,41,72
cyt-ham:fbr 10 mg/L	MUREAV 39,1,76
cyt-grb-unk 100 mg/kg	MUREAV 26,199,74
TXDS: orl-rat TDLo:63 gm/kg/9W-C TFX:NEO	CNREAB 37,2943,77
ipr-rat LD50:1350 mg/kg	NCIBR* NIH-NCI-E-68-1311,10,73
ipr-mus LD50:1154 mg/kg	NCIBR* NIH-NCI-E-68-1311,10,73
imp-mus TDLo:176 mg/kg TFX:NEO	SCIEAS 167,996,70
orl-rat TD :112 gm/kg/6W-C TFX:NEO	CNREAB 37,2943,77
orl-rat TD :610 gm/kg/87W-C TFX:ETA	CEINAB 11,225,75
CARCINOGENIC DETERMINATION:ANIMAL POSITIVE	IARC** 22,55,80
REVIEW: TOXICOLOGY REVIEW	IDJOAS 23(2),328,73
REVIEW: TOXICOLOGY REVIEW	MUREAV 39,1,76
REVIEW: TOXICOLOGY REVIEW	AEHLAU 23,6,71
REVIEW: TOXICOLOGY REVIEW	WMWOA4 121,515,71
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980	

GV7450000 CYCLOHEXANESULFONAMIDE
UPDT:7901 CAS: 2435-32-2 MW: 163.24 MOLFM: C6-H13-N-O2-S

TXDS: orl-rat LD50:80 mg/kg	JPETAB 90,260,47

CYCLOHEXANESULPHAMIC ACID see: GV0950000
CYCLOHEXANESULPHAMIC ACID, MONOSODIUM SALT see: GV7350000

GV7500000 1,1,3,3-CYCLOHEXANETETRAPROPIONITRILE, 2-OXO-
UPDT:7901 CAS: 5283-05-6 MW: 310.44 MOLFM: C18-H22-N4-O
SYN: 2-OXO-1,1,3,3-CYCLOHEXANETETRAPROPIONITRILE

TXDS: ivn-mus LD50:180 mg/kg	CSLNX* NX#03574

GV7525000 CYCLOHEXANETHIOL
UPDT:7908 CAS: 1569-69-3 MW: 116.24 MOLFM: C6-H12-S
SYN: CYKLOHEXYLMERKAPTAN (Czech)

IRDS: skn-rbt 500 mg/24H SEV	26ZPAK -,167,72
eye-rbt 500 mg/24H SEV	26ZPAK -,167,72
TXDS: orl-rat LD50:556 mg/kg	26ZPAK -,167,72
CRIT DOS: OCCUPATIONAL EXPOSURE TO CYCLOHEXANETHIOL recm std-air:Cl 0.5 ppm/15M	NTIS**
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980	

CYCLOHEXANE, 1-(TRICHLOROSILYL)- see: VV2090000

GV7610000 CYCLOHEXANE, 1-TRIFLUOROMETHYL-1,2,2,3,3,4,4,5,5,6,6-UNDECAFLUORO-
UPDT:7908 CAS: 355-02-2 MW: 350.07 MOLFM: C7-F14
SYN: PERFLUOROMETHYLCYCLOHEXANE

TXDS: ihl-rat LCLo:525 ppm/14H	IJFYAN 3,90,63
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980	

GV7650000 CYCLOHEXANE, 1,1,3-TRIMETHYL-
UPDT:7905 CAS: 3073-66-3 MW: 126.27 MOLFM: C9-H18
SYN: 1,1,3-TRIMETHYLCYCLOHEXANE

TXDS: ivn-mus LD50:15 mg/kg	CSLNX* NX#04716

GV7700000 CYCLOHEXANEVALERIC ACID, alpha,2,2,6-TETRAMETHYL-beta-CYANO-, SODIUM SALT
UPDT:7901 CAS: 693-12-5 MW: 287.42 MOLFM: C16-H26-N-O2-Na
SYN: beta-CYANO-2,2,6-TRIMETHYLCYCLOHEXYLBUTANECARBOXYLIC ACID, SODIUM SALT * SODIUM SALT of alpha-2,2,6-TETRAMETHYL-beta-CYANOCYCLOHEXANEVALERIC ACID

TXDS: ipr-mus LD50:65 mg/kg	PJPPAA 27(4),399,75

GV7875000 CYCLOHEXANOL
UPDT:8002 CAS: 108-93-0 MW: 100.18 MOLFM: C6-H12-O
SYN: ADRONAL * ANOL * CICLOESANOLO (Italian) * CYCLOHEXYL ALCOHOL * CYCLOHEKSANOL (Polish) * HEXAHYDROPHENOL * HEXALIN * HYDRALIN * HYDROPHENOL * HYDROXYCYCLOHEXANE * NAXOL * PHENOL HEXAHYDRO-

MTDS: dnd-mom:lym 150 mmol/L	PNASA6 48,686,62
IRDS: eye-hmn 100 ppm	JIHTAB 25,282,43
skn-rbt 14600 ug 24H open MLD	AIHAAP 23,95,62
ver-rbt 2 mg SEV	AJOPAA 29,1363,46
ihl-hmn TCLo:75 ppm TFX:IRR	JIHTAB 25,282,43
ipr-rat LD50:2060 mg/kg	MDTEAK 8,244,67
ivn-mus LD50:2450 mg/kg	REMBAB 5,7,67
ivn-mus LD50:1030 mg/kg	JNCIAZ 21,342,62
orl-rbt LDLo:2200 mg/kg	JIHTAB 25,199,43
skn-rbt LDLo:12 gm/kg	JIHTAB 25,199,43
ipr-rbt LDLo:1420 mg/kg	JPMPAR 3,1,28
AQTX: AQUATIC TOXICITY RATING: Tlm:96:100-10 ppm	WQCHM* 2,-,74
REVIEW: THRESHOLD LIMIT VALUE-air:50 ppm	DFLVS* 4,111,80
REVIEW: TOXICOLOGY REVIEW	27/TAP 3,44,69
REGS: OSHA STANDARD-air:TWA 50 ppm (SCP-E)	FEREAC 39,23540,74
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S54	
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980	

CYCLOHEXANOL, ACETATE see: AG5075000

GV8100000 CYCLOHEXANOL, 1-ALLYL-
UPDT:7901 CAS: 1123-34-8 MW: 140.23 MOLFM: C9-H16-O
SYN: 1-ALLYL-1-CYCLOHEXANOL

TXDS: ivn-mus LD50:100 mg/kg	CSLNX* NX#04164

CYCLOHEXANOL, 3-ALLYL-, PROPIONATE see: GV6735000

GV8400000 CYCLOHEXANOL, 1-AMINO-3-AMINOMETHYL-3,5,5-TRIMETHYL-
UPDT:7901 CAS: 2855-13-2 MW: 156.24 MOLFM: C10-H22-N2-O
SYN: 1-AMINO-3-AMINOMETHYL-3,5,5-TRIMETHYLCYCLOHEXANOL

TXDS: orl-rat LD50:1500 mg/kg	ARZNAD 30,470,69

GV8425000 CYCLOHEXANOL, 4-((N-(2-AMINO-3,5-DIBROMOBENZYL)AMINO)-, HYDROCHLORIDE (E)-
UPDT:7901 CAS: 18683-91-5 MW: 414.61 MOLFM: C13-H18-Br2-N2-O .Cl-H
SYN: AMBROXOL * trans-4-((2-AMINO-3,5-DIBROMOBENZYL)AMINO)CYCLOHEXANOL HYDROCHLORIDE * NA 872

TXDS: orl-rat LD50:13400 mg/kg	ARZNAD 28,889,78
ipr-rat LD50:380 mg/kg	ARZNAD 28,889,78
orl-mus LD50:2720 mg/kg	ARZNAD 28,889,78
ipr-mus LD50:768 mg/kg	ARZNAD 28,889,78
ivn-mus LD50:138 mg/kg	ARZNAD 28,889,78
orl-dog LD50:500 mg/kg	ARZNAD 28,889,78
ipr-dog LD50:125 mg/kg	ARZNAD 28,889,78
orl-rbt LDLo:10 mg/kg	ARZNAD 28,889,78
ipr-gpg LDLo:400 mg/kg	ARZNAD 28,889,78
ivn-rbt LDLo:80 mg/kg	ARZNAD 28,889,78
orl-gpg LD50:1160 mg/kg	ARZNAD 28,889,78
ipr-gpg LD50:260 mg/kg	ARZNAD 28,889,78

GV8450000 CYCLOHEXANOL, 2-AMINOMETHYL-1-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 73906-40-3 MW: 235.36 MOLFM: C14-H21-N-O2
SYN: 2-AMINOMETHYL-1-(m-METHOXYPHENYL)CYCLOHEXANOL

TXDS: orl-mus LD50:466 mg/kg	ARZNAD 28,107,78

GV8575000 CYCLOHEXANOL, 4-(2-AMINOPROPYL)-, HYDROBROMIDE
UPDT:7901 CAS: 64011-65-0 MW: 238.21 MOLFM: C9-H19-N-O .Br-H
SYN: 1-(p-HYDROXYCYCLOHEXYL)-2-AMINO-PROPANE HYDROBROMIDE

TXDS: ipr-mus LD50:1000 mg/kg	JPETAB 92,207,48

CYCLOHEXANOLAZETAT (German) see: AG5075000

GV8620000 CYCLOHEXANOL, 2-(N-BENZYL-N-METHYLAMINOMETHYL)-1-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 73506-41-4 MW: 339.52 MOLFM: C22-H29-N-O2
SYN: 2-(N-BENZYL-N-METHYLAMINOMETHYL)-1-(m-METHOXYPHENYL)CYCLOHEXANOL

TXDS: orl-mus LD50:404 mg/kg	ARZNAD 28,107,78

GV8640000 CYCLOHEXANOL, 1-BENZYLOXY-2-(DIMETHYLAMINOMETHYL)-
UPDT:7901 CAS: 73806-42-5 MW: 339.52 MOLFM: C22-H29-N-O2
SYN: 1-BENZYLOXY-2-(DIMETHYLAMINOMETHYL)CYCLOHEXANOL

TXDS: orl-mus LD50:172 mg/kg	ARZNAD 28,107,78

GV8645000 CYCLOHEXANOL, 1-(2-BROMOETHYNYL)-
UPDT:7903 CAS: 13957-27-2 MW: 203.10 MOLFM: C8-H11-Br-O
SYN: 1-BROMOAETHINYL-CYCLOHEXANOL-(1) (German) * 1-BROMOETHYNYLCYCLOHEXANOL * SEDLNOL

TXDS: scu-mus LD50:560 mg/kg	ARZNAD 5,161,55

GV8650000 CYCLOHEXANOL, 1,1'-BUTADIYNYLENEDI-
UPDT:7901 CAS: 5765-10-5 MW: 246.38 MOLFM: C16-H22-O2
SYN: BIS(1-HYDROXYCYCLOHEXYL)BUTADIYNE

TXDS: ivn-mus LD50:56 mg/kg	CSLNX* NX#02803

GV8750000 CYCLOHEXANOL, 4-tert-BUTYL-
UPDT:7908 CAS: 98-52-2 MW: 156.30 MOLFM: C10-H20-O
SYN: 4-tert-BUTYLCYCLOHEXANOL * USAF DO-20

TXDS: orl-rat LD50:4200 mg/kg	FCTXAV 12,807,74
ipr-mus LD50:50 mg/kg	NTIS** AD277-689
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980	

CYCLOHEXANOL, 4-tert-BUTYL-, ACETATE see: AF7117000

GV8800000 1-CYCLOHEXANOL, 4-tert-BUTYL-1-ETHYNYL-
UPDT:7901 CAS: 20225-03-5 MW: 180.32 MOLFM: C12-H20-O
SYN: 4-tert-BUTYL-1-ETHYNYLCYCLOHEXANOL

TXDS: ivn-mus LD50:56 mg/kg	CSLNX* NX#00335

GV8820000 CYCLOHEXANOL, 1-(((CHLOROMETHYL)DIMETHYLSILYL)ETHYNYL)-
UPDT:7901 CAS: 25911-25-5 MW: 230.84 MOLFM: C11-H19-Cl-O-Si
SYN: CYCLOHEXAN-1-OL, 1-[beta-CHLOROMETHYLDIMETHYLSILYLETHYNYL]- * 1-(beta-CHLOROMETHYLDIMETHYLSILYLETHYNYLCYCLOHEXAN-1-OL * SILANE, (CHLOROMETHYL)DICHLORO(1-HYDROXYCYCLOHEXYLETHYNYL)-

TXDS: ivn-mus LD50:56 mg/kg	CSLNX* NX#02574

CYCLOHEXAN-1-OL, 1-(beta-CHLOROMETHYLDIMETHYLSILYL)ETHYNYL- see: GV8820000

GV8830000 CYCLOHEXANOL, 1-(m-CHLOROPHENYL)-2-(DIMETHYLAMINOMETHYL)-
UPDT:7903 CAS: 73806-44-7 MW: 267.83 MOLFM: C15-H22-Cl-N-O
SYN: 1-(m-CHLOROPHENYL)-2-(DIMETHYLAMINOMETHYL)CYCLOHEXANOL

TXDS: orl-mus LD50:201 mg/kg	ARZNAD 28,107,78

GV8835000 CYCLOHEXANOL, 4-(CYCLOHEXYLMETHYL)-
UPDT:8011 MW: 196.37 MOLFM: C13-H24-O
SYN: 4-CYCLOHEXYLMETHYLCYCLOHEXANOL

TXDS: ivn-mus LD50:56 mg/kg	CSLNX* FIX#10067

GV8840000 CYCLOHEXANOL, 2-DIALLYLAMINOMETHYL-1-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 73906-43-7 MW: 275.50 MOLFM: C20-H29-N-O2
SYN: 2-DIALLYLAMINOETHYL-1-(m-METHOXYPHENYL)CYCLOHEXANOL

TXDS: orl-mus LD50:348 mg/kg	ARZNAD 28,107,78

GV8850000 CYCLOHEXANOL, 1-(p-(3-DIETHYLAMINOPROPYL)PHENETHYL)-
UPDT:7901 CAS: 14893-41-5 MW: 317.57 MOLFM: C21-H35-N-O
SYN: 1-(2-(p-(3-DIETHYLAMINOPROPYL)PHENYL)ETHYL)CYCLOHEXANOL

TXDS: scu-mus LD50:258 mg/kg	RPTOAN 37(5),217,74

GV8870000 CYCLOHEXANOL, 1-(2-(p-(3-DIETHYLAMINO-1-PROPYNYL)PHENYL)ETHYNYL)-
UPDT:7901 CAS: 5076-60-8 MW: 339.49 MOLFM: C21-H29-N-O
SYN: 1-(2-(p-(3-DIETHYLAMINO-1-PROPYNYL)PHENYL)ETHYNYL)CYCLOHEXANOL

TXDS: scu-mus LD50:1394 mg/kg	RPTOAN 37(5),217,74

GV8875000 CYCLOHEXANOL, 2-(DIMETHYLAMINOMETHYL)-1-(m-ETHOXYPHENYL)-
UPDT:7901 CAS: 29164-83-6 MW: 277.45 MOLFM: C17-H27-N-O2
SYN: 2-(DIMETHYLAMINOMETHYL)-1-(m-ETHOXYPHENYL)CYCLOHEXANOL

TXDS: orl-mus LD50:274 mg/kg	ARZNAD 28,107,78

GV8880000 CYCLOHEXANOL, 2-(DIMETHYLAMINOMETHYL)-1-(m-FLUOROPHENYL)-
UPDT:7901 CAS: 73806-44-7 MW: 251.38 MOLFM: C15-H22-F-N-O
SYN: 2-(DIMETHYLAMINOMETHYL)-1-(m-FLUOROPHENYL)CYCLOHEXANOL

TXDS: orl-mus LD50:310 mg/kg	ARZNAD 28,107,78

GV8885000 CYCLOHEXANOL, 2-(DIMETHYLAMINOMETHYL)-1-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 29164-27-4 MW: 263.42 MOLFM: C16-H25-N-O2
SYN: 2-DIMETHYLAMINOMETHYL-1-(m-METHOXYPHENYL)CYCLOHEXANOL

TXDS: orl-mus LD50:395 mg/kg	ARZNAD 28,107,78

APPENDIX B

HOMEOWNER'S AGREEMENT

In this Agreement, made as of _____, 1985, between _____ and spouse _____ residing at _____, County of _____, State of _____, and Martin Marietta Energy Systems, Inc., a Delaware Corporation with an office at Oak Ridge, Tennessee 37831, acting under its Contract DE-AC05-84OR21400 with the United States of America as represented by the Department of Energy with research facilities at Oak Ridge National Laboratory;

Acquisition of additional data on indoor air quality in residential settings has been identified as a research need. The Health and Safety Research Division of Oak Ridge National Laboratory will be conducting an indoor air quality field study in the Tennessee Valley region during 1985-86. The field study is supported by several agencies including the Department of Energy (DOE), the Tennessee Valley Authority (TVA), the Environmental Protection Agency (EPA), and the Consumer Product Safety Commission (CPSC). The primary component of the study, on which other activities will build, will involve measurement of radon and radon progeny in 60 houses in four states. Additional pollutants that will be monitored include formaldehyde and nitrogen dioxide. Air exchange rates between indoor and outdoor air will also be measured. Other parameters that cannot be measured in all 60 homes will be measured in a subset of homes. Examples include measurement of volatile organic compounds and particulate matter. The houses will be visited by a monitoring team once or twice each quarter for one year to perform sampling. Measurements are to begin in the summer of 1985. The 60 houses selected for the study will be chosen from the list of candidate houses based on various selection criteria.

NOW, THEREFORE, the parties agree as follows:

Martin Marietta Energy Systems, Inc. will

[1] provide data collection equipment and install said equipment on participants' premises and subsequently remove it;
[2] maintain and service such equipment at its expense during the term of this agreement;
[3] periodically monitor the air on the premises;
[4] release perfluoromethylcyclohexane and perfluorodimethylcyclohexane into the house allowing concentration no greater than 0.0001 ppm (the lowest known levels at which these chemicals affect rats is greater than 100 ppm);
[5] occasionally release Freon 12 (i.e., dichlorodifluoromethane) into 6 houses in the Oak Ridge area allowing concentrations no greater than 600 ppm (the lowest known level at which Freon affects humans is 200,000 ppm and occupational exposure is limited to 900 ppm);
[6] make available to the Participants the results of the data collected from the Participants' premises;

HOMEOWNER'S AGREEMENT

In this Agreement, made as of _____, 1985, between _____ and spouse _____ residing at _____, County of _____, State of _____, and Martin Marietta Energy Systems, Inc., a Delaware Corporation with an office at Oak Ridge, Tennessee 37831, acting under its Contract DE-AC05-840R21400 with the United States of America as represented by the Department of Energy with research facilities at Oak Ridge National Laboratory;

Acquisition of additional data on indoor air quality in residential settings has been identified as a research need. The Health and Safety Research Division of Oak Ridge National Laboratory will be conducting an indoor air quality field study in the Tennessee Valley region during 1985-86. The field study is supported by several agencies including the Department of Energy (DOE), the Tennessee Valley Authority (TVA), the Environmental Protection Agency (EPA), and the Consumer Product Safety Commission (CPSC). The primary component of the study, on which other activities will build, will involve measurement of radon and radon progeny in 60 houses in four states. Additional pollutants that will be monitored include formaldehyde and nitrogen dioxide. Air exchange rates between indoor and outdoor air will also be measured. Other parameters that cannot be measured in all 60 homes will be measured in a subset of homes. Examples include measurement of volatile organic compounds and particulate matter. The houses will be visited by a monitoring team once or twice each quarter for one year to perform sampling. Measurements are to begin in the spring of 1985. The 60 houses selected for the study will be chosen from the list of candidate houses based on various selection criteria.

NOW, THEREFORE, the parties agree as follows:

Martin Marietta Energy Systems, Inc. will

[1] provide data collection equipment and install said equipment on participants' premises and subsequently remove it;
[2] maintain and service such equipment at its expense during the term of this agreement;
[3] periodically monitor the air on the premises;
[4] make available to the Participants the results of the data collected from the Participants' premises;
[5] assume responsibility for any damage to Participants' property directly caused by its representatives monitoring the air or by the installation or removal of the data collection equipment, or for claims brought by third persons for personal injury or damage to property directly related to the installation of the equipment or monitoring of the air during the term of this agreement, subject to the availability of funds;
[6] to the extent possible by law, withhold from the public the name(s) of occupants or owners of residences that are studied;
[7] notify Participants at least 24 hours in advance of the date access to the premises is desired; and
[8] pay Participants $50 upon acceptance into the final group of 60 houses and $50 upon completion of the study.

HOMEOWNERS AGREEMENT 60-House Study

Participants will

[1] permit representatives of Martin Marietta Energy Systems, Inc., reasonable access to Participants' premises for the purpose of sampling air indoors and outdoors;
[2] allow the installation, servicing, and removal of data collection equipment;
[3] allow Martin Marietta Energy Systems, Inc., representatives to take photographs at Participants' premises;
[4] allow Martin Marietta Energy Systems, Inc., to disseminate information collected to the public; and
[5] participate for the full year of the study if accepted into the final group of 60 houses.

PARTICIPANTS

By _____
Date _____

By _____
Date _____

Martin Marietta Energy Systems, Inc.

By _____
Title _____
Date _____

\K RIDGE NATIONAL LABORATORY
ERATED BY MARTIN MARIETTA ENERGY SYSTEMS, INC

POST OFFICE BOX X
OAK RIDGE, TENNESSEE 37831

October 8, 1986

Ms. Lynn M. Reeves
Secretary
ORNL Human Studies Committee
Medical Division, Room D110
Oak Ridge Associated University
Badger Avenue
Oak Ridge, TN 37830

Dear Lynn:

Updated Copy of Homeowner's Agreement for New Jersey Radon Study

Enclosed is an updated copy of the Homeowner's Agreement for our New Jersey Radon Mitigation Study. This copy has been reviewed by the legal staff. Please substitute this latest version of the Homeowner's Agreement in your files on this project.

Thank you for your assistance.

Sincerely,

A. R. Hawthorne, PhD
Group Leader
Measurement Applications Group
Health and Safety Research Division

ARH:lgj

Enclosure

cc: C. S. Dudney
T. G. Matthews

1048248

HOMEOWNER'S AGREEMENT

In this Agreement, made as of _____, 1986, between _____ and spouse _____ residing at _____, County of _____, State of New Jersey, and Martin Marietta Energy Systems, Inc., a Delaware Corporation with an office at Oak Ridge, Tennessee 37831, acting under its Contract DE-AC05-84OR21400 with the United States of America as represented by the Department of Energy with research facilities at Oak Ridge National Laboratory;

Whereas acquisition of additional data on time-dependent indoor radon levels in residential settings and evaluation of the effectiveness of various mitigation measures to reduce radon levels has been identified as research needs by state and federal agencies, the Health and Safety Research Division of Oak Ridge National Laboratory and the Center for Energy and Environmental Studies of Princeton University, as a subcontractor to Martin Marietta Energy Systems, Inc., are conducting a detailed study of seven New Jersey homes to address these needs. Other subcontractors may be engaged to implement a specific control measure. This study is supported by several agencies including the Environmental Protection Agency (EPA), the New Jersey Department of Environmental Protection (DEP), and the Department of Energy (DOE), and is a subset of a larger study managed by Lawrence Berkeley Laboratory (LBL). The primary study goals are:

1. field evaluation and refinement of diagostic protocols for implementation of effective mitigation stategies,

2. improved understanding of the physical processes leading to elevated radon levels in homes and the impact of mitigation measures on these processes, and

3. systematic reduction of radon levels in the study homes via implementation of approved mitigation plans.

The study will begin in September 1986 and last for a period of one year.

NOW, THEREFORE, the parties agree as follows:

Martin Marietta Energy Systems, Inc., and Princeton University will

[1] provide monitoring equipment for radon and radon progeny, environmental parameters (such as temperature, relative humidity, and pressure differences), house characteristics (air exchange rates, house leakage, internal mixing), and other such equipment as might be needed, and install said equipment on Participants' premises and subsequently remove it;
[2] maintain and service such equipment at their expense during the term of this agreement;
[3] shall pay for installation, monthly charges, and removal (upon completion of the study) of an additional telephone line for data transmission from monitoring equipment;

[4] monitor the air on the premises;
[5] notify Participants in advance of the time access to the premises is desired;
[6] release perfluoromethylcyclohexane and perfluorodimethylcyclohexane into the house for air exchange rate measurements, allowing concentration no greater than 0.001 ppm (the lowest known levels at which these chemicals affect rats is greater than 100ppm);
[7] produce house specific mitigation plans for Participants' approval;
[8] attempt to reduce radon levels (one house will be a control and will not be mitigated until near the end of the study); if, however, reductions cannot be accomplished, then to ensure that levels will be no greater that in the unmitigated structure;
[9] provide mitigation measures that will become the property of the Participants upon completion of the study;
[10] conduct baseline testing of active mitigation measures (i.e., switch off the devices) to evaluate their effectiveness for radon control--levels will not be allowed to exceed values determined by EPA to be excessive;
[11] make available to the Participants the results of the data collected from the Participants' premises;
[12] assume responsibility for damage to Participants' property directly caused by their representatives monitoring the home or by the installation or removal of the data collection equipment, or for claims brought by third persons for personal injury or damage to property directly related to the installation of the equipment or monitoring in the home during the term of this agreement, subject to the availability of funds; and
[13] to the extent possible by law, withhold from the public the name(s) of occupants or owners of residences that are studied.

Participants will

[1] permit representatives of Martin Marietta Energy Systems, Inc., and Princeton University reasonable access to Participants' premises for the purpose of monitoring radon and related parameters;
[2] allow the installation, servicing, and removal of data collection equipment;
[3] allow the installation and removal of an additional telephone line for data transmission from monitoring equipment;
[4] review and approve specific mitigation plan for Participants' home;
[5] allow implementation, including modification of the house, of Participant approved mitigation plan;
[6] indemnify and hold harmless Martin Marietta Energy Systems, Inc., Princeton University, and/or the U.S. Government and/or the State of New Jersey for any injury to person or damage to property that may occur as a result of the work done or omitted as part of this study, including without limitation, modifications to the house design and structure and the installation of mitigation devices. We have been advised that the process of installation and evaluation may result in a temporary increase in radon concentrations on the premises.

[7] allow Martin Marietta Energy Systems, Inc., and Princeton University representatives to take photographs at Participants' premises;
[8] allow Martin Marietta Energy Systems, Inc., and Princeton University to disseminate information collected to the public.

PARTICIPANTS

By _____

Date_____

Martin Marietta Energy Systems, Inc.

By_____

Title_____

Date_____

Princeton University

By_____

Date_____

By_____

Title_____

Date_____

HOMEOWNER'S AGREEMENT

In this Agreement, made as of _____, 1986, between _____ and spouse _____ residing at _____, County of _____, State of New Jersey, and Martin Marietta Energy Systems, Inc., a Delaware Corporation with an office at Oak Ridge, Tennessee 37831, acting under its Contract DE-AC05-84OR21400 with the United States of America as represented by the Department of Energy with research facilities at Oak Ridge National Laboratory;

Whereas acquisition of additional data on time-dependent indoor radon levels in residential settings and evaluation of the effectiveness of various mitigation measures to reduce radon levels have been identified as research needs by state and federal agencies, the Health and Safety Research Division of Oak Ridge National Laboratory and the Center for Energy and Environmental Studies of Princeton University, as a subcontractor to Martin Marietta Energy Systems, Inc., are conducting a detailed study of seven New Jersey homes to address these needs. Other subcontractors may be engaged to implement specific control measures. This study is supported by several agencies including the Environmental Protection Agency (EPA), the New Jersey Department of Environmental Protection (DEP), and the Department of Energy (DOE), and is a subset of a larger study managed by Lawrence Berkeley Laboratory (LBL). The primary study goals are:

1. field evaluation and refinement of diagnostic protocols for implementation of effective mitigation strategies,

2. improved understanding of the physical processes leading to elevated radon levels in homes and the impact of mitigation measures on these processes, and

3. systematic reduction of radon levels in the study homes via implementation of approved mitigation plans.

The study will begin in September 1986 and last for a period of one year.

NOW, THEREFORE, the parties agree as follows:

Martin Marietta Energy Systems, Inc., will

[1] provide monitoring equipment for radon and radon progeny, environmental parameters (such as temperature, relative humidity, and pressure differences), house characteristics (air exchange rates, house leakage, internal mixing), and other such equipment as might be needed, and install said equipment on Participants' premises and subsequently remove it;
[2] maintain and service such equipment at their expense during the term of this agreement;
[3] pay for installation, monthly charges, and removal (upon completion of the study) of an additional telephone line for data transmission from monitoring equipment;
[4] monitor the air on the premises;

[5] notify Participants in advance of the time access to the premises is desired;
[6] release perfluoromethylcyclohexane and perfluorodimethylcyclohexane into the house for air exchange rate measurements, allowing concentration no greater than 0.001 ppm (the lowest known levels at which these chemicals affect rats is greater than 100 ppm);
[7] produce house specific mitigation plans for Participants' approval;
[8] attempt to reduce radon levels (one house will be a control and will not be mitigated until near the end of the study); if, however, reductions cannot be accomplished, then to ensure, within the available funding, that levels will be no greater than in the unmitigated structure based on pre- and post-mitigation measurements performed during the same seasonal conditions;
[9] make available to the Participants the results of the data collected from the Participants' premises;
[10] assume responsibility for damage to Participants' property directly caused by their representatives monitoring the home or by the installation or removal of the data collection equipment, or for claims brought by third persons for personal injury or damage to property directly related to the installation of the equipment or monitoring in the home during the term of this agreement, subject to the availability of funds; and
[11] to the extent possible by law, withhold from the public the name(s) of occupants or owners of residences that are studied.

Participants will

[1] permit representatives of Martin Marietta Energy Systems, Inc., and their subcontractors reasonable access to Participants' premises for the purpose of monitoring radon and related parameters;
[2] allow the installation, servicing, and removal of data collection equipment;
[3] allow the installation and removal of an additional telephone line for data transmission from monitoring equipment;
[4] review and approve specific mitigation plan for Participants' home;
[5] allow implementation, including modification of the house, of Participant approved mitigation plan;
[6] indemnify and hold harmless Martin Marietta Energy Systems, Inc., Princeton University, and/or the U.S. Government and/or the State of New Jersey for any injury to person or damage to property that may occur as a result of the work done or omitted as part of this study, including without limitation, modifications to the house design and structure and the installation of mitigation devices. We have been advised that the process of installation and evaluation may result in a temporary increase in radon concentrations on the premises.
[7] allow Martin Marietta Energy Systems, Inc., representatives to take photographs at Participants' premises;
[8] allow Martin Marietta Energy Systems, Inc., to disseminate information collected to the public.

PARTICIPANTS

Martin Marietta Energy Systems, Inc.

By _____

Date_____

By_____

Title_____

Date_____

By_____

Date_____

Ident. No. _____

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date: 04/22/85

Principal Investigators: Charles S. Dudney, Ph.D.
Thomas G. Matthews, Ph.D.

Co-Investigators: William G. Dreibelbis, C.I.H
Alan R. Hawthorne, Ph.D.

Title of Project: Indoor Air Quality Study in 60 Houses in the Tennessee Valley

I. OBJECTIVES OF STUDY:

The Health and Safety Research Division of Oak Ridge National Laboratory will be conducting a study of indoor air quality in 60 houses in the Tennessee Valley under the sponsorship of several federal agencies.

There will be two major operational elements of this study. One will be the collection of data from all of the houses in the study and will emphasize use of relatively small, passive sampling devices that can be analyzed to yield information on time-weighted average levels of chemical or naturally occurring radioactive species in the homes. The other major element will be the collection of data in six of the 60 homes and will emphasize the use of more elaborate sampling devices for one-week intervals in the summer and winter quarters. The six-home subset will be limited to houses in the area surrounding Oak Ridge.

The objective of one aspect of the study, applicable to all of the houses and defined by the TVA-supported IAG (#40-1459-84) which funds the major part of this study, is to determine the mean and standard deviation of the levels of radon and radon progeny in 60 selected homes during a one-year interval. Exposure to the short-lived radioactive progeny of radon has been associated with increased incidence of lung cancer among various uranium-mining populations. Various products from the phosphate-mining operations in central Florida have been shown to emanate radon at rates

1. Radon

Once each quarter track etch detectors will be placed in the houses. A track etch detector is about the size and mass of a paper cup. There is a filter across the opening to prevent the entry of particles on which most of the radon progeny reside. Inside is a plastic detector. Subsequent radioactive decays within the chamber give rise to tracks that are detected during analysis. The density of tracks is proportional to the time-weighted average radon concentration.

Once each quarter each home will be visited by a specially equipped van. Samples of the air will be analyzed by high resolution alpha spectroscopy to determine radon levels.

2. Radon Progeny

For one week each quarter a radon progeny integrating sampling unit, known as a MOD, will be installed and operated in each house. A MOD is a box about the size of a table radio and requires 60 Hz 120 VAC for operation. The device pumps air (~0.1L/min) through a filter behind which is a TLD chip to detect radioactive decay events. Since radon passes through the filter only decay events from progeny on particulate material are detected.

During visits by the specially equipped van, levels of the progeny will be measured using alpha spectroscopy.

3. Air Exchange

In each house, sources of perflourocarbon gases will be installed. Two different kinds of sources will be installed, with one kind on the upper level and another kind on the lower level. For one week each quarter, passive samplers will be installed in several locations in each house and subsequently analyzed to estimate time-weighted average air exchange rates. This method was developed by Dietz and Cote (1982) and has been extensively used to measure air exchange rates in homes.

2. Air Exchange.

Continuous measurements of the air infiltration rate will be performed using tracer gas decay measurements. Freon 12 will be injected into the indoor atmosphere; its decaying concentration will be monitored as a function of time with a Miran infrared absorption spectrometer. This instrument will be located outside the home in an instrumented van with an air sampling tube running indoors. The concentration of the tracer gas will be microprocessor controlled in a range of approximately 1-10 ppm. When the concentration reaches 1 ppm, the control unit will open a valve to a small tank of freon located inside the home. The valve will subsequently be closed as the Freon concentration approaches 10 ppm. Fans will be used during and after freon injection to mix the gas throughout the home.

3. Formaldehyde

Continuous formaldehyde vapor concentration measurements will be performed indoors using a CEA Instrument Inc. Analyzer. This instrument will be located in an instrumented van outside the home with an air sampling tube running indoors.

4. Nitrogen Oxides, Nitrogen Dioxide

Total nitrogen oxides and specifically nitrogen dioxide will be monitored continuously using a Monitor Labs, Inc., nitrogen oxides analyzer. This instrument will be located in an instrumented van outside of the home with an air sampling tube running indoors

5. Carbon Monoxide

A Interscan electrochemical analyzer will be used to perform continuous measurements of carbon monoxide indoors. This instrument will be located in an instrumented van outside of the home with an air sampling tube running indoors.

Name	TLV	Toxicity
Dichlorodifluoromethane (Freon 12)	4,950 mg/m3	200,000 ppm/30 min TClo inhal/human
Perfluoromethylcyclohexane (PMCH)	NA	825 ppm/14 hr. TClo inhal/rat
Perfluorodimethylcyclohexane(PDCH)	NA	100 ppm/14 hr. TClo inhal/rat/guinea pig

Appendix A provides copies of the entries for these chemicals from the latest issue of the NIOSH Registry of Toxic Effects of Chemicals.

Under normal operation, the microprocessor-controlled, Freon injection system will limit Freon concentrations to approximately 10 ppm, which is one percent of the Occupational Safety and Health Administration threshold limit value (TLV) for eight hours of exposure to Freon. The air inside the homes would be mixed during and after Freon injection to prevent abnormally high concentrations from developing near the injection point. The source of Freon will be limited such that total system failure, in which all the Freon was released, would result in concentrations less than 3,000 mg/m^3 (~60% of TLV) for a very tight (i.e., zero air exchange) house having 750 square feet of floor space and 8 foot ceilings. For houses that are either larger or leakier the levels would be less.

In all 60 houses, the perfluorocarbons tracers will be released passively from pellets. The rate of release is less than 1 mg/day for each pellet and three pellets for each tracer will be used in each house. For a house having 750 square feet of floor space and 8-foot ceilings with an air exchange rate greater than 0.2 h^{-1} then the levels of PMCH and of PDCH would be less than 0.00123 mg/m^3 (less than 0.0001 ppm).

Safety will be considered during the house selection process. For example, homes with young children will be excluded unless the homeowner feels certain that the children will not be left unattended with the sampling equipment and the investigators feel that the homeowner will responsibly oversee any resident children.

The principal investigators will follow the procedures of the Committee on Human Studies in obtaining "informed consent" from each of the subjects in the study. The investigators recognize that they retain the primary responsibility for safe-guarding the interests of the participants in the study. Any significant changes in the study protocols or the development of any unexpected risks will be brought to the attention of the Committee on Human Studies.

Starting Date: June 1, 1985

Signatures: _____ Principal Investigator

_____ Principal Investigator

_____ Co-Investigator

_____ Co-Investigator

DIVISION REVIEW:

The application described above has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Official signing for the institution:

Signature _____

Title _____

Institution _____

Date _____

Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical and
Health Sciences
Division

April 17, 1986

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: ~~Drs~~ Dudney + Matthews

FROM: Lynn Reeves, Secretary
ORAU/ORNL Committee on Human Studies

SUBJECT: PROGRESS REPORTS

The guidelines for the ORAU/ORNL Committee on Human Studies require that yearly all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by ~~May 5,~~ 1986. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: Indoor Air Quality Study in 60 Houses in the Tennessee Valley

Proposal No. ORNL-14 Date ~~1984~~ 1985

Charles A. Dudney Thomas D. Matthews
Signatures of Principal Investigators

4/25/86
Date Signed

1. Report progress made in the past year.
Measurements have been made for three calendar quarters. Also intensive study of six local homes has been completed. The following numbers of measurements have been made:

Radon (3 month): 557	Formaldehyde (1-week): 391	NO_2 (1-week): 947	
Radon (grab): 409	Vapor-phase PNAs (1-week): 172	VOC (grab): 200	
Rn Progeny (1 week): 277	Water vapor (1-week): 465		
Rn Progeny (grab): 349	Air Exchange (1-week): 674		

2. Report any complications.
Only two homeowners have quit the study. Ten new homes were added to the study at the mid point and will be studied from Win 86 to Fall 86

1048260

3. Are there any planned changes?
None other than the addition of ten new homes

4. Do you wish the project to be continued?
We wish the project to continue through Jan 87

5. Comments.
Given the size and geographic scope of this study it has gone ~~smo~~ more smoothly than we expected.
To our knowledge, there have been no homeowner complaints and no unsafe events in these homes because of our study activities.
One homeowner, who is still in the study, did ~~f~~ complain about the intensive study last summer.

ihl-hmn TCLo:500 ppm/1Y-I TFX:CNS — ABMYAE 43,1123.68
ihl-hmn TCLo:500 ppm/8H TFX:BLD — SCIEAS 176,295.72
orl-rat LD50:167 mg/kg — DOWSD* 1/26/76
ihl-rat LC50:88000 mg/m3/30M — FAVUAI 7,35,75
ihl-rat TCLo:500 ppm/6M/2Y TFX:ETA — TXAPA9 48 A183,79
ihl-mus LC50:144000 ppm/7H — NIMBAZ 191,1,49
ipr-mus LD50:1500 mg/kg — TXAPA9 9,139.66
scu-mus LD50:6480 mg/kg — TXAPA9 4,354.62
orl-dog LDLo:3200 mg/kg — QJPPAL 7,205,34
ihl-dog LCLo:14108 ppm/7H — NIMBAZ 191,1,49
ipr-dog LDLo:950 mg/kg — TXAPA9 10,119.67
scu-dog LDLo:2700 mg/kg — QJPPAL 7,205,34
ivn-dog LDLo:200 mg/kg — QJPPAL 7,205,34
ihl-rat LCLo:43400 mg/m3/4.5H — AMBAAM 116,131,36
orl-rbt LDLo:1600 mg/kg — H8TXAC 1,94,36
scu-rbt LDLo:2700 mg/kg — QJPPAL 7,205,34
ihl-gpg LCLo:5000 ppm/2H — FLCRAP 1,197,67

AQTX: AQUATIC TOXICITY RATING: TLm96:1000-100 ppm — WQCHM* 3,-,74
REVIEW: CARCINOGENIC DETERMINATION:INDEFINITE — IARC** 20,449,79
REVIEW: THRESHOLD LIMIT VALUE-air:100 ppm — DTLVS* 4,275.80
REVIEW: TOXICOLOGY REVIEW — FAZMAE 18,365,74
REVIEW: TOXICOLOGY REVIEW — 27ZTAP 3,94,69
REGS: OSHA STANDARD-air:TWA 500 ppm;CI 1000;Pt 2000/5M/2H (SCP-J) — FEREAC 39,22340,74
DOT-ORM-A, LABEL:NONE — FEREAC 41,57018,76
CRIT DOC OCCUPATIONAL EXPOSURE TO METHYLENE CHLORIDE recm std-air:TWA 75 ppm;Pt 500 ppm/15M — NTIS**
STATUS: CURRENTLY TESTED BY NTP FOR CARCINOGENESIS BY STANDARD BIOASSAY PROTOCOL AS OF SEPT 1980
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 1 127, VOL 2 S329
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8100000 METHANE, DICHLOROBIS(METHYLSULFONYL)-

UPDT:8007 CAS: 32436-32-1 MW: 241.11 MOLFM: C3-H6-Cl2-O4-S2
SYN: BISMETHYLSULFONYLDICHLOROMETHANE * DICHLOROBIS(METHYLSULFONYL)METHANE
TXDS: — CSLNX* NX#09537

[redacted]

SYN: ALGOFRENE TYPE 2 * F 12 * FC 12 * ARCTON 6 * DICHLORODIFLUOROMETHANE * DICHLORODIFLUOROMETHANE (DOT) * DIFLUORODICHLOROMETHANE * DWUCHLORODWUFLUOROMETAN (Polish) * ELECTRO-CF 12 * FLUOROCARBON-12 * FREON 12 * ESKIMON 12 * FREON 9-12 * FRIGEN 12 * GEMETRON 12 * HALON * ISCEON 122 * ISOTRON 12 * LEDON 12 * PROPELLANT 12 * REFRIGERANT 12 * UCON 12
TXDS: ihl-hmn TCLo:200000 ppm/30M TFX:EYE — JETOAS 9,385,76
ihl-hmn TCLo:200000 ppm/30M TFX:CNS — JETOAS 9,385,76
ihl-rat LC50:80 pph/30M — JETOAS 9,385,76
ihl-mus LC50:76 pph/30M — JETOAS 9,385,76
ihl-rbt LC50:80 pph/30M — JETOAS 9,385,76
ihl-gpg LC50:80 pph/30M — JETOAS 9,385,76
AQTX: AQUATIC TOXICITY RATING: TLm96:over 1000 ppm — WQCHM* 3,-,74
REVIEW: THRESHOLD LIMIT VALUE-air:1000 ppm — DTLVS* 4,128.80
REVIEW: TOXICOLOGY REVIEW — FAZMAE 18,365,74
REVIEW: TOXICOLOGY REVIEW — NYSJAM 74(11),1939,74
REGS: OSHA STANDARD-air:TWA 1000 ppm (SCP-H) — FEREAC 39,23540,74
DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS — FEREAC 41,57018,76
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S111
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8220000 METHANE, DICHLORODIFLUORO- mixed with CHLORODIFLUOROMETHANE

UPDT:7905 CAS: 70231-20-0
SYN: DICHLORODIFLUOROMETHANE-MONOCHLORODIFLUOROMETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS — FEREAC 41,57018,76

PA8250000 METHANE, DICHLORODIFLUORO- mixed with DICHLOROTETRAFLUOROETHANE

UPDT:7901 CAS: 57107-42-9
SYN: DICHLORODIFLUOROMETHANE-DICHLOROTETRAFLUOROETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS — FEREAC 41,57018,76

PA8260000 METHANE, DICHLORODIFLUORO- mixed with 1,1-DIFLUOROETHANE

UPDT:7901 CAS: 36273-41-3
SYN: DICHLORODIFLUOROMETHANE and DIFLUOROETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS — FEREAC 41,57018,76

PA8275000 METHANE, DICHLORODIFLUORO- mixed with FLUOROTRICHLOROMETHANE

UPDT:7907
SYN: DICHLORODIFLUOROMETHANE-TRICHLOROMONOFLUOROMETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS — FEREAC 41,57018,76

PA8278000 METHANE, DICHLORODIFLUORO-, mixed with TRICHLOROFLUOROMETHANE (1:1)

UPDT:7903 MW: 258.27 MOLFM: C-Cl3-F.C-Cl2-F2
SYN: DICHLOROFLUOROMETHANE-TRICHLOROFLUOROMETHANE (DOT)
TXDS: ihl-rat LC50:20 pph/30M — JETOAS 9,385,76
ihl-mus LC50:72 pph/30M — JETOAS 9,385,76
ihl-gpg LC50:50 pph/30M — JETOAS 9,385,76

PA8278500 METHANE, DICHLORODIFLUORO- and METHANE, FLUOROTRICHLORO- mixed with CHLORODIFLUOROMETHANE

UPDT:7905
SYN: DICHLORODIFLUOROMETHANE-TRICHLOROMONOFLUOROMETHANE-MONOCHLORODIFLUOROMETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS — FEREAC 41,57018,76

PA8280000 METHANE, DICHLORODIFLUORO- mixed with TRICHLOROTRIFLUOROETHANE

UPDT:7901
SYN: DICHLORODIFLUOROMETHANE-TRICHLOROTRIFLUOROETHANE MIXTURE (DOT)
REGS: DOT-NONFLAMMABLE GAS, LABEL:NONFLAMMABLE GAS — FEREAC 41,57018,76

PA8300000 METHANE, DICHLORODINITRO-

UPDT:7907 CAS: 1587-41-3 MW: 174.93 MOLFM: C-Cl2-N2-O4
SYN: DICHLORODINITROMETHANE
TXDS: ipr-mam LDLo:200 mg/kg — CORFAF 171,1396,20
ipr-mus LD50:20 mg/kg — KHFZAN 10(6),53,76

PA8400000 METHANE, DICHLOROFLUORO-

UPDT:7908 CAS: 75-43-4 MW: 102.92 MOLFM: C-H-Cl2-F
SYN: ALGOFRENE TYPE 3 * ARCTON 7 * DICHLOROFLUOROMETHANE * DICHLOROMONOFLUOROMETHANE * DWUCHLOROWOFLUOROMETAN (Polish) * FLUORODICHLOROMETHANE * FREON 21 * GENETRON 21
TXDS: ihl-gpg LCLo:10 ppk/1H — FLCRAP 1,197,67

REVIEW: THRESHOLD LIMIT VALUE-air:10 ppm — DTLVS* 4,132.80
REVIEW: TOXICOLOGY REVIEW — FAZMAE 18,365,74
REGS: OSHA STANDARD-air:TWA 1000 ppm (SCP-H) — FEREAC 39,23540,74
STATUS: NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S109
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8440000 METHANE, DICUMENYL-

UPDT:7908 CAS: 25550-72-1 MW: 282.43 MOLFM: C19-H26
SYN: DICUMYLMETHANE * DSM (Russian)
TXDS: orl-mus LDLo:15 gm/kg — TPKVAL 6,73,64
ihl-mus LCLo:122 mg/m3 — TPKVAL 6,73,64
scu-mus LDLo:19 gm/kg — TPKVAL 6,73,64

METHANE, DICYANO- see: OO1150000

PA8500000 METHANE, DIETHOXY-

UPDT:7908 CAS: 462-95-3 MW: 104.17 MOLFM: C5-H12-O2
SYN: ETHYLAL
TXDS: orl-rbt LD50:2604 mg/kg — PSEBAA 29,730,32
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8575000 METHANE, DIIODO-

UPDT:7908 CAS: 75-11-6 MW: 267.83 MOLFM: C-H2-I2
SYN: DIIODOMETHANE * METHYLENE IODIDE
TXDS: scu-mus LD50:830 mg/kg — TXAPA9 4,354,62
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8750000 METHANE, DIMETHOXY-

UPDT:8007 CAS: 109-87-5 MW: 76.11 MOLFM: C3-H8-O2
SYN: APRESTHENYL * DIMETHOXYMETHANE * FORMAL * FORMALDEHYDE DIMETHYLACETAL * METHYLAL * METHYLENE DIMETHYL ETHER * METHYLAL (DOT) * METYLAL (Polish)
TXDS: ihl-rat LC50:15000 ppm — NPIRI* 1,73,74
orl-rbt LD50:5708 mg/kg — PSEBAA 29,730,32
scu-gpg LDLo:3013 mg/kg — BJIMAG 8,279,51
REVIEW: THRESHOLD LIMIT VALUE-air:1000 ppm — DTLVS* 4,262,80
REGS: OSHA STANDARD-air:TWA 1000 ppm (SCP-F) — FEREAC 39,23540,74
DOT-FLAMMABLE LIQUID, LABEL:FLAMMABLE LIQUID — FEREAC 41,57018,76
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S71
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA8800000 METHANE, DINITROFLUORO-

UPDT:8012 CAS: 7182-87-8 MW: 124.04 MOLFM: C-H-F-N2-O4
SYN: DINITROFLUOROMETHANE
TXDS: ipr-mus LD50:24 mg/kg — KHFZAN 10(6),53,76

METHANEDIOL, DIACETATE see A:9075000

PA8925000 METHANEDIOL, DIMETHANESULFONATE

UPDT:8011 CAS: 126-72-9 MW: 204.22 MOLFM: C3-H8-O6-S2
SYN: METHANESULFONIC ACID, METHYLENE ESTER * METHYLENE BIS(METHANESULFONATE) * METHYLENE DIMETHANESULFONATE
MTDS: dnd-rat-ipr 10 mg/kg — CBINAB 3,149,71
dlt-rat-ipr 15 mg/kg — CCPTAY 13,639,76
mic-mus/sym 50 umol/L — MUREAV 25,107,74
TXDS: ipr-rat TDLo:13 mg/kg/13D preg) TFX:TER — JRPAA4 17,325,68

PA8990000 METHANE, DIPHENYL-

UPDT:7908 CAS: 101-81-5 MW: 168.25 MOLFM: C13-H12
SYN: BENZENE, BENZYL- * BENZYLBENZENE * DIPHENYLMETHANE * DITAN * DITANE * TOLUENE, alpha-PHENYL-
TXDS: orl-rat LDLo:5000 mg/kg — AMIHAB 19,403,59
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

METHANEDITHIOL, S,S-DIESTER with O,O-DIETHYL PHOSPHORODITHIOATE see TE4550000
METHANE (DOT) see PA1490000
METHANE, ETHOXY see KO0260000
METHANE, FLUOROTRICHLORO- see: FS6125000

PA9150000 METHANE, FLUOROTRICHLORO- with NITROMETHANE (99.7:0.3)

CEP Contains 0.3% NITROMETHANE in addition to FREON-11 (TOIZAG 13,363,71)
UPDT:7901
SYN: FREON-11 S
TXDS: ipr-mus LD50:2799 mg/kg — TOIZAG 13(2),363,71

PA9200000 METHANE, FLUOROTRINITRO-

UPDT:7902 CAS: 1840-42-2 MW: 169.04 MOLFM: C-F-N3-O6
SYN: FLUOROTRINITROMETHANE
TXDS: ipr-mus LD50:57300 ug/kg — KHFZAN 10(6),53,76
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

METHANE, (2-HYDROXYETHOXY)METHOXY- see: KL6475000
METHANE, HYDROXYIMINOBIS(2-METHYLCYCLOPROPYL)- see GZ3015000

PA9450000 METHANE, IODO-

UPDT:8007 CAS: 74-88-4 MW: 141.94 MOLFM: C-H3-I
SYN: HALON 10001 * IODOMETANO (Italian) * IODOMETHANE * IODURE DE METHYLE (French) * JOD-METHAN (German) * JODOMETHAAN (Dutch) * METHYL IODIDE * METHYLJODID (German) * METHYLJODIDE (Dutch) * METYLU JODEK (Polish) * MONOIODURO DI METILE (Italian)
MTDS: mmo-sal 2 uL/plate — JNCIAM 62,873,79
mmo-sal 2 uL/plate — JNCIAM 62,873,79
dnr-esc 10 ug/disc — JNCIAM 62,873,79
mrc-smc 1000 ppm — JNCIAM 62,901,79
mmo-mus/ivm 50 mg/L/4H — MUREAV 59,61,79
mic-mus/ivm 15 mg/L/2H — MUREAV 59,61,79
IRDS: ihl-hmn 1 gm/10M MLD — BJIMAG 7,122,50
ihl-rat 1 gm/30M MLD — BJIMAG 7,122,50
TXDS: orl-rat LD50:150 mg/kg — BJIMAG 7,122,50
ihl-rat LCLo:3790 ppm/15M — NRLR** No.23,50
skn-rat LDLo:800 mg/kg — KODAK* -,-,71
scu-rat LDLo:150 mg/kg — BJIMAG 7,122,50
scu-rat TDLo:50mg/kg TFX:ETA — ZEKRAI 74,241,73
ihl-mus LCLo:5000 mg/m3/11H — BJIMAG 7,122,50
ipr-mus TDLo:44 mg/kg/8W-I TFX:NEO — CNREAB 25,1411,75
scu-mus TD50:110 mg/kg — TXAPA9 4,354,62
REVIEW: CARCINOGENIC DETERMINATION-ANIMAL POSITIVE — IARC** 15,245,77
REVIEW: THRESHOLD LIMIT VALUE-air:2 ppm (skin) — DTLVS* 4,231,80
REVIEW: TOXICOLOGY REVIEW — 27ZTAP 3,95,69
REGS: OSHA STANDARD-air:TWA 5 ppm (skin) (SCP-H) — FEREAC 39,23540,74
STATUS: NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S98
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

PA9500000 METHANE, IODOTRINITRO-

UPDT:7907 CAS: 6070-08-8 MW: 276.94 MOLFM: C-I-N3-O6
SYN: IODOTRINITROMETHANE
TXDS: orl-mus LD50:20 mg/kg — KHFZAN 10(6),53,76

PA9540000 METHANE, ISOCYANATO- mixed with DICHLOROPROPANES or DICHLOROPROPENES (1:4)

UPDT:7901 CAS: none 01-1
SYN: EP-162 * TRAPEX * VORLEX
TXDS: orl-rat LD50:305 mg/kg — GUCHAZ 6,532,73

PA9625000 METHANE, ISOTHIOCYANATO-

UPDT:7903 CAS: 556-61-6 MW: 73.12 MOLFM: C2-H-N-S
SYN: EP-162 * ISOTHIOCYANATE DE METHYLE (French) * ISOTHIOCYANATOMETHANE * ISOTHIOCYANIC ACID, METHYL ESTER * ISOTIOCIANATO DI METILE (Italian) * METHYLISOTHIOCYANAT (Dutch) * METHYLISOTHIOCYANAT (German) * METHYL ISOTHIOCYANATE * METHYL MUSTARD OIL * METHYLSENFOEL (German) * MIC * MIT * MITC * MORTON EP-162 * TRAPEX * TRAPEXIDE * VORLEX * VORTEX * WN 12
TXDS: orl-rat LD50:97 mg/kg — ASCHAN 22,183,59

TOXICITY DATA HAS NOT BEEN EVALUATED
OMISSION OF A SUBSTANCE OR NOTATION DOES NOT IMPLY ANY RELIEF FROM REGULATORY RESPONSIBILITY.

STATUS: REPORTED IN EPA TSCA INVENTORY, 1980
CYCLOHEXANE, dono-1,2,3,4,5,6-HEXACHLORO- see: GV4550000

GV4900000 CYCLOHEXANE, 1,2,3,4,5,6-HEXACHLORO-, gamma-isomer
UPDT 8011 CAS: 58-89-9 MW: 290.82 MOLFM: C6-H6-Cl6
SYN: AALINDAN * AFICIDE * AGRISOL G 20 * AGROCIDE * AGROCIDE 2 * AGROCIDE 6G * AGROCIDE 7 * AGROCIDE III * AGROCIDE WP * AGRONEXIT * AMEISENMITTEL MERCK * AMEISENATOD * APARASIN * APHTIRIA * APLIDAL * ARBITEX * BBH * BEN-HEX * BENTOX 10 * BENZENE HEXACHLORIDE gamma-isomer * gamma-BENZENE HEXACHLORIDE * BEXOL * BHC * gamma-BHC * CELANEX * CHLORESENE * CODECHINE * DBH * DETMOL-EXTRAKT * DETOX 25 * DEVORAN * DOL GRANULE * DRILL TOX-SPEZIAL AGLUKON * ENT 7,796 * ENTOMOXAN * EXAGAMA * FORLIN * GALLOGAMA * GAMACID * GAMAPHEX * GAMMAHEXA * GAMMAHEXANE * GAMMALIN * GAMMALIN 20 * GAMMATERR * GAMMEX * GAMMEXANE * GAMMOPAZ * GEXANE * HCCH * HCH * gamma-HCH * HECLOTOX * HEXA * HEXACHLORAN * gamma-HEXACHLORAN * HEXACHLORANE * gamma-HEXACHLORANE * gamma-HEXACHLOROBENZENE * 1-alpha,2-alpha,3-beta,4-alpha,5-alpha,6-beta-HEXACHLOROCYCLOHEXANE * gamma-HEXACHLOROCYCLOHEXANE * 1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE, gamma-ISOMER * gamma-1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE * HEXATOX * HEXAVERM * HEXICIDE * HEXYCLAN * HGI * HORTEX * INEXIT * ISOTOX * JACUTIN * KOKOTINE * KWELL * LENDINE * LENTOX * LIDENAL * LINDAFOR * LINDAGAM * LINDAGRAIN * LINDAGRANOX * LINDANE * LINDANE (DOT) * gamma-LINDANE * LINDAPOUDRE * LINDATOX * LINDOSEP * LINTOX * LOREXANE * milbol 49 * MSZYCOL * NCI-C00204 * NEO-SCABICIDOL * NEXEN FB * NEXIT * NEXIT-STARK * NEXOL-E * NICOCHLORAN * NOVIGAM * OMNITOX * OVADZIAK * OWADZIAK * PEDRACZAK * PFLANZOL * QUELLADA * SANG gamma * SILVANOL * SPRITZ-RAPIDIN * SPRUEHPFLANZOL * STREUNEX * TAP 85 * TRI-6 * VITON

MTDS:	cyt-ham:fbr 63 mg/L/48H	MUREAV 48,337,77
TXDS:	orl-chd LDLo:180 mg/kg	CMEP** -,1,56
	orl-chd TDLo:111 mg/kg TFX:SYS	AEHLAU 25,374,72
	orl-rat LD50:76 mg/kg	SPEADM 74-1,-,74
	skn-rat LD50:500 mg/kg	WRPCA2 9,119,70
	ipr-rat LDLo:35 mg/kg	AEPPAE 212,463,51
	orl-mus LD50:86 mg/kg	FEPRA7 6,386,47
	orl-mus TDLo:25 gm/kg/73W-C TFX:NEO	FCTXAV 11,433,73
	ipr-mus LDLo:75 mg/kg	TXAPA9 23,288,72
	orl-dog LD50:40 mg/kg	SPEADM 74-1,-,74
	ivn-dog LDLo:5 mg/kg	TIEUA7 5,61,50
	orl-rbt LD50:60 mg/kg	JHEMA2 22,115,78
	skn-rbt LD50:50 mg/kg	AFDOAQ 16,3,52
	ivn-rbt LDLo:4500 ug/kg	JPETAB 92,140,48
	orl-gpg LD50:127 mg/kg	FEPRA7 6,386,47
	orl-ham LD50:360 mg/kg	JETOAS 7,159,74
	orl-bwd LDLo:100 mg/kg	TIEUA7 5,61,50
	ims-bwd LDLo:26 mg/kg	TIEUA7 5,61,50
AQTX:	AQUATIC TOXICITY RATING: TLm96:under 1 ppm	WQCHM* 3,-,74
REVIEW:	CARCINOGENIC DETERMINATION:ANIMAL POSITIVE	IARC** 20,195,79
REVIEW:	CARCINOGENIC DETERMINATION:INDEFINITE	IARC** 5,47,74
REVIEW:	THRESHOLD LIMIT VALUE-air:0.5 mg/m3 (skin)	DTLVS* 4,246,80
REVIEW:	TOXICOLOGY REVIEW	CNDQAB 10(3),43,75
REVIEW:	TOXICOLOGY REVIEW	RREVAH 56,107,75
REVIEW:	TOXICOLOGY REVIEW	PMDCAY 10,85,74
REVIEW:	TOXICOLOGY REVIEW	DTTIAF 80(20),485,73
REVIEW:	TOXICOLOGY REVIEW	ARDEAC 113(3),353,77
REVIEW:	TOXICOLOGY REVIEW	CTOXAO 13,231,78
REGS:	OSHA STANDARD-air:TWA 500 ug/m3 (skin) (SCP-T)	FEREAC 39,23540,74
	DOT-ORM-A, LABEL:NONE	FEREAC 41,57018,76

STATUS: NCI CARCINOGENESIS BIOASSAY COMPLETED;RESULTS NEGATIVE (NCITR* NCI-CG-TR-14,77)
STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 3 S290
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV4950000 CYCLOHEXANE, 1,2,3,4,5,6-HEXACHLORO-, (mixed isomers)
DEF:Technical BHC contains about 64% alpha, 10% beta, 13% gamma, 9% delta and 1% epsilonisomers of 1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE (IARC** 5,47,74)
UPDT 8011 CAS: 608-73-1 MW: 290.82 MOLFM: C6-H6-Cl6
SYN: BENZAHEX * BENZENEHEXACHLORIDE, mixed isomers * BENZEX * DOL * DOLMIX * FBHC * FHCH * 1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE (mixture of isomers) * HEXAFOR * HEXYCLAN * KOTOL * SOPROCIDE * TECHNICAL BHC * TECHNICAL HCH

TXDS:	orl-mus TDLo:13 gm/kg/24W-C TFX:NEO	GANNA2 62,431,71
REVIEW:	CARCINOGENIC DETERMINATION:ANIMAL POSITIVE	IARC** 20,195,79
REVIEW:	CARCINOGENIC DETERMINATION:ANIMAL POSITIVE	IARC** 5,47,74

[redacted] CAS: 26637-65-3 [redacted] M: C8-F16
SYN: FORESHOT

TXDS:	ihl-rat LCLo:100 ppm/14H	11FYAN 3,78,63
	ihl-mus LCLo:550 ppm/14H	11FYAN 3,78,63
	ihl-gpg LCLo:100 ppm/14H	11FYAN 3,78,63

GV5000000 CYCLOHEXANE, 1,2,3,4,5,6-HEXAKIS(2-CYANOETHOXY)-
UPDT 7901 CAS: 2035-56-3 MW: 456.60 MOLFM: C24-H30-N6-O6
SYN: 1,2,3,4,5,6-HEXAKIS(2-CYANOETHOXY)-CYCLOHEXANE
TXDS: ivn-mus LD50:180 mg/kg CSLNX* NX#02784
CYCLOHEXANE, 5-ISOCYANATO-1-(ISOCYANATOMETHYL)-1,3,3-TRIMETHYL- (9CI) see: NQ5400000

GV5030000 CYCLOHEXANE, ISOPROPYL-
UPDT 7903 CAS: 696-29-7 MW: 126.27 MOLFM: C9-H18
SYN: ISOPROPYLCYCLOHEXANE
AQTX: AQUATIC TOXICITY RATING: TLm96:1000-100 ppm WQCHM* 2,-,74
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980
delta-alpha-1,alpha-CYCLOHEXANEMALONONITRILE see: OO3735250
CYCLOHEXANEMETHANAMINE see: GV6128000

GV5075000 CYCLOHEXANEMETHANOL
UPDT 7908 CAS: 100-49-2 MW: 114.21 MOLFM: C7-H14-O
SYN: BENZYL ALCOHOL, HEXAHYDRO- * CYCLOHEXANECARBINOL * CYCLOHEXYLCARBINOL * CYCLOHEXYLMETHANOL * HEXAHYDROBENZYL ALCOHOL * HYDROXYMETHYLCYCLOHEXANE * METHANOL, CYCLOHEXYL- * USAF DO-49
TXDS: ipr-mus LD50:250 mg/kg NTIS** AD277-689
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980
CYCLOHEXANEMETHANOL, alpha-(2-BROMOETHYNYL)- see: UK5080000
CYCLOHEXANEMETHANOL, alpha-(2-CHLOROETHYNYL)- see: UK5085000
CYCLOHEXANEMETHANOL, alpha-ETHYNYL- see: UK5090000

GV5200000 CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, ACETATE
UPDT 8003 MW: 180.27 MOLFM: C11-H16-O2
SYN: ACETIC ACID 1-CYCLOHEXYL-2-PROPYN-1-YL ESTER
TXDS: orl-mus LD50:1200 mg/kg ARZNAD 7,85,57
CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, BENZOATE see: DG5775100
CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, BUTYRATE see: ES0935000
CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, CARBAMATE see: FC8676000
CYCLOHEXANEMETHANOL, alpha-ETHYNYL-, PROPIONATE see: UF0655000

GV5425000 CYCLOHEXANEMETHANOL, 4-HYDROXY-alpha-(ISOPROPYLAMINOMETHYL)-
UPDT 7901 CAS: 63960-63-2 MW: 201.35 MOLFM: C11-H23-N-O2
SYN: ETHANOL, 2-ISOPROPYLAMINO-1-(4-HYDROXYHEXYL)- * WIN 5579
TXDS: ivn-mus LD50:460 mg/kg JPETAB 106,341,52

GV5600000 CYCLOHEXANEMETHANOL, 4-HYDROXY-alpha-(METHYLAMINOMETHYL)-
UPDT 7901 CAS: 63916-66-3 MW: 173.29 MOLFM: C9-H19-N-O2
SYN: ETHANOL, 2-(METHYLAMINO)-1-(4-HYDROXYCYCLOHEXYL)- * N-METHYL-2-(4-HYDROXYCYCLOHEXYL)ETHANOLAMINE * WIN 5580

TXDS:	ipr-mus LD50:620 mg/kg	JPETAB 105,341,52
	ivn-mus LD50:795 mg/kg	JPETAB 105,341,52

GV5950000 CYCLOHEXANEMETHANOL, alpha-(METHYLAMINOMETHYL)-
UPDT 7901 CAS: 23261-44-8 MW: 157.29 MOLFM: C9-H19-N-O
SYN: ETHANOL, 2-(METHYLAMINO)-1-CYCLOHEXYL- * alpha-(METHYLAMINOMETHYL)CYCLOHEXANEMETHANOL * N-METHYL-2-CYCLOHEXYLETHANOLAMINE * WIN 5581

TXDS:	ivn-mus LD50:37 mg/kg	JPETAB 105,341,52
	ipr-mus LD50:260 mg/kg	JPETAB 105,341,52

CYCLOHEXANEMETHANOL, alpha-PHENYL- see: PC1935000

GV5965000 CYCLOHEXANEMETHANOL, 1-PHENYL-
UPDT 8007 MW: 190.31 MOLFM: C13-H18-O
SYN: 1-PHENYL CYCLOHEXANEMETHANOL
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#07313

GV6125000 CYCLOHEXANE, METHYL-
UPDT 7908 CAS: 108-87-2 MW: 98.21 MOLFM: C7-H14
SYN: CYCLOHEXYLMETHANE * HEXAHYDROTOLUENE * METHYLCYCLOHEXANE * METHYLCYCLOHEXANE (DOT) * METYLOCYKLOHEKSAN (Polish) * SEXTONE B * TOLUENE HEXAHYDRIDE * TOLUENE, HEXAHYDRO-

TXDS:	orl-rbt LDLo:4000 mg/kg	JIHTAB 25,199,43
REVIEW:	THRESHOLD LIMIT VALUE-air:400 ppm	DTLVS* 4,271,80
REVIEW:	TOXICOLOGY REVIEW	27ZTAP 3,89,69
REGS:	OSHA STANDARD-air:TWA 500 ppm (SCP-G)	FEREAC 39,23540,74
	DOT-FLAMMABLE LIQUID, LABEL:FLAMMABLE LIQUID	FEREAC 41,57018,76

STATUS: 'NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S94
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV6128000 CYCLOHEXANEMETHYLAMINE
UPDT 8211 CAS: 3218-02-8 MW: 113.23 MOLFM: C7-H15-N
SYN: (AMINOMETHYL)CYCLOHEXANE * CYCLOHEXANEMETHANAMINE * CYCLOHEXYLMETHANAMINE * CYCLOHEXYLMETHYLAMINE
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#10002
CYCLOHEXANEMETHYLAMINE, N,N'-(1,4-BICYCLO(2.2.2)OCTYLENEDIMETHYLENE)BIS-, DIHYDROCHLORIDE see: DT7920000

GV6133000 CYCLOHEXANEMETHYLAMINE, N-(2-CHLOROETHYL)-N-ETHYL-PHENYL-, HYDROCHLORIDE
UPDT 8007 MW: 316.35 MOLFM: C17-H26-Cl-N .Cl-H
SYN: N-(2-CHLOROETHYL)-N-ETHYL-1-PHENYLCYCLOHEXANEMETHYLAMINE * 1-PHENYL-1-(N-(2-CHLOROETHYL)-N-ETHYLAMINOMETHYL)CYCLOHEXANE, HYDROCHLORIDE
TXDS: ivn-mus LD50:55 mg/kg CSLNX* NX#07316

GV6135000 CYCLOHEXANEMETHYLAMINE, 2-CHLORO-2-(m-METHOXYPHENYL)-
UPDT 7902 CAS: 73806-28-9 MW: 279.86 MOLFM: C14-H22-Cl-N-O
SYN: 2-CHLORO-2-(m-METHOXYPHENYL)CYCLOHEXANEMETHYLAMINE
TXDS: orl-mus LD50:390 mg/kg ARZNAD 28,107,78
CYCLOHEXANEMETHYLAMINE, N,N'-(1,4-CYCLOHEXENYLENEDI)BIS-, DIACETATE see: GW2545000
CYCLOHEXANEMETHYLAMINE, N,N'-(1,4-CYCLOHEXYLENEDIMETHYLENE)DI-, DIHYDROCHLORIDE, (E)- see: GU7047000
CYCLOHEXANEMETHYLAMINE, N,N'-(1,4-CYCLOHEXYLENEDIMETHYLENE)DI-, DIHYDROCHLORIDE, (Z)- see: GU7049000

GV6150000 CYCLOHEXANEMETHYLAMINE, N,N-DIMETHYL-2-(m-METHOXYPHENYL)-
UPDT 7901 CAS: 73806-39-0 MW: 247.42 MOLFM: C16-H25-N-O
SYN: N,N-DIMETHYL-2-(m-METHOXYPHENYL)CYCLOHEXANEMETHYLAMINE
TXDS: orl-mus LD50:214 mg/kg ARZNAD 28,107,78
CYCLOHEXANEMETHYLAMINE, N-(2-HYDROXYETHYL)-N-ETHYL-1-PHENYL- see: KL0260000

GV6300000 CYCLOHEXANEMETHYLAMINE, N-METHYL-
UPDT 7901 CAS: 25756-29-0 MW: 127.26 MOLFM: C8-H17-N
SYN: N-METHYL-N-(CYCLOHEXYLMETHYL) AMINE

TXDS:	orl-rat LDLo:1410 mg/kg	AIHAAP 30,470,69
	skn-rbt LD50:630 mg/kg	AIHAAP 30,470,69

GV6400000 CYCLOHEXANEMETHYLAMINE, 1-PHENYL-
UPDT 8007 MW: 189.33 MOLFM: C13-H19-N
SYN: 1-PHENYLCYCLOHEXANEMETHYLAMINE
TXDS: ivn-mus LD50:18 mg/kg CSLNX* NX#07306
CYCLOHEXANE, 1-METHYL-n-AMINOETHYLTHIOAZO- see: XH2540000

GV6670000 CYCLOHEXANE, 1,1,2,2,3,4,4,5,6-NONAFLUORO-
UPDT 7901 CAS: 22150-31-2 MW: 246.09 MOLFM: C6-H3-F9
SYN: 1H,2H,4H-NONAFLUOROCYCLOHEXANE
TXDS: ihl-mus LCLo:17000 ppm/10M ANASAB 16,3,61

GV6678000 CYCLOHEXANE, PIPERIDINOMETHYL-
UPDT 7901 CAS: 5005-72-1 MW: 181.36 MOLFM: C12-H23-N
SYN: PMC

TXDS:	orl-mus LD50:160 mg/kg	AIPTAK 167,273,67
	ipr-mus LD50:55 mg/kg	AIPTAK 167,273,67
	ivn-mus LD50:20 mg/kg	AIPTAK 167,273,67

GV6680000 CYCLOHEXANE, PIPERIDINOMETHYL-, CAMPHOSULFATE SALT
UPDT 7901 CAS: 62916-34-1 MW: 413.65 MOLFM: C12-H23-N .C10-H16-O4-S
SYN: PIPERIDINOMETHYLCYCLOHEXANE, CAMPHOSULFATE * SD 210-37

TXDS:	orl-mus LD50:370 mg/kg	AIPTAK 167,273,67
	ipr-mus LD50:370 mg/kg	AIPTAK 167,273,67
	ivn-mus LD50:41 mg/kg	AIPTAK 167,273,67

GV6690000 CYCLOHEXANE, PIPERIDINOMETHYL-, HYDROCHLORIDE
UPDT 7901 CAS: 5005-71-0 MW: 217.82 MOLFM: C12-H23-N .Cl-H
SYN: PIPERIDINOMETHYLCYCLOHEXANE CHLORHYDRATE SALT * SD 210-32

TXDS:	orl-mus LD50:205 mg/kg	AIPTAK 167,273,67
	ipr-mus LD50:65 mg/kg	AIPTAK 167,273,67
	ivn-mus LD50:25 mg/kg	AIPTAK 167,273,67

GV6735000 CYCLOHEXANEPROPIONIC ACID, ALLYL ESTER
UPDT 7908 CAS: 2705-87-5 MW: 196.32 MOLFM: C12-H20-O2
SYN: ALLYL CYCLOHEXANEPROPIONATE * 3-ALLYLCYCLOHEXYL PROPIONATE * ALLYL HEXAHYDROPHENYLPROPIONATE * CYCLOHEXANOL, 3-ALLYL-, PROPIONATE

TXDS:	orl-rat LD50:585 mg/kg	FCTXAV 2,327,64
	orl-gpg LD50:380 mg/kg	FCTXAV 2,327,64

STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV6760000 CYCLOHEXANEPROPIONIC ACID, alpha-CYCLOPENTYL-, 2-(DIETHYLAMINO)ETHYL ESTER, HYDROCHLORIDE
UPDT 7901 CAS: 67227-07-5 MW: 360.04 MOLFM: C20-H37-N-O2 .Cl-H
SYN: alpha-CYCLOPENTYLCYCLOHEXANEPROPIONIC ACID 2-(DIETHYLAMINO)ETHYL ESTER HYDROCHLORIDE
TXDS: ipr-mus LD50:220 mg/kg JACSAT 69,1849,47

GV6825000 CYCLOHEXANEPROPYLAMINE, N,N-DIMETHYL-gamma-PHENYL-, HYDROCHLORIDE
UPDT 7901 CAS: 15826-61-6 MW: 281.91 MOLFM: C17-H27-N .Cl-H
SYN: N,N-DIMETHYL-3-CYCLOHEXYL-3-PHENYL PROPYLAMINE HYDROCHLORIDE * GAMFEXINE HYDROCHLORIDE * WIN 1344
TXDS: orl-hmn TDLo:5 mg/kg TFX:PSY CTCEA? 9,549,67
CYCLOHEXANESPIRO-5'-HYDANTOIN see: HM2460000

GV6950000 CYCLOHEXANESULFAMIC ACID
UPDT ... CAS: 100-88-9 MW: 179.26 MOLFM: C6-H13-N-O3-S
SYN: CYCLAMATE * CYCLOHEXANESULPHAMIC ACID * CYCLOHEXYLAMIDOSULPHURIC ACID * CYCLOHEXYLAMINESULFONIC ACID * CYCLOHEXYLSULPHAMIC ACID * N-CYCLOHEXYLSULPHAMIC ACID * HEXAMIC ACID * SUCARYL * SUCARYL ACID * SULFAMIC ACID, CYCLOHEXYL- (9CI)
TXDS: orl-man TDLo:27 gm/kg/78W-C TFX:ETA JOURAA 118,258,/

TOXICITY DATA HAS NOT BEEN EVALUATED
OMISSION OF A SUBSTANCE OR NOTATION DOES NOT IMPLY ANY RELIEF FROM REGULATORY RESPONSIBILITY.

1048263

Y-358956 0563(50)(28-DEC-81-18:03:26)

ivn-mus LD50:180 mg/kg CSLNX* NX#01774
REVIEW: CARCINOGENIC DETERMINATION:NO DATA IARC** 22,55,80
US REPORTED IN EPA TSCA INVENTORY 1980

00 CYCLOHEXANESULFAMIC ACID, BARIUM SALT
UPDT:8001 CAS: [illegible] MW: [illegible] MOLFM: [illegible]
SYN: [illegible]
orl-rat LDLo:250 mg/kg NCNSA6 5,40,53
CYCLOHEXANISULFAMIC ACID, CALCIUM SALT see: GV7100000

GV7100000 CYCLOHEXANESULFAMIC ACID, CALCIUM SALT (2:1)
UPDT:8009 CAS: 139-05-9 MW: 276.38 MOLFM: C12-H26-N2-O6-S2 Ca
SYN: CALCIUM CYCLAMATE * CALCIUM CYCLOHEXANESULFAMATE * CALCIUM CYCLOHEXANE SULFAMATE * CALCIUM CYCLOHEXYLSULFAMATE * CALCIUM CYCLOHEXYLSULPHAMATE * CYCLAMATE CALCIUM SALT * CYCLAMATE CALCIUM * CYCLOHEXANESULFAMIC ACID, CALCIUM SALT * CYCLAM * CYCLOHEXYLSULPHAMIC ACID, CALCIUM SALT * CYLAN * DIETIL * KALZIUM-CYKLAMAT (German) * SUCARYL CALCIUM
MTDS: cyt-hmn:lev 250 mg/L SCIEAS 164,568,69
cyt-hamlib 10 mg/L MUREAV 39,1,76
cyt-hamsing 100 mg/L MEREAY 70,271,72
cyt-grbsipr 150 mg/kg CNJGAB 13,189,71
TXDS: orl-rat LDLo:10 mg/kg CLDND*
orl-rat TDLo:3465 gm/kg/88W-C TFX:NEO JNCIAM 49,751,72
scu-rat TDLo:45 gm/kg/66W-I TFX:ETA FCTXAV 9,463,71
ivn-rat LDLo:3550 ug/kg CLDND*
orl-mus LDLo:10 mg/kg CLDND*
ivn-mus LDLo:3500 ug/kg CLDND*
REVIEW: CARCINOGENIC DETERMINATION:ANIMAL POSITIVE IARC** 22,55,80
REVIEW: TOXICOLOGY REVIEW MUREAV 39,1,76
REVIEW: TOXICOLOGY REVIEW WMWOA4 121,515,71
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV7175000 CYCLOHEXANESULFAMIC ACID, CALCIUM SALT, DIHYDRATE
UPDT:7901 CAS: 5897-16-3 MW: 432.62 MOLFM: C12-H24-N2-O6-S2 .2H2-O .Ca
TXDS: scu-rat LD50:100 mg/kg FAONAU 44A,83,67

GV7350000 CYCLOHEXANESULFAMIC ACID, MONOSODIUM SALT
UPDT:8012 CAS: 139-05-9 MW: 169.18 MOLFM: C6-H12-N-O3 Na
SYN: ASSUGRIN * ASSUGRIN FEIPISUSS * ASSURGRYN VOLKSUSS * ASUGRYN * CYCLAMATE * CYCLAMATE SODIUM * CYCLAMATE, SODIUM SALT * CYCLOHEXANESULFAMIC ACID, MONOSODIUM SALT * CYCLOHEXYLSULPHAMATE SODIUM * CYCLOHEXYLSULPHAMIC ACID, MONOSODIUM SALT * DIUZOR-ETAS * HACHI-SUGAR * IEOSUC * NATREEN * NATRIUM-CYKLAMAT (German) * SODIUM CYCLAMATE * SODIUM CYCLOHEXANESULFAMATE * SODIUM CYCLOHEXANESULPHAMATE * SODIUM CYCLOHEXYL SULFAMATE * SODIUM CYCLOHEXYL AMIDOSULPHATE * SODIUM CYCLOHEXYL SULPHAMATE * SODIUM CYCLOHEXYLSULPHAMIDATE * SODUM SUCARYL * SUCARYL SODIUM * SUCCARIL * SUCROSA * SUCRUM 7 * SUESSETTE * SUESTAMIN * SUGARIN * SUGARON
MTDS: cyt-hmn:lev 10 umol/L/3H MUREAV 39,1,76
cyt-hma:fbr 500 mg/L ACYTAN 16,41,72
cyt-hamifbr 10 mg/L MUREAV 39,1,76
cyt-grbhunk 100 mg/kg MUREAV 26,199,74
TXDS: orl-rat TDLo:63 gm/kg/9W-C TFX:NEO CNREAB 37,2943,77
ipr-rat LD50:1350 mg/kg NCIBR* NIH-NCI-E-68-1311,10,73
ipr-mus LD50:1154 mg/kg NCIBR* NIH-NCI-E-68-1311,10,73
ivn-mus TDLo:176 mg/kg TFX:NEO SCIEAS 167,996,70
orl-rat TD :112 gm/kg/8W-C TFX:NEO CNREAB 37,2943,77
orl-rat TD :610 gm/kg/87W-C TFX:ETA CEINAB 11,225,75
CARCINOGENIC DETERMINATION:ANIMAL POSITIVE IARC** 22,55,80
REVIEW: TOXICOLOGY REVIEW IDJOAS 23(2),328,73
REVIEW: TOXICOLOGY REVIEW MUREAV 39,1,76
REVIEW: TOXICOLOGY REVIEW AEHLAU 22,6,71
REVIEW: TOXICOLOGY REVIEW WMWOA4 121,515,71
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV7450000 CYCLOHEXANESULFONAMIDE
UPDT:7901 CAS: 1455-32-2 MW: 163.26 MOLFM: C6-H13-N-O2-S
TXDS: orl-rat LD50:80 mg/kg JPETAB 90,260,47
CYCLOHEXANESULPHAMIC ACID see: GV6950000
CYCLOHEXANESULPHAMIC ACID, MONOSODIUM SALT see: GV7350000

GV7500000 1,1,3,3-CYCLOHEXANETETRAPROPIONITRILE, 2-OXO-
UPDT:7901 CAS: 5883-05-6 MW: 310.44 MOLFM: C18-H22-N4-O
SYN: 2-OXO-1,1,3,3-CYCLOHEXANETETRAPROPIONITRILE
TXDS: ivn-mus LD50:180 mg/kg CSLNX* NX#00374

GV7525000 CYCLOHEXANETHIOL
UPDT:7908 CAS: 1569-69-3 MW: 116.24 MOLFM: C6-H12-S
SYN: CYCLOHEXYLMERCAPTAN (Czech)
IRDS: skn-rbt 500 mg/24H SEV 28ZPAK -,167,72
eye-rbt 500 mg/24H SEV 28ZPAK -,167,72
TXDS: orl-rat LD50:558 mg/kg 28ZPAK -,167,72
CRIT DOS: OCCUPATIONAL EXPOSURE TO CYCLOHEXANETHIOL resm std=airCl 0.5 ppm/15M NTIS**
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

[redacted]
UPDT:7908 CAS: 355-02-2 MW: 350.07 MOLFM: C7-F14
SYN: PERFLUOROHEPTYLCYCLOHEXANE
TXDS: ihl-rat LCLo:325 ppm/14H 11FYAN 3,90,63
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980

GV7650000 CYCLOHEXANE, 1,1,3-TRIMETHYL-
UPDT:7903 CAS: 3073-66-3 MW: 126.27 MOLFM: C9-H18
SYN: 1,1,3-TRIMETHYLCYCLOHEXANE
TXDS: ivn-mus LD50:35 mg/kg CSLNX* NX#04716

GV7700000 CYCLOHEXANEVALERIC ACID, alpha,2,2,6-TETRAMETHYL-beta-CYANO-, SODIUM SALT
UPDT:7901 CAS: 695-12-3 MW: 287.42 MOLFM: C16-H26-N-O2 Na
SYN: beta-CYANO-2,2,6,6-TETRAMETHYLCYCLOHEXYLBUTANECARBOXYLIC ACID SODIUM SALT * SODIUM SALT of alpha-2,2,6,6-TETRAMETHYL-beta-CYANOCYCLOHEXANEVALERIC ACID
TXDS: ipr-mus LD50:65 mg/kg PJPPAA 27(4),399,75

GV7875000 CYCLOHEXANOL
UPDT:8007 CAS: 108-93-0 MW: 100.18 MOLFM: C6-H12-O
SYN: ADRENAL * ANOL * CICLOESANOLO (Italian) * CYCLOHEXYL ALCOHOL * CYCLOHEXYLOL (Polish) * HEXAHYDROPHENOL * HEXALIN * HYDRALIN * HYDROPHENOL * HYDROXYCYCLOHEXANE * HYXOL * PHENOL HEXAHYDRO-
MTDS: dnd-mam:lym 150 mmol/L PNASA6 48,686,62
IRDS: eye-hmn 100 ppm JIHTAB 25,282,43
skn-rbt 16400 ug 24H open MLD AIHAAP 20,95,62
eye-rat 2 mg SEV AJOPAA 29,1363,46
TXDS: ihl-hmn TCLo:75 ppm TFX:IRR JIHTAB 25,282,43
ihl-rat LD50:2000 mg/kg MDZEAK 8 244,67
ivn-mus LD50:1450 mg/kg REMBAB 5,7,67
ivn-mus LD50:1030 mg/kg JSICAZ 21,342,62
orl-rbt LDLo:2200 mg/kg JIHTAB 25,199,43
skn-rbt LDLo:12 gm/kg JIHTAB 25,199,43
ipr-mbt LDLo:1420 mg/kg JPYRAB 3,1,28
AQTX: AQUATIC TOXICITY RATING: TLm96:100-10 ppm WQCHM* 2,-,74
REVIEW: THRESHOLD LIMIT VALUE-air:50 ppm DIEVS* 4,111,80
REVIEW: TOXICOLOGY REVIEW 27ZIAP 3,44,69
REGS: OSHA STANDARD-air TWA 50 ppm (SCP:E) FEREAC 39,23540,74
STATUS: NIOSH MANUAL OF ANALYTICAL METHODS' VOL 2 S54
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980
CYCLOHEXANOL, ACETATE see: AG5075000

GV8100000 CYCLOHEXANOL, 1-ALLYL-
UPDT:7901 CAS: 1123-34-8 MW: 140.23 MOLFM: C9-H16-O
SYN: 1-ALLYL-1-CYCLOHEXANOL
TXDS: ivn-mus LD50:100 mg/kg CSLNX* NX#04164
CYCLOHEXANOL, 3-ALLYL-, PROPIONATE see: GV6735000

GV8400000 CYCLOHEXANOL, 1-AMINO-3-AMINOMETHYL-3,5,5-TRIMETHYL-
UPDT:7901 CAS: 2572-03-0 MW: 186.34 MOLFM: C10-H22-N2-O
SYN: 1-AMINO-3-AMINOMETHYL-3,5,5-TRIMETHYL CYCLOHEXANOL
TXDS: orl-rat LD50:1300 mg/kg AHHAAP 30,470,69

GV8425000 CYCLOHEXANOL, 4-(N-(2-AMINO-3,5-DIBROMOBENZYL)AMINO)-, HYDROCHLORIDE (E)-
UPDT:7901 CAS: 18683-91-5 MW: 414.61 MOLFM: C13-H18-Br2-N2-O Cl-H
SYN: AMBROXOL * trans-4-((2-AMINO-3,5-DIBROMOBENZYL)AMINO)CYCLOHEXANOL HYDROCHLORIDE * WA 872
TXDS: orl-rat LD50:13400 mg/kg ARZNAD 28,889,78
ipr-rat LD50:380 mg/kg ARZNAD 28,889,78
orl-mus LD50:2720 mg/kg ARZNAD 28,889,78
ipr-mus LD50:268 mg/kg ARZNAD 28,889,78
ivn-mus LD50:138 mg/kg ARZNAD 28,889,78
orl-dog LD50:500 mg/kg ARZNAD 28,889,78
ipr-dog LD50:125 mg/kg ARZNAD 28,889,78
orl-rbt LDLo:10 mg/kg ARZNAD 28,889,78
ipr-gpg LDLo:400 mg/kg ARZNAD 28,889,78
ivn-rbt LDLo:80 mg/kg ARZNAD 28,889,78
orl-gpg LD50:1180 mg/kg ARZNAD 28,889,78
ipr-gpg LD50:280 mg/kg ARZNAD 28,889,78

GV8450000 CYCLOHEXANOL, 2-AMINOMETHYL-1-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 73806-40-2 MW: 233.26 MOLFM: C14-H21-N-O2
SYN: 2-AMINOMETHYL-1-(m-METHOXYPHENYL)CYCLOHEXANOL
TXDS: orl-mus LD50:466 mg/kg ARZNAD 28,107,78

GV8575000 CYCLOHEXANOL, 4-(2-AMINOPROPYL)-, HYDROBROMIDE
UPDT:7901 CAS: 6411-65-8 MW: 238.21 MOLFM: C9-H19-N-O .Br-H
SYN: 1-(p-HYDROXYCYCLOHEXYL)-2-AMINO-PROPANE HYDROBROMIDE
TXDS: ipr-mus LD50:1000 mg/kg JPETAB 92,207,48
CYCLOHEXANOLAZETAT (German) see: AG5075000

GV8620000 CYCLOHEXANOL, 2-(N-BENZYL-N-METHYLAMINOMETHYL)-1-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 73806-41-4 MW: 339.52 MOLFM: C22-H29-N-O2
SYN: 2-(N-BENZYL-N-METHYLAMINOMETHYL)-1-(m-METHOXYPHENYL)CYCLOHEXANOL
TXDS: orl-mus LD50:404 mg/kg ARZNAD 28,107,78

GV8640000 CYCLOHEXANOL, 1-BENZYLOXY-2-(DIMETHYLAMINOMETHYL)-
UPDT:7901 CAS: 73806-42-5 MW: 339.52 MOLFM: C22-H29-N-O2
SYN: 1-BENZYLOXY-2-(DIMETHYLAMINOMETHYL)CYCLOHEXANOL
TXDS: orl-mus LD50:172 mg/kg ARZNAD 28,107,78

GV8645000 CYCLOHEXANOL, 1-(2-BROMOETHYNYL)-
UPDT:7903 CAS: 52937-27-3 MW: 203.10 MOLFM: C8-H11-Br-O
SYN: 1-BROMOAETHINYL-CYCLOHEXANOL-(1) (German) * 1-BROMOETHYNYLCYCLOHEXANOL * SEDENOL
TXDS: scu-mus LD50:560 mg/kg ARZNAD 5,161,55

GV8650000 CYCLOHEXANOL, 1,1'-BUTADIYNYLENEDI-
UPDT:7901 CAS: 3753-10-5 MW: 246.38 MOLFM: C16-H22-O2
SYN: BIS(1-HYDROXYCYCLOHEXYL)BUTADIYNE
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#02803

GV8750000 CYCLOHEXANOL, 4-tert-BUTYL-
UPDT:7908 CAS: 98-52-2 MW: 156.30 MOLFM: C10-H20-O
SYN: 4-tert-BUTYLCYCLOHEXANOL * USAF DO-22
TXDS: orl-rat LD50:4200 mg/kg FCTXAV 12,807,74
ipr-mus LD50:50 mg/kg NTIS** AD277-689
STATUS: REPORTED IN EPA TSCA INVENTORY, 1980
CYCLOHEXANOL, 4-tert-BUTYL-, ACETATE see: AF7117000

GV8800000 1-CYCLOHEXANOL, 4-tert-BUTYL-1-ETHYNYL-
UPDT:7901 CAS: 20525-03-5 MW: 180.33 MOLFM: C12-H20-O
SYN: 4-tert-BUTYL-1-ETHYNYLCYCLOHEXANOL
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#00335

GV8820000 CYCLOHEXANOL, 1-(((CHLOROMETHYL)DIMETHYLSILYL)ETHYNYL)-
UPDT:7901 CAS: 25911-23-5 MW: 230.84 MOLFM: C11-H19-Cl-O-Si
SYN: CYCLOHEXAN-1-OL, 1-(beta-CHLOROMETHYLDIMETHYLSILYLETHYNYL)- * 1-(beta-CHLOROMETHYLDIMETHYLSILYLETHYNYL)CYCLOHEXAN-1-OL * SILANE, (CHLOROMETHYL)DICHLORO(1-HYDROXYCYCLOHEXYLETHYNYL)-
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#02574
CYCLOHEXAN-1-OL, 1-(beta-CHLOROMETHYLDIMETHYLSILYLETHYNYL- see: GV8320000

GV8830000 CYCLOHEXANOL, 1-(m-CHLOROPHENYL)-2-(DIMETHYLAMINOMETHYL)-
UPDT:7901 CAS: 73806-23-6 MW: 267.83 MOLFM: C15-H22-Cl-N-O
SYN: 1-(m-CHLOROPHENYL)-2-(DIMETHYLAMINOMETHYL)CYCLOHEXANOL
TXDS: orl-mus LD50:201 mg/kg ARZNAD 28,107,78

GV8835000 CYCLOHEXANOL, 4-(CYCLOHEXYLMETHYL)-
UPDT:8011 MW: 196.37 MOLFM: C13-H24-O
SYN: 4-CYCLOHEXYLMETHYLCYCLOHEXANOL
TXDS: ivn-mus LD50:56 mg/kg CSLNX* NX#10067

GV8840000 CYCLOHEXANOL, 2-DIALLYLAMINOMETHYL-1-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 73516-03-7 MW: 315.50 MOLFM: C20-H29-N-O2
SYN: 2-DIALLYLAMINOMETHYL-1-(m-METHOXYPHENYL)CYCLOHEXANOL
TXDS: orl-mus LD50:348 mg/kg ARZNAD 28,107,78

GV8950000 CYCLOHEXANOL, 1-(p-(3-DIETHYLAMINOPROPYL)PHENETHYL)-
UPDT:7901 CAS: 1482-41-5 MW: 317.57 MOLFM: C21-H35-N-O
SYN: 1-(2-(p-(3-DIETHYLAMINOPROPYL)PHENYL)ETHYL)CYCLOHEXANOL
TXDS: scu-mus LD50:258 mg/kg RPTOAN 37(5),217,74

GV8970000 CYCLOHEXANOL, 1-(2-(p-(3-DIETHYLAMINO-1-PROPYNYL)PHENYL)ETHYNYL)-
UPDT:7901 CAS: 3076-60-8 MW: 339.49 MOLFM: C21-H29-N-O
SYN: 1-(2-(p-(3-DIETHYLAMINO-1-PROPYNYL)PHENYL)ETHYNYL)CYCLOHEXANOL
TXDS: scu-mus LD50:1304 mg/kg RPTOAN 37(5),217,74

GV8875000 CYCLOHEXANOL, 2-(DIMETHYLAMINOMETHYL)-1-(m-ETHOXYPHENYL)-
UPDT:7901 CAS: 29166-93-6 MW: 277.45 MOLFM: C17-H27-N-O2
SYN: 2-(DIMETHYLAMINOMETHYL)-1-(m-ETHOXYPHENYL)CYCLOHEXANOL
TXDS: orl-mus LD50:274 mg/kg ARZNAD 28,107,78

GV8880000 CYCLOHEXANOL, 2-(DIMETHYLAMINOMETHYL)-1-(m-FLUOROPHENYL)-
UPDT:7901 CAS: 73806-44-7 MW: 251.36 MOLFM: C15-H22-F-N-O
SYN: 2-(DIMETHYLAMINOMETHYL)-1-(m-FLUOROPHENYL)CYCLOHEXANOL
TXDS: orl-mus LD50:310 mg/kg ARZNAD 28,107,78

GV8885000 CYCLOHEXANOL, 2-(DIMETHYLAMINOMETHYL)-1-(m-METHOXYPHENYL)-
UPDT:7901 CAS: 29166-27-4 MW: 263.42 MOLFM: C16-H25-N-O2
SYN: 2-DIMETHYLAMINOMETHYL-1-(m-METHOXYPHENYL)CYCLOHEXANOL
TXDS: orl-mus LD50:395 mg/kg ARZNAD 28,107,78

APPENDIX B

HOMEOWNER'S AGREEMENT

In this Agreement, made as of _____, 1985, between _____ and spouse _____ residing at _____, County of _____, State of _____, and Martin Marietta Energy Systems, Inc., a Delaware Corporation with an office at Oak Ridge, Tennessee 37831, acting under its Contract DE-AC05-84OR21400 with the United States of America as represented by the Department of Energy with research facilities at Oak Ridge National Laboratory;

Acquisition of additional data on indoor air quality in residential settings has been identified as a research need. The Health and Safety Research Division of Oak Ridge National Laboratory will be conducting an indoor air quality field study in the Tennessee Valley region during 1985-86. The field study is supported by several agencies including the Department of Energy (DOE), the Tennessee Valley Authority (TVA), the Environmental Protection Agency (EPA), and the Consumer Product Safety Commission (CPSC). The primary component of the study, on which other activities will build, will involve measurement of radon and radon progeny in 60 houses in four states. Additional pollutants that will be monitored include formaldehyde and nitrogen dioxide. Air exchange rates between indoor and outdoor air will also be measured. Other parameters that cannot be measured in all 60 homes will be measured in a subset of homes. Examples include measurement of volatile organic compounds and particulate matter. The houses will be visited by a monitoring team once or twice each quarter for one year to perform sampling. Measurements are to begin in the spring of 1985. The 60 houses selected for the study will be chosen from the list of candidate houses based on various selection criteria.

NOW, THEREFORE, the parties agree as follows:

Martin Marietta Energy Systems, Inc. will

[1] provide data collection equipment and install said equipment on participants' premises and subsequently remove it;
[2] maintain and service such equipment at its expense during the term of this agreement;
[3] periodically monitor the air on the premises;
[4] make available to the Participants the results of the data collected from the Participants' premises;
[5] assume responsibility for any damage to Participants' property directly caused by its representatives monitoring the air or by the installation or removal of the data collection equipment, or for claims brought by third persons for personal injury or damage to property directly related to the installation of the equipment or monitoring of the air during the term of this agreement, subject to the availability of funds;
[6] to the extent possible by law, withhold from the public the name(s) of occupants or owners of residences that are studied;
[7] notify Participants at least 24 hours in advance of the date access to the premises is desired; and
[8] pay Participants $50 upon acceptance into the final group of 60 houses and $50 upon completion of the study.

HOMEOWNERS AGREEMENT 60-House Study

Participants will

[1] permit representatives of Martin Marietta Energy Systems, Inc., reasonable access to Participants' premises for the purpose of sampling air indoors and outdoors;
[2] allow the installation, servicing, and removal of data collection equipment;
[3] allow Martin Marietta Energy Systems, Inc., representatives to take photographs at Participants' premises;
[4] allow Martin Marietta Energy Systems, Inc., to disseminate information collected to the public; and
[5] participate for the full year of the study if accepted into the final group of 60 houses.

PARTICIPANTS

By _____
Date _____

By _____
Date _____

Martin Marietta Energy Systems, Inc.

By _____
Title _____
Date _____

1048267

REVIEW AND ACTION

ORAU/ORNL Committee on Human Studies

Principal Investigator Charles S. Dudney & Thomas G. Matthews Ident. No. ORNL-14

Project Title INDOOR AIR QUALITY STUDY IN 60 HOUSES IN THE TENNESSEE VALLEY

1. In the opinion of this committee the rights and welfare of the subjects in this project or activity will be protected. The committee states that adequate safeguards against any untoward effects have been provided.

2. In the opinion of the committee the informed consent procedures to be used in this project will be both appropriate and adequate. The committee also finds that no inappropriate psychological or sociological risks will exist for the subjects involved in this project.

3. The committee seeks continuing communication with the investigator(s) on this project along the following lines:

4. Other committee comments: —

Approve ✓

Disapprove ___

Karl F. Hubner
Chairman of Committee

May 6, 1985

1048268

ORAU-ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title ORNL-14 INDOOR AIR QUALITY STUDY IN 60 HOUSES IN THE TENNESSEE VALLEY

Principal Investigator Charles S. Dudney, Ph.D., and Thomas G. Matthews, Ph.D.

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.	Martha L Wray	✓			5/6/85
2.	Ruby A Miller	✓			5/6/85
3.	[illegible]				5/6/85
4.	Kenneth E. Hunt	✓			5/6/85
5.	[illegible]	✓			5/6/85
6.	William W Lockwood	✓			5/6/85
7.	[illegible]	✓			5/6/85
8.	Shirley A. Fry				5/6/85
9.	Karl F. Hubner				5/6/85
10.					5/6/85
11.					5/6/85
12.					5/6/85
13.					5/6/85
14.					5/6/85

Chairman's statement of Committee consensus:

Approved pending a change in the content from saying what and how much will be released into the air. Also the consent form should include a statement that the participant may withdraw from the study at any time.

Karl F. Hubner
DATE
May 6, 1985

1048269

file

Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

May 17, 1985

M E M O R A N D U M

To: Dr. Charles S. Dudney
Dr. Thomas G. Matthews

From: Lynn Reeves, Secretary
ORAU/ORNL Committee on Human Studies

Subject: PROPOSAL ORNL-14
INDOOR AIR QUALITY STUDY IN 60 HOUSES
IN THE TENNESSEE VALLEY

This proposal was approved at the recent Committee meeting pending a change in the consent form saying what and how much will be released into the homes and the consent form should include a statement that the participant may withdraw from the study at any time.

Please submit a revised consent form to me and it will be reviewed within the Committee. When it has been approved, I will let you know.

lmr

May 31, 1985

To: Lynn Reeves, Secretary, ORAU/ORNL Committee on Human Studies

From: C. S. Dudney (6-2712) CSD

Subject: Proposal ORNL-14: Revised Consent Form

The consent form has been revised and is being reviewed by this committee as well as by the law department and purchasing. Attached is a copy of the draft consent form. Please call me if there are any questions.

CSD:lgw

cc: A. R. Hawthorne
T. G. Matthew

HOMEOWNER'S AGREEMENT

In this Agreement, made as of _____, 1985, between _____ and spouse _____ residing at _____, County of _____, State of _____, and Martin Marietta Energy Systems, Inc., a Delaware Corporation with an office at Oak Ridge, Tennessee 37831, acting under its Contract DE-AC05-84OR21400 with the United States of America as represented by the Department of Energy with research facilities at Oak Ridge National Laboratory;

Acquisition of additional data on indoor air quality in residential settings has been identified as a research need. The Health and Safety Research Division of Oak Ridge National Laboratory will be conducting an indoor air quality field study in the Tennessee Valley region during 1985-86. The field study is supported by several agencies including the Department of Energy (DOE), the Tennessee Valley Authority (TVA), the Environmental Protection Agency (EPA), and the Consumer Product Safety Commission (CPSC). The primary component of the study, on which other activities will build, will involve measurement of radon and radon progeny in 60 houses in four states. Additional pollutants that will be monitored include formaldehyde and nitrogen dioxide. Air exchange rates between indoor and outdoor air will also be measured. Other parameters that cannot be measured in all 60 homes will be measured in a subset of homes. Examples include measurement of volatile organic compounds and particulate matter. The houses will be visited by a monitoring team once or twice each quarter for one year to perform sampling. Measurements are to begin in the summer of 1985. The 60 houses selected for the study will be chosen from the list of candidate houses based on various selection criteria.

NOW, THEREFORE, the parties agree as follows:

Martin Marietta Energy Systems, Inc. will

[1] provide data collection equipment and install said equipment on participants' premises and subsequently remove it;
[2] maintain and service such equipment at its expense during the term of this agreement;
[3] periodically monitor the air on the premises;
[4] release perfluoromethylcyclohexane and perfluorodimethylcyclohexane into the house allowing concentration no greater than 0.0001 ppm (the lowest known levels at which these chemicals affect rats is greater than 100 ppm);
[5] occasionally release Freon 12 (i.e., dichlorodifluoromethane) into 6 houses in the Oak Ridge area allowing concentrations no greater than 600 ppm (the lowest known level at which Freon affects humans is 200,000 ppm and occupational exposure is limited to 900 ppm);
[6] make available to the Participants the results of the data collected from the Participants' premises;

[7] assume responsibility for any damage to Participants' property directly caused by its representatives monitoring the air or by the installation or removal of the data collection equipment, or for claims brought by third persons for personal injury or damage to property directly related to the installation of the equipment or monitoring of the air during the term of this agreement, subject to the availability of funds;
[8] to the extent possible by law, withhold from the public the name(s) of occupants or owners of residences that are studied;
[9] notify Participants at least 24 hours in advance of the date access to the premises is desired; and
[10] pay Participants $50 upon acceptance into the final group of 60 houses and $50 upon completion of the study.

Participants will

[1] permit representatives of Martin Marietta Energy Systems, Inc., reasonable access to Participants' premises for the purpose of sampling air indoors and outdoors;
[2] allow the installation, servicing, and removal of data collection equipment;
[3] allow Martin Marietta Energy Systems, Inc., representatives to take photographs at Participants' premises;
[4] allow Martin Marietta Energy Systems, Inc., to disseminate information collected to the public;
[5] receive $50.00 if accepted into the final group of 60 houses; and
[6] receive $50.00 if they participate in the study for the full year.

PARTICIPANTS

By _____
Date _____

By _____
Date _____

Martin Marietta Energy Systems, Inc.

By _____
Title _____
Date _____

Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical and
Health Sciences
Division

April 1, 1985

M E M O R A N D U M

To: Dr. Charles Dudney

From: Lynn Reeves, Secretary
ORAU/ORNL Committee on Human Studies

Subject: GUIDELINES FOR PREPARING PROPOSALS FOR SUBMISSION TO THE COMMITTEE ON HUMAN STUDIES

I am enclosing six documents which should assist you in preparing your proposal. Please note that the next Committee meeting is in early May.

If you have further questions, please call me at 6-3087 and I will try to get the information you require.

Enclosures
Outline for submission
Sample proposal
Guidelines
NIH notice on informed consent
Code of Federal Regulations (consent form)
Sample consent form for blood procurement

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37830

Medical and
Health Sciences
Division

April 26, 1985

M E M O R A N D U M

To: Dr. Charles S. Dudney

From: Lynn Reeves, Secretary
ORAU/ORNL Committee on Human Studies

Subject: PROPOSAL ORNL-14
INDOOR AIR QUALITY STUDY IN 60 HOUSES
IN THE TENNESSEE VALLEY

The Committee on Human Studies plans to meet May 6, 1985, in the second floor conference room of ORAU's Medical and Health Sciences [redacted]

Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

June 10, 1985

M E M O R A N D U M

To: Dr. Karl F. Hubner, Chairman
ORAU/ORNL Committee on Human Studies

From: Lynn Reeves, Secretary

Subject: PROPOSAL ORNL-14
INDOOR AIR QUALITY STUDY IN 60
HOUSES IN THE TENNESSEE VALLEY

Enclosed is a copy of the revised consent form submitted for this proposal. I have highlighted the portions which say what and how much will be released into homes. There is no specific statement that the participant may withdraw from the study at any time but it is clear from [6] under "Participants will" that withdrawl is possible.

Do you feel Mr. Koons should examine this form because a specific statement is missing?

I am also enclosing a copy of my letter to Drs. Dudney and Matthews. How much review of this form is needed?

Enclosures
LMR letter of May 17
CSD letter of May 31 and attachment

f-up 7/22

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

July 12, 1985

M E M O R A N D U M

TO: Dr. Karl F. Hubner, Chairman
ORAU/ORNL Committee on Human Studies

FROM: Lynn Reeves, Secretary

SUBJECT: HOMEOWNER'S AGREEMENT

I believe the enclosed consent form now complies with the committee's request.

bjj

Enclosure
Homeowner's Agreement Form

Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

To: Dr. Charles Dudney

From: Lynn Reeves, Secretary
ORAU/ORNL Committee on Human Studies

Date: September 30, 1985

SUBJECT: ORNL-14 INDOOR AIR QUALITY STUDY IN 60 HOUSES IN THE TENNESSEE VALLEY

Here is the written copy of the approval of your request presented to the ORAU/ORNL Committee on Human Studies at it's May 6, 1985, meeting. Would you please sign the original and return it to me.

I had noted the approval in my file and spoke with you by phone you to let you know, but I didn't forward the paperwork to you. I'm sorry to send this to you at such a late date.

cc: Dr. Karl Hubner, Chairman

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

Title of Proposal: INDOOR AIR QUALITY STUDY IN 60 HOUSES IN THE TENNESSEE VALLEY

Proposal No.: ORNL-14 Principal Investigator: Dr. Charles Dudney

Date of Approval: July 29, 1985 Date of Disapproval: _____

Acknowledgment of Principal Investigator:

Charles S. Dudney

Signature

7 Oct 85

Date

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Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Dudney/Matthews

FROM: Becky Hawkins/Secretary, Committee on Human Studies B. Hawkins

RE: Status Reports on Active Proposals

DATE: May 1987

The guidelines for the ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by May 1, 1987. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: ORNL-14 Indoor Air Quality Study in 60 Houses in the Tennessee Valley

Proposal No. ORNL-14 Date Approved: 1985

Charles S. Dudney
Signature of Principal Investigator

28 April 1987
Date Signed

1. Report progress made in the past year.
All experimental phases of the study were completed by January 31, 1987.

2. Report any complications.
None

3. Are there any planned changes?

No

4. Do you wish the project to be continued?

No

5. Comments.

We are currently preparing the final project report.

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical
Sciences
Division

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Charles S. Dudney
4500S, MS 6113, ORNL

FROM: Karl Hubner/Chairman, Committee on Human Studies KH

RE: COMMITTEE ACTION ON YOUR PROPOSAL

DATE: July 15, 1991

Your project number ORNL-14, "Indoor Air Quality Study in 60 Houses in the Tennessee Valley," was reviewed. It is my opinion that your project meets the criteria for expedited review and approval for reactivating this project is granted at this time.

Progress reports of all active proposals are reviewed yearly at our meeting usually held in June or July.

bh

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117
Medical Sciences Division

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Dudney

FROM: Marta V. Rivera/Secretary, Committee on Human Studies

RE: Status Reports on Active Proposals

DATE: May 12, 1992

The guidelines for the ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by May 26. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: Final Review of Homeowner's Contract for Radon Research in Homes

Proposal No. ORNL-14 DATE APPROVED: 1991 (re-activated)

Charles S Dudney
Signature of Principal Investigator

6/1/92
Date Signed

1. Report progress made in the past year.

Data logging Studies of radon and air pressure were made in 5 occupied houses during the year. In one house, we looked for, but did not detect, dichloro-difluoro-methane released in a nearby cave.

2. Report any complications.

None

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3. Are there any planned changes?

no substantive changes are planned

4. Do you wish the project to be continued?

yes

5. Comments.

ORISE

OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION

ORISE/ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Dudney

FROM: Marta V. Rivera/Secretary, Committee on Human Studies

RE: Status Reports on Active Proposals

DATE: April 28, 1993

The guidelines for the ORISE/ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by **May 14.** (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: Final Review of Homeowner's Contract for Radon Research in Homes

Proposal No. ORNL-14 DATE APPROVED: 1991 (re-activated)

Charles S Dudney
Signature of Principal Investigator

17 May 1993
Date Signed

1. Report progress made in the past year.
Radon measurements were made in 125 homes in New Jersey.

2. Report any complications.
None

P. O. BOX 117, OAK RIDGE, TENNESSEE 37831-0117

1048285

Managed and operated by Oak Ridge Associated Universities for the U.S. Department of Energy

3. Are there any planned changes?

No

4. Do you wish the project to be continued?

Yes

5. Comments.

Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

To: Dr. Charles Dudney

From: Dr. Karl Hubner, Chairman
Committee on Human Studies

Date: August 5, 1992

Re: Committee Action on Active Proposals

Your project number ORNL-14 "Final Review of Homeowner's Contract for radon Research in Homes" was reviewed and approved for continuation at our last meeting on July 31, 1992.

Progress reports of all active proposals will again be reviewed at our next meeting to be held in the fall of 1992.

/mvr

Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

To: Dr. Charles Dudney

From: Dr. William Calhoun, Chairman
Committee on Human Studies

Date: June 29, 1993

Re: Committee Action on Active Proposals

Your project number ORNL-14 "Final Review of Homeowner's Contract for radon Research in Homes" was reviewed and approved for continuation at our last meeting on June 25, 1993.

Progress reports of all active proposals will again be reviewed at our next meeting to be held in the fall of 1993.

/mvr

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title

Indoor Air Quality in Occupied Spaces

2. Principal Investigator

CS Dudney

Telephone Number

(615) 576-2712

Mailing Address — Include full name of performing institution.

Health Sciences Research Division
Oak Ridge National Laboratory, PO Box 2008, Oak Ridge, TN 37831-6379

3. Institutional Assurance Number (If issued)[1]

4. Project Number[2]

ORNL-14

5. Annual Funding:

Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☐ Actual Funding $ _____

☐ $10,000 ☐ $100,000 ☒ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources

A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

	Contact Person	Telephone Number

B. Non-DOE Source

U.S. Postal Service

Non-DOE Source

U.S. Navy

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

☒ Full Board
For a list of research not requiring IRB review, see Attachment.

☐ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☐ New ☒ Annual Renewal ☐ Other

C. IRB Approval Date

8. This Project involves the following collaborating institutions (list a maximum of two):

na

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ **Minors** ☐ **Mentally Disabled** ☐ **Prisoners**

☐ **Fetuses, Pregnant Women, In Vitro Fertilization** ☐ **Economically or Educationally Disadvantaged**

10. Type of Research
Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
- ☐ Using data collected directly from human subjects.
- ☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☐ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
- ☐ Specimens collected directly from human subjects for this project.
- ☐ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☐ Instrument development and testing using human subjects.

☒ Surveys that collect personally identifiable data.

☒ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☐ Other. Please identify _____

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11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

Indoor air quality (IAQ) research routinely involves (1) collection of questionnaire data on building characteristics and (2) experimental measurement of air flow patterns (usually air exchange rate). Building questionnaire data usually include some indentifying characteristic such as address. Air flow measurements usually involve release of non-toxic tracer gases.

B. Specify the number of human subjects involved each year.

There is large fluctuation but in the last 10 years, air exchange measurements were made in about 500 locations and radon measurements in about 1,000 locations.

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

The radon measurements are completely passive with no chemicals released or radiation of any form emitted in occupied spaces.

The air exchange measurements have involved short-lived concentrations of up to (1) 1 ppm dichlorodifluoromethane or up to 0.1 ppm of either perfluorinated methylcyclohexane or perfluorinated dimethyloyclohexane. Review of data in $NIOSA_A$ RTECS indicates that laboratory animals are asphyxicted at concentrations below those that lead to toxic effects.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

dichlorodifluoromethane
perfluorinated methylcyclohexane
perfluorinated dimethyloyclohexane

Exposure is by inhalation.

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year.	
Signature of Institution Official David E Reichle	**Date** Jan. 25, 1994
Printed or Typed Name Dr. David E. Reichle	**Telephone Number**

PCO

For DOE Use Only

Date Received by ER-70	**Date** ☐ **Accepted** _____ ☐ **Returned to Originator** _____
Reason for Return	
DOE Reviewers	

1048292

Indent No. ORNL-17

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

TO: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities (ORAU)
and Oak Ridge National Laboratory (ORNL)

Date: January 5, 1987

Principal Investigator: Michael R. Guerin, Ph.D. (ORNL)

Co-Investigator: Roger A. Jenkins, Ph.D. (ORNL)

Title of Project: MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

I. Objective of Experiment:

The objective of this study is to determine whether analytical chemical methods used to measure human exposure to environmental tobacco smoke (ETS) by ambient air sampling are valid. This includes the quantitative reliability of both the sampling and measurement methods and a consideration of the physical state (particulate or vapor phase) of the marker chemical being measured. The results of this study will be analytical methods which can be used to determine human exposure to environmental tobacco smoke.

II. Methods of Procedure:

Ambient air samples will be taken and/or instrumental measurements will be made at various locations over various periods of time in occupied spaces in the presence and absence of active smokers. Collected samples will be returned to the laboratory for analysis. Smokers will smoke normally. No intervention is planned other than a request to note the number of cigarettes smoked or to save the cigarette butts as a record. Spaces to be sampled include offices, conference rooms, eating areas, and public areas.

REVIEW AND ACTION

ORAU/ORNL Committee on Human Studies

Principal Investigator Michael R. Guerin, PhD Ident. No. ORNL-17

Project Title Measurement of Environmental Tombacco Smoke Constituents in Occupied Spaces

1. In the opinion of this committee the rights and welfare of the subjects in this project or activity will be protected. The committee states that adequate safeguards against any untoward effects have been provided.

2. In the opinion of the committee the informed consent procedures to be used in this project will be both appropriate and adequate. The committee also finds that no inappropriate psychological or sociological risks will exist for the subjects involved in this project.

3. The committee seeks continuing communication with the investigator(s) on this project along the following lines:

4. Other committee comments:

Approve x 1048294

Disapprove

Carl F. Hubner
Chairman of Committee

Jan. 20, 1987

\K RIDGE NATIONAL LABORATORY
OPERATED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.

POST OFFICE BOX X
OAK RIDGE, TENNESSEE 37831

January 5, 1987

To: Committee on Human Studies

Review of Project "Measurement of Environmental Tobacco Smoke Constituents in Occupied Spaces"

Research underway in my Section for the National Cancer Institute and the Council for Tobacco Research includes the development of analytical methods for the chemical characterization of environmental tobacco smoke (ETS). An important components of this work involves sampling and monitoring of natural ETS. This requires that spaces occupied by smokers be sampled.

It is not clear whether this work constitutes a "human study". An application form is included for your review.

Please inform me as soon as possible if Human Studies Committee approval is not required.

Sincerely,

M. R. Guerin, Head
Organic Chemistry Section
Analytical Chemistry Division

MRG:pmt

Enclosure

cc: A. S. Garrett, Jr., ORNL Medical

17

Indent No. ORNL-16

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

TO: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities (ORAU)
and Oak Ridge National Laboratory (ORNL)

Date: January 5, 1987

Principal Investigator: Michael R. Guerin, Ph.D. (ORNL)

Co-Investigator: Roger A. Jenkins, Ph.D. (ORNL)

Title of Project: MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

I. Objective of Experiment:

The objective of this study is to determine whether analytical chemical methods used to measure human exposure to environmental tobacco smoke (ETS) by ambient air sampling are valid. This includes the quantitative reliability of both the sampling and measurement methods and a consideration of the physical state (particulate or vapor phase) of the marker chemical being measured. The results of this study will be analytical methods which can be used to determine human exposure to environmental tobacco smoke.

II. Methods of Procedure:

Ambient air samples will be taken and/or instrumental measurements will be made at various locations over various periods of time in occupied spaces in the presence and absence of active smokers. Collected samples will be returned to the laboratory for analysis. Smokers will smoke normally. No intervention is planned other than a request to note the number of cigarettes smoked or to save the cigarette butts as a record. Spaces to be sampled include offices, conference rooms, eating areas, and public areas.

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Sampling and monitoring will be carried out using pumps, collection media and instrumentation common to industrial hygiene monitoring. Three types of study conditions will be involved. These are:

a) area monitoring of occupied spaces under conditions of normal use.

b) personal monitoring of individuals under conditions of normal activity, and

c) area and personal monitoring of smokers in a conference room which has been thoroughly characterized in terms of ventilation, temperature, and humidity.

III. Possible Hazards and Their Evaluation:

No health hazard is posed specifically by this study. Only current smokers are involved in the study and they are allowed to smoke their regular brand normally.

IV. Radioisotopes and New Drugs:

None.

V. Responsibility of Principal Investigator:

The principal investigator will follow the procedures of the Committee on Human Studies in obtaining informed consent from the subjects involved in this study. The investigator recognizes that he retains the primary responsibility for safe-guarding the interests of participants involved in the study. Any significant changes in methods of procedure or the development of unexpected risks will be immediately brought to the attention of the Committee on Human Studies.

Starting Date January 15, 1987

Signatures _____ Principal Investigator

_____ Co-Investigator

DIVISION REVIEW:

The application described above has been reviewed and approved.

Official signing for the institution:

Signature: _____

Title: _____

Institution: _____

Date: _____

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical and
Health Sciences
Division

January 13, 1987

M E M O R A N D U M

To: Dr. Karl Hubner, Chairman
ORAU/ORNL Committee on Human Studies

From: Becky Hawkins, Secretary

Subject: ORNL-17
MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS
IN OCCUPIED SPACES

I received the enclosed application for the use of humans as experimental subjects last week from Dr. Michael Guerin.

Please let me know whether this application should go to the expedited review committee or be presented to the full committee.

bsh

Oak Ridge
Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical and
Health Sciences
Division

January 20, 1987

M E M O R A N D U M

TO: Michael R. Guerin, Ph.D.
Roger A. Jenkins, Ph.D.

FROM: Dr. Karl Hubner/Chairman Karl Hubner M.D. 1/20/87
ORAU/ORNL Committee on Human Studies

SUBJECT: ORNL-17
MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS
IN OCCUPIED SPACES

I have reviewed your proposal for the use of humans in experiments to measure exposure to environmental tobacco smoke. Thank you for clarifying your statement "personal monitoring of individuals under conditions of normal activity." It is understood that you will attach a trapping device to humans to measure their exact exposure levels.

According to the guidelines of the Committee on Human Studies, this proposal can be approved by the Expedited Review Process. Since there is no health hazard and no violations of privacy, you do not need a consent form to do these studies.

The Committee needs to be notified of any new proposals and yours will be presented to the Committee for their comments at the next scheduled meeting early this spring.

If you have any further questions or comments, please contact Becky Hawkins at 576-3086.

KFH:bh

APR 13 1987

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Michael Guerin

FROM: Becky Hawkins/Secretary, Committee on Human Studies B. Hawkins

RE: Status Reports on Active Proposals

DATE: May 1987

The guidelines for the ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by May 1, 1987. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: ORNL-17 MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

Proposal No. ORNL-17 Date Approved: 1987

M.P. Guerin
Signature of Principal Investigator

5/11/87
Date Signed

1. Report progress made in the past year.

Samples of ambient indoor air have been taken in several office and work areas and those samples have been analyzed for nicotine content by two methods. Results are appended as "Table 4" from a progress report to our sponsor.

2. Report any complications.

No complications.

1048301

3. Are there any planned changes?

No changes are planned.

4. Do you wish the project to be continued?

Yes. Additional field sampling will be required to validate methods.

5. Comments.

None.

Table 4
Comparison of Mean Ambient Nicotine Levels
(Mean +/- one standard deviation)

	TREATED FILTER METHOD Nicotine, ug/m3	TENAX METHOD Nicotine, ug/m3
Office #1	9.8 +/- 2.4	14.0 +/- 0.5
Office #1 (repeat)	21.0 +/- 3.9	19.7 +/- 1.8
Office #2	5.5 +/- 0.3	5.4 +/- 0.5
Office #3	6.9 +/- 0.6	8.2 +/- 0.1
Print Office	1.7	4.1
Print Room	2.2	0
Labor Shack Trial #1	31.9 +/- 1.6	30.1 +/- 0.9
Labor Shack Trial #2	58.7 +/- 2.2	60.3 +/- 2.1
Labor Shack Trial #3	45.6 +/- 1.0	53.2 +/- 0.9
Labor Shack Trial #4	23.4 +/- 0.3	23.3 +/- 2.9
Labor Shack Trial #5	41.2 +/- 0.6	39.8 +/- 0.1
Labor Shack Trial #6	12.8 +/- 1.3	12.6 +/- 1.3
Office #4 Trial #1	2.8 +/- 0.6	2.1 +/- 0.0
Office #4 Trial #2	0.5 +/- 0.1	2.8 +/- 0.0
Office #4 Trial #3	0.9 +/- 0.3	2.5 +/- 0.0
Office #4 Trial #4	0.7 +/- 0.5	2.8 +/- 0.1
Office #5 Trial #1	0.4 +/- 0.3	1.8 +/- 0.1
Office #5 Trial #2	1.8 +/- 0.7	0.9 +/- 0.1
Machine Shop Trial #1	4.4 +/- 0.6	3.8 +/- 0.1
Machine Shop Trial #2	2.4 +/- 0.2	2.3 +/- 0.9
Machine Shop Trial #3	1.2 +/- 0.6	1.0 +/- 0.4
Common Room Trial #1	1.2 +/- 0.7	2.4 +/- 0.1
Common Room Trial #2	0.8 +/- 0.8	2.5 +/- 0.0
Common Room Trial #3	0.5 +/- 0.5	2.0 +/- 0.0

Submitted to EST

A THERMAL DESORPTION METHOD FOR THE DETERMINATION OF NICOTINE IN INDOOR ENVIRONMENTS [1]

Cyril V. Thompson*, Roger A. Jenkins, and Cecil E. Higgins

Organic Chemistry Section, Analytical Chemistry Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee, 37831

[1] Research sponsored by the Council for Tobacco Research, Inc., under Interagency Agreement DOE No. ERD-85-471, CTR Project No. 132 with Martin Marietta Energy Systems, Inc., under Contract DE-AC05-840R21400 with the U. S. Department of Energy.

Nicotine, the major, unique component of the gas phase of environmental tobacco smoke (ETS), has been employed as a marker for estimating exposure to ETS. A personal monitoring system for the determination of exposure to nicotine has been developed. The system consists of a sampling cartridge packed with 200 mg of Tenax GC ® and a small, constant flow, personal sampling pump. After sampling, the cartridges are analyzed by triethylamine-assisted thermal desorption gas chromatography with nitrogen-selective detection. Collection and desorption efficiencies for the cartridges have been determined. The system has been evaluated in controlled-atmosphere chambers, and applied in a variety of work sites, and in 36 restaurants, where measured concentrations of nicotine ranged from 0.5 to 37.2 $\mu g/m^3$.

Introduction

One of the major public health concerns of the 1980s has been indoor air pollution and its effects on the individual. Environmental tobacco smoke (ETS), which is the diluted and aged mixture of side-stream smoke emanating from the smoldering cigarette and main-stream smoke exhaled by the smoker, represents a potentially significant contribution to this pollution. Concentrations of ETS respirable suspended particulates (RSP) have been reported to range from 0 to 700 $\mu g/m^3$ in indoor environments (1). A number of procedures have been applied for estimating ETS concentrations based on the measurement of concentrations of particular ETS constituents, such as CO (2-5), oxides of nitrogen (NO_x) (3-5), and particulate matter (4-9). However, these constituents of tobacco smoke are also the products of other

combustion processes, an aspect which limits their utility as markers for estimating ETS levels, especially in complex atmospheres such as those which exist in indoor environments. Estimates of personal exposure to ETS have been made by measuring carboxyhemoglobin (COHb) (10-11), urinary hydroxyproline (HOP) (12), and nicotine and cotinine (a metabolite of nicotine) in the blood, urine and saliva (10-11, 13).

Several methods have been developed for determinating nicotine concentrations at fixed sampling locations in industrial settings. The NIOSH method for nicotine utilizes a resin-filled cartridge (XAD-2) with a personal sampling pump for collection of samples followed by solvent extraction and analysis by gas chromotography (14). However, this method's 300 $\mu g/m^3$ limit-of-detection (LOD) makes it unsuitable for measuring ETS because associated concentrations of nicotine are well below this LOD. Another industrial method, also limited by its relatively high LOD (40 $\mu g/m^3$), collects nicotine in a series of water-filled bubblers (15).

Williams et al. (16) have reported a method using a cold Petri dish as the means for collecting nicotine. Although the reported nicotine concentration range associated with the method was low enough to be applicable for measuring ETS, the method had several deficiencies which would severely limit its value (17). Other methods reported in the literature detail the use of untreated glass fiber filters (4) or diffusion denuder tubes (18) for collection of ambient nicotine.

The development and testing of a number of personal monitoring systems which measure individual exposures to ETS as determined by ambient nicotine concentrations have been reported recently in the literature. Solvent desorption-based systems include personal sampling pumps coupled with commercially available XAD-4 cartridges (19, 20, 21) and $NaHSO_4$-treated,

Teflon-coated glass fiber filters (22), and a passive sampling system utilizing the treated filters (23). The limitation of using solvent extraction of samples is that only a small fraction of the analyte is actually analyzed. This necessarily raises the theoretical LOD for such methods relative to those such as thermal desorption, that use all of the acquired sample. Two thermal desorption-based personal monitoring systems for nicotine have been reported, one by Proctor (24) that employs an unspecified adsorbent and analysis system and another by Muramatsu et al. (25, 26), that utilizes an ammonia purge of the sample cartridge during desorption into a gas chromatograph (gc). This method requires modification of the gc and desorption system by placing an ammonia bubbler in-line with the carrier gas.

This paper discusses the development, evaluation in controlled ETS atmospheres in chambers and offices, and field testing of a thermal desorption-based personal monitoring system for nicotine using Tenax GC as the adsorption material. This system is similar to the system developed by Muramatsu; its difference - and advantage - is that it lacks the mechanical complexities of the ammonia purge during desorption.

Methods and Material

Personal Monitoring Systems - Air sampling cartridges were 16 cm sections of ¼ in. O.D. borosilicate glass tubing which was treated with NH_4OH (immersion in 15% NH_4OH over-night, followed by air-drying) and then fire polished on both ends and packed with approximately 200 mg of Tenax GC, 35-60 mesh, acquired from Alltech Associates (Deerfield, IL). Before use,

cartridges were conditioned at 250° C, in a stream of N_2 flowing at 40 mL/min. for at least two hours. After the cartridges had cooled, both ends were sealed with ¼ in. plastic caps obtained from Alltech Associates (Deerfield, IL). The cartridges were also reused after washing (with 2-3 mL of methanol) and reconditioning.

Alpha-2 personal sampling pumps, available from DuPont (Kennett Square, PA), were used for sample collection in most experiments (DuPont P-4000 pumps were used in a few initial chamber experiments), and were chosen for their light weight (410 g) and low-noise level during operation. For experiments performed in the chambers and offices, pumps were connected to Tenax cartridges with a section of flexible tubing, and air from the area sampled was drawn through the cartridge. For sampling conducted in restaurants, the pumps were worn under jackets. A section of Tygon® tubing connected the pump to the Tenax cartridge, which was clipped to the inside lapel of the jacket so that the inlet end was within 25 cm of the mouth and nose of the individual conducting the sampling. All samples were collected for at least one hour with the pump operating at a flow rate of 170 mL/min. Flow rates were checked with a bubble meter before and after sample acquisition. Immediately after completion of sampling, Swagelok ¼ in. stainless steel end caps fitted with Teflon ferrules were placed on each end of the cartridge, and the cartridge was refrigerated at 3°C until analysis.

Analytical Method - Nicotine standards were prepared by diluting redistilled nicotine (98%) obtained from Eastman Kodak (Rochester, NY) in ethyl acetate which contained 0.01% triethylamine (TEA). (It has been found that addition of a basic material such as TEA (19) or NH_4OH (27) to nicotine standards prevents adsorption, by the glass of the container, of nicotine from

solution.) Internal standards employing quinoline were prepared by diluting quinoline in a solution of ethyl acetate/5% TEA. Fresh nicotine and quinoline standards were prepared every 15 days.

Analyses were performed with a Varian Model 3700 gas chromatograph equipped with a nitrogen/phosphorous detector (gc/NPD) and a 2 m x 2 mm i. d. glass column packed with 10% Carbowax 20M/2% KOH on 80-100 mesh Chromosorb W-AW (obtained from Alltech Associates, Inc., Deerfield, IL). Flow rates were He (carrier gas) = 40 mL/min., H_2 = 4.5 mL/min., and air = 175 mL/min. Temperature settings were injector and detector = 250°C; and column oven initial temperature = 70°C for 8 min., programmed at a rate of 46°C/min. to 175°C for 4 min. At these settings, nicotine elutes at 13.4 minutes and quinoline at 14.0 minutes.

In the initial developmental work for the method, multi-point calibrations with nicotine standards were performed daily. For the field sampling, a calibration curve was generated from the desorption of 9 duplicate sets of Tenax traps loaded with amounts of nicotine ranging from 1.5 to 700 ng and with 250 ng of quinoline internal standard. Because the response of the nitrogen/phosphorous detector tended to be nonlinear at higher trap loadings (>1000 ng), data from the analyses were fitted to a second order polynomial regression. In practice, there was no difference between first and second order regressions in the 0-700 ng concentration range. For example, the first and second order correlation coefficients (R^2) for one calibration run were both 0.995, and for another, both were 0.997.

Response factors (RF) for all standards were calculated with the formula:

$$RF = \frac{(\text{AREA COUNTS NICOTINE})}{(\text{AREA COUNTS QUINOLINE})} \cdot \frac{(\text{CONCENTRATION OF QUINOLINE})}{(\text{CONCENTRATION OF NICOTINE})} \quad (1)$$

Averages and standard deviations computed from the RF data were used to assess control of the method in day-to-day operation. If results for daily control standards were more than two standard deviations from the average for the calibration, the method was judged to be out of control, thus requiring recalibration. Control was observed throughout the study.

Test Atmospheres - The initial experimental atmospheres for the development of the Tenax method were generated in two stainless steel chambers with volumes of 0.4 and 1.4 m^3 (obtained from Young and Bertke Co. Cincinnati, OH). Side-stream smoke from a 2R1 Kentucky Reference cigarette (procured from the University of Kentucky Tobacco and Health Research Institute, Lexington, KY) smoldering in a laminar flow smoke generator (28), was pulled into the smaller chamber at a rate of 30 L/min. and diluted with an air flow of 250 to 1000 L/min., the exact rate depending on the concentration of ETS needed. Concentrations for this chamber ranged from 700 to 3500 $\mu g/m^3$ particulate matter (PM) and 100-500 $\mu g/m^3$ nicotine. Low concentrations of ETS, 50-300 $\mu g/m^3$ PM and 10-70 $\mu g/m^3$ nicotine, were generated by diluting a portion of the atmosphere from the small chamber into that of the large chamber. Concentrations of particulate matter in the chambers were monitored with a TSI-5000 piezoelectric balance (acquired from TSI, St. Paul, MN) and an RAS-1 light scattering sensor (purchased from GCA Instruments, Bedford, MA), which was modified in our laboratory to enhance its sensitivity. The nicotine and PM concentrations utilized for these experiments are much higher than what would be typically observed in real life situations and were used only to determine the potential utility and the upper analytical limits of the method. After development experiments

involving the chamber were concluded, other experiments were conducted in an un-occupied office. ETS was produced by generating sidestream smoke from 1R4F Kentucky Reference cigarettes smoked (one 35 mL puff per minute) on an ADL-II machine (obtained from Arthur D. Little Co., Cambridge, MA). Mainstream smoke was collected in sealed Tedlar bags (acquired from SKC Inc., Eighty Four, PA), and ETS concentrations were varied by adjusting the smoking rate from 1 minute of smoking (2 second puff, 58 seconds smolder) per 10 minutes elapsed time up to continuous cigarette smoking. PM levels were monitored with a TSI-5000 piezoelectric balance.

Additional laboratory evaluations of the method's performance were conducted in an 18 m^3 environmental chamber (29) used for ETS studies and located at the R. J. Reynolds Tobacco Company's facilities in Winston-Salem, N. C. PM concentrations in the chamber were monitored with a TSI-5000 piezo-electric balance. Initial field evaluations were conducted in work areas, offices, common areas, and dining areas at Oak Ridge National Laboratory.

Sampling Site Selection - Field sampling was conducted in establishments which were both listed under the "Restaurant" heading in the Yellow Pages of the Knoxville, TN telephone directory and located in the Knoxville, TN, Standard Metropolitan Statistical Area (SMSA) (Knox, Blount, and Anderson counties). Restaurant selection was conducted by assigning each restaurant a number and then choosing 43 out of the 419 restaurants with a random number generator. Three of these restaurants were eliminated because they had gone out of business, three because they were carry-out only, and one because the personal safety of the sampling team was called into question. The remaining 36 were sampled, and for each sample, information was recorded

TABLE III

RESULTS FROM DETERMINATIONS OF NICOTINE

BY TENAX AND XAD-4 METHODS

RUN No.	Particulate Matter Concentration ($\mu g/m^3$)	MEAN NICOTINE CONCENTRATION, ($\mu g/m^3$) TENAX[a]	ORNL[b] XAD-4	RJR (A)[c] XAD-4	RJR (B)[c] XAD-4
1	55	2.5	-	-	-
2	14	1.8	-	-	-
3	103	5.0	-	-	-
4	62	4.1	4.1	4.3	4.3
5	16	2.1	2.1	2.2	2.3
6	128	5.5	5.5	5.9	5.7

(a) N = 3 determinations (b) Analyzed by the authors using the method developed at R. J. Reynolds Tobacco Co. N = 2 determinations. (c) Analyzed at R. J. Reynolds Tobacco Co (30). N = 2 determinations. RJR (A) analyzed using 0.53 mm i. d. capillary column with direct injection. RJR (B) analyzed using 0.32 mm i. d. capillary column with split injection.

TABLE IV

NICOTINE CONCENTRATIONS MEASURED AT SELECTED LOCATIONS WITHIN OAK RIDGE NATIONAL LABORATORY

LOCATION	AMBIENT NICOTINE LEVEL ($\mu g/m^3$)
Offices	4.2 ± 0.1[a]
	4.0 ± 3.5[a]
	4.5 ± 0.5[a]
	6.7 ± 0.9
	0.7 ± 1.0
	1.1 ± 1.5
	0.6 ± 0.8
	0.6 ± 0.8
	0.6 ± 0.9
	0.3 ± 0.4
Dining Area	4.4 ± 0.8
	2.3[b]
Work Area	2.0 ± 0.3
Common Area	30.0 ± 0.9
	60.3 ± 2.1
	53.1 ± 2.8[a]
	23.2 ± 2.9
	39.7 ± 0.1
	12.6 ± 1.2
Work Area	3.8 ± 0.1
	2.2 ± 0.9
	1.0 ± 0.4
Common Area	0.9 ± 1.3
	1.7 ± 0.8
	0.8 ± 1.1

(a) N = 3 determinations. (b) N = 1. All others, N = 2 determinations.

TABLE V

NICOTINE LEVELS IN RESTAURANTS

SAMPLE NUMBER	# SMOKERS OBSERVED	# CIGARETTES	# CIGARS OR PIPES	ESTIMATED RESTAURANT VOLUME (m^3)	CLOSEST SMOKER (ft.)	NICOTINE CONCENTRATION ($\mu g/m^3$)
34	0	0		179	-	0.5
16	0	0		595	-	0.5
24	1	1		198	6	0.7
21	1	1		41	9	0.8
10	0	0		638	-	1.1
20	7	9		227	5	1.4
31	2	2		272	12	1.5
14	1	2		283	20	1.5
25	1	1		136	8	1.6
18	2	2		1204	15	2.3
19	0	0		453	-	2.3
27	2	2		317	10	2.4
29	6	8		1700	10	2.4
9	8	9		510	5	2.5
2	7	8		113	8	3.3
26	6	7		213	2	3.3
22	4	3	1	170	3	3.5
11	12	14		204	5	4.1
12	9	9		1785	7	4.2
15	4	4		198	5	4.3
35	10	11		623	4	4.5
32	5	7		397	5	4.8
33	6	10		1063	14	4.8
23	5	8	1	238	10	4.9
7	8	11		2380	5	5.6
1	15	18	1	744	2	5.7
6	6	8		340	2	5.9
4	4	3		179	7	7.3
5	4	3		179	7	7.4
17	19	35	1	680	4	7.8
28	10	15		204	5	8.0
13	9	10		177	6	9.3
30	19	25		793	4	12.1
3	33	43		1666	5	12.6
8	14	18		680	5	13.5
36	-	30		272	8	37.2

TABLE VI

NICOTINE LEVELS IN FOOD COURTS

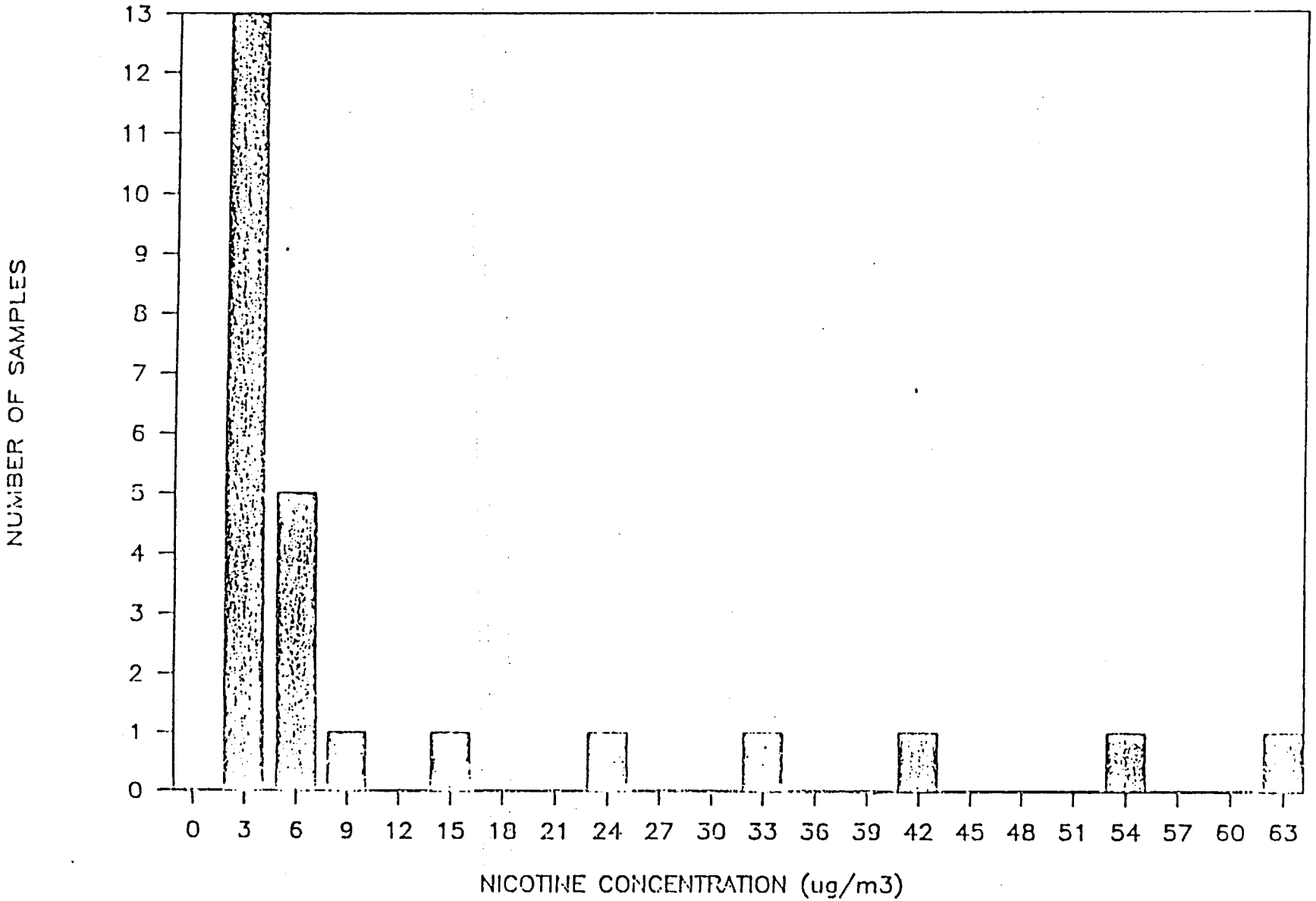
SAMPLE	# SMOKERS OBSERVED	# CIGARETTES	# CIGARS OR PIPES	CLOSEST SMOKER (ft.)	NICOTINE CONCENTRATION ($\mu g/m^3$)
37	6	6		15	1.6
38	16	16		4	1.6
39	8	11		4	2.1
40	7	7	1	7	2.5
42	17	19		15	3.0
41	34	34		6	3.1

LIST OF CAPTIONS FOR FIGURES

Figure 1. Distribution of nicotine levels for work sites at ORNL. Note that nicotine concentrations listed are the maxima for the individual cells.

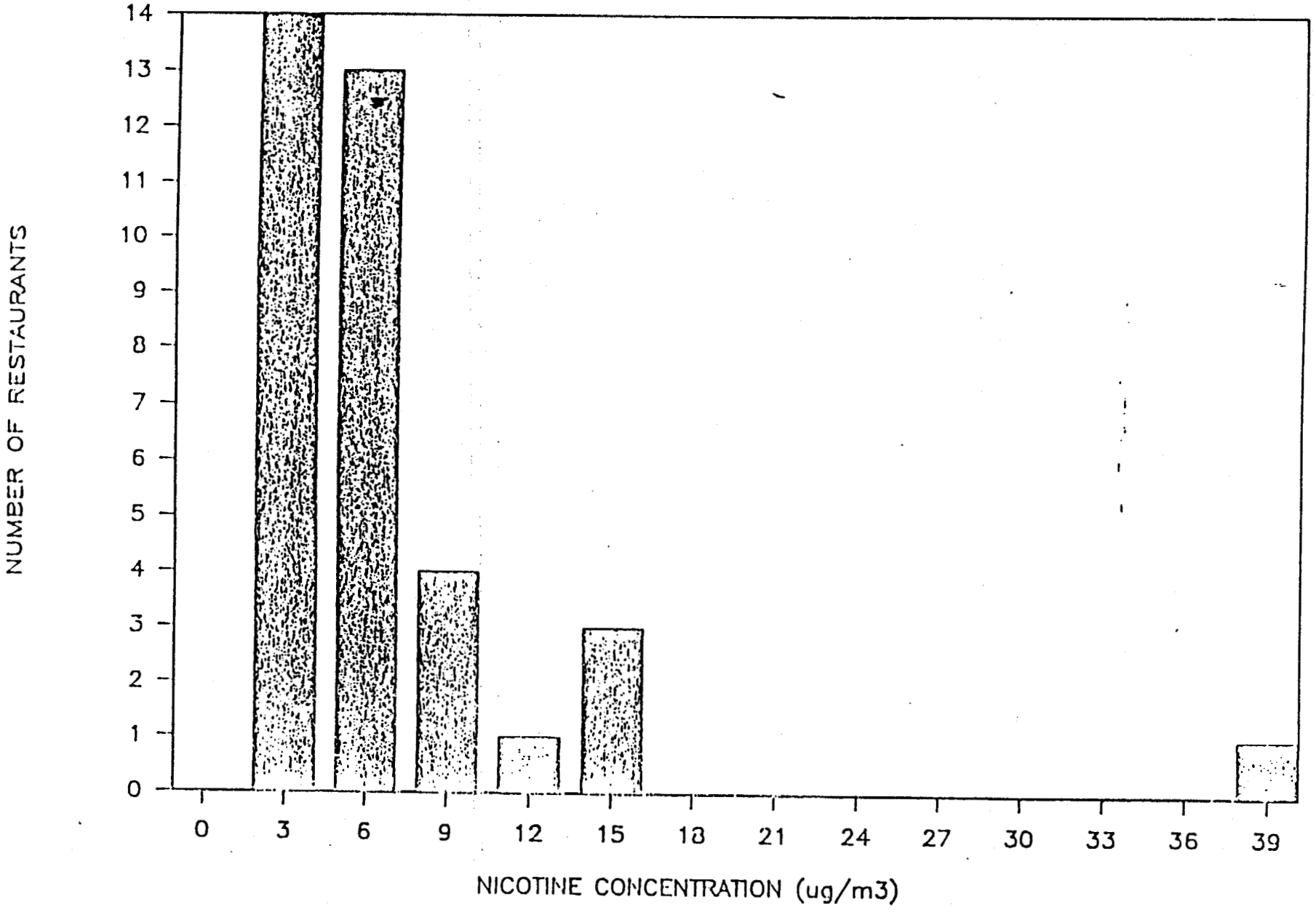
Figure 2. Distribution of nicotine results in selected Knoxville, Tennessee area restaurants. Note that nicotine concentrations listed are the maxima for the individual cells.

ORNL DWG 88 8850



1048317

ORNL DWG 88-8849



regarding the number of smokers, the number of cigarettes, cigars, and pipes observed to have been smoked, the distance to the closest observed smoker the type of meal served (lunch or dinner), crowd density, and restaurant volume. In addition to the samples acquired in restaurants, two samples were acquired on a Saturday afternoon at each of three food courts in shopping malls.

Results and Discussion

Results of initial experiments with Tenax cartridges showed evidence of incomplete desorption of nicotine, with up to 10% of the nicotine remaining on the cartridge. In order to enhance nicotine desorption, an internal standard solution was prepared which included 5% TEA. Internal standard spikes thus contained about 200 μg of TEA, which, as a stronger base, displaced nicotine from acidic sites within the sampling cartridge or analysis train.

Experiments conducted in the 0.4 and 1.4 m^3 chambers were performed to determine the functional capabilities of the method and the nicotine collection efficiency. Table I gives the results from sampling of both dilute and concentrated simulated ETS environments in the large and small chambers, respectively. The ratios of nicotine to particulate matter in these experiments are substantially higher than what has been reported in typical indoor environments (30). This discrepancy was judged of little consequence since investigation of nicotine levels was the sole focus of the study.

Experiments to determine sample volumes at which nicotine breakthrough became significant were conducted by placing two Tenax cartridges in series and sampling from simulated ETS environments in the chambers. Results indicated not more than 1% breakthrough for sample volumes ranging from 20 to 45 L and nicotine concentrations ranging from 70-250 $\mu g/m^3$. At lower sample volumes, breakthrough percentages are expected to be correspondingly lower.

In Table II are listed the results from sampling of ETS in the unoccupied office. This range of nicotine and PM levels more closely approximated that which would be expected from sampling in public places. Agreement between nicotine and particulate levels was particularly good in this experiment, with the correlation coefficient of 0.976 for a first order regression analysis of these two parameters.

The detection limit of the method was determined by sampling, in triplicate, a very dilute environment of ETS generated in the office [air changes per hour (ACH) = 2.4] with one puff and one minute of smoldering from a 1R4F Kentucky reference cigarette. Following a one hour sampling period, analysis of the cartridges showed an average of 3.0 ± 0.3 ng per cartridge, corresponding to 0.3 $\mu g/m^3$ nicotine, with a relative standard deviation (RSD) of 10%. A second experiment conducted at a slightly lower ETS concentration gave an average nicotine loading per cartridge of 2.3 ± 0.6 ng corresponding to a concentration of 0.2 $\mu g/m^3$ and an RSD of 26%. This level of variation was arbitrarily considered to be unacceptable for the method, so the detection limit was defined as 0.3 $\mu g/m^3$ for a 10 L sample. In practice, the detection limit may be as low as 0.08 $\mu g/m^3$ assuming a sample volume of 40 L. Experiments indicated that breakthrough would be insignificant even at that relatively large sample volume.

In Table III are listed the results from sampling conducted in the 18 m^3 chamber at R. J. Reynolds. An evaluation of the method for ambient nicotine developed by Ogden et al. (31) was also being conducted at the same facilities. This presented an opportunity for comparison of the two methods. In general, the data indicated that agreement between the two methods was excellent. The nicotine levels sampled for this experiment are near the mean of the level determined in the field study (see below) but represent only a fraction of the range expected to be encountered during field sampling in general. However, given that the greatest difficulty associated with the analysis of trace quantities of nicotine is adsorption losses in the analytical system, a method which can accurately determine these concentrations should also be able to correctly assess higher concentrations.

For all experiments where PM concentration data were available, mean ratios of nicotine to PM were calculated. The ratios obtained from experiments involving the 1.4 and 0.4 m^3 chambers were 0.52 ± 0.07 and 0.39 ± 0.05, respectively. The ratio for experiments performed in the unoccupied office was 0.16 ± 0.06, and for experiments conducted in the 18 m^3 chamber, 0.08 ± 0.04. The considerable differences among the ratios is expected in view of the differences in ETS levels, air handling methods, and air exchange rates and the theory that as ETS ages, nicotine tends to be adsorbed by the various surfaces present (27). For the two smaller chambers, air exchange rates ranged from 21 to 150 ACH. allowing little opportunity for nicotine adsorption by the chamber walls. The office, with an air exchange of 5.4 ACH and non-recirculated ventilation, exhibited lower nicotine/PM ratios, and the 18 m^3 chamber, with an air exchange rate of 0.05 (32) and complete recirculation in a static system, showed the lowest levels

of nicotine relative to the particulate levels. These data appear to support the above-mentioned theory.

Listed in Table IV are the results from samples collected at Oak Ridge National Laboratory facilities. The arithmetic mean and standard deviation of nicotine concentrations for all sample sites is 10.5 ± 17.2 $\mu g/m^3$. However, the relatively high concentrations measured in the first common area (36.5 ± 18.1 $\mu g/m^3$) influence the average disproportionately. As can be seen in Figure 1, the data appear to be distributed in a log normal pattern; thus the geometric mean of 3.2 $\mu g/m^3$ (with 95% confidence boundaries of 1.8 and 6.0 $\mu g/m^3$) may be more appropriate for this data set.

Results from the field determinations of nicotine concentrations in restaurants are shown in Table V. Samples 28 and 29 were acquired simultaneously from the same restaurant, with an RSD for these two samples of 1%, suggesting good reproducibility for the method.

Nicotine concentrations found in the restaurants ranged from 0.5 to 37.2 $\mu g/m^3$ with an arithmetic mean of 5.4 ± 6.4 $\mu g/m^3$. As in the treatment of the data from the in-house sampling, a plot of the distribution of the concentration data indicates that it fits a log normal rather than Gaussian pattern (Fig. 2). The geometric mean of 3.5 $\mu g/m^3$, with 95% confidence boundaries on the median of distribution of 2.5 and 4.8 $\mu g/m^3$, is somewhat lower than the arithmetic mean but is still comparable to data results cited by the researchers listed below.

Muramatsu et al. (25) reported a range of 7.1 to 27.8 $\mu g/m^3$ nicotine with an average of 14.8 $\mu g/m^3$ for eight samples taken in five restaurants. Hinds and First (33) have reported an average of 5.2 $\mu g/m^3$ nicotine for four samples from restaurants. Oldaker et al. (21) reported a range of 0-24 $\mu g/m^3$ nicotine with an average of 5 $\mu g/m^3$ for 170 samples acquired in

restaurants. For air samples taken in offices, Hammond et al. (22) have reported 3-48 $\mu g/m^3$ nicotine, while Muramatsu et al. (25) have reported 9-32 $\mu g/m^3$ and 6-20 $\mu g/m^3$ nicotine (26). For 156 office samples, Oldaker et al. (21) reported an average of 5 $\mu g/m^3$ nicotine with a range of 0-70 $\mu g/m^3$. Nicotine concentrations in public common areas such as lobbies and waiting rooms were reported to be 2-36 $\mu g/m^3$ by Muramatsu et al. (25) and 1-3 $\mu g/m^3$ by Hinds and First (33). For samples taken in the smoking sections of airplanes, Muramatsu et al. (26) have reported 14 $\mu g/m^3$ and 6-29 $\mu g/m^3$ with an average of 15 $\mu g/m^3$ (25). Oldaker and Conrad (20) have reported 0-112 $\mu g/m^3$ nicotine, with an average of 9 $\mu g/m^3$ in airplane smoking sections, and 0-40 $\mu g/m^3$ nicotine, with an average of 6 $\mu g/m^3$ in non-smoking sections.

Major factors likely to affect nicotine concentrations in a restaurant are the number of cigarettes smoked, the volume of the room, the proximity of smokers to the sample location, and the air exchange rate (data relative to this last factor were not acquired). The Pearson's correlation coefficients (r) for first order regressions of nicotine concentration to number of cigarettes, number of smokers, restaurant volume, and distance to the closest smoker are 0.669, 0.783, 0.049, and -0.155, respectively. The significance levels (p) (an indicator of the probability of correlation between the nicotine concentration and the above-mentioned factors) for the regressions are 0.0001, 0.0001, 0.776, and 0.396, respectively. A correlation is thus indicated between nicotine concentration and both the number of cigarettes and number of smokers. If sample 36 is eliminated from the regression analysis for nearest smoker, then $p = 0.03$, indicating a correlation between nicotine concentration and this parameter. Attempts to increase the degree of correlation by normalizing for various combinations of these factors were unsuccessful. No data were acquired regarding other

factors which could have some impact on the nicotine concentration, such as the history of the number of cigarettes smoked prior to sampling, and the direction of air flow in the restaurants.

In Table VI are listed the data from samples acquired in the food courts of the shopping malls. The range of nicotine concentrations from the mall food court samples was 1.6 to 3.1 $\mu g/m^3$ with an arithmetic mean and standard deviation of 2.3 ± 0.7 $\mu g/m^3$. Although use of the geometric mean could not be justified for this sample set, it was calculated for comparison purposes and is the same as the arithmetic value. The average nicotine concentration for these samples is lower than that from the restaurant data (notwithstanding the large number of cigarettes observed to have been smoked) and is probably attributable to the much greater volumes of the food courts, which begin to approximate open-air restaurants.

Conclusion

A procedure for the determination of personal exposure to concentrations of nicotine in indoor environments has been developed that has a low detection limit and is unobtrusive in its use. Developmental studies have again pointed to the need for the use of a basic compound for sample modification or desorption enhancement, when trace quantities of nicotine are being processed or analyzed. The Tenax method has been applied to the determination of nicotine concentrations in a number of restaurants; results are comparable to those obtained by other researchers utilizing different methods for sampling in restaurants and other public places.

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TABLE I

NICOTINE AND PM CONCENTRATIONS MEASURED IN 0.4 AND 1.4 m^3 STAINLESS STEEL CHAMBERS[a]

Nicotine ($\mu g/m^3$)	Particulate Matter ($\mu g/m^3$)
34	80
42	83
43	79
44	74
282	757
263	667
302	684
291	659
238	708
224	684
271	643

(a) Air changes per hour (ACH) ranged from 21 to 150.

TABLE II

CONCENTRATIONS OF NICOTINE AND PARTICULATE MATTER MEASURED IN AN UN-OCCUPIED OFFICE

TRIAL NO.	PARTICULATE MATTER ($\mu g/m^3$)	NICOTINE CONCENTRATION ($\mu g/m^3$)
1	14.6	1.8
2	23.2	1.9
3	28.2	2.4
4	15.2	3.7
5	58.6	4.8
6	59.6	8.2
7	113.0	21.7
8	115.4	27.3
9	257.0	48.3
10	248.8	49.0

JUN 0 7 1988

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Michael Guerin

FROM: Becky Hawkins/Secretary, Committee on Human Studies B. Hawkins

RE: Status Reports on Active Proposals

DATE: June 1988

The guidelines for the ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by June 17, 1988. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: ORNL-17 MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

Proposal No. ORNL-17 DATE APPROVED: 1987

MR Guerin
Signature of Principal Investigator

6/13/88
Date Signed

1. Report progress made in the past year.

   Analyses for ambient nicotine in Knoxville area restaurants and for volatile organic components of environmental tobacco smoke in an investigators home were completed. A paper illustrating some of the work is appended.

2. Report any complications.

   No complications.

3. Are there any planned changes?

No

4. Do you wish the project to be continued?

Yes

5. Comments.

None

June 30, 1988

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

STATUS REPORTS ON ACTIVE PROPOSALS

Investigator: Dr. Michael Guerin

Title of Project: ORNL-17 MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

Date Approved: 1987

1. Report progress made in the past year.

   Analyses for ambient nicotine in Knoxville area restaurants and for volatile organic commponents of environmental tobacco smoke in an investigator's home were completed. A paper illustrating some of the work is appended.

2. Report any complications.

   No complications

3. Are there any planned changes:

   No

4. Do you wish the project to be continued?

   Yes

5. Comments.

   None

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Michael Guerin

FROM: Becky Hawkins/Secretary, Committee on Human Studies

RE: Status Reports on Active Proposals

DATE: April 6, 1989

The guidelines for the ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by May 8, 1989. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: ORNL-17 MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

Proposal No. ORNL-17 DATE APPROVED: 1987

MP Guerin
Signature of Principal Investigator

5/2/89
Date Signed

1. Report progress made in the past year.

Field studies of ambient nicotine concentrations in public places were completed and the results published (reference attached). A new agreement has been signed for related work to compare area- and personal breathing zone - sampling for nicotine exposure assessment. New analytical technology has been developed which shows promise for determining nicotine in physiological fluids.

2. Report any complications.

No complications.

3. Are there any planned changes?

No changes are planned for studies of ambient air nicotine exposure. Normal public environments are sampled. No intervention or human subject manipulation is required.

We plan to add a study of the applicability of our new analytical method to the determination of nicotine and cotinine in urine and blood. See comments.

4. Do you wish the project to be continued?

Yes.

5. Comments.

We are proposing to evaluate thermal desorption ion trap mass spectrometry for the rapid determination of nicotine and cotinine in urine and blood as part of our National Cancer Institute Smoking and Health Research Program in FY 1990. Blood will be examined only if if can be acquired from excess sample taken as part of routine physical examinations at ORNL or it is provided from excess sample taken by collaborating researchers addressing other issues using normal healthy adults. Urine and blood will only be used as a matrix to which known quantities of nicotine and cotinine are added. No subject intervention or manipulation is planned.

Environ. Sci. Technol. 1989, 23, 429-435

A Thermal Desorption Method for the Determination of Nicotine in Indoor Environments

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■ Nicotine, the major, unique component of the gas phase of environmental tobacco smoke (ETS), has been employed as a marker for estimating exposure to ETS. A personal monitoring system for the determination of exposure to nicotine has been developed. The system consists of a sampling cartridge packed with 200 mg of Tenax GC and a small, constant-flow, personal sampling pump. After sampling, the cartridges are analyzed by triethylamine-assisted thermal desorption gas chromatography with nitrogen-selective detection. Collection and desorption efficiencies for the cartridges have been determined. The system has been evaluated in controlled-atmosphere chambers, and applied in a variety of work sites, and in 36 restaurants, where measured concentrations of nicotine ranged from 0.5 to 37.2 $\mu g/m^3$.

Introduction

One of the major public health concerns of the 1980s has been indoor air pollution and its effects on the individual. Environmental tobacco smoke (ETS), which is the diluted and aged mixture of sidestream smoke emanating from the smoldering cigarette and mainstream smoke exhaled by the smoker, represents a potentially significant contribution to this pollution. Concentrations of ETS respirable suspended particulates (RSP) have been reported to range from 0 to 700 $\mu g/m^3$ in indoor environments (*1*). A number of procedures have been applied for estimating ETS concentrations based on the measurements of concentrations of particular ETS constituents, such as CO (*2–5*), oxides of nitrogen (NO_x) (*3–5*), and particulate matter (*4–9*). However, these constituents of tobacco smoke are also the products of other combustion processes, an aspect that limits their utility as markers for estimating ETS levels, especially in complex atmospheres such as those existing in indoor environments. Estimates of personal exposure to ETS have been made by measuring carboxyhemoglobin (COHb) (*10, 11*), urinary hydroxyproline (HOP) (*12*), and nicotine and cotinine (a metabolite of nicotine) in the blood, urine, and saliva (*10, 11, 13*).

Several methods have been developed for determining nicotine concentrations at fixed sampling locations in industrial settings. The NIOSH method for nicotine utilizes a resin-filled cartridge (XAD-2) with a personal sampling pump for collection of samples followed by solvent extraction and analysis by gas chromatography (*14*). However, this method's 300 $\mu g/m^3$ limit-of-detection (LOD) makes it unsuitable for measuring ETS because associated concentrations of nicotine are well below this LOD. Another industrial method, also limited by its relatively high LOD (40 $\mu g/m^3$), collects nicotine in a series of water-filled bubblers (*15*).

Williams et al. (*16*) have reported a method using a cold Petri dish as the means for collecting nicotine. Although the reported nicotine concentration range associated with the method was low enough to be applicable for measuring ETS, the method had several deficiencies that would severely limit its value (*17*). Other methods reported in the literature detail the use of untreated glass fiber filters (*4*) or diffusion denuder tubes (*18*) for collection of ambient nicotine.

The development and testing of a number of personal monitoring systems that measure individual exposures to ETS as determined by ambient nicotine concentrations have been reported recently in the literature. Solvent desorption based systems include personal sampling pumps coupled with commercially available XAD-4 cartridges (19–21) and $NaHSO_4$-treated, Teflon-coated glass fiber filters (*22*), and a passive sampling system utilizing the treated filters (*23*). The limitation of using solvent extraction of samples is that only a small fraction of the analyte is actually analyzed. This necessarily raises the theoretical LOD for such methods relative to those such as thermal desorption that use all of the acquired sample. Two thermal desorption based personal monitoring systems for nicotine have been reported, one by Proctor (*24*) that employs an unspecified adsorbent and analysis system and another by Muramatsu et al. (*25, 26*) that utilizes an ammonia purge of the sample cartridge during desorption into a gas chromatograph (GC). In initial laboratory evaluation studies, we found the experimental arrangement used by Muramatsu to be cumbersome and mechanically complex. In addition, we found that repeated exposures of the analytical column to the ammonia gas caused rapid deterioration of the column. Furthermore, the collection cartridge utilizes a packing, the support for which is a very unique diatomaceous earth, that is difficult to obtain in the United States.

This paper discusses the development, evaluation in controlled ETS atmospheres in chambers and offices, and field validation of a thermal desorption based personal monitoring system for nicotine using Tenax-GC as the adsorption material. Tenax is a poly(*p*-2,6-diphenylphenylene oxide) which is porous and stable up to 400 °C (*27*). It has a high affinity for semivolatile organic compounds and can be used repeatedly. It has been used for a number of indoor air characterization studies (*28, 29*), and its performance characteristics are relatively well understood. The nitrogen-selective detector used in the analysis procedure affords improved sensitivity and selectivity over a conventional flame ionization system when assaying complex atmospheres and has been employed similarly by several investigators (*19, 20*). The experimental arrangement used for the field sampling is similar to that employed by other investigators. The analytical system lacks the mechanical complexities of the system developed by Muramatsu.

Methods and Material

Personal Monitoring Systems. Air-sampling cartridges were 16-cm sections of $^1/_4$-in.-o.d. borosilicate glass tubing which were treated with NH_4OH (immersion in 15% NH_4OH overnight, followed by air drying) and then fire polished on both ends and packed with approximately 200 mg of Tenax GC, 35–60 mesh, acquired from Alltech Associates (Deerfield, IL). Before use, the packed cartridges were conditioned at 250 °C by attaching them to a manifold in the oven of a gas chromatograph and passing

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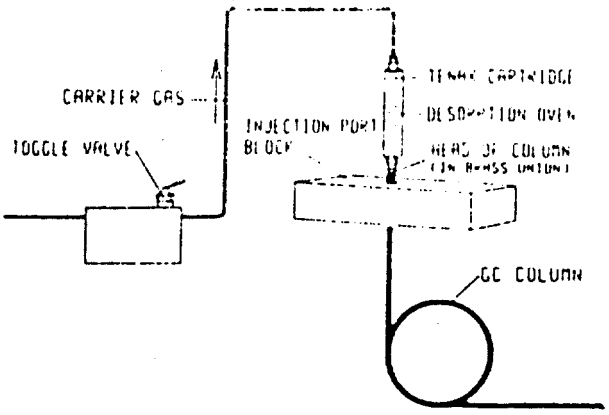

Figure 1. Schematic diagram of analytical system.

a stream of N_2 flowing at 40 mL/min through each cartridge for at least 2 h. After the cartridges had been cooled with continued N_2 flow, both ends were sealed with $^1/_4$-in. plastic caps obtained from Alltech Associates. The cartridges could be reused by first washing them with 2–3 mL of methanol and thermally reconditioning them according to the procedure given above.

Alpha-2 personal sampling pumps, available from Du Pont (Kennett Square, PA), were used for sample collection in most experiments (Du Pont P-4000 pumps were used in a few initial chamber experiments) and were chosen for their light weight (410 g) and low noise level during operation. This latter feature was especially important for unobtrusive performance. For experiments performed in the chamber and work areas, in which occupants were aware of the sampling being conducted, pumps were connected to Tenax cartridges with a section of flexible tubing, and air from the area sampled was drawn through the cartridge. For sampling conducted in restaurants, in which the occupants were unaware of the sample collection, the pumps were worn on belt clips under jackets. A section of Tygon tubing was used to connect the pump to the Tenax cartridge, the latter being clipped to the inside lapel of the jacket so that the inlet end of the cartridge was within 25 cm of the mouth and nose of the individual conducting the sampling. All samples were collected for at least 1 h with the pump operating at a flow rate of 170 mL/min. Flow rates were checked with a bubble meter before and after sample acquisition. Immediately after completion of sampling, Swagelok $^1/_4$-in. stainless steel end caps fitted with Teflon ferrules were placed on each end of the cartridge and tightened, and the cartridge was refrigerated at 3 °C until analysis.

Analytical Method. Nicotine containing solution standards were prepared by diluting redistilled nicotine (98%) obtained from Eastman Kodak (Rochester, NY) in ethyl acetate that contained 0.01% triethylamine (TEA). Internal standards employing quinoline were prepared by diluting quinoline in a solution of ethyl acetate/5% TEA. Fresh nicotine and quinoline standards were prepared every 15 days.

Analyses were performed with a Varian Model 3700 gas chromatograph equipped with a nitrogen/phosphorus detector (GC/NPD) and a 2 m × 2 mm i.d. glass column packed with 10% Carbowax 20M/2% KOH on 80–100 mesh Chromosorb W-AW (obtained from Alltech Associates). Flow rates were He (carrier gas) 40 mL/min, H_2 4.5 mL/min, and air 175 mL/min. Temperature settings were injector and detector 250 °C and column oven initial temperature 70 °C for 8 min, programmed at a rate of 46 °C/min to 175 °C for 4 min. At these settings, nicotine elutes at 13.4 min and quinoline at 14.0 min.

In Figure 1 is portrayed a schematic diagram of the analytical experimental configuration. The system is designed to be mechanically simple and to minimize the opportunity for the nicotine vaporized from the Tenax trap to contact any materials prior to entering the analytical column. The carrier gas is directed through a toggle valve so that it can be interrupted when the Tenax cartridges are being changed. (When the system is not in use, a clean glass tube replaces the cartridge.) The analysis is performed by loosening the fittings at both ends of the desorption oven, inserting the cartridge, tightening the fittings, and resuming the carrier gas flow. Although the desorption oven remains at operating temperature during this operation, the elapsed time for connecting the cartridge is less than 5 s. The desorption begins when the carrier gas is turned on.

Because the manner in which the analyte is introduced into the gas chromatograph affects the peak shape and ultimately the apparent quantitity of analyte present in the aliquot, it was critical that the analyte in the calibration standards be introduced in a manner identical with that of those in the samples. To accomplish this, clean Tenax-filled cartridges were spiked with small aliquots of nicotine standard solutions (on the downstream end to simulate sample loading) by using a conventional 10-μL syringe. The volume of the aliquots ranged from 1.8 to 6 μL, depending on the desired amount of standard. Next, the cartridges were spiked with 5 μL of the ethyl acetate solution containing the quinoline internal standard and the TEA desorption modifier on the upstream end so as to facilitate desorption of the entire cartridge. In order to maintain direct comparability, this was the same quinoline/TEA solution that was added to the ETS samples. In the initial developmental work for the method, multipoint calibrations with nicotine standards were performed daily. For the field sampling, a calibration curve was generated from the desorption of nine sets of duplicate Tenax traps loaded with amounts of nicotine ranging from 1.5 to 700 ng and with 250 ng of quinoline internal standard prior to any sample analysis. The first set of standards was run in one random order and the second set of standards was run in a different random order. Daily standards of 3, 100, and 700 ng of nicotine were analyzed during sample analysis to ensure analytical control. Field blank cartridges were analyzed periodically.

Because the response of the nitrogen/phosphorus detector tended to be nonlinear at higher trap loadings (>1000 ng), data from the analyses were fitted to a second-order polynomial regression. In practice, there was no difference between first- and second-order regressions in the 0–700-ng concentration range. For example, the first- and second-order correlation coefficients (R^2) for one calibration run were both 0.995, and for another, both were 0.997.

Response factors (RF) for all standards were calculated with the formula

$$RF = \left(\frac{\text{area counts nicotine}}{\text{area counts quinoline}}\right) \times \left(\frac{\text{concentration of quinoline}}{\text{concentration of nicotine}}\right) \quad (1)$$

Averages and standard deviations computed from the RF data were used to assess control of the method in day-to-day operation. If results for daily control standards were more than two standard deviations from the average for the calibration, the method was judged to be out of control, thus requiring recalibration. Control was observed

throughout the analysis of the samples from the public areas.

Test Atmospheres. The initial experimental atmospheres for the development of the Tenax method were generated in two stainless steel chambers with volumes of 0.4 and 1.4 m^3 (obtained from Young and Bertke Co. Cincinnati, OH). Sidestream smoke from a 2R1 Kentucky Reference cigarette (procured from the University of Kentucky Tobacco and Health Research Institute, Lexington, KY), smoldering in a laminar flow smoke generation (*30*), was pulled into the smaller chamber at a rate of 30 L/min and diluted with an air flow of 250–1000 L/min, the exact rate depending on the concentration of ETS needed. Concentrations for this chamber ranged from 700 to 3500 $\mu g/m^3$ particulate matter (PM) and from 100 to 500 $\mu g/m^3$ nicotine. Low concentrations of ETS, 50–300 $\mu g/m^3$ PM and 10–70 $\mu g/m^3$ nicotine, were generated by diluting a portion of the atmosphere from the small chamber into that of the large chamber. Concentrations of particulate matter in the chambers were monitored with a TSI-5000 piezoelectric balance (acquired from TSI, St. Paul, MN) and an RAS-1 light-scattering sensor (purchased from GCA Instruments, Bedford, MA), which was modified in our laboratory to enhance its sensitivity. The nicotine and PM concentrations utilized for these experiments are much higher than what would be typically observed in real life situations and were used only to determine the potential utility and the upper analytical limits of the method. After development experiments involving the chamber were concluded, other experiments were conducted in an unoccupied office. ETS was produced by generating sidestream smoke from 1R4F Kentucky Reference cigarettes smoked (one 35-mL puff/min) on an ADL-II machine obtained from Arthur D. Little Co., Cambridge, MA). Mainstream smoke was collected in sealed Tedlar bags (acquired from SKC Inc., Eightly Four, PA), and ETS concentrations were varied by adjusting the smoking rate from 1 min of smoking (2-s puff, 58-s smolder) per min of elapsed time up to continuous cigarette smoking. PM levels were monitored with a TSI-5000 piezoelectric balance.

Additional laboratory evaluations of the method's performance were conducted in an 18-m^3 environmental chamber (*31*) used for ETS studies and located at the R. J. Reynolds Tobacco Company's facilities in Winston-Salem, NC. PM concentrations in that chamber were monitored with a TSI-5000 piezoelectric balance. Initial field evaluations were conducted in work areas, offices, common areas, and dining areas at Oak Ridge National Laboratory.

Sampling Site Selection. Field sampling was conducted in establishments that were both listed under the "Restaurant" heading in the Yellow Pages of the Knoxville, TN, telephone directory and located in the Knoxville, TN, Standard Metropolitan Statistical Area (SMSA) (Knox, Blount, and Anderson counties). Restaurant selection was conducted by assigning each restaurant a number and then choosing 43 out of the 419 restaurants with a random number generator. Three of these restaurants were eliminated because they had gone out of business, three because they were carry out only, and one because the personal safety of the sampling team was called into question. The remaining 36 were sampled, and for each sample, information was recorded regarding the number of smokers, the number of cigarettes, cigars, and pipes observed to have been smoked, the distance to the closest observed smoker, the type of meal served (lunch or dinner), crowd density, and restaurant volume. All of the information was recorded on a sampling data sheet during the time of sampling. A unique sample number was assigned to each cartridge immediately following sampling. No attempt was made to assess air exchange within the facility, as this would have compromised the unobtrusive nature of the sampling. Also, no determination of the number of smokers smoking at any one time or smoker turnover was made. In addition to the samples acquired in restaurants, two samples were acquired on a Saturday afternoon at each of three food courts in shopping malls.

Table I. Nicotine and Particulate Matter (PM) Concentrations Measured in 0.4- and 1.4-m^3 Stainless Steel Chambers[a]

	nicotine, $\mu g/m^3$	PM, $\mu g/m^3$	nicotine/PM ratio
	34	80	0.425
	42	83	0.506
	43	79	0.544
	44	74	0.595
mean ±1 SD[b]	40.8 ± 4.6	79.0 ± 3.7	0.518 ± 0.072
	282	757	0.373
	263	667	0.394
	302	684	0.442
	291	659	0.442
	238	708	0.336
	224	684	0.328
	271	643	0.421
mean ±1 SD[b]	267 ± 28	686 ± 36	0.391 ± 0.047

[a] Air changes per hour (ACH) ranged from 21 to 150. [b] SD, standard deviation.

Results and Discussion

Results of initial experiments with Tenax cartridges, in which the responses to standard quantities of nicotine spiked on to the cartridges and subsequently desorbed were compared with those of the same sized aliquot directly injected on to the head of the GC column, showed evidence of incomplete desorption of nicotine, with up to 10% of the nicotine remaining on the cartridge. In order to enhance nicotine desorption, an internal standard solution was prepared that included 5% TEA. It has been found that addition of a strongly basic material such as TEA (*19*) or NH_4OH (*32*) to nicotine standards prevents adsorption, by the glass of the container, of nicotine from solution. The base probably functions by displacing nicotine or other weaker bases from the adsorptive sites. Internal standard spikes thus contained about 200 μg of TEA, which, as a stronger base, displaced nicotine from acidic sites within the sampling cartridge or analysis train.

Experiments conducted in the 0.4- and 1.4-m^3 chambers were performed to determine the functional capabilities of the method and the nicotine collection efficiency. Table I gives the results from sampling of both dilute and concentrated simulated ETS environments in the large and small chambers, respectively. The ratios of nicotine to particulate matter in these experiments are substantially higher than what has been reported in typical indoor environments (*33*). This discrepancy was judged of little consequence since investigation of nicotine levels was the sole focus of the study. However, the consistency of the ratios is about ±15% or less, which was judged to be indicative of both a constant atmosphere in the chamber and consistent nicotine and particulate mass concentration determinations.

Experiments to determine sample volumes at which nicotine breakthrough became significant were conducted by placing two Tenax cartridges in series and sampling from simulated ETS environments in the chambers. Re-

Table II. Concentrations of Nicotine and Particulate Matter (PM) Measured in an Unoccupied Office

trial no.	PM, $\mu g/m^3$	nicotine, $\mu g/m^3$	trial no.	PM, $\mu g/m^3$	nicotine, $\mu g/m^3$
1	14.6	1.8	6	59.6	8.2
2	23.2	1.9	7	113.0	21.7
3	28.2	2.4	8	115.4	27.3
4	15.2	3.7	9	257.0	48.3
5	58.6	4.8	10	248.8	49.0

Table III. Results from Determination of Nicotine by the Tenax Method in a Minimal Air Exchange Controlled Atmosphere Chamber

run no.	PM, $\mu g/m^3$	nicotine,* $\mu g/m^3$	run no.	PM, $\mu g/m^3$	nicotine,* $\mu g/m^3$
1	55	2.5	4	62	4.1
2	14	1.8	5	16	2.1
3	103	5.0	6	128	5.5

*N = 3 determinations.

sults indicated not more than 1% breakthrough for sample volumes ranging from 20 to 45 L and nicotine concentrations ranging from 70 to 250 $\mu g/m^3$. At lower sample volumes, breakthrough percentages are expected to be correspondingly lower.

In Table II are listed the results from sampling of ETS in the unoccupied office. This range of nicotine and PM levels more closely approximated that which would be expected from sampling in public places. Proportionality between nicotine and particulate levels was particularly good in this experiment, with the correlation coefficient of 0.976 for a first-order regression analysis of these two parameters.

The limits of detection and quantitation were determined according to published guidelines (*34*). These are comparable to 3 and 10 times the standard deviation above the mean value of a series of field blanks, respectively. Signal response of the blanks (in microvolt seconds) was related to a series of calibration standards run within the lower quantitation region. According to these criteria, under the sampling conditions described above, the limit of detection was equivalent to 0.07 $\mu g/m^3$ nicotine, and the limit of quantitation was 0.17 $\mu g/m^3$. This calculated level is in good agreement with experiences with sampling actual low-concentration ETS atmospheres in an office environment. These experiments indicated that within the range of 0.2–0.3 $\mu g/m^3$, variation among multiple samples acquired near the same point in space became unacceptably large. Presumably, the effective limit of detection could be lowered by simply increasing the sampling duration.

In Table III are listed the results from sampling conducted in an 18-m^3 chamber at R. J. Reynolds. The purpose of these experiments was to determine the performance of the method in a chamber whose atmosphere had been well characterized in a number of studies (*19*, *31*), especially at low nicotine concentrations, and to compare nicotine with ETS PM levels in a controlled environment that had been contaminated with ETS only. The nicotine levels sampled for this experiment are near the mean of the level determined in the field study (see below) but represent only a fraction of the range expected to be encountered during field sampling in general. For this and all the experiments where PM concentration data were available, mean ratios of nicotine to PM were calculated. The ratios obtained from experiments involving the 1.4- and 0.4-m^3 chambers were 0.52 ± 0.07 and 0.39 ± 0.05, respectively. The ratio for experiments performed in the unoccupied office was 0.16 ± 0.06, and for experiments conducted in the 18-m^3 chamber, 0.08 ± 0.04. The considerable differences among the ratios are expected in view of the differences in ETS levels, air handing methods, and air exchange rates and the theory that as ETS ages, nicotine tends to be adsorbed by the various surfaces present (*18*, *26*). For the two smaller chambers, air exchange rates ranged from 21 to 150 ACH, allowing little opportunity for nicotine adsorption by the chamber walls. The office, with an air exchange of 5.4 ACH and nonrecirculated ventilation, exhibited lower nicotine/PM ratios, and the 18-m^3 chamber, with an air exchange rate of 0.05 ACH (*35*) and complete recirculation in a static system, showed the lowest levels of nicotine relative to the particulate levels. These data appear to support the above-mentioned theory.

Table IV. Nicotine Concentrations Measured at Selected Locations within Oak Ridge National Laboratory

location	ambient nicotine level, $\mu g/m^3$	location	ambient nicotine level, $\mu g/m^3$
offices	4.2 ± 0.1*	common area	30.0 ± 0.9
	4.0 ± 3.5*		60.3 ± 2.1
	4.5 ± 0.5*		53.1 ± 2.8*
	6.7 ± 0.9		23.2 ± 2.9
	0.7 ± 1.0		39.7 ± 0.1
	1.1 ± 1.5		12.6 ± 1.2
	0.6 ± 0.8	work area	3.8 ± 0.1
	0.6 ± 0.8		2.2 ± 0.9
	0.6 ± 0.9		1.0 ± 0.4
	0.3 ± 0.4	common area	0.9 ± 1.3
dining area	4.4 ± 0.8		1.7 ± 0.8
	2.3†		0.8 ± 1.1
work area	2.0 ± 0.3		

*N = 3 determinations. †N = 1. All others, N = 2 determinations.

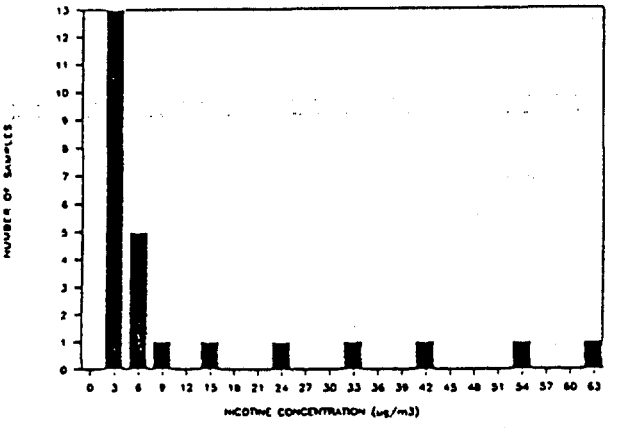

Figure 2. Distribution of nicotine levels for work sites at ORNL. Note that nicotine concentrations listed are the maximums for the individual cells

Listed in Table IV are the results from samples collected at Oak Ridge National Laboratory facilities. The arithmetic mean and standard deviation of nicotine concentrations for all sample sites is 10.5 ± 17.2 $\mu g/m^3$. However, the relatively high concentrations measured in the first common area (36.5 ± 18.1 $\mu g/m^3$) influence the average disproportionately. As can be seen in Figure 2, the data appear to be distributed in a log normal pattern; thus, the geometric mean of 3.2 $\mu g/m^3$ (with 95% confidence boundaries of 1.8 and 6.0 $\mu g/m^3$) may be more appropriate for this data set. For the lower nicotine level environments, there is considerable variation (±100%) within duplicate samples taken near the same point in space. For the environments containing higher nicotine levels, the coefficient of variation within duplicate samples was usually about ±10%.

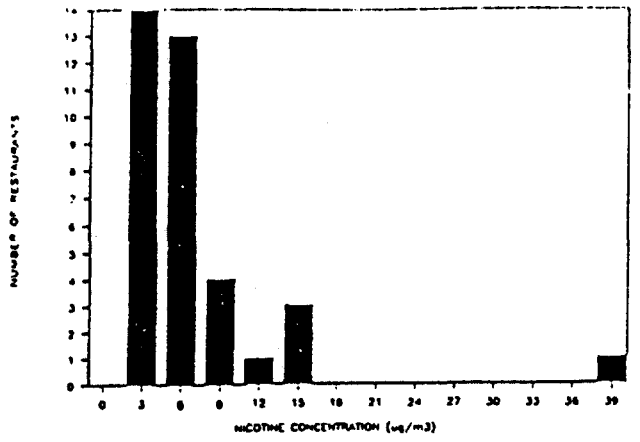

Figure 3. Distribution of nicotine resultsin selected Knoxville, TN, area restaurants. Note that nicotine concentratons listed are the maximums for the individual cells.

Results from the field determinations of nicotine concentrations in restaurants are shown in Table V. Nicotine concentrations found in the restaurants ranged from 0.5 to 37.2 $\mu g/m^3$ with an arithmetic mean of 5.4 ± 6.4 $\mu g/m^3$. As in the treatment of the data from the in-house sampling, a plot of the distribution of the concentration data indicates that it fits a log normal, rather than Gaussian, pattern (Figure 3). The geometric mean of 3.5 $\mu g/m^3$, with 95% confidence boundaries on the median of distribution of 2.5 and 4.8 $\mu g/m^3$, is somewhat lower than the arithmetic mean but is still comparable to data results cited by the researchers listed below.

Muramatsu et al. (25) reported a range of 7.1–27.8 $\mu g/m^3$ nicotine with an average of 14.8 $\mu g/m^3$ for eight samples taken in five restaurants. Hinds and First (36) have reported an average of 5.2 $\mu g/m^3$ nicotine for four samples from restaurants. Oldaker et al. (21) reported a range of 0–24 $\mu g/m^3$ nicotine with an average of 5 $\mu g/m^3$ for 170 samples acquired in restaurants. For air samples taken in offices, Hammond et al. (22) have reported 3–48 $\mu g/m^3$ nicotine, while Muramatsu et al. (25) have reported 9–32 and 6–20 $\mu g/m^3$ nicotine (26). For 156 office samples, Oldaker et al. (21) reported an average of 5 $\mu g/m^3$ nicotine with a range of 0–70 $\mu g/m^3$. Nicotine concentrations in public common areas such as lobbies and waiting rooms were reported to be 2–36 $\mu g/m^3$ by Muramatsu et al. (25) and 1–3 $\mu g/m^3$ by Hinds and First (36). For samples taken in the smoking sections of airplanes, Muramatsu et al. (26) have reported 14 and 6–29 $\mu g/m^3$ with an average of 15 $\mu g/m^3$ (25). Oldaker and Conrad (20) have reported 0–112 $\mu g/m^3$ nicotine, with an average of 9 $\mu g/m^3$ in airplane smoking sections, and 0–40 $\mu g/m^3$ nicotine, with an average of 6 $\mu g/m^3$ in nonsmoking sections.

Major factors likely to affect nicotine concentrations in a public location include the number of cigarettes smoked and the time required for smoking, the volume of the room, the proximity of smokers to the sample location, and the air exchange rate. Under the conditions of the field sampling validation for this study, not all of these parameters could be easily determined, nor were they necessary to assess the performance of the experimental personal monitor in a realistic situation. However, to assess the impact of the easily determined factors, the relationship between those factors and ambient nicotine concentrations were determined. The Pearson's correlation coefficients (r) for first-order regressions of nicotine concentration to number of cigarettes, number of smokers, restaurant volume, and distance to the closest smoker were computed to be 0.669, 0.783, 0.049, and –0.155, respectively. The significance levels (p) (an indicator of the probability of

Table V. Nicotine Levels in Restaurants

sample no.	smokers obsd, no.	cigarettes, no.	cigars or pipes, no.	est restaurant vol, m^3	closest smoker, ft	nicotine concn. $\mu g/m^3$	sample no.	smokers obsd, no.	cigarettes, no.	cigars or pipes, no.	est restaurant vol, m^3	closest smoker, ft	nicotine concn. $\mu g/m^3$
34	0	0		179		0.5	12	9	9		1785	7	4.2
16	0	0		595		0.5	15	4	4		198	5	4.3
24	1	1		198	6	0.7	35	10	11		623	4	4.5
21	1	1		41	9	0.8	32	5	7		397	5	4.8
10	0	0		638		1.1	33	6	10		1063	14	4.8
20	7	9		227	5	1.4	23	5	8	1	238	10	4.9
31	2	2		272	12	1.5	7	8	11		2380	5	5.6
14	-	2		283	20	1.5	1	15	18	1	744	2	5.7
25	1	1		136	8	1.6	6	6	8		340	2	5.9
18	2	2		1204	15	2.3	4	4	3		179	7	7.3
19	0	0		453		2.3	5	4	3		179	7	7.4
27	2	2		317	10	2.4	17	19	35	1	680	4	7.8
29	6	8		1700	10	2.4	28	10	15		204	5	8.0
9	8	9		510	5	2.5	13	9	10		177	6	9.3
2	7	8		113	8	3.3	30	19	25		793	4	12.1
26	6	7		213	2	3.3	3	33	43		1666	5	12.6
22	4	3	1	170	3	3.5	8	14	18		680	5	13.5
11	12	14		204	5	4.1	36		30		272	8	37.2

Table VI. Nicotine Levels in Food Courts

sample	smokers obsd, no.	cigarettes, no.	cigars or pipes, no.	closest smoker, ft	nicotine concn, $\mu g/m^3$
37	6	6		15	1.6
38	16	16		4	1.6
39	8	11		4	2.1
40	7	7	1	7	2.5
42	17	19		15	3.0
41	34	34		6	3.1

correlation between the nicotine concentration and the above-mentioned factors) for the regressions are 0.0001, 0.0001, 0.776, and 0.396, respectively. A relationship is thus indicated between nicotine concentration and both the number of cigarettes and number of smokers. If sample 36 is eliminated from the regression analysis for nearest smoker, then $p = 0.03$, indicating a correlation between nicotine concentration and this parameter. Attempts to increase the degree of correlation by normalizing for various combinations of these factors were unsuccessful. No data were acquired regarding other factors that could have some impact on the nicotine concentration, such as the history of the number of cigarettes smoked prior to sampling, and the direction of air flow in the restaurants.

In Table VI are listed the data from samples acquired in the food courts of the shopping malls. The range of nicotine concentrations from the mall food court samples was 1.6–3.1 $\mu g/m^3$ with an arithmetic mean and standard deviation of 2.3 ± 0.7 $\mu g/m^3$. Although use of the geometric mean could not be justified for such a small sample set, it was calculated for comparison purposes and is the same as the arithmetic value. The average nicotine concentration for these samples is lower than that from the restaurant data (notwithstanding the large number of cigarettes observed to have been smoked) and is probably attributabe to the much greater volumes of the food courts, which begin to approximate open-air restaurants.

Conclusions

A procedure and experimental arrangement for the determination of personal exposure to concentrations of nicotine in indoor environments has been developed that has a low detection limit and is unobtrusive in its use. Developmental studies have again pointed to the need for the use of a basic compound for sample modification or desorption enhancement when trace quantities of nicotine are being processed or analyzed. The Tenax method has been applied to the determination of nicotine concentrations in a number of restaurants; results are comparable to those obtained by other researchers utilizing different methods for sampling in restaurants and other public places.

Acknowledgments

We thank J. H. Moneyhun for his assistance in generation of simulated ETS atmospheres in the stainless steel chambers and in sample acquisition. We also thank C. D. Varnadore for his assistance in sample acquisition.

Registry No. TEA, 121-44-8; Tenax GC, 24938-68-9; nicotine, 54-11-5.

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Aerobic and Anaerobic Microbial Dissolution of Toxic Metals from Coal Wastes: Mechanism of Action

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■ Microbial dissolution of toxic metals from two types of coal-cleaning wastes, one high in pyrite and trace metals and low in organic carbon (fines fraction) and a second lower in trace metals and higher in organic carbon (filter cake), was studied. Under aerobic conditions, native autotrophic bacteria solubilized varying amounts of As, Cr, Cu, Mn, Ni, Pb, and Zn from the filter cake and fines fraction. Dissolution of the above metals was increased by severalfold when the inorganic nutrients N and P were supplemented. Under anaerobic conditions, concentrations of Fe, Cr, and Mn increased due to native anaerobic bacterial activity from filter cake amended with carbon and nitrogen. Concentrations of soluble Ni and Zn in filter cake decreased, probably due to sulfate reduction and formation of insoluble metal sulfides. Selective chemical extractions of coal wastes indicate that most trace metals were associated with pyrite, ferric oxides, and a soluble phase, possibly ferric sulfate. The predominant mechanism of dissolution of metals from coal wastes under aerobic conditions is due to bacterial oxidation of pyrite; under anaerobic conditions it is due to bacterial reduction of iron and manganese oxides and the release of trace metals coprecipitated with the oxides.

Introduction

Over 3 billion tons of coal-cleaning residues have accumulated in the United States and the current levels of production exceed 100 million tons per year. Nearly one-third of the mined coal is discarded after physical cleaning. This refuse varies in size and generally contains waste coal, slate, carbonaceous and pyritic shales, clay, and other impurities associated with a coal seam (*1*). Currently, most coal-preparation plants dewater the fine refuse and dispose of it, along with coarse refuse, in landfills or disposal ponds. The types of contaminants released from the disposal areas include organic compounds, metal ions, and acidity primarily due to chemical and microbiological action.

Bacterial oxidation of pyrite and metal sulfide minerals by *Thiobacillus ferrooxidans* and *Thiobacillus thiooxidans* has been extensively studied (*2*, *3*). Although a variety of other types of microorganisms have been found in coal waste (*4*-*7*), there is limited information on their effects on dissolution of metals. In addition to autotrophic microbial activity, an increase in heterotrophic microbial activity due to biodegradation of organic compounds in the residue (*8*) also can have an appreciable effect on the dissolution, mobilization, and immobilization of toxic metals from the residues. However, the extent and mechanisms of metal dissolution from coal refuse under the oxidizing and reducing conditions commonly encountered in the field (*9*) are incompletely understood.

In this study, two samples of coal-cleaning residue, one high in trace metals and relatively low in organic carbon (fines fraction) and the second low in trace metals and relatively high in organic carbon (filter cake) were used to investigate the extent and mechanism of microbial dissolution of toxic metals by the native microflora in the residue under aerobic and anaerobic conditions.

Materials and Methods

Source of Samples. Coal-cleaning residues (fines fraction and filter cake) were collected from active circuits of the coal-washing plant of the Bradford Coal Co., Bigler, Clearfield County, Pa, in July 1983. This plant processes a mixture of bituminous coals from central and northwestern Pennsylvania. The samples were collected in clean 5-gal polyethylene containers, sealed, and shipped to the laboratory in a cooler with ice. Upon receipt at the laboratory, the samples were immediately analyzed for microbiological and chemical characteristics. Unused portions of the samples were stored in air-tight containers in a refrigerator.

Microbiological Analysis. The total number of bacteria in the fines fraction and filter cake were enumerated by Acridine Orange direct counts (AODC) (*10*, *11*). Total viable aerobic and anaerobic bacteria as colony-forming units (CFU) were determined by using Trypticase soy agar (Difco) and 50% diluted thioglycolate medium (Difco), respectively (*12*). Sulfur- and iron-oxidizing bacteria were enumerated by the most probable number (MPN) technique. Iron-oxidizing bacteria were determined by using 9K medium (*13*). Sulfur-oxidizing bacteria were determined by using thiosulfate medium containing the following: $(NH_4)_2SO_4$, 1.3 g; K_2HPO_4, 0.28 g; $MgSO_4 \cdot 7H_2O$, 0.25 g; $CaCl_2 \cdot 2H_2O$, 0.07 g; and 900 mL of distilled water.

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical Sciences Division

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Michael Guerin

FROM: Becky Hawkins/Secretary, Committee on Human Studies

RE: Status Reports on Active Proposals

DATE: May 2, 1990

The guidelines for the ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by May 17. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: ORNL-17 MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

Proposal No. ORNL-17 DATE APPROVED: 1987

R Guerin
Signature of Principal Investigator

5/13/90
Date Signed

1. Report progress made in the past year.

   Area sampling has been compared with personal sampling for estimating exposure to environmental tobacco smoke (ETS). Samples have been taken using both methods in various public and business environments. Analytical methods have been compared by sampling an office-like environment at ORNL experimentally contaminated with ETS.

2. Report any complications.

   There have been no complications.

3. Are there any planned changes?

None

4. Do you wish the project to be continued?

Yes

5. Comments.

None

June 28, 1990
ORAU/ORNL COMMITTEE ON HUMAN STUDIES

STATUS REPORTS ON ACTIVE PROPOSALS

Investigator: Dr. Michael Guerin

Title of Project: ORNL-17 MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

Date Approved: 1987

1. Report progress made in the past year.

   Area sampling has been compared with personal sampling for estimating exposure to environmental tobacco smoke (ETS). Samples have been taken using both methods in various public and business environments. Analytical methods have been compared by sampling an office-like environment at ORNL experimentally contaminated with ETS.

2. Report any complications.

   There have been no complications.

3. Are there any planned changes:

   None.

4. Do you wish the project to be continued?

   Yes

5. Comments.

   None

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical
Sciences
Division

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Michael Guerin

FROM: Karl Hubner/Chairman, Committee on Human Studies KH

RE: Committee Action on Active Proposals

DATE: June 28, 1990

Your project number ORNL-17 "MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES" was reviewed and approved at our last meeting on June 28, 1990.

Progress reports of all active proposals will again be reviewed at our next meeting to be held in the spring of 1991.

bh

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117
Medical Sciences Division

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Michael Guerin

FROM: Becky Hawkins/Secretary, Committee on Human Studies

RE: Status Reports on Active Proposals

DATE: April 22, 1991

The guidelines for the ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by May 17. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: ORNL-17 MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

Proposal No. ORNL-17 DATE APPROVED: 1987

M. Guerin
Signature of Principal Investigator

5/15/91
Date Signed

1. Report progress made in the past year.

Airborne nicotine concentrations in restaurants and other public access environments were determined and correlated with observed smoking patterns. Stationary area-samplers were compared with personal breathing zone samplers. Urine and saliva samples were provided by a smoker associated with the program to test a new method for determining nicotine and metabolites in physiological media.

2. Report any complications.

None

1048347

3. **Are there any planned changes?**

None

4. **Do you wish the project to be continued?**

Yes. Continuing related work is expected to be funded by the National Cancer Institute and the Center for Indoor Air Research.

5. **Comments.**

All samples taken under normal prevailing conditions. No manipulation of environments or subjects is carried out in this Program.

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831 0117
Medical Sciences Division

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Guerin

FROM: Dr. Karl Hubner/Chairman, Committee on Human Studies

RE: COMMITTEE ACTION ON ACTIVE PROPOSALS

DATE: September 7, 1991

Your project number ORNL-20 "Measurement of Environmental Tobacco Smoke Constituents in Occupied Spaces" was reviewed and approved at our last meeting on June 6, 1991. The committee has no objection to the continuation of this project.

Progress reports of all active proposals will again be reviewed at our next meeting to be held in the spring of 1992.

bh

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117
Medical Sciences Division

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Michael Guerin

FROM: Marta V. Rivera/Secretary, Committee on Human Studies

RE: Status Reports on Active Proposals

DATE: May 12, 1992

The guidelines for the ORAU/ORNL Committee on Human Studies require that all principal investigators of ongoing proposals present a progress report to the Committee on the status of their proposals each year. Each proposal must be reviewed by the Committee yearly for research projects to continue. Please answer the questions below and add any other information you feel pertinent and return by May 26. (If additional space is needed, please use the back of this form or attach extra sheets.)

Title of Project: MEASUREMENT OF ENVIRONMENTAL TOBACCO SMOKE CONSTITUENTS IN OCCUPIED SPACES

Proposal No. ORNL-17 DATE APPROVED: 1987

M C Guerin
Signature of Principal Investigator

7/29/92
Date Signed

1. Report progress made in the past year.

Experimental work in this period was limited to optimizing instrument operating parameters for the gas chromatographic analysis of environmental tobacco smoke and for the mass spectrometric determination of nicotine and cotinine. Field studies of exposure were postponed pending sponsoring agencies review of previously generated data.

2. Report any complications.

There have been no complications.

1048350

3. Are there any planned changes?

Year three of the renewal proposal being considered by the National Cancer Institute includes soliciting volunteers who work in areas contaminated with environmental tobacco smoke to wear breathing zone air samplers and provide urine samples. This is to allow comparison between exposure assessed by air sampling with that assessed by nicotine/cotinine measures. Volunteers will go about their normal activities.

4. Do you wish the project to be continued?

Yes. The National Cancer Institute has expressed interest in continuing work on nicotine exposure.

5. Comments.

Task 2 of the National Cancer Institute proposal is appended.

Clarifying information provided earlier (memo of 11/14/89, appended) remains correct.

TECHNICAL PROPOSAL

ENVIRONMENTAL CARCINOGEN MEASUREMENT

Current Interagency Agreement

Collection, Separation, and Elucidation of
The Components of Cigarette Smoke

DOE (ERDA/AEC) 0485-0485-A1
NIH (NCI) Y01-CP-90508

New Agreement Designation

Collection and Evaluation of Environmental Carcinogenesis
Including Combustion and Smoking Relation Exposures

NIH (NCI) Y01-CP-20512-13
DOE 0485-F053-A1

M.R. Guerin, Program Director
M.V. Buchanan, Principal Investigator

Analytical Chemistry Division
Oak Ridge National Laboratory*
P.O. Box 2008
Oak Ridge, Tennessee 37831-6120

June 1, 1992

Program Term: October 1, 1992 to September 30, 1995

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*Operated by Martin Marietta Energy Systems, Inc., under Contract No. DE-AC05-84OR21400 with the U.S. Department of Energy.

TABLE OF CONTENTS

TASK 2

RAPID DETERMINATION OF MARKERS OF CHEMICAL EXPOSURE

OBJECTIVE

The objective of this work is to develop a rapid, cost-effective method for the measurement of exposure-related chemicals in physiological media. The approach is based on highly promising results of work conducted in the previous contract period that addressed the potential utility of Direct Sampling Ion Trap Mass Spectrometry for such applications. Nicotine and cotinine in urine as they relate to environmental tobacco smoke exposure will receive primary attention. The simultaneous measurement of other nicotine metabolites and of creatinine will also be considered. The general utility of the method will be surveyed by considering blood and saliva analysis for nicotine and cotinine and by considering its utility for measuring urinary and exhaled volatile organic chemicals.

APPROACH

We propose to develop a rapid, cost effect method for the measurement of exposure-related chemicals in physiological media, building upon our progress to date on the applicability of ITMS for the rapid analysis of trace components in urine and other physiological fluids. The measurement of nicotine and cotinine in physiological fluids, which is widely used as a means of assessing human exposure to environmental tobacco smoke [14,15], will be our starting point. Several analytical methods have been developed for the determination of nicotine and cotinine in physiological matrices. Typically, an extraction procedure is required to isolate the analyte from the matrix and to preconcentrate the sample prior to analysis. Analysis of the extracted samples is then performed by gas chromatographic separation and specific detection with a nitrogen detector [16,17] or a mass spectrometer [18,19]. Other analytical methods that have been used successfully include liquid chromatography [20,21] and radioimmunoassay [22,23]. The major limitations of these methods are that they are labor intensive and/or time consuming and therefore have reduced sample throughput and/or and considerable expense for each analysis.

As an alternative approach, direct sampling ion trap mass spectrometry will be evaluated for the rapid and quantitative determination of nicotine and its metabolites in urine. Using a combination of chemical ionization and tandem mass spectrometry techniques, the ITMS can often selectively detect target compounds in a complex mixture without the need for chromatographic separation and with little or no sample cleanup steps. Eliminating these time-consuming procedures would translate into the ability to analyze more samples in a more cost effective manner. Further, it opens the possibility of obtaining time-resolved exposure data. Previous studies using direct sampling ITMS have demonstrated the ability to detect nicotine and cotinine at levels of 0.010 μg/mL in 1 uL of untreated urine in less than three minutes total analysis time.

As a first step in the proposed work, this direct sampling ITMS technique will be optimized to establish the limit of detection for nicotine and cotinine in urine. Desorption conditions (i.e., purge flow, quantity injected, and temperature) and different sorbent materials will be evaluated to maximize the desorption efficiency of the analyte and to minimize contamination from the sample

matrix. In the preliminary studies, only one microliter of raw urine was analyzed. It is possible that the quantity of urine analyzed by thermal desorption ITMS could be increased to tens of microliters to allow lower detection limits to be achieved without interference from the sample matrix.

If it is not possible to inject more sample directly into the ITMS to lower the limits of detection into the range of low level passive smoking (< 5 ng/mL) [24], rapid sample isolation steps based on solid phase filtration will be evaluated. This approach has been recently demonstrated in our laboratory to allow larger sample volumes to be processed and to lower the achievable limits of detection. The solid phase filters are small fiberglass filter disks modified with different types of solid sorbents (Toxi-Labs, Irvine, CA). Preliminary work will focus on sample filtration followed by direct

and/or cotinine conjugates into the free base may occur during the thermal desorption process. Desorption characteristics of these compounds will be investigated to ascertain to what extent this degradation is occurring.

It is likely that some nicotine metabolites and conjugates will be sufficiently polar (and/or thermally unstable) to make them unsuitable for analysis by thermal desorption techniques. In these cases alternative sample introduction techniques such as electrospray will be evaluated for direct introduction of these compounds from solution into the ITMS. In this technique [25,26] solutions are introduced directly into the mass spectrometer through a needle which is held at a potential of several hundred or thousand of volts relative to ground. Under these conditions, the analyte compounds are ionized directly from solution and detected by the mass spectrometer. Because polar metabolites are excellent candidates for efficient ionization by electrospray techniques, this approach will be investigated for the direct detection of these compounds in urine. Solid phase extraction techniques will also be investigated for use with electrospray ionization if clean-up steps are required, especially in the case of analysis of blood.

In the third year of this study, a pilot study will be conducted to determine whether detectable airborne concentrations of nicotine can be detected by the DSMS method in urine. Air samples will be collected from a variety of establishments (i.e., restaurants, bars, and others) in which smoking is permitted to establish airborne levels of nicotine, for example. Physiological samples from volunteers working in these establishments will be collected for multicomponent analysis (nicotine, cotinine, creatinine, and others) by DSMS. Measurement of actual dose by analysis of physiological fluids should provide a much better indication of exposure and a better estimate of risk than currently used personal air monitoring methods. The DS ITMS analysis should offer substantial improvement over current analytical methodologies for the detection of compounds in urine with respect to speed and cost effectiveness. Because the technique is so rapid and requires small sample sizes, it also has the potential of allowing studies of time-resolved exposure. The developed technologies would have a wide range of potential applications in addition to monitoring exposure to environmental tobacco smoke. Other important chemical markers of exposure, for example, metabolites of vinyl chloride indicative of exposure to plastics could be investigated using the same TD ITMS methodology. As part of this work a literature survey will be conducted to identify other physiological metabolites that are markers of chemical dosimetry and are possible candidates for study by direct sampling ITMS techniques. Markers of ETS exposure such as butyronitile and 3-vinylpyridine which may better track gas phase carcinogens will be especially sought.

METHODS

Standards: Samples for TD ITMS analysis will be prepared using standard reference chemicals spiked into reconstituted freeze-dried urine. Urinary metabolite lyophilizate from human male urine will be obtained from Sigma Chemical Company, St. Louis, MO. Nicotine and cotinine standards are available from Aldrich, Milwaukee, WI. Standards of other nicotine metabolites, such as cotinine-N-oxide and trans-3-hydroxycotinine, will either be obtained commercially or synthesized according to standard literature methods. Deuterated reference standards of nicotine and cotinine for use as internal standards will be obtained from Sigma.

Thermal desorption: Sample introduction will be performed using a direct thermal desorption/capillary restrictor interface. Rapid vaporization by flash thermal desorption can be achieved for samples trapped on sorbent tubes packed with an appropriate resin or by direct injection of liquid samples onto glass wool. The thermal desorption interface to be used in these experiments was described in detail in Task 1 of this proposal.

ITMS: A Finnigan MAT Ion Trap Mass Spectrometry (ITMS) will be used as a rapid, selective, and sensitive detector for the determination of chemical markers of exposure in physiological fluids. This instrument was described in detail in Task 1 of this proposal. Compound identification and specificity will be achieved through a combination of selective CI reactions and CID tandem mass spectrometry. Isobutane CI will be used to selectively protonate the nitrogen-containing target analytes, forming $(M + H)^+$, without interference from less basic urinary constituents. Collision induced dissociation will be used to generate characteristic fragment ions which are used to identify the analytes of interest. Quantification will be achieved by integrating the ion current for the characteristic ions from the analyte and an internal standard, deuterated cotinine, and comparing with acalibration curve. Quality assurance parameters will be established and validated, including linearity of calibration, reproducibility, and limits of detection using spiked urine samples.

Electrospray Ionization: For non-volatile metabolites and conjugates of nicotine, electrospray ionization will be evaluated for direct analysis of physiological samples. A Vestec electrospray ionization source interfaced to the ITMS will be used in these experiments.

Sample Isolation Steps: Filter disks imbedded with various sorbents will be evaluated for effective isolation of the target analyte. These filter disks will be obtained from Toxi-Lab (Irvine, CA). It is possible that these disks can be directly desorbed into the ITMS for analysis, especially with relatively simple matrices, such as urine and saliva. For more complex matrices, such as blood, or for more polar analytes which do not thermally desorb, the isolated material may be eluted with a small amount of solvent prior to analysis.

Detection of Airborne Nicotine Exposure: Personal air sampling pumps (Dupont Alpha 2) will be used to introduce ambient nicotine onto triple sorbent traps [27] containing Tenax GC, Ca, and Ambersorb XE-340. The traps will be thermally desorbed and analyzed by either GC/MS or DSITMS using methods described in Tasks 1 and 2.

SCHEDULE

Subtasks Completed	Project Month
Optimize Limit of Detection for Nicotine/Cotinine in Standards	2
Develop Methods for Multicomponent Analysis	4
Evaluate Direct Thermal Desorption of Urine for Detection of Nicotine/Cotinine	6
Develop Rapid Isolation Methods for Nicotine/ Cotinine in Urine and Other Matrices	12
Develop methods for detection of nicotine conjugates/metabolites	24
Correlation of nicotine conjugates/metabolites as indicators of dosimetry	36

July 29, 1992

Marta V. Rivera, Secretary, Committee on Human Studies

Proposal Status Report

This is to request continuation of our Project ORNL-17 entitled "Measurement of Environmental Tobacco Smoke in Occupied Spaces" originally approved in 1987.

I apologize for this very late submission. We only recently learned that the National Cancer Institute is interested in re-starting this work.

M. R. Guerin, 4500S, MS-6120 (4-4862)

MRG:pmt

cc: M. V. Buchanan

MARTIN MARIETTA ENERGY SYSTEMS, INC.

November 14, 1989

Seaton Garrett, Human Studies Committee, 4500N, MS-6220

Human Studies Committee

You asked for further information on changes in workscope that might affect our Human Studies Committee approval. The work in question deals with human exposure to cigarette smoke and especially to environmental tobacco smoke (ETS). Studies are sponsored by the National Cancer Institute and by the Center for Indoor Air Research.

We expect to continue studies previously reported to the Human Studies Committee which involve ambient air sampling in ETS-containing environments. These involve area sampling (a stationary air sampling device in the room being studied) and personal sampling (a breathing zone ambient air sampler carried by an individual). The samples are subsequently returned to the laboratory for determinations of nicotine and/or other constituents of tobacco smoke. Natural indoor environments are sampled. No environmental nor subject manipulation is involved.

We propose two additional tasks (unrelated to one another) that may require Human Studies Committee approval and/or guidance. These are as follows.

1. We have recently found that a new analytical technique, Direct Sampling Ion Trap Mass Spectrometry (ITMS), might allow the rapid determination of nicotine and cotinine in physiological fluids. We wish to test this technique by comparing ITMS results with results generated by others using current methods. This would involve analyzing urine and/or blood samples provided by NIH or tobacco industry scientists from their excess samples taken in the course of their on-going studies. Prior to this study, however, it will be necessary to develop sample preparation and ITMS operating conditions for the analysis. This requires access to non-smoker urine and blood to serve as media for methods development. Analytical chemical grade nicotine and cotinine will be added to the urine and blood at known concentrations to calibrate the instrument and to determine whether natural constituents of urine or blood interfere with the measurements of nicotine and cotinine. We propose to employ pooled samples of urine from at least three male and three female non-smokers who are working on this or related projects in the Organic Chemistry Section of the Analytical Chemistry Division. Provided we can arrange for the assistance of the ORNL Health Division, we propose to employ blood samples donated by at least one of the non-smoking staff members who are involved in this project.

2. Current studies of ambient air sampling methods for nicotine and other measures of ETS contamination require that test atmospheres be generated under as realistic conditions as possible. We propose to generate natural levels of ETS contamination by machine-smoking of cigarettes in an unoccupied office-like room and an unoccupied conference room. Research staff engaged in machine-generation of cigarette smoke, in sampling the room air, or in operating the monitoring instrumentation would require access to the room and thus be exposed to ETS at naturally occurring concentrations.

Please contact me (4-4862) or Roger Jenkins (6-8594) if you have any further questions.

M. R. Guerin, 4500S, MS-6120 (4-4862)

MRG:pmt

Attachments

cc: R. A. Jenkins

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title

Determination of Human Exposure to Environmental Tobacco Smoke

2. Principal Investigator

Roger A. Jenkins, Ph.D.
Michael R. Guerin, Ph.D.

Telephone Number

615-576-8594
615-574-4862

Mailing Address — Include full name of performing institution.

Oak Ridge National Laboratory, P.O. Box 2008, 4500-S, MS-6120

Oak Ridge, Tennessee 37831-6120

3. Institutional Assurance Number (if issued)[1]

4. Project Number[2]

ERD-88-812 ORNL-17

5. Annual Funding:

Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☒ Actual Funding $ 250,000

☐ $10,000 ☐ $100,000 ☐ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources

A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

N/A

Contact Person	Telephone Number

B. Non-DOE Source

Center for Indoor Air Research

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

1048362

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

☐ Full Board
For a list of research not requiring IRB review, see Attachment.

☒ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☒ New ☐ Annual Renewal ☐ Other

C. IRB Approval Date

February 22, 1993

8. This Project involves the following collaborating institutions (list a maximum of two):

Bellomy Research, Inc.

R. J. Reynolds Tobacco Company

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. Type of Research
Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
- ☐ Using data collected directly from human subjects.
- ☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☒ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
- ☒ Specimens collected directly from human subjects for this project.
- ☐ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☐ Instrument development and testing using human subjects.

☒ Surveys that collect personally identifiable data.

☐ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☐ Other. Please identify _____

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

The objective of this study is a definitive determination of human exposure to environmental tobacco smoke (ETS). Exposure is assessed across a broad geographic region of the United States, and is conducted in such a manner as to determine exposure in the workplace and in private residences. Subjects wear sampling pumps, which collect a small sample of the air near their breathing zone while at work, and at home and during other activities. Exposure is determined to both particle phase and vapor phase species through the use of chemical markers (respirable suspended particulates (RSP), ultraviolet absorbing and fluorescing particulate matter (UVPM and FPM), solanesol, and vapor phase nicotine and 3-vinyl pyridine). Confirmation of human subject smoking status is determined by acquiring a small sample of the participant's saliva, and analyzing it for cotinine, a metabolite of nicotine.

B. Specify the number of human subjects involved each year.

Approximately 100 subjects are recruited in each of 16 cities, for a total of 1600 subjects.

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

Following telephone recruitment, subjects:

1. Come to field service site, and are trained in the use of personal air sampling pumps.
2. Provide a pre-test saliva sample.
3. Wear a personal sir sampling pump as they go about their <u>normal activities</u> at home and at work.
4. Return to field service site and return pumps and questionnaires.
5. Provide final saliva sample and exit the study.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

Not applicable.

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year.	
Signature of Institution Official David E Reichle	**Date** Jan. 25, 1994
Printed or Typed Name David E. Reichle	**Telephone Number** (615) 574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ **Accepted** _____ ☐ **Returned to Originator** _____
Reason for Return	
DOE Reviewers	

1048365

Identification No. ORNL-24

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities (ORAU) and
Oak Ridge National Laboratory (ORNL)

June 30, 1992

Principal Investigator: Richard J. Carter (ORNL), 574-6454, MS-6360

Title of Project: Development of a Portable Driver Performance Data Acquisition System for Human Factors Research

I. Objectives of Research

The overall objective of the research is to develop a portable driver performance data acquisition system for the National Highway Traffic Safety Administration. The data acquisition system is to be used to evaluate new Intelligent Vehicle/Highway System technologies. The system will allow driver performance data to be collected using a large variety of vehicle types and that would be capable of being installed on a given vehicle within a short time frame.

The proposed system will be developed and implemented in two phases. During the first phase a feasibility study of developing the data acquisition system will be conducted. Human factors research needs will be evaluated, and existing methods, measures, techniques, hardware, and software for evaluating driver/vehicle/environment in relation to crash avoidance research will be identified. In the second phase the prototype driver performance data acquisition system will be constructed and evaluated. The evaluation will serve as a basis for developing a final set of design specifications that could be used to construct additional data acquisition systems.

II. Methods of Procedure

During Phase II of the research a pilot test of the driver performance data acquisition system will be conducted. Vehicles driven by humans will be part of the evaluation. The pilot test will evaluate the impact on driveability of the vehicle and obtrusiveness of the data acquisition system to the driver. ORNL is to ensure that the data acquisition system does not compromise safety from the standpoint of vehicle handling and/or visibility. ORNL is also to ensure that the system is as unobtrusive to the

driver of the vehicle as possible. All instances where either the operation of the vehicle or performance of the driver is unavoidably compromised by the data acquisition system are to be documented. At no time, however, is the safety of the driver to be compromised.

An evaluation plan is to be prepared 17 months after the project begins (i.e., December 1993). At that time the methods to be employed in the test, number and types of participants, total number of sessions, etc., will be determined.

The actual pilot test will be completed within 3 months of initiation. The test is to be conducted both at a test track and on open road.

III. Possible Hazards and their Evaluation

All possible hazards of the driver performance data acquisition system on the driver will be considered during the design and development of the system. By the time the data acquisition system is pilot tested all of the possible hazards to the human will have been identified and the system designed so that none of the hazards can or will occur. Invasive clinical procedures will not be applied.

IV. Radioisotopes and New Drugs

No materials of this kind will be involved in the research.

V. Responsibility of Principal Investigator

The rights of the participants in the pilot test will be protected. None of the testing procedures will violate the rights of the human. A form will be prepared asking for the consent of the drivers before they engage in the pilot test.

V. Responsibility of Principal Investigator (Continued)

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

Starting Date: March 1994

Signature: Richard J Carter Principal Investigator

DIVISION REVIEW:

The application described above has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Official signing for the institution:

Signature Robert C. Ward/D. E. Reichle RCWard

Title Director, Engineering Physics and Mathematics Division

Institution Oak Ridge National Laboratory

Date June 30, 1992

David E. Reichle, Associate Director
Oak Ridge National Laboratory

1048368

Engineering Physics and Mathematics Division
OAK RIDGE NATIONAL LABORATORY

CONSENT FOR RESEARCH STUDY

Title of Project: Development of a Portable Driver Performance Data Acquisition System for Human Factors Research

Principal Investigator: Richard J. Carter

Name of Volunteer: _____ **Age:** _____

The purpose of the study: The objective of the study is to pilot test a driver performance data acquisition system for the National Highway Traffic Safety Administration. Volunteers will drive a vehicle (automobile or truck) on a test track and/or on the open road. While they are driving their behavior/performance will be monitored. The recorded data will be used to analyze and validate the data acquisition system.

The procedures to be done are as follows: I will drive a vehicle during which time my driver behavior/performance will be gathered. My steering behavior, brake application, accelerator application, fidget index (movement in the seat), eye/head movement, vigilance, attention/distraction, speed maintenance, and headway/speed differential will be monitored. These measurements will be taken as unobtrusively as possible.

Potential benefits of the study: Since the intent of the proposed pilot test is test/validate an ORNL data acquisition system for human performance research, I understand that there are no anticipated benefits to me as an automobile or truck driver. I further understand that this pilot test is part of a research program and the data will be used to validate the driver performance data acquisition system.

TO PERSONS WHO AGREE TO PARTICIPATE IN THIS STUDY:

The information on this form has been given to me to inform me about this project and my participation in it. I have been asked to read this form carefully. All my questions about the study and the procedures required to do the study have been answered by Mr. Richard Carter at ORNL, (615) 574-6454.

I understand the purpose of the study, the procedures involved, and the possible risks and potential benefits.

I have been informed that I may decline to participate in the study. I freely and voluntarily choose to participate.

Date _____ _____
Signature of Volunteer

_____
Signature of Witness

1048369

ORAU-ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title

Development of a Portable Driver Performance Data Acquisition System for Human Factors Research

Principal Investigator Richard J. Carter

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.					
2.					
3.					
4.					
5.					
6.					
7.					
8.					
9.					
10.					
11.					
12.					
13.					
14.					

Chairman's statement of Committee consensus:

1-31-92
Date

1048370

REVIEW AND ACTION

ORAU/ORNL Committee on Human Studies

Principal Investigator Richard J. Carter Ident. No 24

Project Title Development of a Portable Driver Performance Data Acquisition System for Human Factors Research

1. In the opinion of this committee the rights and welfare of the subjects in this project or activity will be protected. The committee states that adequate safeguards against any untoward effects have been provided.

2. In the opinion of the committee the informed consent procedures to be used in this project will be both appropriate and adequate. The committee also finds that no inappropriate psychological or sociological risks will exist for the subjects involved in this project.

3. The committee seeks continuing communication with the investigator(s) on this project along the following lines:

4. Other committee comments:

Approve ✓

Disapprove _____

Karl F. Hlum
Chairman of Committee

7/31/92
Date

1048371

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical
Sciences
Division

MEMORANDUM

TO: Richard J. Carter
Bill Knee
ORNL MS 6360

FROM: Dr. Karl Hubner, Chairman
ORAU/ORNL Committee on Human Studies

DATE: July 1, 1992

RE: DEVELOPMENT OF A PORTABLE DRIVER PERFORMANCE DATA ACQUISITION SYSTEM FOR HUMAN FACTORS RESEARCH

After reviewing the summary of your proposal, and after discussion of the subject with two other committee members, I have determined that the proposal should be reviewed by the full ORAU/ORNL Committee on Human Studies at its next scheduled meeting the last week of July 1992. I hope this does not inconvenience you or delay the start of your project. The starting date indicated on the bottom of page two of the application indicates that a delay of four weeks will not make a significant difference.

Please submit 16 copies of your entire proposal, along with your proposed consent form, to Ms. Marta Rivera, ORISE/MSD, for distribution to the committee by the end of next week. You will be informed of the committee decision during first week of August 1992.

If you have any questions, please contact Ms. Becky Hawkins (6-1725) who is assisting Ms. Rivera during the transition of the committee's secretarial duties.

KFB:bh

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37831-0117

Medical
Sciences
Division

MEMORANDUM

TO: Richard J. Carter
Bill Knee
ORNL MS 6360

FROM: Dr. Karl Hubner, Chairman
ORAU/ORNL Committee on Human Studies

DATE: July 6, 1992

RE: DEVELOPMENT OF A PORTABLE DRIVER PERFORMANCE DATA ACQUISITION SYSTEM FOR HUMAN FACTORS RESEARCH

I have discussed your proposal again with Mr. Mel Koons, and have determined that your proposal does, in fact, meet the criteria for expedited review. Approval for this project is granted at this time with the understanding that it will be reviewed by the full committee at the time of our next meeting at the end of July.

Please submit 16 copies of your proposal to Ms. Marta Rivera, ORISE/MSD, by the end of this week for distribution to the committee.

KFB:bh

ORISE
OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION

MEDICAL SCIENCES DIVISION

ORAU/ORNL COMMITTEE ON HUMAN STUDIES

TO: Dr. Richard Carter

FROM: Dr. William Calhoun WC/mvr
Chairman, Committee on Human Studies

RE: COMMITTEE ACTION ON NEW PROPOSALS

DATE: August 3, 1992

Your project number ORNL-24 "Development of A Portable Driver Performance Acquisition System for Human Factors Research" was reviewed and approved at our last meeting held on July 31, 1992. The Committee feels that the consent form should be revised to keep confidentiality of the driver's record.

Progress reports of all active proposals will again be reviewed at our next meeting to be held in the fall of 1992.

mvr

P. O. BOX 117, OAK RIDGE, TENNESSEE 37831-0117

Managed and operated by Oak Ridge Associated Universities for the U.S. Department of Energy

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title
Development of a Portable Driver Performance Data Acquisition System for Human Factors Research

2. Principal Investigator
Richard J. Carter

Telephone Number
(615 574-6454

Mailing Address — Include full name of performing institution.
Oak Ridge National Laboratory, P. O. Box 2008, Bethel Valley Road
Building 6025, Mail Stop 6360, Oak Ridge, TN 37831-6360

3. Institutional Assurance Number (If issued)[1]

4. Project Number[2] ORNL-24
DOE No. 2088-F077-A1

5. Annual Funding:
Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☐ Actual Funding $ _____

☐ $10,000 ☐ $100,000 X ☒ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources
A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

	Contact Person	Telephone Number

B. Non-DOE Source
National Highway Traffic Safety Administration

Non-DOE Source
Michael J. Goodman (202) 366-5677

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

☒ Full Board
For a list of research not requiring IRB review, see Attachment.

☐ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☐ New ☐ Annual Renewal ☒ Other

C. IRB Approval Date

July 31, 1992

8. This Project involves the following collaborating institutions (list a maximum of two):

None

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. Type of Research
Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
- ☐ Using data collected directly from human subjects.
- ☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☐ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
- ☐ Specimens collected directly from human subjects for this project.
- ☐ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☒ Instrument development and testing using human subjects.

☐ Surveys that collect personally identifiable data.

☐ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☐ Other. Please identify _____

1048376

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

The overall objective of the research is to develop a portable driver performance data acquisition system which will be used to evaluate new Intelligent Vehicle/Highway System Technologies. The system will allow driver performance data to be collected using a large variety of vehicle types and that would be capable of being installed on a given vehicle within a short time frame. The proposed system will be developed and implemented in two phases. During the first phase a feasibility study of developing the data acquisition system will be conducted. In the second phase the prototype driver performance data acquisition system will be constructed and evaluated.

B. Specify the number of human subjects involved each year.

2-4 The drivers will be either ORNL or NHTSA employees.

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

During Phase II of the research a pilot of the driver performance data acquisition system will be conducted. Vehicles driven by humans will be part of the evaluation. The pilot test will evaluate the impact on driveability of the vehicle and obtrusiveness of the data acquisition system to the driver. ORNL is to ensure that the data acquisition system does not compromise safety from the standpoint of vehicle handling and/or visibility. ORNL is also to ensure that the system is as unobtrusive to the driver of the vehicle as possible. All instances where either the operation of the vehicle or performance of the driver is unavoidably compromised by the data acquisition system are to be documented. At no time, however, is the safety of the driver to be compromised.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

None

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year.	
Signature of Institution Official David E Reichle	**Date** 1/28/94
Printed or Typed Name David E. Reichle	**Telephone Number** (615) 574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ Accepted _____ ☐ Returned to Originator _____
Reason for Return	
DOE Reviewers	

Identification No. ORNL-25

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities (ORAU) and
Oak Ridge National Laboratory (ORNL)

Date: March 8, 1993

Principal Investigators: Joseph H. Goldberg, Ph.D. (ORNL) 4-6198; 6025 MS-6360
(visiting scientist from Penn State University; ORAU Faculty Fellowship Program)

Jack C. Schryver, Ph.D. (ORNL) 4-4710; 6025 MS-6360

Co-Investigators: (none)

Title of Project: Discrimination of User Zoom Intent from Eye-Gaze

I. Objective of Experiment:

This experiment will obtain empirical data on eye-gaze characteristics just prior to a decision of whether to zoom-in or zoom-out at a computer interface. This information is necessary to determine if cameras or process control simulations may be controlled by a user's real-time eye-gaze. If definable eye-gaze patterns do exist prior to such operations, then the zoom control aspects of these interfaces may be controlled by eye-gaze, freeing up the hands for routine interface and telerobotic control. New applications for those with certain disabilities may also be possible.

II. Methods of Procedure:

About 20 subjects will participate in this study of eye-gaze characteristics just prior to zoom-in or zoom-out decisions. During the experimental trials, each subject will participate in a single session for 30-60 minutes. Subjects will be recruited from ORNL employee volunteers, and possibly from local colleges and universities depending upon availability.

Each subject, tested separately in a private office, will sit in front of a Unix computer workstation, and asked to view and compare a series of 96 trials of stimuli on the screen. On each trial, an initial test stimulus will be presented for the subject to memorize. Following a short pause, a comparison stimulus will be presented. To express whether the test and comparison stimuli are the same, the subject will make a "same" or "different" response by pressing "s" or "d" keys on the computer keyboard. On most trials, the subject will need to zoom-in or zoom-out from the comparison stimulus, prior to making a response, to obtain additional information. The zoom-in and zoom-out are effected by pressing the left or right mouse buttons, respectively. The subject's eye-gaze locations on the screen during the trial will be collected by a commercial, non-invasive eye-tracking system, as explained below. The camera from the eye-tracking system is not attached to the subject, and resides just under the computer display. The subject will rest his chin in a comfortable chin rest during these trials.

A calibration procedure for the eye-tracking system precedes the experimental trials described above. For this procedure, the subject places his chin in the chin rest to maintain a reasonably stationary head position, then looks into the infrared-sensitive eye-tracking camera with 75 mm lens. A computer-controlled sequence of circles presented on the display is then initiated. The subject fixates each of the 10 circles as they are displayed. The system repeats the calibration until a criterion accuracy is achieved.

III. Possible Hazards and Their Evaluation:

This study involves behavioral research with minimal risk to human subjects. Subjects will be tested individually in a private office environment, without invasive clinical procedures. Subjects will perform simple visual scanning and comparison of displayed objects at a workstation. This will be done in a self-paced manner, without stress. The procedure includes no deceptive or behavioral manipulations, and confidentiality will be ensured via numerical encoding of all subject identities.

The eye-tracking hardware, manufactured by LC Technologies, Fairfax, VA, uses a pupil-center/corneal-reflection algorithm to determine eye-gaze direction. A small, low-power, infrared light-emitting diode (LED) located at the center of the camera lens illuminates the pupil of the eye. The LED generates both a bright pupil for camera view enhancement and a corneally reflected light glint. The relative relationship of the glint to the modeled pupil is used by the computer software to infer gazepoint direction. The LED wavelength is 880 nm (near-infrared), and has a beam width of 20 degrees between half power points. The radiated power is 20 mW, over the 20 degree beam width; the safety factor is 5. At a range of 15 inches, the LED illumination on the eye is 20% of the US Dept. of Health and Human Services maximum permissible exposure. The only noticeable effect of LED illumination is that prolonged exposure (i.e., several hours) sometimes dries the eye. In this study, subjects will be provided with several rest periods over the course of experimental testing. In addition, subjects will be instructed to take a break whenever they feel it is necessary, as the task is self-paced.

IV. Radioisotopes and New Drugs:

No materials of this kind are involved in this study.

V. Responsibility of Principal Investigators:

The principal investigators will follow the procedures of the Committee on Human Studies. The experimental protocol has minimal risk, and visual search of computer displays is an accepted daily occurrence in office work environments. The eye tracking procedure is well-accepted and non-invasive. Informed consent will be obtained from all participants, as shown in an attached sample form, which also contains the explanation of study.

The principal investigators recognize their primary responsibility for safe-guarding the interests of the participants under study. Significant changes in methods of this procedure, and development of unexpected risks will be brought to the attention of the Committee on Human Studies.

Engineering Physics and Mathematics Division
OAK RIDGE NATIONAL LABORATORY

Explanation of Research Study and Informed Consent Form

Project: Discrimination of User Zoom Intent from Eye-Gaze

Principal Investigators: Joseph H. Goldberg, Ph.D. (574-6198)
Jack C. Schryver, Ph.D. (574-4710)

Participant's Name: _____

Participant Number/ID: _____

EXPLANATION OF STUDY

Purpose of Study:

This study will obtain empirical data on eye-gaze characteristics just prior to a decision of whether to zoom-in or zoom-out at a computer interface. This information is necessary to determine if cameras or process control simulations may be controlled by a user's real-time eye-gaze. If definable eye-gaze patterns do exist prior to such operations, then the zoom control aspects of these interfaces may be controlled by eye-gaze, freeing up the hands for routine interface and telerobotic control. New applications for those with certain disabilities may also be possible.

Study Procedure:

During the study, you will need to place your chin in a chin rest. This will ensure that the head is relatively steady. The study will include the following procedures:

1. Calibration to a workstation display to permit the eye-gaze hardware to accurately track your eye movements. You will look into the camera to initiate the calibration, then view small circles sequentially displayed on the computer display. Several calibration cycles may be required to achieve necessary accuracy.

2. About 100 experimental trials will be conducted, during which you will view objects on the computer display, and determine if they represent the same or different objects. You will respond using keys on the computer keyboard, and will zoom-in or zoom-out (when additional information is necessary) using buttons on the mouse. Several seconds will elapse between each trial, and you may take longer rest breaks whenever required. You may also terminate the experiment at any time by telling the experimenter.

Study Duration:

The entire study will take less than an hour, including instruction and practice. Several rest periods will be provided, but if you become fatigued at any time, you may stop and rest.

Discomforts, Inconveniences, or Risks:

A camera with a very low power infrared light source will be used to track your eye position during the experiment. Prolonged exposure to this may cause some dryness in your eyes. If your eyes feel dry, please notify the experimenter so the study may be paused.

Potential Benefits:

This study will determine if any discriminable eye movement patterns or characteristics precede a zooming-in or zooming-out operation at the computer interface. If such characteristics exist across many subjects, then a demonstration program will be written to perform the zooming-in or out in real-time, just from eye-gaze. Ultimately, many computer operations may be controllable from eye-gaze. New applications may then be developed for camera and robotic control, and for those with significant disabilities. Following the study, you may contact either of the principal investigators for follow-up information and published results.

INFORMED CONSENT

The information on this form has been given to me to inform me about this research project and my participation in it. I have read it carefully, and all of my questions about the study, and its procedures, have been answered to my satisfaction.

I have been informed of the purpose of the study and the procedures involved. I understand that confidentiality will be ensured and that my name will not be associated with any results from this study. I understand that any information gained in this study becomes the property of ORNL and may be published in the scientific literature or used for other purposes which ORNL deems proper in the interest of education, knowledge, or research.

I am freely volunteering for this study. I understand that I may, at any time, withdraw from continued participation in this study without suffering any penalty or prejudice. I am freely and voluntarily choosing to participate.

Date:_____ Signature:_____

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

INSTITUTIONAL REVIEW AND APPROVAL

STARTING DATE: March 22, 1993 (or as soon as approved)

SIGNATURES: _____
Principal Investigator

_____
Principal Investigator

DIVISION REVIEW:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: _____

Title: Director, Engineering Physics and Mathematics Division

Institution: Oak Ridge National Laboratory

Date: March 18, 1993

INSTITUTIONAL APPROVAL:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: _____

Title: Associate Director, Environmental, Life, and Social Sciences

Institution: Oak Ridge National Laboratory

Date: March 18, 1993

THE EYEGAZE™ DEVELOPMENT SYSTEM

A TOOL FOR HUMAN FACTORS APPLICATIONS

LC Technologies, Inc.

4415 Glenn Rose Street
Fairfax, Virginia 22032

(800) 733-5284
(703) 425-7509
FAX: (703) 323-4782

ORAU/ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title: Discrimination of User Zoom Intent from Eye-Gaze

Principal Investigator: Joseph Goldberg, Ph.D.; ORNL
Jack C. Schryver, Ph.D.; ORNL

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.	Karl F. Hoffman	✓			6/25/93
2.	Howard Frisch	✓			6/25/93
3.	Robert Hall	✓			6/25/93
4.	M E Koons	✓			6/25/93
5.	Teaching 2	✓			6/25/93
6.	Shirley A. Fry	✓			6.25.93
7.	R J Michael Fry			Abstain	6.25.93
8.	Sun Tong	✓			6/25/93
9.	Cuellar Fisher	✓			6/25/93
10.					
11.					
12.					
13.					
14.					

Chairman's statement of Committee consensus:

Date

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title

Discrimination of User Zoom Intent from Eye-Gaze

2. Principal Investigator

Jack C. Schryver

Telephone Number

(615) 574-4710

Mailing Address — Include full name of performing institution.

Oak Ridge National Laboratory
Bldg. 6025, Mail Stop 6360

P. O. Box 2008, Oak Ridge, TN 37831

3. Institutional Assurance Number (if issued)[1]

4. Project Number[2]

ORNL - 25

5. Annual Funding:

Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☒ Actual Funding $ 0.00

☐ $10,000 ☐ $100,000 ☐ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources

A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

Office of Advanced Reactor Programs

Contact Person

Harry Alter

Telephone Number

(301) 903-3766

B. Non-DOE Source

Oak Ridge Associated Universities

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

1048386

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

☐ Full Board
For a list of research not requiring IRB review, see Attachment.

☒ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☒ New ☐ Annual Renewal ☐ Other

C. IRB Approval Date

March 22, 1993

8. This Project involves the following collaborating institutions (list a maximum of two):

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. Type of Research
Check all categories that apply.

☐ Epidemiology (using personally identifiable data)—
☐ Using data collected directly from human subjects.
☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☐ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the category checked in Item 11).

The objective of this research was to develop methodologies to discriminate user intent solely from eye-gaze. In this experiment, zoom intent was investigated for application to development of a natural interface for camera zoom, pan, and tilt in teleoperated robotic platforms. Testing of human subjects occurred while participants were seated before a computer workstation monitor. The participants performed an eye tracker calibration procedure with the head supported in a chin rest. They were briefed on all phases of the procedure, and then performed a few practice trials. The participants completed approximately 100 test trials. The trials were simple repetitive problem-solving tasks completed at the workstation. A same/different comparison procedure was used in which participants were first shown a simple test stimulus and then a comparison stimulus. The subject zoomed-in or zoomed-out from the comparison stimulus to make the same/different determination. Eye gaze measurements were recorded during the zoom intent phase. Experimental sessions were approximately 60 minutes in duration.

B. Specify the number of human subjects involved each year.

Eleven human subjects participated during the FY-1993.

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

The participants completed tasks at a computer workstation while their performance was recorded. The tasks were not significantly different from those ordinarily performed by office workers on computers. Eye movements were recorded by an Eye-Gaze System marketed by L. C. Technologies. Inc. of Fairfax, VA. The eyetracker utilized an infrared LED source mounted on a camera lens to illuminate the pupil and generate a corneal glint. These phenomena were detected and utilized by the eyetracker to calculate eye-gaze point-of-regard. The amount of infrared illumination on the eye at a range of 15 inches is 20% of the HEW maximum permissible exposure according to vendor performance specifications.

D. List the number of radioactive materials, if any, that are used in the study, and identify the route of exposure.

NA

See reverse for additional signatures.

1048388

The official signing [illegible] certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals and submissions of project summaries, which are all required at least once a year.	
Signature of Institutional Official	**Date** Jan. 25, 1994
Printed or Typed Name David E. [illegible]	**Telephone Number** (615) 574-4333

For DOE Use Only

Date Received by EH-70	**Date** ☐ **Accepted** _____ ☐ **Returned to Originator** _____
Reason for Return	
DOE Reviewers	

1048389

OAK RIDGE NATIONAL LABORATORY
MANAGED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.
FOR THE U.S. DEPARTMENT OF ENERGY

POST OFFICE BOX 2008
OAK RIDGE, TENNESSEE 37831

June 22, 1993

Dr. William H. Calhoun, Chair
ORNL/ORAU Committee on Human Studies
312 Austin Peay Hall
Department of Psychology
University of Tennessee
Knoxville, TN 37996-0900

Dear Dr. Calhoun:

Enclosed you will find a review application for the proposed involvement of human subjects in a Native Hawaiian Ethnographic Survey for the Hawaii Geothermal Project Environmental Impact Statement. This environmental assessment is being prepared by ORNL staff under the direction of the Department of Energy.

The enclosed application includes a rationale for obtaining informed consent and a sample informed consent document designed to meet the requirements described in the Committee's guidelines, "Assurance of Compliance with HHS Regulations for Protection of Human Research Subjects (p. 6). " However, the document does not describe "discomforts" or "alternative procedures" because the study involves no human health risks and only minimal risks to individuals' well-being as described in the guidelines (p. 17). The research involves neither "[manipulation of] subjects' behavior... [nor] stress to subjects (p. 17)." ORNL staff therefore request approval of this modification on the basis of DOE's regulations on Protection of Human Subjects [10 CFR Ch. III 745.116 (d) (1)], which state that a review board may approve a consent procedure which does not include, or which alters, some of the basic elements of informed consent, provided the research involves no more than minimal risk to the subjects. Furthermore, since the study described involves no more than minimal risk to human subjects, we also request an expedited review, as outlined in the Assurance of Compliance guidelines (pp. 16-17).

We appreciate any comments the Committee may have on how best to safeguard the interests of participants in this survey. Any changes to the informed consent document recommended by the Committee, or that result from a concurrent review being conducted by DOE, will be adopted as necessary.

Sincerely,

James Saulsbury

JWS:sgs

Application for the Use of Humans as Experimental Subjects

To: Committee on Human Studies
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date 6/22/93

Principal Investigator: James Saulsbury

Title of Project: Native Hawaiian Ethnographic Survey,
Hawaii Geothermal Project Environmental Impact Statement

Oak Ridge National Laboratory (ORNL) is currently assisting the Department of Energy (DOE) in identifying and evaluating the potential environmental impacts of the 500-megawatt Hawaii Geothermal Project (HGP), a project proposed to Congress by the State of Hawaii in 1990. To assist DOE in complying with federal and State legislation pertaining to the protection of cultural resources and Native Hawaiian cultural and religious practices, ORNL has subcontracted with a team of professional consultants located in Hawaii to conduct a Native Hawaiian ethnographic survey. This team, an unincorporated affiliation of individual consultants known as Community Action Network Developing Options (CANDO), consists of Dr. Luciano Minerbi, Dr. Jon Matsuoka, and Dr. Davianna McGregor. Their fields of expertise at the University of Hawaii include (respectively) planning, sociology, and ethnic studies.

I. Objectives of Study

To comply with various federal and State laws pertaining to the protection of Native Hawaiian culture, preparers of the environmental impact statement (EIS) need information from Native Hawaiians on their cultural resources and practices, and on potential impacts to those resources and practices. To obtain this information, the CANDO team will conduct a Native Hawaiian ethnographic survey in two stages. Tasks for Stage 1 include: identify all Native Hawaiian groups and individuals likely to consider themselves affected by the HGP, produce a background literature review using archival and other primary sources, prepare a letter report on Native Hawaiian concerns regarding archaeological investigation, develop procedures for maintaining confidentiality of sensitive information, and complete a research design study plan.

Tasks for Stage 2 include: select participants for focus groups and ethnographic interviews; collect data (conduct group meetings and interviews), analyze data, and produce a final report. The report will include detailed analysis of traditional Native Hawaiian sites, and of cultural and religious values, practices, and beliefs associated with natural resources and prehistoric or historic sites. The report will also identify potential impacts from the proposed HGP to cultural practices and resources, and identify appropriate preservation measures or mitigation strategies.

II. Methods of Procedure

Methods of soliciting information on such topics as gathering practices, religious rituals, and sacred sites, and on Native Hawaiian concerns regarding their protection, will include focus group discussions, moderated by a facilitator, and in-depth directed and nondirected participant-observation interviews conducted by individuals with training in ethnographic interviewing techniques.

III. Possible Hazards

There are no potential human health hazards associated with this project. However, the use of informed consent documents is warranted according to DOE guidelines on the protection of human subjects [10 CFR Ch. III, prt. 745 (January 1, 1992)] for the following reasons: First, it may be difficult to ensure complete anonymity for participants. Even if sources remain unnamed, traditional experts might still be identified by members of their communities based on the content of their information [745.101 (b)(4)]. Given the sensitive nature of information about gathering practices, sacred places, and burial sites, and given the lack of consensus among native people about the potential extent of impacts to some of those practices and resources, damage to individuals' reputations could occur [745.101 (b) (2) (i-ii)].

Second, some information is likely to be considered private rather than publicly identifiable[745.101 (b)(4)]. Survey information on gathering practices, sacred places, and burial sites could range from evidence of observable public behavior to individual opinion or private knowledge, with many gray areas in between. Native people sometimes refuse to speak for their community, tribe, or ethnic group, and maintain that their opinions are their own. Many express concern that they not be identified as spokespeople for the larger group.

IV. Radioisotopes and New Drugs

The study involves no use of radioisotopes or drugs.

V. Responsibility of Principal Investigator

By approving the use of an informed consent document for this survey, DOE maintains the right to cite subjects who grant permission (pending review of their statements) for their names to be cited in a public document. DOE also builds evidence of a good faith effort to fully inform subjects of the nature and intent of the survey and to ensure the maximum possible confidentiality for those who indicate that they prefer to remain anonymous. The attached sample informed consent document provides basic elements of informed consent, as described in "Assurance of Compliance with HHS Regulations for Protection of Human Research Subjects (p. 6)." However, because the study involves only minimal risks to individuals (p. 17), the document does not describe "discomforts" or "alternative procedures."

The principal investigator will follow the procedures of the Committee on Human Studies in obtaining informed consent. The investigator recognizes that he retains the primary responsibility for safe-guarding the interests of the participants under study. Any significant changes in methods of procedure or the development of unexpected risks will be brought to the attention of the Committee immediately.

AGREEMENT TO PARTICIPATE IN

A Native Hawaiian Ethnographic Survey
for the
Hawaii Geothermal Project
Environmental Impact Statement

Sponsored by the U.S. Department of Energy

Oak Ridge National Laboratory (ORNL) is currently assisting the Department of Energy (DOE) in identifying and evaluating the potential environmental impacts of the 500-megawatt Hawaii Geothermal Project (HGP), a project proposed to Congress by the State of Hawaii in 1990. To assist DOE in complying with federal and State legislation on the protection of cultural resources and Native Hawaiian customs and religion, ORNL has subcontracted with a team of professional consultants located in Hawaii to conduct a survey of Native Hawaiian customs and religion. This team of consultants, who use the name Community Action Network Developing Options, consists of Dr. Luciano Minerbi, Dr. Jon Matsuoka, and Dr. Davianna McGregor. Their fields of expertise at the University of Hawaii include (respectively) planning, sociology, and ethnic studies.

These consultants request your participation in a survey to gather information on Native Hawaiian traditional and religious practices, and on potential impacts to those practices from the proposed geothermal project. They will conduct group meetings and individual interviews to gather the required information. Participation is completely voluntary, and you may withdraw from a group survey or interview at any time. You may also indicate, below, whether you wish to remain anonymous.

I certify that I have been told of possible risks involved in this project; that I have been given satisfactory answers to my questions concerning project procedures and other matters; and that I have been advised that I am free to withdraw my consent and to stop my participation in the project or activity at any time.

I wish my identity to remain anonymous.

_____ _____
Signature of Individual Participant Date

Given the opportunity to first review any statement attributed to me, I would allow citation in a public document.

_____ _____
Signature of Individual Participant Date

For more information about the survey, please contact Dr. Jon K. Matsuoka, University of Hawaii at Manoa, School of Social Work, 2500 Campus Road, Honolulu, HI 96822, (808) 956-6123.

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

INSTITUTIONAL REVIEW AND APPROVAL

STARTING DATE: 6/7/93

SIGNATURES: _____
Principal Investigator

R. M. Reed
Principal Investigator

DIVISION REVIEW:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: J B Cannon

Title: Associate Director, Energy Division

Institution: Oak Ridge National Laboratory

Date: 6-24-93

INSTITUTIONAL APPROVAL:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: David E. Reichle
David E. Reichle

Title: Associate Director, Environmental, Life, and Social Sciences

Institution: Oak Ridge National Laboratory

Date: 6/29/93

ORAU/ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title:

Native Hawaiian Ethnographic Survey, Hawaii Geothermal Project Environmental Impact Statement.

Principal Investigator: James Saulsbury

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.	[signature]	X			11-10-93
2.	[signature]	X			11.10.93
3.	[signature]	X			"
4.	[signature]	X			"
5.	[signature]		abstain		11/10/93
6.	[signature]	X			11/10/93
7.	[signature]	X			11/10/93
8.					
9.					
10.					
11.					
12.					
13.					
14.					

Chairman's statement of Committee consensus:

Date

1048395

OAK RIDGE NATIONAL LABORATORY
MANAGED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.
FOR THE U.S. DEPARTMENT OF ENERGY

POST OFFICE BOX 2008
OAK RIDGE, TENNESSEE 37831

June 22, 1993

Dr. William H. Calhoun, Chair
ORNL/ORAU Committee on Human Studies
312 Austin Peay Hall
Department of Psychology
University of Tennessee
Knoxville, TN 37996-0900

Dear Dr. Calhoun:

Enclosed you will find a review application for the proposed involvement of human subjects in a Cultural Resources Survey for the Hawaii Geothermal Project Environmental Impact Statement. This environmental assessment is being prepared by ORNL staff under the direction of the Department of Energy.

The study involves no human health risks and only minimal risks to individuals' well-being as described in the Committee's guidelines, "Assurance of Compliance with HHS Regulations for Protection of Human Research Subjects (p. 17). " The research involves neither "[manipulation of] subjects' behavior... [nor] stress to subjects (p. 17)." ORNL staff therefore request an expedited review, as outlined in the Assurance of Compliance guidelines (pp. 16-17).

We appreciate any comments the Committee may have on how best to safeguard the interests of participants in this survey. Any changes recommended by the Committee will be adopted as necessary.

Sincerely,

James Saulsbury

JWS:sgs

Application for the Use of Humans as Experimental Subjects

To: Committee on Human Studies
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date 6/22/93

Principal Investigator: James Saulsbury

Title of Project: Cultural Resources Survey,
Hawaii Geothermal Project Environmental Impact Statement

Oak Ridge National Laboratory (ORNL) is currently assisting the Department of Energy (DOE) in identifying and evaluating the potential environmental impacts of the 500-megawatt Hawaii Geothermal Project (HGP), a project proposed to Congress by the State of Hawaii in 1990. To assist DOE in complying with federal and State legislation pertaining to the protection of cultural resources and Native Hawaiian cultural and religious practices, ORNL has subcontracted with a State-approved archaeological firm, International Archaeological Research Institute, Inc. (IARII), located in Hawaii, to conduct Phase I surveys of cultural resources in two project areas on the islands of Hawaii and Maui. Cultural resources to be identified include prehistoric, historic, and traditional sites.

I. Objectives of Study

To comply with various federal and State laws pertaining to the protection of cultural resources, preparers of the environmental impact statement (EIS) must solicit information on cultural resources, determine the significance of those resources, and evaluate potential impacts to the resources from the proposed project. To obtain the necessary information for the HGP EIS, a cultural resources survey will be conducted in two stages. In Stage 1, IARII will develop two regionally-specific research designs resulting in a predictive model for a Phase I cultural resources survey of the Big Island project area and a general plan for a Phase I cultural resources survey of the Maui project area. These research designs will provide the basis for locating cultural remains in each of the two project areas and for determining their potential eligibility for listing in the National Register of Historic Places according to criteria listed in 36 CFR, Part 60, of the National Historic Preservation Act. In Stage 2, IARII will conduct a verification survey for each of the two project areas. Following completion of each survey and analysis of results, the subcontractors will produce a separate final report on the Phase I survey of cultural resources for each project area.

II. Methods of Procedure

In Stage 1, IARII will conduct a background literature review of previous archaeological research and other relevant documents (such as aerial photographs and environmental studies) that illuminate prehistoric and historic land use in the project area. IARII then will conduct a preliminary reconnaissance survey of each project area. The

reconnaissance surveys will consist of: a helicopter survey of each project area to identify factors relevant to conducting the full verification survey; a windshield survey to identify access routes, potential survey problems, and major cultural resources; and a limited ground survey of easily accessible sample areas. These initial surveys will familiarize personnel with the topography and vegetation of the project corridor, enable personnel to determine the best means of access for the survey crew, and identify problems that might be encountered during verification surveys.

In Stage 2, IARII will conduct a verification survey for each of the two project areas to provide data from a cross section of topographic and geological formations, soil types, and historic land use patterns. Field verification of the Big Island predictive model will consist of stratified sampling of an appropriate percentage of the total acreage, along with areas of probable density, to be determined by the predictive model. Field verification in the Maui project area will consist of a pedestrian reconnaissance survey of a 20-mile long, 200-foot wide corridor, following as closely as possible the proposed transmission corridor.

Most of the information required for this study is collected by means of physical archaeological procedures and a background literature review. However, IARII staff may need to consult with local people on occasion. In the case of traditional Native Hawaiian sites, such as burial sites or sacred places, local informants' knowledge could be valuable.

III. Possible Hazards

There are no potential human health hazards and only minimal risks of other kinds to human subjects associated with this project. In accordance with DOE guidelines on the protection of human subjects [10 CFR Ch. III, prt. 745 (January 1, 1992)], the requirement for informed consent does not apply to this study for two reasons. First, in the case of sensitive cultural information concerning burial sites and sacred places, archaeological reports prepared for public release typically maintain strict confidentiality of locations and sources. Examples of federal regulations addressing confidentiality of sensitive cultural information include the Department of Energy's Implementing Procedures and Guidelines for the National Environmental Policy Act [10 CFR 1021.340 (a-b) (April 24, 1992)] and the National Historic Preservation Act of 1966, as amended in 1992 [16 U.S.C 470w-3, Sec. 304 (a)]. Thus, it is reasonable to assume that anonymity of human subjects can be maintained, as required in [745.101 (b)(4)] of the DOE guidelines.

Second, in the case of non-sensitive cultural information, the risk of damage or stress to human subjects is small because the study emphasizes physical evidence about culturally significant sites and artifacts. With the exception of traditional cultural sites (many of which require confidential treatment), the evidence required for documentation is largely physical. Information gathered from local informants serves a supplemental role. Should such information assume an uncharacteristically prominent or controversial role in this study, an informed consent document could be modeled after the one currently proposed for a companion study, a Native Hawaiian Ethnographic Survey, that does require documentation of informed consent from participants in interviews and group meetings. However, due to the extensive protection afforded sensitive cultural information by existing regulations and by standard archaeological procedures which minimize attention to human subjects, damage to reputation or stress to subjects as defined in [745.101 (b) (2) (i-ii)] of the DOE guidelines is unlikely.

IV. Radioisotopes and New Drugs

The study involves no use of radioisotopes or drugs.

V. Responsibility of Principal Investigator

The principal investigator will follow, and will direct subcontractors to follow, the procedures of the Committee on Human Studies in obtaining informed consent. The investigator recognizes that he retains the primary responsibility for safe-guarding the interests of the participants under study. Any significant changes in methods of procedure or the development of unexpected risks will be brought to the attention of the Committee immediately.

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

INSTITUTIONAL REVIEW AND APPROVAL

STARTING DATE: 6/7/93

SIGNATURES: _____
Principal Investigator

_____
Principal Investigator

DIVISION REVIEW:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: _____

Title: Associate Director, Energy Division

Institution: Oak Ridge National Laboratory

Date: 6-24-93

INSTITUTIONAL APPROVAL:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: _____
David E. Reichle

Title: Associate Director, Environmental, Life, and Social Sciences

Institution: Oak Ridge National Laboratory

Date: June 28, 1993

ORNL-26-a

ORAU/ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title:

Cultural Resources Survey, Hawaii Geothermal Project Environmental Impact Statement.

Principal Investigator: James Saulsbury

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.	[signature]	X			11-10-93
2.	[signature]	X			11.10.93
3.	[signature]	X			"
4.	[signature]	X			"
5.	[signature]	X			"
6.	[signature]	✓			11/10/93
7.					
8.					
9.					
10.					
11.					
12.					
13.					
14.					

Chairman's statement of Committee consensus:

Date

1048401

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title Hawaii Geothermal Project Environmental Impact Statement (Cultural Resources Survey)

2. Principal Investigator
R. M. Reed

Telephone Number
(615) 574-5756

Mailing Address — Include full name of performing institution.
Oak Ridge National Laboratory
P.O. Box 2008, Oak Ridge, TN 37831-6200

3. Institutional Assurance Number (if issued)[1]

4. Project Number[2]
3345-3350 ORNL-26a

5. Annual Funding:
Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☒ Actual Funding $ 205,000

☐ $10,000 ☐ $100,000 ☐ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources
A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office
Energy Efficiency and Renewable Energy

Contact Person
R. R. Kessler

Telephone Number
(202) 586-8089

B. Non-DOE Source

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

1048402

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

❑ Full Board
For a list of research not requiring IRB review, see Attachment.

☒ Expedited The project has been approved for expedited review, but the review is not complete.
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

❑ New ❑ Annual Renewal ❑ Other

C. IRB Approval Date

8. This Project involves the following collaborating institutions (list a maximum of two):

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

❑ This project involves the following vulnerable populations:

❑ Minors ❑ Mentally Disabled ❑ Prisoners

❑ Fetuses, Pregnant Women, In Vitro Fertilization ❑ Economically or Educationally Disadvantaged

10. Type of Research

Check all categories that apply.

❑ Epidemiology(using personally identifiable data)—
- ❑ Using data collected directly from human subjects.
- ❑ Using existing data.

❑ Diagnostic studies using radiation or chemical agents in tracer amounts.

❑ Therapeutic studies using radiation or chemical agents.

❑ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
- ❑ Specimens collected directly from human subjects for this project.
- ❑ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

❑ Instrument development and testing using human subjects.

☒ Surveys that collect personally identifiable data.

❑ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

❑ Other. Please identify _____

1048403

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

See attached

B. Specify the number of human subjects involved each year.

Unknown

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

Human subjects might be consulted on sensitive topics concerning Native Hawaiian sites (e.g., burial sites). They would not be exposed to any type of risk.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year	
Signature of Institution Official David E Reichle	**Date** Jan. 25, 1994
Printed or Typed Name David E. Reichle	**Telephone Number** (615) 574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ **Accepted** _____ ☐ **Returned to Originator** _____
Reason for Return	
DOE Reviewers	

1048405

Human Subjects Research, ORNL 26-A

Title of Project: Cultural Resources Survey,
Hawaii Geothermal Project Environmental Impact Statement

Oak Ridge National Laboratory (ORNL) is currently assisting the Department of Energy (DOE) in identifying and evaluating the potential environmental impacts of the proposed 500-megawatt Hawaii Geothermal Project (HGP). To assist DOE in complying with federal and state legislation pertaining to the protection of cultural resources and Native Hawaiian cultural and religious practices, ORNL has subcontracted with a state-approved archaeological firm, International Archaeological Research Institute, Inc. (IARII), located in Hawaii, to conduct Phase I surveys of cultural resources in two project areas on the islands of Hawaii and Maui. Cultural resources to be identified include prehistoric, historic, and traditional sites.

The IARII team will collect information for ORNL staff to use in preparing sections of an environmental impact statement (EIS) on cultural resources in the vicinity of the two project areas, and on potential impacts to those resources. To obtain this information, IARII will conduct a cultural resources survey in two stages. Stage I consists of developing two regionally-specific research designs resulting in a predictive model for a Phase I cultural resources survey of the Big Island project area and a general plan for a Phase I cultural resources survey of the Maui project area. Stage II consists of conducting a verification survey for each of the two project areas. IARII completed Stage I in November 1993. Fieldwork for Stage II began in December 1993 and is scheduled for completion in March 1994. Following the analysis of survey results, IARII will produce a separate final report on the Phase I survey of cultural resources for each project area.

Most of the information required for this study is collected by means of physical archaeological procedures and a background literature review. However, in the case of traditional Native Hawaiian sites, such as burial sites or sacred places, local informants' knowledge could be valuable and IARII staff might need to consult with them on sensitive topics. In such cases, IARII uses an informed consent form approved by DOE and the ORAU/ORNL Human Subjects Committee to determine whether participants wish to remain anonymous or will allow themselves to be cited in public documents. Research designs for both project areas indicate that access to confidential information is restricted.

OAK RIDGE NATIONAL LABORATORY
MANAGED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.
FOR THE U.S. DEPARTMENT OF ENERGY

POST OFFICE BOX 2008
OAK RIDGE, TENNESSEE 37831

June 15, 1993

Dr. William H. Calhoun, Chair
ORNL/ORAU Committee on Human Studies
312 Austin Peay Hall
Department of Psychology
University of Tennessee
Knoxville, TN 37996-0900

Dear Dr. Calhoun:

We are sending a research proposal to DOE on a collaborative project with the Thompson Cancer Survival Center (TCSC) on **"Advanced Biomedical Diagnostics and Therapy"**, which involves the development of laser-induced *in vivo* autofluorescence detection of human tissue during routine endoscopy performed at TCSC.

The protocol has been approved by the TCSC Institutional Review Board (see enclosed letter on December, 1992 to Dr. M. Panjehpour).

We are waiting for your review and approval in order to send the proposal to DOE. Please, FAX your reply at your earliest convenience.

Best regards

Tuan Vo-Dinh, Ph. D.
Group Leader
Advanced Monitoring Development Group
Tel: 574-6259
FAX:576-7651

TV:st
Encl.

DOE Form 6120.2 (Page 1)
(12-87)

U.S DEPARTMENT OF ENERGY
OAK RIDGE OPERATIONS

FIELD WORK PROPOSAL

PROGRAM: KP - BIOLOGICAL AND ENVIRONMENTAL RESEARCH

1. WORK PROPOSAL NO.	2. REVISION NO.	3. DATE PREPARED	
ERKP905	0	04-22-93	08

4. WORK PROPOSAL TITLE: Advanced Biomedical Diagnostics and Therapy

5. BUDGET AND REPORTING CODE: KP 01 02 00 0

6. WORK PROPOSAL TERM
Begin: - - End: OPEN

PATENT STATUS
This proposal is being transmitted in advance of patent review for evaluation purposes only. No further dissemination or publication shall be made without prior approval of the Assistant General Counsel for Patents, DOE.

7. Is This Work Proposal Included in the Institutional Plan?
☐ Yes ☒ No

8. HEADQUARTERS/OPERATIONS OFFICE PROGRAM MANAGER:
Goldstein, Gerald (301) (903-5348)

11. HEADQUARTERS ORGANIZATION: Energy Research

14. DOE ORGANIZATION CODE: ER

9. OPERATIONS OFFICE WORK PROPOSAL REVIEWER:
Wolfe, Sylvia Jane (615) (576-4065)

12. OPERATIONS OFFICE: Oak Ridge Operations

15. DOE ORGANIZATION CODE: ON

10. CONTRACTOR WORK DISPOSAL PRINCIPAL INVESTIGATOR(S)/MANAGER:
Vo-Dinh, T. (615-574-6249)
Panjehpour, M. (615-541-1281)
Overholt, B.J. (615-541-1433)
Frazier, D. (615-974-5577)

13. CONTRACTOR NAME:
Martin Marietta Energy Systems, Inc.
Oak Ridge National Laboratory
Oak Ridge, Tennessee 37831

16. DOE CONTRACTOR CODE: 41

17. WORK PROPOSAL DESCRIPTION (Approach, anticipated benefits in 200 words or less)

The long-term objective of this research project is to develop novel and/or improved spectroscopic methods and instrumentation for cancer diagnostics and treatment. The specific aims of this research project are: (a) Investigation of the laser-induced fluorescence (LIF) technique for autofluorescence and drug fluorescence, (b) development of a new approach based on synchronous luminescence (SL) for cancer diagnostics, (c) Development of a new SL prototype instrument, and (d) Evaluation in animal studies and clinical applications.

The LIF study will include: i) in vivo laser-induced auto fluorescence analysis of normal and dysplastic tissues in the esophagus and colon; and ii) spectral decomposition study to determine the origin of spectral characteristics of normal and dysplastic tissue; (iii) fluorescence analysis of a drug (e.g., PHOTOFRIN) in rat tissues. A unique aspect of this project is the development of a novel SL detection methodology for monitoring small changes in fluorescence profiles of normal and tumor tissues. The conventional laser-induced fluorescence (LIF) technique does not often provide the spectral specificity needed to provide clear "spectral fingerprints" of normal and tumor tissues. This novel SL detection scheme could lead to significant advances in effective detection of tumors and in the understanding of cancer therapy in general. Sensitivity and selectivity enhancement techniques will be evaluated. The potential of the new SL diagnostic approach and the LIF technique will be assessed for clinical evaluations in collaboration with the Thompson Cancer Survival Center (M. Panjehpour, Ph.D.; B. Overholt, M.D.). An interdisciplinary approach to the proposed research tasks will be pursued throughout the entire project.

Keywords: Biomedical diagnostics; Cancer treatment, Laser Fluorescence Spectroscopy

18. CONTRACTOR WORK PROPOSAL MANAGER: (Name and FTS No.)
Barry A. Berven (615) (574-5845) - -
Signature: Date:

19. OPERATIONS OFFICE REVIEW OFFICIAL
(Signature) (Date)

20. DETAIL ATTACHMENTS: (See instructions for page 3)

☒ a. Facility Requirements	☒ d. Background	☒ g. Future accomplishments	☒ j. Explanation of Milestones
☒ b. Publications	☒ e. Approach	☒ h. Relationships to other projects	☒ k. Other (specify): Budget
☒ c. Purpose	☒ f. Technical progress	☐ i. Environmental assesment	

December 16, 1992

Masoud Panjehpour, Ph.D.
Thompson Cancer Survival Center
1915 White Avenue
Knoxville, TN 37916

RE: TCSC 9203 - Laser-Induced Fluorescence Detection of Malignant Tissue Phase II: In Vivo Autofluorescence Measurement During Routine Endoscopy

Dear Dr. Panjehpour,

The Thompson Cancer Survival Center Institutional Review Board met December 16, 1992 and approved the protocol - Masoud Panjehpour, Ph.D. (Principal Investigator) and Bergein F. Overholt, M.D. (Sub-Investigator) as submitted for the above mentioned study.

The Informed Consent Form (dated December 16, 1992) was approved contingent upon the following changes:

In Section 2, Procedures to be Followed, the paragraph "It has been explained to me that during my endoscopy, fluorescence measurements will be performed on my esophagus/colon (normal/tumor) and that the results of the fluoreaccence studies will be correlated with results of the histological examination of my tumor (if any)."

was changed to

"It has been explained to me that during my endoscopy, fluorescence (light) measurements will be performed on my esophagus/colon (normal/tumor) and that the results of the light measurements will be compared with results of the microscopic examination of my tumor (if any). If any tumor is seen, a biopsy will be obtained."

Continuing approval of this protocol is contingent upon a receipt of a report from you, on an annual basis after the approval date (December 16, 1992) on the progress of this study. It is the investigator's responsibility to submit these reports directly to the TCSC Institutional Review Board.

Federal Regulations, under the Investigational New Drug Application Rewrite effective 6/17/87, (21CRF312.3(b)) state: "An investigator means an individual who actually conducts a clinical investigation; i.e., under whose immediate direction the drug is administered or dispensed to a subject. In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. 'Subinvestigator' includes any other individual member of that team."

The Institutional Review Board presumes that you fully understand the implications of accepting this responsibility.

You are required to notify the Board of the following at any time during the conduct of this study:

1. Protocol changes.
2. Deviations from the conduct of the study.
3. Adverse events that occur to study patients. Serious adverse events are to be reported within 10 days of occurrance of same.

The Board is to be notified of the completion date of the study; and a timely, final report on the conduct and results of the trial is required.

Please contact us if we can furnish additional assistance or information.

Sincerely,

William Reid Bell, M.D., Chairman
Institutional Review Board
Thompson Cancer Survival Center

ORAU/ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title:

Advanced Biomedical Diagnostic and Therapy.

Principal Investigator: Tuan Vo-Dinh, Ph.D.

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.	William Hollaway	X			
2.	Shirley M. Tang	X			11.10.93
3.	[illegible]	X			11/10/93
4.	[illegible]	X			"
5.	[illegible]	X			"
6.	[illegible]	✓			11/10/93
7.					
8.					
9.					
10.					
11.					
12.					
13.					
14.					

Chairman's statement of Committee consensus:

Date

1048411

OAK RIDGE NATIONAL LABORATORY
MANAGED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.
FOR THE U.S. DEPARTMENT OF ENERGY

POST OFFICE BOX 2008
OAK RIDGE, TENNESSEE 37831

February 7, 1994

Dr. William H. Calhoun, Chair
ORAU/ORNL Committee on Human Subjects
Oak Ridge Associated Universities
P.O. Box 117
Oak Ridge, TN 37831-0117

Dear Dr. Calhoun:

Per your request, please find enclosed the consent form used by the Thompson Cancer Survival Center for the project, "Advanced Biomedical Diagnostics and Therapy."

Thank you for your assistance.

Sincerely,

Tuan Vo-Dinh, Ph.D.
Group Leader
Advanced Monitoring Development Group

TVD:jc

Enclosure

File - TVD

THOMPSON CANCER SURVIVAL CENTER

SPECIAL PERMIT SHEET

CONSENT FOR SPECTROSCOPY MEASUREMENT

PATIENT NAME: _____ AGE: _____

DATE: _____ 19 ___ TIME: _____

PHYSICIAN: _____ PLACE: _____

I, _____ a patient of THOMPSON CANCER SURVIVAL CENTER hereby give permission for spectroscopic measurement to be performed during my endoscopy and further release THOMPSON CANCER SURVIVAL CENTER from any legal or other responsibility for protecting my rights in the release or use of the data obtained.

_____
Signature

_____
Witness

1048413

WHAT IS FLUORESCENCE SPECTROSCOPY ?

Using Fluorescence to Detect Tumors

When tissue is exposed to certain colors of light, it fluoresces similar to fluorescent markers under violet light. Fluorescence of normal and cancerous tissue are different. This fluorescence difference may be used to detect tumors without taking any biopsies.

How is Tissue Fluorescence Measured?

Fluorescence spectroscopy is a technique that measures fluorescence of tissue. During the endoscopy procedure, a small fiber is lightly touched to the tissue to measure its fluorescence. The measurement is non-invasive (painless). Each measurement is completed in less than two seconds.

The Need For Volunteers

Volunteers are needed to collect fluorescence of normal and tumor tissues to further develop this non-invasive technique. Development of this method, ultimately, will allow detection of tumors without taking any biopsies.

Oak Ridge
Associated
Universities

Post Office Box 117
Oak Ridge, Tennessee 37831-0117

COPY

December 30, 1993

Tuan Vo-Dinh, Ph.D.
Advanced Monitoring Development Group
Oak Ridge National Laboratory
P.O. Box 2008
Oak Ridge, Tennessee 37831

Dear Dr. Vo-Dinh:

I apologize for the delay in getting this letter written. The ORAU/ORNL Institutional Review Board met on November 10, 1993. I had approved your proposals for the Committee as they qualified for expedited review. Yet, the full committee does have to review the proposals at the next regular meeting and note any concerns.

Some general concerns applied to all proposals we reviewed that day. The Institutional Review and Approval Sheets were often incomplete. These sheets must contain the title of the project and the project code number, in your case ORNL-27. The secretary for the Committee assigns these numbers, and I will ensure that all proposals go first to her to ensure the Review and Approval sheet is complete and that she assigns a project code. In some cases the sheets did not include the signatures of all persons required to approve the projects. On future proposals, I will return them to the PI to obtain the full signatures before approving projects.

The Committee asked that I write you to obtain a copy of the consent form which is used by the Thompson Cancer Survival Center for our files. Otherwise, there were no concerns regarding your proposal.

I wish you success with your research projects.

Sincerely yours,

William H. Calhoun, Chair
ORAU/ORNL Committee on Human Subjects

WHC:mvr

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title
Advanced Biomedical Diagnostics and Therapy

2. Principal Investigator
Tuan Vo-Dinh

Telephone Number
615-574-6249

Mailing Address — Include full name of performing institution.
Oak Ridge National Laboratory, P.O. Box 2008, Bldg. 4500S, MS-6101
Oak Ridge, TN 37831-6101

3. Institutional Assurance Number (If issued)[1]

4. Project Number[2]
ORNL-27

5. Annual Funding:
Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☐ Actual Funding $ N/A

☐ $10,000 ☐ $100,000 ☐ $500,000 ☐ $1,000,000 ☐ $5,000,000 (submitted proposal)

6. Funding Sources
A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office
Office of Health and Environmental Research

Contact Person
Gerry Goldstein

Telephone Number
301-903-5348

B. Non-DOE Source

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

1048416

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

☒ Full Board
For a list of research not requiring IRB review, see Attachment.

☐ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☒ New ☐ Annual Renewal ☐ Other

C. IRB Approval Date Letter from Thompson Cancer Survival Center (1/20/94) and from University of Tennessee Medical Center (2/11/94)

8. This Project involves the following collaborating institutions (list a maximum of two):

Thompson Cancer Survival Center

University of Tennessee Medical Center

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. Type of Research
Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
- ☐ Using data collected directly from human subjects.
- ☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☒ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
- ☐ Specimens collected directly from human subjects for this project.
- ☒ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☒ Instrument development and testing using human subjects.

☐ Surveys that collect personally identifiable data.

☐ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☐ Other. Please identify _____

1048417

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

This project involves the development of novel or improved biomedical diagnostic and therapeutic technologies. A new diagnostic procedure based on laser-induced fluorescence is developed for direct *in-vivo* cancer diagnosis without requiring biopsy surgery. The methodology was applied to differentiate normal and malignant tumors of the esophagus. Endogenous fluorescence of normal and malignant tissues were measured directly using a fiberoptic probe inserted in an endoscope at the Thompson Cancer Survival Center (TCSC). The measurements were performed *in-vivo* during routine endoscopy. The fiber-optic probe was designed so that it could be inserted into the biopsy channel of an endoscope. The detector was an intensified photodiode

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year.	
Signature of Institution Official	**Date** 2/15/94
Printed or Typed Name Dr. David E. Reichle	**Telephone Number** 574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ Accepted _____ ☐ Returned to Originator _____
Reason for Return	
DOE Reviewers	

1048419

OAK RIDGE NATIONAL LABORATORY
MANAGED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.
FOR THE U.S. DEPARTMENT OF ENERGY

POST OFFICE BOX 2008
OAK RIDGE, TENNESSEE 37831

Dr. Virginia H. Dale
Environmental Sciences Division
Building 1505, MS-6038
Telephone: 615-576-8043
FAX: 615-576-8646
Email:Bitnet VHD@ORNLSTC
Internet: VHD@ORNL.GOV

September 22, 1993

Dr. William H. Calhoun, Chair
ORNL/ORAU Committee on Human Studies
312 Austin Peay Hall
Department of Psychology
The University of Tennessee
Knoxville, Tennessee 37996-0900

Dear Dr. Calhoun:

Enclosed you will find a review application for the proposed involvement of human subjects in a proposal being submitted to the U.S. Environmental Protection Agency (EPA). This environmental assessment is being prepared by ORNL staff under the direction of the Department of Energy.

The study involves no human health risks and only minimal risks to individuals' well-being as described in the Committee's guidelines, "Assurance of Compliance with HHS Regulations for Protection of Human Research Subjects." We believe that the research described in this application is exempted from the DOE Policy for the Protection of Human Subjects in accordance with 10CFR Part 745, Section 101(a)(2), due to the protection of anonymity of the participants in the surveys used in this research.

We appreciate any comments the Committee may have on the human subject aspects of our proposed research. Any changes recommended by the Committee will be adopted as necessary.

Because we are trying to submit a proposal to the EPA in a timely fashion, we would appreciate a guick response regarding this application. If you concur that the research is exempted, please sign the concurrence block below and telefax this letter to me at 576-8646. Please call me if you need any additional information.

Sincerely,

Virginia Dale

Virginia Dale

VHD:sjw

Attachment

cc: S. G. Hildebrand
D. E. Reichle
M. Rivera (ORAU)
D. S. Shriner
R. I. Van Hook

CONCURRENCE:

_____ _____

W. H. Calhoun, Chair Date
ORNL/ORAU Committee on Human Studies

INSTITUTIONAL REVIEW AND APPROVAL

PROJECT TITLE: Relating Ecological Indicators to Societal Values

IDENTIFICATION NO.: _____

STARTING DATE: January 1, 1994

The principal investigator will follow the procedures of the Committee on Human Studies in obtaining "informed consent" from the subjects under study. The investigator recognizes acceptance of primary responsibility for safeguarding the interests of the participants under study. The investigator is responsible for notifying the ORAU/ORNL Committee on Human Studies of any significant changes in methods of procedure or of the development of unexpected risks.

SIGNATURES:

Virginia H. Dale 9-21-93
Principal Investigator — Date

Carolyn T. Hunsaker 9-21-93

Sl W. Suter II 9/21/93
Co-Principal Investigator(s) — Date

DIVISION REVIEW:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: _____

Title: _____

Institution: Oak Ridge National Laboratory

Date: _____

INSTITUTIONAL APPROVAL:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: _____
David E. Reichle

Title: Associate Director, Environmental, Life, and Social Sciences

Institution: Oak Ridge National Laboratory

Date: _____

Identification No. ___

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: Committee on Human Studies
Oak Ridge Associated Universities
Oak Ridge National Laboratory

Date: September 21, 1993

Principal Investigator: Virginia H. Dale

In-plant mailing address: Ms 6038, Building 1505, ORNL

Telephone number: 6-8043 (fax 6-8646)

Co-investigators: Carolyn Hunsaker and Glenn Suter, Environmental Sciences Division, ORNL

Title of Project: Relating environmental indicators to societal values

Anticipated sponsor: U.S. Environmental Protection Agency

Estimated annual funding: $268,655 (first year)
$544,819 (two years)

I. Objectives of experiment

We propose to develop and test three alternative methods for conveying information about environmental indicators to members of the public (society) and for soliciting their rankings of combinations of those indicators that characterize different states of ecological systems. The particular systems and indicators used will be defined by our case-study region: the forests, surface waters, and integrated resources of the Southern Appalachian Man and Biosphere region. The data available for this region are extensive and include information on current status and some projections of changes over time for the Great Smoky Mountains National Park and for the Oak Ridge Reservation and surrounding counties.

II. Method of Procedure

a. Identification of Relevant Indicators and Other Variables for Data Collection

The examination of societal environmental values and the ways in which they can best be assessed requires identifying the relevant ecosystem indicators that best reflect these broader values and can be understood by the public and individual and research design characteristics that may influence the nature of responses. Decisions about elements within each of these categories that will be included in the data collection protocols will be guided

by several sources. These include reports of relevant research conducted to date, pertinent documents about the case study ecosystem, and interviews of knowledgeable individuals, and focus groups comprised of both members of the public and active stakeholders in environmental debates and decisions.

b. Development and pre-testing of data collection protocols

The major aim of our study is to examine the utility of three different data collection strategies (a mail questionnaire, a telephone survey, and a video-based in-person questionnaire) for collecting public valuations of the case study ecosystem conditions (Table 1). By keeping certain aspects of each constant (e.g., employing the same core set of questions) but manipulating the format, especially the use of visual information, and procedures for gathering the individual valuations, it should be possible to investigate the effects of these data collection modes on responses [e.g., whether supplementing pure word questions (as in the phone survey) with static images (as in the mail survey) alters the distribution of value rankings, results in a higher level of individual confidence in their assessments, and/or decreases the proportion of "don't know" responses]. These results, in turn, should identify which approach(es) for assessing public societal values appear most promising in any future EMAP efforts.

c. Development of data collection protocols

The findings from the previously described activities will be used to design three more formal protocols for data collection, each of which incorporates a distinct assessment strategy and methodology for obtaining public valuations. These are: (1) a telephone survey protocol that uses words to present the information (e.g., indicators and alternative system conditions), to pose questions, and to obtain responses and that will be administered to a probability sample of the target population; (2) a mail questionnaire that relies on both words and static images (e.g., graphs, drawings, and still photos) for distribution to another probability sample; and (3) a video and accompanying questionnaire that combine words, static illustrations, and moving images to be administered to a random sample of visitors to a shopping mall serving the target population, following the procedures used by Viscusi and his colleagues (e.g., Viscusi et al. (1991b).

Each protocol will cover the same domains, indicators, demographic, and other variables, sharing a standard core of questions for obtaining data on:

- The individual's assessment of the overall relative value of the respective ecosystem and its alternative conditions;
- The person's judged level of confidence in his/her responses to each of the above sections;
- Respondent evaluations regarding the ease of answering the survey items (e.g., their clarity), length of the survey, and any other aspects of the procedure about which they wish to comment; and

Table 1. Similarities and Differences in the Proposed Data Collection Strategies

Attribute	Telephone Survey	Mail Survey	Video Survey
Target population	Adult residents of a locale in the case-study region	Adult residents of a locale in the case-study region	Adult residents of a locale in the case-study region
Sampling frame	Published residential telephone directory listings (reverse telephone directory) for the appropriate geographic area, i.e., county	Published residential telephone directory listings (reverse telephone directory) for the appropriate geographic area, i.e., county	Visitors to a mall in the locale during specified time periods
Sampling strategy	Probability sample, using systematic sampling procedures	Probability sample, using systematic sampling procedures	Systematic sampling of visitors during randomly varied time periods and mall locations
Total *N* in sample	1,138	610	?
Expected completed protocols (*N*)	391	391	391
Protocol format	Words only	Words and static images	Words, static images, and sophisticated images and displays
Mode of recruitment	Prenotification letter followed by interviewer phone call	Mailed cover letter	Face-to-face request from a research staff person
Mode of administration	Interviewer-administered	Paper-and-pencil	Paper-and-pencil (after instructions from a research staff person)
Expected period required for actual data collection	4 weeks	8-10 weeks	4 weeks
Elements used in calculations of actual data collection cost (excludes professional time required for development of core items, data entry, and analysis costs	Sample selection Xeroxing, supplies, assembly, and postage for pre-notification letter Interviewer hiring, training, and supervision Interviewer pay Xeroxing of data collection protocols Phone lines and charges	Sample selection Xeroxing, supplies, assembly, and postage for cover letter Clerical staff for survey personalization techniques Xeroxing of data collection protocols and follow-up mailings Postage for initial mailing and follow-up mailings Research staff time for telephone follow-up request	Sample selection and recruitment by research staff Preparation of video Acquisition of video equipment Payment of research staff for recruitment and participant instructions Xeroxing of data collection protocols

- Selected demographic and other characteristics that may potentially affect responses (e.g., rural vs. urban residence, educational attainment, and previous exposure to the case-study ecosystem).

The study design will permit empirically-grounded comparisons of how the survey (especially the information transfer characteristics) contribute to the types and quality of data obtained.

d. Exemption

The study involves no human health risk and only minimal risks to individuals' well-being as described in the Committee's guidelines, "Assurance of Compliance with HHS Regulations for Protection of Human Research Subjects." The research described in the application is exempted from the DOE Policy for the Protection of Human Subjects, in accordance with 10 CFR Part 745 section 101 (a)(2), due to the protection of anonymity of the participants in the surveys used in the research.

III. Possible Hazards and their Evaluation

There are no potential human health hazards and only minimal risks of other kinds to human subjects associated with this project. Because this research is exempt from the DOE Policy on the Protection of Human Subjects, the requirement for informed consent does not apply, as given in the 10 CFR Part 745, section 116. The anonymity of participants is this study will be maintained, which is the central basis for exemption from the Policy for this research.

IV. Radioisotopes and New Drugs

The study involves no use of radioisotopes or drugs.

V. Responsibility of Principal Investigator

The principal investigator will follow, and will direct subcontractors to follow, the procedures of the Committee on Human Studies in conducting the research described in this application. The investigator recognizes that she retains the primary responsibility for safe-guarding the interests of the participants under study. Any significant changes in methods of procedure or the development of unexpected risks will be brought to the attention of the Committee immediately.

ORNL-28

ORAU/ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title:

Relating Ecological Indicators to Societal Values

Principal Investigator: Virginia Dale

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.	[signature]	X			11-10-93
2.					
3.	[signature]	✓			11/10/93
4.	[signature]	X			11.10.93
5.	[signature]	X			11/10/93
6.	[signature]	X			"
7.	[signature]	✓			"
8.					
9.					
10.					
11.					
12.					
13.					
14.					

Chairman's statement of Committee consensus:

Date

1048427

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title

Relating Ecological Indicators to Societal Values

2. Principal Investigator

Virginia H. Dale

Telephone Number

615-576-8043

Mailing Address — Include full name of performing institution.

Environmental Sciences Division, Oak Ridge National Laboratory,

P.O. Box 2008, Oak Ridge, TN 37831-6038

3. Institutional Assurance Number (if issued)[1]

4. Project Number[2]

ORNL- 28

5. Annual Funding:

Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☐ Actual Funding $ 268,655

☐ $10,000 ☐ $100,000 ☐ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources

A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

Contact Person

Telephone Number

B. Non-DOE Source

U.S. Environmental Protection Agency

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

1048428

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

☐ Full Board
For a list of research not requiring IRB review, see Attachment.

☒ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☒ New ☐ Annual Renewal ☐ Other

C. IRB Approval Date

9-28-93

8. This Project involves the following collaborating institutions (list a maximum of two):

Vanderbilt University

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. Type of Research

Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
- ☐ Using data collected directly from human subjects.
- ☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☐ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
- ☐ Specimens collected directly from human subjects for this project.
- ☐ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☐ Instrument development and testing using human subjects.

☐ Surveys that collect personally identifiable data.

☐ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☒ Other. Please identify Survey that collect data that cannot be identified to a person

1048429

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

We propose to develop and test three alternative methods for conveying information about environmental indicators to members of the public (society) and for soliciting their rankings of combinations of those indicators that characterize different states of ecological systems. The particular systems and indicators used will be defined by our case-study region: the forests, surface waters, and integrated resources of the Southern Appalachian Man and Biosphere region. Human subjects will be queried via phone, mail, and in-person surveys concerning environmental indicators. The identity of the persons surveyed will remain anonymous.

B. Specify the number of human subjects involved each year.

About 2,200 surveys will be distributed; we anticipate about 1,200 will be completed and returned.

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

Volunteer subjects will be asked to sign an informed consent form prior to participating in the survey. Information will be given to volunteers on the aquatic and terrestrial environment and environmental indicators. There is no risk to the persons involved in the survey.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

None used.

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year.	
Signature of Institution Official David E Reichle	**Date** 1/28/94
Printed or Typed Name David E. Reichle	**Telephone Number** (615)-574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ Accepted _____ ☐ Returned to Originator _____
Reason for Return	
DOE Reviewers	

1048431

Ident. No._____

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date _____

Principal Investigator: Stephen J. Kennel, Ph.D. (ORNL Biology)

Co-Investigators: Scott Robertson, Student (Cell & Molecular Biology Program, U. of TN)

Title of Project: MONOCLONAL ANTIBODIES TO VASCULAR ENDOTHELIUM OF RENAL CELL CARCINOMA

I. Objective of Experiment:

The objective of this study is to develop monoclonal antibodies (MAb) to blood vessels of renal carcinomas. It is hoped that some of these MAb will react selectively with tumor endothelium, providing a reagent for the specific targeting of cytotoxic agents to the tumor. Identification of the target molecules reacting with these MAb will extend our knowledge of the linings of blood vessels and their unique structure and functions at different anatomical sites.

II. Methods of Procedure:

Excess tissues from RCC patients, obtained during standard resection surgery, will be used in these studies. Extracts of membrane proteins from tumor tissue or from cultured human umbilical vein endothelial cells (from a commercial source) will be used to immunize mice in preparation for hybridoma production. Hybridomas producing MAb will be identified by ELISA on membrane protein preparations. Promising MAb will be tested in immunohistochemistry on frozen or fixed sections of human tissue. MAb reacting specifically with endothelium or tumor will be characterized further. Western blot and immunoprecipitation will be done on cell and tissue extracts to identify proteins for the MAbs.

III. Possible hazards and their evaluation:

These experiments will have no bearing on the patients' diagnosis or treatment. Only excess tissues obtained at standard surgery will be used and the patients will not be identified by name. Precautions will be taken when handling and disposing of tissue. Gloves and lab coats will be worn at all times tissue is present. Extracts will be done in a chemical exhaust hood and centrifugation in capped tubes. All waste materials will be bagged and autoclaved before disposal.

Title of Project: MONOCLONAL ANTIBODIES TO VASCULAR ENDOTHELIUM OF RENAL CELL CARCINOMA

Ident. No. _____

IV. Radioisotopes and New Drugs:

N/A

V. Responsibility of the Principal Investigator:

Patients will not be affected by this project and will not be identified by name. The main concern of the P.I. is the proper handling and disposal of tissue. Human samples will be treated as biohazardous materials. Gloves and lab coats will be worn and waste will be autoclaved in plastic bags before disposal. Any significant changes in these procedures will be brought to the attention of the Committee on Human Studies.

Starting Date: _____

Signatures: Stephen J. Kennel _____ Principal Investigator

_____ Co-Investigator

DIVISION REVIEW:

The application described above has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Official signing for the institution:

Signature _____

Title _____

Institution _____

Date _____

OAK RIDGE NATIONAL LABORATORY
MANAGED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.
FOR THE U.S. DEPARTMENT OF ENERGY

POST OFFICE BOX 2009
OAK RIDGE, TENNESSEE 37831

July 21, 1993

Dr. William Calhoun
Committee on Human Studies
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Dear Dr. Calhoun:

In 1988 I spoke with Dr. Lushbaugh about this project. He indicated that it qualified for a waiver from getting approval of the Committee since the subjects were not affected or identified by name. I am submitting this brief application to insure that under current rules our project meets with your approval. Please contact me if more information is needed.

Sincerely,

Stephen J. Kennel, Ph.D.
Biology Division

SJK:sa

Enclosure: Application

cc: File - RC

Idcnt. No._____

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities and
Oak Ridge National Laboratory

Date _____

Principal Investigator: Stephen J. Kennel, Ph.D. (ORNL Biology)

Co-Investigators: Scott Robertson, Student (Cell & Molecular Biology Program, U. of TN)

Title of Project: MONOCLONAL ANTIBODIES TO VASCULAR ENDOTHELIUM OF RENAL CELL CARCINOMA

I. Objective of Experiment:

The objective of this study is to develop monoclonal antibodies (MAb) to blood vessels of renal carcinomas. It is hoped that some of these MAb will react selectively with tumor endothelium, providing a reagent for the specific targeting of cytotoxic agents to the tumor. Identification of the target molecules reacting with these MAb will extend our knowledge of the linings of blood vessels and their unique structure and functions at different anatomical sites.

II. Methods of Procedure:

Excess tissues from RCC patients, obtained during standard resection surgery, will be used in these studies. Extracts of membrane proteins from tumor tissue or from cultured human umbilical vein endothelial cells (from a commercial source) will be used to immunize mice in preparation for hybridoma production. Hybridomas producing MAb will be identified by ELISA on membrane protein preparations. Promising MAb will be tested in immunohistochemistry on frozen or fixed sections of human tissue. MAb reacting specifically with endothelium or tumor will be characterized further. Western blot and immunoprecipitation will be done on cell and tissue extracts to identify proteins for the MAbs.

III. Possible hazards and their evaluation:

These experiments will have no bearing on the patients' diagnosis or treatment. Only excess tissues obtained at standard surgery will be used and the patients will not be identified by name. Precautions will be taken when handling and disposing of tissue. Gloves and lab coats will be worn at all times tissue is present. Extracts will be done in a chemical exhaust hood and centrifugation in capped tubes. All waste materials will be bagged and autoclaved before disposal.

Title of Project: MONOCLONAL ANTIBODIES TO VASCULAR ENDOTHELIUM OF RENAL CELL CARCINOMA

Ident. No. _____

IV. Radioisotopes and New Drugs:

N/A

V. Responsibility of the Principal Investigator:

Patients will not be affected by this project and will not be identified by name. The main concern of the P.I. is the proper handling and disposal of tissue. Human samples will be treated as biohazardous materials. Gloves and lab coats will be worn and waste will be autoclaved in plastic bags before disposal. Any significant changes in these procedures will be brought to the attention of the Committee on Human Studies.

Starting Date: _____

Signatures: Stephen J. Kennel _____ Principal Investigator

_____ Co-Investigator

DIVISION REVIEW:

The application described above has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Official signing for the institution:

Signature _____

Title _____

Institution _____

Date _____

ORNL-29

ORAU/ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title:

Monoclonal Antibodies to Vascular Endothelium of Renal Cell Carcinoma

Principal Investigator: Stephen J. Kennel, Ph.D.

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.	William Walker	✓			11-10-93
2.	Howard Frazier	✓			11/10/93
3.	Shirley A. Fry				11.10.93.
4.	Donna Davis	✓			11/10/93
5.	Melanie E. Evans	X			"
6.	Teaching Faculty	X			11/10/93
7.					
8.					
9.					
10.					
11.					
12.					
13.					
14.					

Chairman's statement of Committee consensus:

Date

1048437

ORISE
OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION
MEDICAL SCIENCES DIVISION

July 30, 1993

Stephen J. Kennel
ORNL
PO Box 2009
Oak Ridge, TN 37831

Dear Dr. Kennel,

I have reviewed your proposal titled "Monoclonal Antibodies to Vascular Endothelium of Renal Cell Carcinoma" and can approve the project by expedited review.

Please inform the Committee of any changes in protocol and file an annual report of progress and any untoward effects you have observed.

I wish you success on your research.

Sincerely,

William H. Calhoun

/sa

cc: Riveria

1048438

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title

Monoclonal Antibodies to Vascular Endothelium of Renal Cell Carcinoma

2. Principal Investigator

Stephen J. Kennel

Telephone Number

615-574-0825

Mailing Address — Include full name of performing institution.

P.O. Box 2009, Biology Division

Oak Ridge National Laboratory, Oak Ridge, TN 37831-8077

3. Institutional Assurance Number (if issued)[1]

4. Project Number[2]

ORNL-29

5. Annual Funding:

Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☐ Actual Funding $ 16,500

☐ $10,000 ☐ $100,000 ☐ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources

A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

Contact Person

Telephone Number

B. Non-DOE Source

Jewish Hospital, Cincinati, OH

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Pa.t 745.

A. Type of Review

☐ Full Board
For a list of research not requiring IRB review, see Attachment.

☒ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☒ New ☐ Annual Renewal ☐ Other

C. IRB Approval Date

November 30, 1993

8. This Project involves the following collaborating institutions (list a maximum of two):

University of Tennessee; Knoxville, TN

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. Type of Research
Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
- ☐ Using data collected directly from human subjects.
- ☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☐ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
- ☐ Specimens collected directly from human subjects for this project.
- ☐ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☐ Instrument development and testing using human subjects.

☐ Surveys that collect personally identifiable data.

☐ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☒ Other. Please identify Excess tissue samples from non-identified individuals from secondary sources

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

The objective of this study is to develop monoclonal antibodies (MAb) to blood vessels of renal carcinomas. It is hoped that some of these MAb will react selectively with tumor endothelium, providing a reagent for the specific targeting of cytotoxic agents to the tumor. Identification of the target molecules reacting with these MAb will extend our knowledge of the linings of blood vessels and their unique structure and functions at different anatomical sites.

Excess tissues from RCC patients, obtained during standard resection surgery, will be used in these studies. Extracts of membrane proteins from tumor tissue or from cultured human umbilical vein endothelial cells (from a commercial source) will be used to immunize mice in preparation for hybridoma production. Hybridomas producing MAb will be identified by ELISA on membrane protein preparations. Promising MAb will be tested in immunohistochemistry on frozen or fixed sections of human tissue. MAb reacting specifically with endothelium or tumor will be characterized further. Western blot and immunoprecipitation will be done on cell and tissue extracts to identify proteins for the MAbs.

B. Specify the number of human subjects involved each year.

10

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

Excess tissues obtained at surgery or autopsy are received from a secondary source. Individual patients are not identified.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

N/A

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year.	
Signature of Institution Official	**Date** January 25, 1994
Printed or Typed Name D. E. Reichle	**Telephone Number** (615)574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ **Accepted** _____ ☐ **Returned to Originator** _____
Reason for Return	
DOE Reviewers	

Identification No. ORNL-30

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

TO: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities (ORAU) and
Oak Ridge National Laboratory (ORNL)

Date: July 2, 1993

Principal Investigators: Jack C. Schryver, Ph.D. (ORNL) 4-4710; 6025 MS-6360

Co-Investigators: (none)

Title of Project: Investigation of Cognitive Workload Measurement Techniques

I. Objective of Experiment:

The objective is to identify techniques for cognitive workload measurement, develop criteria to evaluate these techniques, and perform an experiment to evaluate the techniques for measuring cognitive workload during tasks that require navigation through computer-based display networks. The workload measures to be compared include response latencies, errors, keystrokes/mouse clicks, and eye-gaze scan paths. The results will be used to provide recommendations for review of computer-based operator workstations.

II. Methods of Procedure:

About 12 subjects will participate in this study of cognitive workload metrics associated with navigating display networks. During the experimental trials, each subject will participate in a single session for 60-90 minutes. Subjects will be recruited from ORNL employee volunteers to include research staff and facility operators.

Each subject, tested separately in a private office, will sit in front of a Unix computer workstation. The subject's eye-gaze locations on the screen during the trial will be collected by a commercial, non-invasive eye-tracking system, as explained below. The camera from the eye-tracking system is not attached to the subject, and resides just under the computer display. The subject will rest his chin in a comfortable chin rest during these trials and will be asked to perform a series of simple tasks on the screen. On each trial, the subject will be requested to retrieve information from a computer display, navigate a display network with mouse clicks, and find a target display. The subjects will type in answers to questions based on the information in a pop-up window.

A calibration procedure for the eye-tracking system precedes the experimental trials described above. For this procedure, the subject places his chin in the chin rest to maintain a reasonably stationary head position, then looks into the infrared-sensitive eye-tracking camera with 75 mm lens. A computer-controlled sequence of circles presented on the display is then initiated. The subject fixates each of the 10 circles as they are displayed. The system repeats the calibration until a criterion accuracy is achieved.

III. Possible Hazards and Their Evaluation:

This study involves behavioral research with minimal risk to human subjects. Subjects will be tested individually in a private office environment, without invasive clinical procedures. Subjects will perform simple visual scanning and manipulation of windows at a workstation. This will be done in a self-paced manner, without stress. The procedure includes no deceptive or behavioral manipulations, and confidentiality will be ensured via numerical encoding of all subject identities.

The eye-tracking hardware, manufactured by LC Technologies, Fairfax, VA, uses a pupil-center/corneal-reflection algorithum to determine eye-gaze direction. A small, low-power, infrared light-emitting diode (LED) located at the center of the camera lens illuminates the pupil of the eye. The LED generates both a bright pupil for camera view enhancement and a corneally reflected light glint. The relative relationship of the glint to the modeled pupil is used by the computer software to infer gazepoint direction. The LED wavelength is 880 nm (near-infrared), and has a beam width of 20 degree beam width; the safety factor is 5. At a range of 15 inches, the LED illumination on the eye is 20% of the US Dept. of Health and Human Services maximum permissible exposure. The only noticeable effect of LED illumination is that prolonged exposure (i.e., several hours) sometimes dries the eye. In this study, subjects will be provided with several rest periods over the course of experimental testing. In addition, subjects will be instructed to take a break whenever they feel it is necessary, as the task is self-paced.

IV. Radioisotopes and New Drugs:

No materials of this kind are involved in this study.

V. Responsibility of Principal Investigators:

The principal investigators will follow the procedures of the Committee on Human Studies. The experimental protocol has minimal risk, and manipulation computer displays is an accepted daily occurrence in office work environments. The eye tracking procedure is well-accepted and non-invasive. Informed consent will be obtained from all participants, as shown in an attached sample form, which also contains the explanation of study.

The principal investigators recognize their primary responsibility for safe-guarding the interests of the participants under study. Significant changes in methods of this procedure, and development of unexpected risks will be brought to the attention of the Committee on Human Studies.

THE EYEGAZE™ DEVELOPMENT SYSTEM

A TOOL FOR HUMAN FACTORS APPLICATIONS

LC Technologies, Inc.

4415 Glenn Rose Street
Fairfax, Virginia 22032

(800) 733-5284
(703) 425-7509
FAX: (703) 323-4782

Engineering Physics and Mathematics Division
Oak Ridge National Laboratory

Explanation of Research Study and Informed Consent Form

Project: Investigation of Cognitive Workload Measurement Techniques

Principal Investigator: Jack C. Schryver, Ph.D. (574-4710)

Participant's Name: _____

Participant Number/ID: _____

EXPLANATION OF STUDY

Purpose of Study

The objective is to identify techniques for cognitive workload measurement, develop criteria to evaluate these techniques, and perform an experiment to evaluate the techniques for measuring cognitive workload during tasks that require navigation through computer-based display networks. The workload measures to be compared include response latencies, errors, keystrokes/mouse clicks, and eye-gaze scan paths. The results will be used to provide recommendations for review of computer-based operator workstations.

Study Procedure:

During the study, you will need to place your chin in a chin rest. This will ensure that the head is relatively steady. The study will include the following procedures:

1. Calibration to a workstation display to permit the eye-gaze hardware to accurately track your eye movements.

2. About 50 experimental trials will be conducted, during which you will view computer displays which resemble a safety parameter display system for a Pressurized Water Reactor. You will retrieve information from the display, and then navigate to a target display using the mouse. You will respond to questions regarding the information using keys on the computer keyboard.

ORISE
OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION

MEDICAL SCIENCES DIVISION

July 21, 1993

Jack D. Schryver, Ph.D.
ORNL
PO Box 2008
Oak Ridge, TN 37831

Dear Dr. Schryver,

I have reviewed your proposal and agree that it can be approved by expedited review.

Please file an annual progress report and notify the Committee if there are any changes in the protocol.

I wish you success on the project.

Sincerely,

William H. Calhoun,
Chair, Human Subjects Committee

/sa

cc: Riveria

1048447

APPROVAL SLIP

APPROVAL SEQUENCE
[Type in names. When routing does not apply, type NA on that line.]

		DATE
MEH by Id Ek	Typist/Telephone Marion E. Hall	07/02/93
	Proofreader/Telephone	
	Author Jack C. Schryver Jcs.	07/02/93
Id Ek	Supervisor H. E. Knee, Group Ldr.	07/02/93
RCM	Dept./Sect. Head Reinhold C. Mann	07/02/93
RCM for RCW	Div. Dir.(s) Robert C. Ward	07/02/93
	Prog. Dir.(s)	
	Fin. Off./Mgr.	
	Fin. & Mat. Div. Dir.	
	Adm. Serv. Dir.	
	Programmatic Assoc. Dir. Copy of Appleton	
	Associate Dir.	
	Deputy Dir.	
	Laboratory Dir.	

Commitment System No. _____ /Due Date _____

Delivered to Lab Records on _____ (Date)

For Issue on July 7, 1993 (Date of correspondence)

For Signature of David E. Reichle
[Flag document(s) on which final signature(s) is required.] (Committee Members)

Subject Investigation of Cognitive Workload Measurement Techniques

Type Style _____

* Information Copy to Divisional Assoc. Dir. sent by _____ (Name) on _____ (Date)

Dollar Level
This Increment _____
Cumulative _____

** Concurrence(s) received:

_____
_____
_____
_____
_____
_____

** Responsibility of division office to send copy to divisional Associate Director in conjunction with forwarding document to Programmatic Associate Director.*

*** Responsibility of "hold position" in concurrence sequence.*

Jack Schryver
#44710

UCN-11096
(3 11-90)

1048448

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

INSTITUTIONAL REVIEW AND APPROVAL

STARTING DATE: July 7, 1993 (OR AS SOON AS APPROVED)

SIGNATURE Jack C. Schuyler
Principal Investigator

DIVISION REVIEW:

THE APPLICATION DESCRIBED HEREIN HAS BEEN REVIEWED AND APPROVED FOR SUBMISSION TO THE ORAU/ORNL COMMITTEE ON HUMAN STUDIES.

SIGNATURE: RCW Reichard Ward for R.C. Ward

TITLE: Director, Engineering Physics and Mathematics Division

INSTITUTION: Oak Ridge National Laboratory

DATE: 7/2/93

INSTITUTIONAL APPROVAL:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

SIGNATURE: David E. Reichle

TITLE: Associate Director, Environmental, Life, and Social Sciences

INSTITUTION: Oak Ridge National Laboratory

DATE: _____

MARCH 12, 1993

Engineering Physics and Mathematics Division
Oak Ridge National Laboratory

Explanation of Research Study and Informed Consent Form

Project: Investigation of Cognitive Workload Measurement Techniques

Principal Investigator: Jack C. Schryver, Ph.D. (574-4710)

Participant's Name: _____

Participant Number/ID: _____

EXPLANATION OF STUDY

Purpose of Study

The objective is to identify techniques for cognitive workload measurement, develop criteria to evaluate these techniques, and perform an experiment to evaluate the techniques for measuring cognitive workload during tasks that require navigation through computer-based display networks. The workload measures to be compared include response latencies, errors, keystrokes/mouse clicks, and eye-gaze scan paths. The results will be used to provide recommendations for review of computer-based operator workstations.

Study Procedure:

During the study, you will need to place your chin in a chin rest. This will ensure that the head is relatively steady. The study will include the following procedures:

1. Calibration to a workstation display to permit the eye-gaze hardware to accurately track your eye movements.

2. About 50 experimental trials will be conducted, during which you will view computer displays which resemble a safety parameter display system for a Pressurized Water Reactor. You will retrieve information from the display, and then navigate to a target display using the mouse. You will respond to questions regarding the information using keys on the computer keyboard.

Study Duration:

The entire study will take from 60-90 minutes including instruction and practice. Several rest periods will be provided, but if you become fatigued at any time, you may stop and rest.

Discomforts, Inconveniences, or Risks:

A camera with a very low power infrared light source will be used to track your eye position during the experiment. Prolonged exposure to this may cause some dryness in your eyes. If your eyes feel dry, please notify the experimenter so the study may be paused.

Potential Benefits:

The study to determine the sensitivity and construct validity of various measures of cognitive workload while operators or users navigate a large display network. Ultimately, the results may allow new review procedures to be devised that will verify that computer display networks are not too difficult to use for operators. Following the study, you may contact either of the principal investigators for follow-up information and published results.

INFORMED CONSENT

The information on this form has been given to me to inform me about this research project and my participation in it. I have read it carefully, and all of my questions about the study, and its procedures, have been answered to my satisfaction.

I have been informed of the purpose of the study and the procedures involved. I understand that confidentiality will be ensured and that my name will not be associated with any results from this study. I understand that any information gained in this study becomes the property of ORNL and may be published in the scientific literature or used for other purposes which ORNL deems proper in the interest of education, knowledge, or research.

I am freely volunteering for this study. I understand that I may, at any time, withdraw from continued participation in this study without suffering any penalty or prejudice. I am freely and voluntarily choosing to participate.

Date:_____ Signature_____

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title
Investigation of Cognitive Workload Measurement Techniques

2. Principal Investigator
J. C. Schryver

Telephone Number
(615) 574-4710

Mailing Address — Include full name of performing institution.
Oak Ridge National Laboratory, Bldg. 6025, Mail Stop 6360

P. O. Box 2008, Oak Ridge, TN 37831

3. Institutional Assurance Number (if issued)[1]

4. Project Number[2]
ORNL-30

5. Annual Funding:
Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☒ Actual Funding $ 43,000

☐ $10,000 ☐ $100,000 ☐ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources
A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

Contact Person

Telephone Number

B. Non-DOE Source
U. S. Nuclear Regulatory Commission
Office of Nuclear Regulatory Research, Human Factors Branch

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

7. **The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.**

A. **Type of Review**

☐ Full Board
For a list of research not requiring IRB review, see Attachment.

☒ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. **Type of Approval**

☒ New ☐ Annual Renewal ☐ Other

C. **IRB Approval Date**

July 21, 1993

8. **This Project involves the following collaborating institutions (list a maximum of two):**

9. **Vulnerable Populations**

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. **Type of Research**
Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
- ☐ Using data collected directly from human subjects.
- ☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☐ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
- ☐ Specimens collected directly from human subjects for this project.
- ☐ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☐ Instrument development and testing using human subjects.

☐ Surveys that collect personally identifiable data.

☐ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☐ Other. Please identify _____

1048453

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

The objective of this research was to validate proposed cognitive workload metrics for regulatory review of display navigation tasks which may be performed in advanced digital control rooms. All human subjects testing occurred while the participants were seated before a computer workstation monitor. The participants performed an eyetracker calibration procedure with the head supported in a chin rest. The participants were given instructions and briefed on all aspects of the procedure. After performing a few practice trials, the participants completed approximately 50 test trials. The trials involved repetitive problem-solving tasks at the workstation. For example, a pop-up task window requested the participant to monitor data on the underlying window, and then navigate through a display network to a target window. Questions regarding the monitored data were then answered in a pop-up response window. All participants were debriefed. Experimental sessions were approximately 90 minutes in duration.

B. Specify the number of human subjects involved each year.

Seven human subjects participated during FY-1994

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

The participants completed tasks at a computer workstation while their performance was recorded. The tasks were not significantly different from those ordinarily performed by office workers on computers. Eye movements were recorded by an Eye-Gaze System marketed by LC Technologies, Inc. of Fairfax, VA. The eyetracker utilized an infrared LED sourced mounted on a camera lens to illuminate the pupil and generate a corneal glint. These phenomena were detected and utilized by the eye tracker to calculate eye-gaze point-of regard. The amount of infrared illumination on the eye at a range of 15 inches is 20% of the HEW maximum permissible exposure according to vendor performance specifications.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

NA

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year	
Signature of Institution Official David E. Reichle	**Date** Jan. 25, 1994
Printed or Typed Name David E. Reichle	**Telephone Number** (615) 574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ **Accepted** _____ ☐ **Returned to Originator** _____
Reason for Return	
DOE Reviewers	

Identification No. ORNL-31

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

To: COMMITTEE ON HUMAN STUDIES
Oak Ridge Associated Universities
Oak Ridge National Laboratory

Date: _____

Principal Investigator: Lee M. Hively (Engineering Technology)

In-plant mailing address: K-1225, MS 7294

Telephone number: 615-574-7188

Co-Investigator(s) (Affiliation): N. E. Clapp (Instrumentation & Controls)

C. S. Daw (Engineering Technology)

W. F. Lawkins (Engineering Physics & Math)

Title of Project: Chaos Analysis of EEG Data

Anticipated Sponsor: ORNL Seed Money

Estimated Annual Funding (Current FY): $90K

I. Objective of Experiment:
Include statement why experiment must be done using human subjects, and describe the expected benefits from the knowledge.

Human EEG data must be analyzed to find the onset of epileptic seizures.

II. Methods of Procedure:
Briefly describe methods, all medications including name and dose range, number and types subjects anticipated, time for single session, total number of sessions, total duration of study, methods used to screen subjects, etc. Describe where the work will be done, including collaborative arrangements. Indicate if work will de done by subcontractor to ORNL. Indicate here if you consider your research to meet the requirements for exemptions.

Existing clinical data for 12 patients (2 non-seizure, 10 seizure) will be procured from St. Mary's Medical Foundation, and analyzed via chaos tools. This work meets the exemption requirements.

III. Possible Hazards and their Evaluation:
None (see Attachment for details)

IV. Radioisotopes and New Drugs:
If the study involves radioisotopes, indicate action of the Isotopes Committee. If new drugs are involved, indicate that appropriate application to FDA has been made.

None (see Attachment for details)

V. Responsibility of Principal Investigator:
Include statement of your procedures for protecting rights of the patients and for gaining informed consent.

Standard protocols will be used to assure patient anonymity. Release of this data is covered by existing St. Mary's patient release forms. A counterpart Human Studies application has been approved at St. Mary's Medical Center.

1048456

APPLICATION FOR THE USE OF HUMANS AS EXPERIMENTAL SUBJECTS

INSTITUTIONAL REVIEW AND APPROVAL

PROJECT TITLE: Chaos Analysis of EEG Data

IDENTIFICATION NO.: _____

STARTING DATE: December 1, 1993

The principal investigator will follow the procedures of the Committee on Human Studies in obtaining "informed consent" from the subjects under study. The investigator recognizes acceptance of primary responsibility for safe-guarding the interests of the participants under study. The investigator is responsible for notifying the ORAU/ORNL Committee on Human Studies of any significant changes in methods of procedure or of the development of unexpected risks.

SIGNATURES: Lee M. Hively — Lee M. Hively — 12/17/93
Principal Investigator — Date

N. E. Clapp — N. E. Clapp — 12/20/93
C. S. Daw — C. S. Daw — 12/20/93
W. F. Lawkins — W. F. Lawkins — 12/20/93
Co-Principal Investigator(s) — Date

DIVISION REVIEW:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: John E. Jones Jr.
Title: Director, Engineering Technology Div.
Institution: Oak Ridge National Laboratory
Date: 12/17/93

INSTITUTIONAL APPROVAL:

The application described herein has been reviewed and approved for submission to the ORAU/ORNL Committee on Human Studies.

Signature: David E. Reichle
David E. Reichle
Title: Associate Director, Environmental, Life, and Social Science
Institution: Oak Ridge National Laboratory
Date: 12/20/93

NEW IDEA QUESTIONNAIRE
SEED MONEY FUND
LABORATORY DIRECTED RESEARCH AND DEVELOPMENT PROGRAM

Initiator's Name Lee M. Hively Phone 574-7188

Building K-1225 Mailstop 7294 Division Engineering Technology

Project Title: Chaos Analysis of Electroencephalogram (EEG) Data for Epilepsy Detection

Brief Summary

The DOE Office of Health and Environmental Research and the Office of Naval Research have expressed recent interest in brain research. We propose to apply nonlinear dynamics analysis to electroencephalogram data as a direct indication of brain function for detection of epileptic seizures. Three ORNL divisions (Engineering Technology, Engineering Physics and Mathematics, and Instrumentation and Controls) and St. Mary's NeuroScience Center will collaborate to:

(1) acquire, screen, and digitize EEG data,
(2) graphically and numerically analyze the data for seizure detection, and
(3) document the work as publications and conference papers.

Does your Division Directory agree with the development of the idea in your Division? Yes
Does the proposed work conform with criteria in the ORNL guidelines for Seed Money Fund? Yes
Does your Division have programmatic funding for which this request could be considered a supplement or substitution? No

Author Signature(s) Lee M Hively Badge No. 26906

Principle Division Director's Signature John E. Jones Jr

What other Division(s) are involved in development of the idea? EPM and I&C

Supporting Division Directors' Signature(s) R Ward

Do any environment, safety, and health aspects of this proposal require special review? No

Describe the status of any Technology actions, e.g., invention disclosure, patent application, patent waiver request (planned, submitted, or granted), etc. None

Give amount of money requested. (Include no Laboratory overhead) $120K

Identify the DOE offices or other agencies that may supply future program support.

DOE/OHER, per letter from John C. Wooley to David Reichle (dated 16 June 1993)

Office of Naval Research, per private communication from Mike Shlessinger to Lee Hively (8/9/93)

Submit 18 copies of the completed questionnaire with your proposal attached to the Laboratory Directed R&D Manager, Office of Planning and Management, Building 4500N, Rm 1205P, Mailstop 6251. Send a copy to each Division Director listed above.

BACKGROUND

The theory of chaotic nonlinear dynamics provides a basis for understanding and potentially controlling many complex physical and engineering systems. In particular, brain waves exhibit seemingly random, unpredictable behavior, that is characteristic of deterministic chaos [1]. This proposed research will analyze human neurophysiological functions from a chaos perspective with a long term goal of advanced clinical diagnostic/treatment techniques for brain pathologies. Examples of such disorders include sleep abnormalities, brain injury, stroke, cognition problems (memory, speaking, writing), and dementia. This proposal addresses epilepsy via chaos analysis of EEG data to characterize seizure precursors which present techniques cannot detect.

ORNL staff members have actively developed and applied chaotic time-series diagnostic tools to engineering processes for several years. Indeed, ORNL work has provided leadership in translating theoretical concepts into technology applications. Simultaneously, Dr. Michael Eisenstadt and colleagues at St. Mary's Neuroscience Center (NSC) have created a substantial database of EEG measurements while caring for many patients with neurophysiological disorders. The proposed work will build a collaboration between these two groups, combining the capabilities at St. Mary's (biomedical laboratory facilities, EEG and related diagnostic instrumentation and measurement database, knowledge of neurophysiological function and disorders) and ORNL (chaos theory, data analysis and modelling, chaos control techniques). Dr. Eisenstadt is eager to build a collaboration with ORNL by providing medical expertise, access to biomedical facilities, and EEG data for this project.

We believe that good prospects exist for future funding of this (and related) work. The DOE Office of Health and Environmental Research recently solicited suggestions from ORNL for a Federal initiative on brain research. The Office of Naval Research is interested in chaos analysis of the brain for robotics applications. This proposed research may provide the framework for a practical, real-time, non-intrusive monitoring for epileptic seizure onset and for effects of stress, drug abuse and aging in key workers. These prospects are discussed further below.

The goals of this research are to: (1) demonstrate that EEG data can be meaningfully analyzed via chaotic time-series methods, (2) develop a nonlinear dynamic characterization of the transition from normal to abnormal neurophysiological function during an epileptic seizure, and (3) determine abnormality precursor(s) that are detectable by a practical out-patient sensor. The first goal is very generic and is valuable for the application of chaos tools to advanced diagnostics for other neurological disorders. The second goal is discussed under Task 2. The third goal is addressed in the last section of this proposal.

RESEARCH TASKS

We propose a focussed application of chaos analysis of electroencephalogram (EEG) data as a direct indication of brain function. Present techniques do not access all of the information in EEG signals, so more powerful tools are needed. Analysis tools for chaotic processes over time (chaotic time-series analysis) are appropriate because normal brain waves show strong evidence of chaos [1]. An important objective of this proposal is development of tools for systematic analysis of chaotic structure to distinguish normal function from epilepsy. Also, these tools must cope with the noisy data that is typical in biomedical diagnostics. The proposed work involves (1) acquisition, screening, and digitization of biomedical data with existing equipment, (2) graphical and numerical analysis of the data, and (3) documentation of the work as publications and conference presentations. These tasks are described more fully below.

Task 1: Data acquisition and digitization

Our collaborators at St. Mary's Neuroscience Center have an extensive library of 16-channel, analog EEG data on VHS tapes. Typically, the data are recorded during long periods of normal neurophysiological function and have been carefully indexed by patient for artifacts. Representative data will be characterized for 'normal' neurophysiological function, as a baseline for identifying epileptic seizures and associated precursors. We note that this latter (abnormal) data constitutes only a small fraction of the total. ORNL will work with the Neuroscience Center to screen the data from this library and digitize selected segments for detailed analysis, as well as to acquire and digitize new data from patients as appropriate. Data screening also will involve a data quality assessment (e.g., minimal noise and availability of all 16 data channels). Automated (computerized) techniques will be studied for data screening. Dr. Eisenstadt will provide the medical expertise for this task; see Attachment 1 for more details. The product of this task will be carefully documented, representative segments of multichannel EEG data for detailed nonlinear analysis under Task 2.

Task 2: Nonlinear dynamical analysis of data

The proposed work will build on our extensive experience in chaos analysis of scalar, time-series data. The 16-channel data from Task 1 contains information about the temporal evolution of neurophysiological dynamics at different spatial locations. Relative to previous work (e.g., Ref. 1), examination of the spatio-temporal data will be a unique feature of this research. In fact, spatio-temporal analysis is an important new problem in chaos research.

Existing computational tools will be extended appropriately to analyze the spatio-temporal data graphically and quantitatively for its nonlinear dynamical structure. We foresee a straight-forward software implementation of improved algorithms.

The first goal of this task is quantitative characterization of normal EEG signals which appear as chaotic and spatially uncorrelated brain waves. At the other extreme, we also will characterize epileptic seizures which appear as periodic and spatially correlated brain waves. The second goal of this task involves quantitative characterization of the transition from normal (chaotic) state to an epileptic seizure (periodic) state. We anticipate that this second goal will require detailed analysis of the evolution of the correlation between spatially separated data channels. Alternatively, the transition might be viewed as an evolution from higher dimensional chaotic dynamics to lower dimensional chaos or to periodicity. The third goal involves the earliest possible detection of this chaotic-to-periodic change for seizure mitigation and treatment, for which we will identify key parameter(s) that are most sensitive to the transition onset.

Examples of the chaos analysis techniques [4-9] include: time-delay embedding; phase-space reconstruction; mutual information; singular value decomposition for principle components analysis; nearest-neighbor dimension; correlation dimension; correlation integral; Kolmogorov entropy; Lyapunov spectrum; noise filtering; and Poincaré return map. Various analyses are possible with these techniques to achieve the goals of the proposal. For example, if brain chaos is dissipative (non-energy-conserving), then the number of dominant degrees-of-freedom (e.g., as determined by the principle components analysis of Broomhead and King [2]) may be low, even if the chaos dimensionality of the full system is much larger. Characterization of the dominant degrees of freedom is an important component of the first goal of the proposed research. Another example is construction of a Poincaré return map during chaotic-to-periodic transition as the intersection of the chaotic orbit with an appropriate multi-dimensional plane

surface. This analysis may identify unstable periodic orbit(s) in the chaotic state, which become stable during seizure (periodic) state.

Task 3: Documentation of the Work

This task will document the work in technical publications and conference presentations. We will provide lucid textual descriptions and graphical (video if possible) displays of the work as a basis for seeking further work for ORNL.

IMPLEMENTATION, COSTS, and PERSONNEL

The proposed work will provide methodologies implemented via computer software and hardware for expert analysts' use on existing PCs, workstations, and high-performance computers, as appropriate, with corresponding documentation. Work will begin immediately after approval of this proposal. We expect to further utilize existing collaborations with University of Tennessee/Knoxville (Ke Nguyen), University of California at San Diego (Henry Abarbanel), University of Maryland (Ed Ott, Celso Gebogi, James Yorke), and Delft University/Netherlands (Prof. Takens). Literature searches can be performed through the ORNL library system. The costs and personnel for FY1994 are shown in Table 1. The cost for Dr. Eisenstadt is for screening and selection of data under Task 1. Deliverables include algorithms, computer software, as well as technical reports and publications documenting the work. Task leaders are indicated by asterisks; Dr. L.M. Hively is the principal investigator.

FOLLOW-ON FUNDING

As noted on the title page, John Wooley (DOE Office of Health and Environmental Research) sent a request to David Reichle on 16 June 1993, asking for brain research ideas. DOE is part of a federal initiative to understand the human brain and nervous system, and to treat its diseases. The federal sponsors of this initiative desire to support new research on anatomical and physiological mapping of the human brain and nervous system via real time physiological monitors, advanced computers, and modeling. Federal interest is motivated by a rising incidence in neurological and behavioral diseases, due to aging, drug abuse, and neuropathic involvement in other ailments such as AIDS. See Attachment 2 for details.

The Office of Naval Research has funded nonlinear dynamics research for many years, including chaos analysis, synchronization of chaotic systems, and control of chaos. Mike Shlessinger (a Program Manager at ONR) informed Lee Hively that one of their current interests is chaos in biological systems. Brain research is particularly interesting to ONR for robotics applications.

While the proposed research involves sophisticated computationally-intensive analysis, simplified methods might be developed for real-time analysis and seizure detection. A practical, out-patient implementation might be a hat or pair of glasses with biomedical sensors and a programmable computer chip that would alert a person to the onset of an epileptic seizure. The person then could stop any critical task (e.g., driving a vehicle) and request help or take medication. This type of diagnostic also might provide real-time, non-intrusive monitoring of key workers for extreme stress, drug abuse, or aging. A more advanced product might allow medical intervention into brain pathology via chaos control techniques [10-11].

Dr. Eisenstadt has provided strong input to this proposal and wants to participate directly in Tasks 2 and 3 (without financial support form ORNL) of the proposed work. Based on his many

Attachment 2

Department of Energy

Washington, DC 20585

JUN 1 6 1993

Dr. David Reichle
Oak Ridge National Laboratory
P.O. Box 2008
Oak Ridge, TN 37831

Dear Dr. Reichle:

In the past few years, the Federal Government and the Department of Energy (DOE) have developed an increasing interest in seeking new and innovative ways to apply the rapidly advancing computer and modelling technologies to understanding the human brain. The interest was sparked by rapid technological advances and a rising incidence of neurological and behavioral diseases affecting millions of people. The rising incidence results from several factors, including the changing demographics of an aging population, drug abuse, and increasing occurrences of neuropathic involvement in diseases such as AIDS.

The Federal interest in understanding the brain and behavior led President Bush to declare the 1990s the "Decade of the Brain." Rapid scientific advancements coupled with that declaration led to the formation of an interagency committee on brain and behavior that issued a report entitled, "Maximizing Human Potential." Following that report, a smaller group of scientists from several Federal agencies agreed to form an informal consortium with a more focused goal of supporting new research efforts aimed at mapping the anatomical and physiological aspects of the human brain.

For decades, the Office of Health and Environmental Research (OHER) has sponsored research to develop new radiological and other advanced technologies to study, treat, and understand diseases of the brain and nervous system. During this period, various other DOE Offices have sponsored development of high technologies, such as real time physiological monitors, powerful computers and complex computer models, networks, and so on. But, altering priorities of the past and meeting the needs of the future require change and creativity. OHER would like to help the Department benefit from these changes. To do this, OHER is exploring the question as to whether its resources, technologies, and research potential can be brought together in new and creative ways to help understand the brain and its diseases.

Attachment 2

By this letter, OHER is asking you and your colleagues in fields such as those named above, to give this question serious consideration. Please discuss the issues among yourselves and, with scientists in the relevant disciplines, and with your colleagues in other laboratories. Let OHER know if you are interested in participating in this exploration and ask your collcagues to do the same. After hearing from all interested parties, we will decide the next step. This may include holding an informal meeting or a conference to exchange ideas and to develop future directions. If you are interested in joining OHER's quest for finding new and exciting ways to bring high technology and brain research together to address very difficult national problems, write to James R. Beall, ER-72, U.S. Department of Energy (GTN), Washington, D.C. 20585 or call (301)-903-4507.

Sincerely,

John C. Wooley

John C. Wooley
Deputy Associate Director
Health and Environmental Research
Office of Energy Research

Marta – I copy for your file per your request. –
Lee Hively
1.3.94

OAK RIDGE NATIONAL LABORATORY
MANAGED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.

POST OFFICE BOX 2003
OAK RIDGE, TENNESSEE 37831

December 30, 1993

Dr. William H. Calhoun
Professor, Psychology
312 D Austin Peay Building
855 West Woodchase
Knoxville, TN 37922

Dear Professor Calhoun:

Please find enclosed a copy of our application for Human Studies Review. If you require any further information to complete the review, please call me at 615-574-7188.

Sincerely,

Lee M. Hively

LMH:jbe

Enclosure: Application for Human Studies Review

1048464

If you have any questions about this research project, don't hesitate to call (615)-545-7539,or (615)-545-7527. We'll be happy to find answers for you. We are looking forward to your participation in this research, as we feel it may be of great importance.

The EEG data we want to use is already recorded on tape, so it will not be necessary for you to return to St. Mary's for us to do any further tests. Your name and picture will not be used. Your help is very important to the success of the project. Thank you in advance if you agree to participate.

Please, sign the enclosed consent form in the presence of an adult and have that adult sign on the line that reads "witness." This form may be witnessed by a family member, guardian, or other adult.

Sincerely,

Walter W. Holland, R.EEG T.

1048465

St. Mary's

St. Mary's Medical Center, Inc.
900 E. Oak Hill Avenue
Knoxville, Tennessee 37917-4556
615-971-6011

Neurodiagnostic Department

We are starting a research project dealing with epileptic seizures. We would like to use your EEG data in this important research effort and would appreciate your permission to do so. Your name and image will not be used. Please sign the attached consent form and mail it to the Neurodiagnostic Center at your earliest convenience. We feel that this project may lead to advances in the diagnosis of seizures. Your cooperation in this effort is very much appreciated.

Sincerely,

Michael L. Eisenstadt, M.D., Ph.D.

1048466

FAX COVER SHEET

To: Prof. Willaim Calhoun 974-3423
Department of Psychology 974-3330 fax
University of Tennesse, Knoxville, Tn

From: Dr. Lee M. Hively 574-7188
Engineering Technology Division, ORNL 574-8481 fax
Oak Ridge, Tn

cc: Marta Rivera 576-3480
Oak Ridge Associated Universities 576-7903 fax
Oak Ridge, Tn

Lee M. Hively

Date: 24 January 1994

Number of pages: 4 (including cover sheet)

The answers to your questions are as follows:

1) Patient identity will be preserved by St. Mary's Medical Center, which will identify each data set by a number. All references to the data set will be by number only.

2) The patients were informed of the use of their EEG data by St. Mary's Medical Center. Copies of the cover letters and an unsigned release form (signed by each patient whose data is to be used) are enclosed.

Please call Lee Hively (574-7188) about any questions. - Thanks.

Neurodiagnostic Department

I_____hereby give permission to the Neurodiagnostic Department at St. Mary's Medical Center to use Video Tape for medical purposes and the electroencephalogram (EEG) data for scientific research purposes.

_____
Signature

_____
Witness

_____
Date

1048468

Oak Ridge Associated Universities
Post Office Box 117
Oak Ridge, Tennessee 37831-0117

January 24, 1994

Lee M. Hively
K-1221, MS 7294
Oak Ridge National Laboratory
Oak Ridge, TN 37831

Dear Dr. Hively:

I have reviewed your proposal for the analysis of EEG data using chaotic time-series methods. I will ask Marta Rivera to assign your project an I. D. number, and ask that you use that number in future communications about your project. Your project seems to fit the category of projects which are exempt from review under 45 CFR 46 as follows: " Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects." Yet, I will need some additional information for the Committee.

It is not clear from your proposal how you plan to identify "subjects" to be included in your study. I assume you are using archival data maintained by St. Mary's Neuroscience Laboratory. There are two things you need to add to your proposal: (1) assurances that the persons from whom the EEG's were originally collected are aware that their data will be used by researchers, and how informed consent was obtained from those persons, and (2) how you will ensure that the identify of the persons will be protected.

I believe you can satisfy point 1 by providing the Committee with a copy of the standard consent forms patients sign before the EEG's are recorded. It is standard practice for any hospital or laboratory to collect such approval. The second point merely reflects the need to ensure that no persons will be identified by name.

If you provide this information, your project is approved. You are expected to keep the Committee informed of any changes in protocol and to file an annual report of progress on the project. If you discontinue the project, please let me know.

I wish you success with your research.

Sincerely,

William H. Calhoun, Chair
ORAU/ORNL Committee on Human Subjects

1048469

Marta – I copy for your files per your request –
Lee Hively
1.3.94

OAK RIDGE NATIONAL LABORATORY
MANAGED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.

POST OFFICE BOX 2003
OAK RIDGE, TENNESSEE 37831

December 30, 1993

Dr. William H. Calhoun
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312 D Austin Peay Building
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Dear Professor Calhoun:

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Sincerely,

Lee M Hively

Lee M. Hively

LMH:jbe

Enclosure: Application for Human Studies Review

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

Directions: Institutions must complete this form, providing the data listed below in the format indicated, for each research activity each year. Forms must be sent to the appropriate DOE Field Office, which will forward them to DOE Headquarters (Protection of Human Subjects, Mail Station ER-70, Office of Health and Environmental Research, U.S. Department of Energy, Washington, DC 20585).

1. Project Title

Chaos Analysis of EEG Data for Epilepsy Detection

2. Principal Investigator

Dr. Lee M. Hively

Telephone Number

615-574-7188

Mailing Address — Include full name of performing institution.

Oak Ridge National Laboratory, P. O. Box 2003

Oak Ridge, TN 37831-7294

3. Institutional Assurance Number (If issued)[1]

4. Project Number[2]

3210-0502 ORNL-31

5. Annual Funding:

Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☒ Actual Funding $ 120,000

☐ $10,000 ☐ $100,000 ☐ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources

A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

	Contact Person	Telephone Number

B. Non-DOE Source

ORNL Seed Money (Mark Reeves, Manager 574-4174)

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

☐ Full Board
For a list of research not requiring IRB review, see Attachment.

☐ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☐ New ☐ Annual Renewal ☒ Other Exempt (Category 4)

C. IRB Approval Date

8. This Project involves the following collaborating institutions (list a maximum of two):

St. Mary's Medical Center, Knoxville, TN

University of Tennessee, Knoxville, TN

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. Type of Research
Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
☐ Using data collected directly from human subjects.
☒ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☐ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
☐ Specimens collected directly from human subjects for this project.
☐ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☐ Instrument development and testing using human subjects.

☐ Surveys that collect personally identifiable data.

☐ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☐ Other. Please identify _____

1048472

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

Existing electroencephalogram (EEG) data is analyzed via nonlinear dynamics tools as a direct indication of brain function for detection of epileptic seizure onset. The tasks are:

(1) screen and digitize EEG data,
(2) graphically and numerically analyze the data for seizure onset detection, and
(3) document the work as publications and conference papers.

Only existing electroenchepalogram data is used, for which no risk exists. Therefore this project belongs in the exempt category.

B. Specify the number of human subjects involved each year.

12

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

Only existing electroenchephalogram data is used, for which no risk exists.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

Not applicable

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year.	
Signature of Institution Official	**Date** 1/25/94
Printed or Typed Name Dr. David E. Reichle	**Telephone Number** 615-574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ Accepted _____ ☐ Returned to Originator _____
Reason for Return	
DOE Reviewers	

STATEMENT OF WORK

for

PHYSIOLOGICAL RESPONSES OF ELECTRIC AND MAGNETIC FIELDS IN HUMANS

The contractor shall furnish personnel, facilities, equipment, materials, supplies and services necessary to conduct the following research.

TASK 1 60-Hz EMF Effects on Cardiovascular Activity : Analysis and Integration

Subtask 1.1

Conduct appropriate statistical analysis of the data obtained in the recent study sponsored by the U.S. Department of Energy investigating the effects of intermittent exposures on the heart rate of human subjects.

Parameters measured in this study, and which are to be statistically analyzed, include: cardiac interbeat interval, pulse transit times, FFT of the heart period, blood pressure, alertness ratings, electrocardiogram, arterial oxygen saturation, sinus arrhythmia, and vital signs. Other measures including respiratory parameters and non-linear dynamics of heart rate may be analyzed as deemed appropriate by the investigators.

Subtask 1.2

Integrate the finding from the analysis of the recent study with data from other completed studies at Midwest Research Institute.

Subtask 1.3

Evaluate the significance and implications of the individual and combined studies at Midwest Research Institute with particular emphasis on:

- dose-response relationships
- relevant exposure parameters
- mechanisms of any observed effects.

Subtask 1.4

Review the interpretations derived from the evaluations in Subtask 1.3 with other scientists and with the DOE quality control team for consensus regarding the conclusions.

Subtask 1.5

Prepare recommendations for future research on the basis of findings to date and submit to the ORNL project manager.

Subtask 1.6

Prepare a comprehensive report in protomanuscript format for review by the ORNL project manager and for submission for publication in the peer-reviewed scientific literature.

TASK 2 60-HZ EMF Effects on Electrophysiological Measures of Brain Activity and Function : Relevant Exposure Characteristics and Dose-Response Relationships.

Subtask 2.1

Conduct two studies using a common intermittent exposure protocol based on evaluation of previously obtained data. In each study 18 male and 18 female volunteer human subjects shall be randomly assigned to three conditions:

200 mG rotating magnetic field exposure
100 mG rotating magnetic field exposure
sham (no field) exposure

Each test session shall consist of at least three periods:

45 minutes pre-exposure period
45 minutes of exposure at the assigned level
45 minutes post exposure period

Electroencephalographic (EEG) data shall be collected in the last 30 minutes of each test period. All sessions shall be conducted in the double-blind mode.

Prior to initiation of this series representatives of the National Institute of Standards and Technology shall verify field levels and uniformity in the exposure facility.

All sessions shall be conducted in accordance with NIH guidelines for the use of human subjects and as approved by both the Midwest Research Institute and the ORNL committees on the use of human subjects.

Subtask 2.1.1

Study 1 - Investigate 60-Hz EMF Effects on Sensory Function and EEG Power Spectra.

The following parameters shall be investigated in this study using standard procedures for recording EEG activity from head sites as defined by the International 10-20 electrode placement system.

- Brain Stem Auditory Evoked Potential. The seven distinct components within the BASEP waveform derived from the EEG allows noninvasive measurement of EMF effects on the auditory system.

- Pattern Reversal Visual Evoked Potential. This widely used technique is a measure of the integrity of the visual system.

- Somatosensory Evoked Potential. SEP will be elicited by presenting brief pneumatic pressure stimuli to the finger tips. Data can be used to differentiate peripheral from central effects within the somatosensory system.

- EEG Power Spectra. Spectral analysis provides information about the bioelectric characteristics of the resting brain. Fast Fourier Transformation Analysis will be performed on the EEG data.

Subtask 2.1.2

Study 2 - Investigate 60-Hz EMF Effects on Cognitive EEG Activity and Performance.

The following parameters shall be investigated in this study using the same recording procedures as in Study 1.

- Auditory Evoked Potential. This widely used and standardized paradigm provides both physiological and performance data.

- Contingent Negative Variation. This is a measure of how the central nervous system prepares to respond to stimuli.

- Visual/Spatial Memory Task. This is an analogy to the radial arm maze technique used in animal studies and is a test of short term memory.

- Time Estimation Task. This is a computerized time estimation technique similar to the DRL task used in animal experiments.

TASK 3 Reporting and Deliverables

Subtask 3.1

Detailed, informative task progress reports shall be prepared and submitted to the ORNL project manager early in the 2nd, 3rd and 4th quarters of the contract year presenting progress, problems, etc., for the respective preceding quarters.

Subtask 3.2

A draft final report in protomanuscript format shall be prepared and submitted to the ORNL project manager for review and shall be submitted for publication in the peer-reviewed scientific literature. Two reports shall be prepared:

- Results of Task 1
- Results of Task 2

Subtask 3.3

Investigators shall prepare and present appropriate reports at scientific meetings; for example, the Bioelectromagnetics Society, FASEB, Annual Review of Power Frequency Research, etc. The ORNL program manager shall review the submissions.

ORISE
OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION
MEDICAL SCIENCES DIVISION

May 13, 1993

Paul C. Gailey
Program Manager
ORNL Electric and Magnetic Fields
Research Program

Dear Dr. Gailey:

I have reviewed the materials you submitted. It is clear that the Midwest Research Institute (MRI) understands the procedures to ensure safety of human subjects used in research. I believe all you need for ORNL to be in compliance with our Committee is to inform us of the research you actually undertake. This information should contain dates, numbers of subjects, and any outward observations.

If you plan to conduct such research locally, a compliance procedure patterned after MRI's would be needed.

I do not expect there will be any delays in your receiving expedited review of such proposals.

I trust this is satisfactory for your purposes.

Sincerely,

William H. Calhoun, Chair
ORAU Human Subjects Committee

/sa

cc: Marta Riveria

P. O. BOX 117, OAK RIDGE, TENNESSEE 37831-0117

Managed and operated by Oak Ridge Associated Universities for the U.S. Department of Energy

ORAU/ORNL COMMITTEE ON HUMAN STUDIES VOTING RECORD

Proposal Number and Title: Physiological Responses of Electric and Magnetic Fields in Humans

Principal Investigator: Dr. Paul Gailey, ORNL

VOTE OF COMMITTEE

	Signature	Approve	Disapprove	Comment	Date
1.	Karl F. Hyland	✓			6/25/93
2.	Howard Frisken	✓			6/25/93
3.	Albert Hall	✓			6/25/93
4.	M. E. Kowal	✓			6/25/93
5.	Thaddeus J. Lee	✓			6/25/93
6.	Shelby A. Fry	✓			6.25.95
7.	R. J. Michael Fry			Abstain	6.25.95
8.	Emily Fry	✓			6.25.95
9.	Lin Callahan	✓			
10.					
11.					
12.					
13.					
14.					

Chairman's statement of Committee consensus:

Date

PROTECTING HUMAN SUBJECTS

Office of Health and Environmental Research — U.S. Department of Energy

PROJECT SUMMARY

Policy: Research activities that involve human subjects and that are funded by the U.S. Department of Energy (DOE), conducted in DOE facilities, or conducted by DOE personnel must be approved or exempted from review in accord with 10 CFR Part 745. Failure to comply with these regulations may prevent DOE from authorizing or funding an activity, or may lead the Department to suspend or terminate the project.

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1. Project Title

Physiological Responses of Electric and Magnetic Fields in Human

2. Principal Investigator

Paul Gailey/
(Dr. Charles Graham*)

Telephone Number

* 816-753-7600 Ext 1161

Mailing Address (Include full name of performing institution)

Oak Ridge National Laboratory, BLDG 3147, MS6070, phone (615)-574-0419
(Midwest Research Institute)
P.O. Box 2008, Oak Ridge, Tennessee 37831-6070
(425 Volker Blvd., Kansas City, Missouri 64110-2299)

3. Institutional Assurance Number (If issued)[1]

M1051 (Health and Human Services)

4. Project Number[2]

ORNL-32

5. Annual Funding:

Give actual funding or check the amount closest to the estimated total for the current Federal fiscal year, whether requested or obtained. Include both direct and indirect costs.

☐ Actual Funding $ _____

☐ $10,000 ☐ $100,000 ☒ $500,000 ☐ $1,000,000 ☐ $5,000,000

6. Funding Sources

A. Name DOE Program Office (see list in attachment), if applicable.
B. Name non-DOE sources of funding (up to two), if applicable.

A. DOE Program Office

Energy Efficiency and Renewable Energy

Contact Person	Telephone Number
Dr. Imre Gyuk	202-586-1482

B. Non-DOE Source

Non-DOE Source

[1] Under 10 CFR Part 745, institutions are required to file an assurance of compliance with the regulations with DOE or the Department of Health and Human Services. The Department involved may then issue an assurance number.

[2] Each project must have a unique identification number assigned by the institution—for example, ANL-94/101.

7. The Project has been reviewed and approved by the Institutional Review Board (IRB) as required under 10 CFR Part 745.

A. Type of Review

☒ Full Board
For a list of research not requiring IRB review, see Attachment.

☐ Expedited
For an explanation of projects that qualify for expedited reviews, see Attachment.

B. Type of Approval

☒ New ☐ Annual Renewal ☐ Other

C. IRB Approval Date

June 29, 1993

8. This Project involves the following collaborating institutions (list a maximum of two):

9. Vulnerable Populations

☒ This project does not involve vulnerable populations.

☐ This project involves the following vulnerable populations:

☐ Minors ☐ Mentally Disabled ☐ Prisoners

☐ Fetuses, Pregnant Women, In Vitro Fertilization ☐ Economically or Educationally Disadvantaged

10. Type of Research
Check all categories that apply.

☐ Epidemiology(using personally identifiable data)—
☐ Using data collected directly from human subjects.
☐ Using existing data.

☐ Diagnostic studies using radiation or chemical agents in tracer amounts.

☐ Therapeutic studies using radiation or chemical agents.

☐ Studies of exposure, effects, health, or monitoring using human urine, blood, other body fluids, cells, or tissues—
☐ Specimens collected directly from human subjects for this project.
☐ Specimens obtained from secondary sources (e.g., hospitals, laboratories).

☐ Instrument development and testing using human subjects.

☐ Surveys that collect personally identifiable data.

☐ Environmental studies using human subjects to evaluate weatherization options, habitat alteration, or similar.

☒ Other. Please identify Studies of the effects of environmental levels of magnetic fields on EEG and performance.

1048482

11. Abstract

Provide a brief abstract that includes the following information:

A. Summarize the objectives and methodology of this research project. (Explain clearly why it belongs in the categories checked in Item 11).

Human volunteers are briefly exposed to controlled 60 Hz magnetic fields while EEG and other performance measures are recorded. The field levels used are comparable to those which may be experienced while riding an electric commuter train or sleeping under an electric blanket. These studies are a critical component of a larger, national EMF Research Program to determine whether or not magnetic field exposures produce any measurable effects in humans.

B. Specify the number of human subjects involved each year.

36 men
36 women

C. Describe the involvement of human subjects and the risks, if any, to which they are exposed.

EEG data are recorded from human volunteers while they participate in simple performance tests. During one-half of a 45 minute period, the subjects are exposed to a 200 mG magnetic field which has been characterized by the National Institute of Standards and Technology. There are no known risks from these environmental levels of 60 Hz magnetic fields.

D. List the chemical or radioactive materials, if any, that are used in the study, and identify the route of exposure.

No chemical or radioactive materials are used in the experiments.

See reverse for approval signatures.

The official signing below certifies that the information provided on this form is correct and that the institution assumes responsibility for future reviews, approvals, and submissions of project summaries, which are all required at least once a year.	
Signature of Institution Official David E. Reichle	**Date** Jan. 25, 1994
Printed or Typed Name David E. Reichle	**Telephone Number** (615) 574-4333

For DOE Use Only

Date Received by ER-70	**Date** ☐ **Accepted** _____ ☐ **Returned to Originator** _____
Reason for Return	
DOE Reviewers	