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INTERIM REPORT

SAND82-7079

Review of Recent Research Sponsored by the Department of Energy That Impacts on the Findings of ICRP30

S. A. Felicetti*
G. E. Runkle**

Internal Report to the
U.S. Nuclear Regulatory Commission

Revision
September 1982

Sandia National Laboratories
Fuel Cycle Risk Analysis Division
Albuquerque, New Mexico 87185

The survey for this report was completed July 1982 and is current to that date.

*University of New Mexico
**Raytheon Service Company

Prepared for
Division of Waste Management
Office of Nuclear Material Safety and Safeguards
U.S. Nuclear Regulatory Commission
Washington, D.C. 20555
Under Memorandum of Understanding DOE 40-550-75
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1.0 INTRODUCTION

This report summarizes recent and ongoing research in the areas of dosimetry and potential health effects from exposure to ionizing radiation. The review includes summaries of conversations with major DOE contractors and preprint data provided by individual researchers. The survey for this report was completed in July 1982 and is current to that date.

This review has focused on the research that is funded by the Department of Energy (DOE) and is not intended to be completely comprehensive. Such a review is timely because of the controversy surrounding the adoption of ICRP Publication 30 (ICRP30, 1979, 1980) in the USA. ICRP30 was proposed to supersede ICRP Publication 2 (ICRP2, 1959) and to update existing standards. The state of the art dosimetric modeling techniques and 20 years of research in the area of dose and dose response from exposure to ionizing radiation were incorporated in ICRP30. However, some of the concepts presented by the ICRP in Publication 30 have major effects on risk estimates for exposure to radioactive material and have generated controversy in the scientific and health physics communities. This report includes recent experimental results which have bearing upon the accuracy and applicability of ICRP30.

This report is divided into two major sections. The first is a summary of recent experimental findings and ongoing research relevant to ICRP issues. The second is a more detailed review of current data and research in these areas. This review is based primarily on personal communications and preprint data provided by the investigators. Individuals were contacted at the following facilities: Argonne National Laboratory (ANL), Battelle Pacific Northwest Laboratories (PNL), Collaborative Radiological Health Laboratory at Colorado State University (CSU), Inhalation Toxicology Research Institute (ITRI), Institut für Genetek and für Toxikologie of West Germany, Los Alamos National Laboratories (LANL), Lawrence Livermore National Laboratory (LLNL), National Radiological Protection Board (NRPB) of England, New York University (NYU), Oak Ridge National Laboratory (ORNL), Oregon State University (OSU), Savannah River Laboratory, Texas A&M, Laboratory for Energy-Related Health Research at University of

2.0 SUMMARY OF DEPARTMENT OF ENERGY RESEARCH PROGRAM: IMPACT ON DOSIMETRY AND RISK ASSESSMENT

2.1 Introduction

This report summarizes the DOE research programs on the biological effects of ionizing radiation with emphasis on existing questions on dosimetry. This research includes parameters of actinide metabolism, especially gastrointestinal (GI) tract absorption, organ distribution and retention, and dose-response to ionizing radiation at low dose. DOE also sponsors research on the environmental behavior of actinides. This report concentrates on studies of interaction of environmentally-released actinides with the biosphere. Some of the recent results from the DOE research program have an impact on dosimetry. These results and relevant ongoing research are summarized below with particular emphasis on the research that impacts the dosimetric assumptions of ICRP2 and ICRP30. Research funded by other agencies that impact on the subject matter, such as the program at CSU, are also included.

2.2 Internal Emitters

2.2.1 Gastrointestinal Absorption

Current research is directed toward establishing realistic values for GI tract absorption and the identification of factors affecting absorption. Few human data are available for absorption of radionuclides. Therefore, it is necessary to rely upon experimental data from laboratory animals. Absorption is affected by the species and nutritional state of the laboratory animal, by the quantity of material ingested, and the chemical form of the ingested material.

In the dosimetric models for the gastrointestinal tract, both ICRP2 and ICRP30 described a parameter (f_1) for the fraction of a stable element which reaches the body fluids following ingestion. The values for f_1 presented in ICRP2 were increased in ICRP30 for a number of actinides, including U, Np and Pu. Prior to the publication of ICRP30, the developers of the INREM code (Killough et al., 1978) recognized that higher gut absorption values than those proposed

TABLE 2.1
Gut Absorption for Neptunium and Plutonium

Neptunium

Species	f_1	Reference
Man	10^{-4}	ICRP2
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Adult rats	5×10^{-4}	Sullivan, 1982
Adult mice (Fed)	3×10^{-4}	Bhattacharyya and Larsen, 1981
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dusts which are mostly to be encountered in the industrial situation. (John Stather, NRPB, and Bruce Boecker, ITRI, personal communications).

Improved models have been developed recently, such as a model developed by Richard Cuddihy of ITRI, and are under consideration by an ICRP Committee II Task Group (John Stather, NRPB, personal communication). These newer models greatly facilitate the extrapolation of data from experimental animals to man and permit consideration of the many compounds which do not fit into any of the three categories proposed by the Task Group on Lung Dynamics (John Stather, NRPB, personal communication).

2.2.3 Organ Distribution and Retention

Accurate dose-response descriptions for the actinides require characterization of organ distribution and retention because the latter parameters determine the dose commitment resulting from a given exposure.

The organ distributions and biological retention times of the actinides are poorly characterized. Also, the extrapolation to man of the available data on actinide metabolism in experimental animals is difficult because of the wide interspecies variability. For example, actinide retention times are measured in weeks in rodents, in months in non-human primates, and years in man (Norman Cohen, NYU, personal communication). Realistic estimates are needed for parameters of actinide distribution and retention in man.

Several studies on actinide metabolism have been proposed by DOE contractors. Studies have been initiated under NRC funding by Robert Larsen (ANL) and Norman Cohen (NYU) (personal communications) on actinide metabolism after gut absorption in baboons. Studies on actinide metabolism in beagles and non-human primates after intratracheal instillation have been initiated at UC Davis (Otto Raabe, UC Davis, personal communication). ITRI plans short-term studies of actinide in non-human primates (Bruce Boecker, ITRI, personal communication).

Projections for the risk of liver cancer in humans with actinides are currently based on thorotrast. These estimates may be inaccurate because thorotrast has a chemical toxicity as well as a radiological effect. Studies on wild mice were initiated at the University of Utah because the liver retention times in the wild species of mice are significantly longer than in the laboratory mice, and therefore are more similar to retention times in man. As part of the study on actinide metabolism in mice, the wild mice species have been injected with overlapping doses of ^{241}Am and with thorotrast. ^{241}Am was chosen over Pu for comparison with thorotrast because Pu is more likely to induce osteosarcomas than to induce liver cancer (Charles Mays, 1982), and the risk of liver cancer might not be detected. Completion of these studies will yield realistic numbers for actinide liver carcinogenicity relative to thorotrast.

PNL and ITRI also are conducting studies on dose-response relations with inhalation exposures to actinides. At PNL, various Pu compounds have been inhaled in dogs (1981 Annual Report). A number of animals exposed to low levels of Pu are still alive and are expected to yield further information on the effect of inhaled Pu in various chemical forms at low exposure levels. Also, rats have been exposed to $^{239}PuO_2$ at levels which will result in low life span doses of 2 to 100 rads (Sanders, 1982). Among the actinide compounds other than Pu, under study at PNL in beagles and rats are $^{241}AmO_2$, $^{244}CmO_2$, uranium aerosols and thorium cycle radionuclides.

At ITRI, studies are ongoing on the dose-response to Pu in rats, dogs and monkeys. The effect of age at exposure on the dose-response relationships is being studied in beagles and monkeys (Muggenburg et al., 1981). Rats have been exposed by inhalation to small amounts of Pu, and a response has been demonstrated at the lowest lung burden of 0.012 μCi/kg (Redman et al., 1981). Also at ITRI, many life-span studies are nearing completion on beagles that inhaled various fission products (Hahn et al., 1981). In these studies, neoplasia has developed in organs which retained relatively little radioisotope. This finding is inconsistent with the concept of a "critical organ" which was

recent publications, the RBEs of neutrons were reported to decrease with decreasing dose in reference to gamma radiation [Storer et al., 1979; Ullrich, Jernigan and Adams, 1979]. That is, the ratio of the effect of neutron irradiation to the effect of gamma irradiation is dependent upon the doses of the two types of radiations. As the dose from neutrons and gamma rays decreases, the neutrons become progressively more efficient relative to the gamma rays in producing biological damage, such as life shortening or neoplastic disease. Also, for gammas, the effect of a given dose of radiation administered over several exposures is less than if the dose is administered acutely. However, for neutrons, fractionation of exposure does not decrease the effect of a given cumulative dose. Furthermore, in the range of 10 to 50 rads, the dose response curves for neutrons appear to be convex (Ullrich, 1982a,b). Therefore, linear extrapolation for exposure to neutrons at doses below 50 rads could result in a significant underestimation of risk.

Similar information on dose-response relationships has been obtained from mouse studies at ANL where 40,000 mice have been exposed to neutron or ^{60}Co gamma irradiation since 1971 (Thomson et al., 1982a). The funding for these studies was reduced by DOE three years ago (Doug Grahn, ANL, personal communication).

Studies are ongoing at ANL at lower dose ranges (0.1-1 rad neutron) and at low dose rate (0.1-10 millirads/minute) to establish the limiting values for the RBE's of neutrons (Doug Grahn, ANL, personal communication). Other studies will address host factors in radiosensitivity; that is, the effect of selection of a given experimental population on the observed dose response relationships. For example, laboratory mice and longer-lived field mice are being compared in their dose-response to ionizing radiation (Doug Grahn, ANL, personal communication).

Other studies have investigated cell transformation in cell culture with fractionated gamma and neutron irradiation (Han and Elkind, 1979, and Han, Hill and Elkind, 1980). Recent results in the cell culture

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in ICRP2 were needed. Therefore, in the INREM code, f_1 values were increased by an order of magnitude for the actinides. The gut absorption parameters are currently under investigation because the choice of f_1 has significant impact on uptake from the gut and the dose commitments to the various organs of the body.

Recent studies have indicated that the value of 10^{-2} presented in ICRP30 for the gut absorption of Np is inaccurate. This value was based on preliminary experimental data in rats. High absorption values in these preliminary studies may have been artifacts resulting from the large masses of Np ingested by the experimental animals. The large quantities administered had toxicological effects on the intestinal mucosa (John Stather, NRPB, and Maurice Sullivan, PNL, personal communications; and Thompson, 1982). More recent studies (see Table 2.1) on Np absorption used low mass quantities and reported absorption values several orders of magnitude lower than the ICRP30 recommendation. For example, 5×10^{-4} was absorbed in adult rats (Sullivan, 1982) and 3×10^{-4} by adult mice (Bhattacharyya and Larsen, 1981).

According to Roy Thompson, PNL, in a recent publication (1982a), the f_1 for Np is too high by at least an order of magnitude. Recently, at a National Health Physics Society Meeting in Las Vegas, Nevada, June 27 to July 1, 1982, Roy Thompson presented findings to confirm a gut absorption value of 10^{-3} for all forms of Np. In ICRP30, a caveat indicated that Np uptake may be lower for forms that have incurred environmental interactions. Thompson removed this caveat and said that 10^{-3} is the appropriate gut uptake for Np for all forms of Np whether in the workplace or in the environment. This value is one order of magnitude lower than the 10^{-2} proposed in ICRP30 for Np. John Stather of the NRPB indicated that a true f_1 for Np is at least 2 or 3 times lower than the 10^{-2} value proposed by ICRP30 (personal communication).

Whereas the value for f_1 for Np is apparently too high, the f_1 for Pu in ICRP30 may be too low. The value for f_1 of Pu was increased from 3×10^{-5} in ICRP2 to 10^{-4} in ICRP30. Robert Larsen (ANL), Maurice Sullivan (PNL), and Roy Thompson (PNL) indicated (private communications) that the true f_1 for

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Pu may be at least 10^{-3}. John Stather (NRPB) indicated that an f_1 of 10^{-4} may be adequate for occupational exposure but the f_1 should be higher for environmental exposures. The experimental evidence for a higher f_1 for Pu are summarized in Table 2.1. Recent studies have used lower quantities of Pu than were used in earlier studies. At higher masses, Pu tends to polymerize, resulting in decreased gut absorption (Robert Larsen, Don Nelson, personal communications), and may explain the low gut absorption values obtained in the earlier experimental results. Gut absorption is also affected by the nutritional state and the species of the experimental animal used in the study (Table 2.1).

Research proposed by DOE contractors on actinide gut absorption includes studies by Maurice Sullivan (PNL) on the absorption of fractionated doses of ingested Np in rodents and studies on the nature of the Np-induced lesions in gut and kidney. Completion of these studies will require additional funding (Maurice Sullivan, personal communication). Robert Larsen (ANL) and Norman Cohen (NYU) have initiated a joint study on the absorption and metabolism of Pu, Am and Cm at low mass quantities in baboons. The continuation of the baboon studies at NYU and ANL, currently funded by the NRC, depends on the availability of additional funds from either DOE or NRC (Norman Cohen, personal communication).

2.2.2 Inhalation Models

ICRP30 proposed the adoption of the 1966 model from the Task Group on Lung Dynamics (ICRP, 1966) for inhalation exposures. The 1966 model (TGLD66) defined three categories of materials based on the rate of clearance from the respiratory tract. These categories are: D (cleared in 10 days), W (cleared in 10 to 100 days) and Y (requires greater than 100 days for clearance). The TGLD66 has some serious limitations, including: (1) the difficulty of extrapolating the data on the clearance of radioactive material from the respiratory tract of experimental animals to man (John Stather, NRPB, personal communication), (2) the inability to accommodate material whose behavior does not fit the D, W or Y categories (John Stather, NRPB, personal communication), and (3) the failure to consider mixed

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Improved models have been developed recently, such as a model developed by Richard Cuddihy of ITRI, and are under consideration by an ICRP Committee II Task Group (John Stather, NRPB, personal communication). These newer models greatly facilitate the extrapolation of data from experimental animals to man and permit consideration of the many compounds which do not fit into any of the three categories proposed by the Task Group on Lung Dynamics (John Stather, NRPB, personal communication).

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Accurate dose-response descriptions for the actinides require characterization of organ distribution and retention because the latter parameters determine the dose commitment resulting from a given exposure.

The organ distributions and biological retention times of the actinides are poorly characterized. Also, the extrapolation to man of the available data on actinide metabolism in experimental animals is difficult because of the wide interspecies variability. For example, actinide retention times are measured in weeks in rodents, in months in non-human primates, and years in man (Norman Cohen, NYU, personal communication). Realistic estimates are needed for parameters of actinide distribution and retention in man.

Several studies on actinide metabolism have been proposed by DOE contractors. Studies have been initiated under NRC funding by Robert Larsen (ANL) and Norman Cohen (NYU) (personal communications) on actinide metabolism after gut absorption in baboons. Studies on actinide metabolism in beagles and non-human primates after intratracheal instillation have been initiated at UC Davis (Otto Raabe, UC Davis, personal communication). ITRI plans short-term studies of actinide in non-human primates (Bruce Boecker, ITRI, personal communication).

At the University of Utah the microdosimetry of Pu compared to Ra is under investigation. ICRP30 classifies Ra as a "volume seeker" which irradiates the entire bone, and Pu is classified as a "surface seeker" from which the majority of radiation is delivered to radiosensitive endosteal cells on the surface of the bone. Recent results (Webster Jee, University of Utah, personal communication) have revealed that: (1) Pu is not uniformly distributed throughout the bone but seeks highly vascularized bone with hematopoietic (red) marrow; (2) surface deposited Pu is subject to processes of bone dynamic remodeling, which result in the burial of substantial amounts of Pu within the interior of bone; and (3) the rate of bone turnover is an important parameter in the effectiveness of a given burden of Pu in producing osteosarcomas (or bone cancers). Because of refinements in the understanding of Pu bone microdosimetry, several investigators (Webster Jee; personal communication, May 1982, Priest et al., 1978) have suggested that the ICRP30 classification of Pu as purely a surface seeker leads to major errors in bone dosimetry.

A group under Webster Jee at the University of Utah is developing simulated "skeletal risk" models which describe the risk of induction of neoplasia (cancer) by actinides relative to the endosteal dose (Webster Jee, 1982). The development of these models will integrate information on bone remodeling and turnover.

Other dose response studies (University of Utah, Annual Budget Submission, FY-1983 and BY-1984) which are ongoing at the University of Utah include: (1) ^{239}Pu and ^{226}Ra in young adult beagles, (2) ^{239}Pu and ^{226}Ra in juvenile vs. mature beagles, and (3) ^{239}Pu and ^{226}Ra in St. Bernards which have a high natural sensitivity to bone cancer, and (4) comparative toxicity of ^{224}Ra in mice, beagles and humans. In addition, toxicity of a number of actinides, administered by intravenous (IV) injections, is being studied in dogs, in laboratory mice and in two species of wild mice. Relationships between microdosimetry and actinide toxicity are being investigated in several dog studies.

Projections for the risk of liver cancer in humans with actinides are currently based on thorotrast. These estimates may be inaccurate because thorotrast has a chemical toxicity as well as a radiological effect. Studies on wild mice were initiated at the University of Utah because the liver retention times in the wild species of mice are significantly longer than in the laboratory mice, and therefore are more similar to retention times in man. As part of the study on actinide metabolism in mice, the wild mice species have been injected with overlapping doses of ^{241}Am and with thorotrast. ^{241}Am was chosen over Pu for comparison with thorotrast because Pu is more likely to induce osteosarcomas than to induce liver cancer (Charles Mays, 1982), and the risk of liver cancer might not be detected. Completion of these studies will yield realistic numbers for actinide liver carcinogenicity relative to thorotrast.

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proposed in ICRP2. In the future, few life-span studies will be initiated at ITRI. Therefore, little further information on dose-response to low levels of inhaled radionuclides, other than in rodents, will be forthcoming. The exceptions to this are studies which have already been initiated, such as the exposure of immature beagles to Pu. The emphasis will be on short-term studies in beagles, rodents and non-human primates (Bruce Boecker, ITRI, personal communication).

At UC Davis, a 20-year study in which dogs were fed ^{90}Sr is nearing completion (Marvin Goldman, UC Davis, personal communication). Responses in these dogs are being compared to the effects in the dogs injected with ^{226}Ra. The relative biological effectiveness (RBE) of Sr relative to Ra has been found to decrease at low dose rates (Raabe, Book and Park, 1981b). The response was dose-rate dependent. Tumors developed in the soft tissue adjacent to the bone at low dose rates (0.1-1 rads/day) of ^{90}Sr (Raabe et al., 1981a). Above 1 rad/day, leukemia developed at cumulative doses near 2000 rads (Raabe et al., 1981a, Otto Raabe, UC Davis, personal communication). Marvin Goldman (UC Davis, personal communication) indicated that these ^{90}Sr studies are inconsistent with ICRP30 because of the high incidence of leukemia and the lack of evidence for a linear response.

2.3 Somatic Effects of Ionizing Radiation

The studies on the somatic effects of external ionizing radiation have concentrated on neoplasia (cancer) because of the evidence that external ionizing radiation shortens life primarily through the induction of neoplastic disease (BEIR III). Current research is directed toward: (1) the shape of dose-response curve at low doses, (2) the effect of fractionated doses, (3) the RBEs of neutrons relative to radiation, (4) the effect of age on radiosensitivity, and (5) the existence of a radiosensitive subpopulation.

Factors which influence the response to external irradiation are studied in the "megamouse" experiments at ORNL. The dose response to and neutron radiation are compared and the dose-response in populations of different radiosensitivities are characterized. In

recent publications, the RBEs of neutrons were reported to decrease with decreasing dose in reference to gamma radiation [Storer et al., 1979; Ullrich, Jernigan and Adams, 1979]. That is, the ratio of the effect of neutron irradiation to the effect of gamma irradiation is dependent upon the doses of the two types of radiations. As the dose from neutrons and gamma rays decreases, the neutrons become progressively more efficient relative to the gamma rays in producing biological damage, such as life shortening or neoplastic disease. Also, for gammas, the effect of a given dose of radiation administered over several exposures is less than if the dose is administered acutely. However, for neutrons, fractionation of exposure does not decrease the effect of a given cumulative dose. Furthermore, in the range of 10 to 50 rads, the dose response curves for neutrons appear to be convex (Ullrich, 1982a,b). Therefore, linear extrapolation for exposure to neutrons at doses below 50 rads could result in a significant underestimation of risk.

Similar information on dose-response relationships has been obtained from mouse studies at ANL where 40,000 mice have been exposed to neutron or ^{60}Co gamma irradiation since 1971 (Thomson et al., 1982a). The funding for these studies was reduced by DOE three years ago (Doug Grahn, ANL, personal communication).

Studies are ongoing at ANL at lower dose ranges (0.1-1 rad neutron) and at low dose rate (0.1-10 millirads/minute) to establish the limiting values for the RBE's of neutrons (Doug Grahn, ANL, personal communication). Other studies will address host factors in radiosensitivity; that is, the effect of selection of a given experimental population on the observed dose response relationships. For example, laboratory mice and longer-lived field mice are being compared in their dose-response to ionizing radiation (Doug Grahn, ANL, personal communication).

Other studies have investigated cell transformation in cell culture with fractionated gamma and neutron irradiation (Han and Elkind, 1979, and Han, Hill and Elkind, 1980). Recent results in the cell culture

studies indicate that transformation in culture may increase with fractionation of neutron dose.

The studies at ORNL and ANL showing that the RBE of neutrons relative to gamma radiation increases at decreasing dose rates may have an important impact on risk assessment. Also important are some recent results, discussed above, for low dose rates in mice at ORNL and in cell culture at ANL that indicate that the dose response curve for neutrons may be convex at low doses. The concern exists that extrapolation of the dose response curve from high exposures may underestimate the health risk from neutron exposure at low doses (Han, ANL, unpublished summary). Contributing to this concern is the evidence cited above that, unlike gamma irradiation, very little repair of neutron-induced damage occurs when exposures are protracted or fractionated.

At ANL, an extensive study is examining the response of beagle dogs to ^{60}Co irradiation. Several important findings are emerging from these studies. At intermediate doses of 5 to 10 rads per day, a high incidence of myeloproliferative disorders (leukemia) is seen (Tolle et al., 1982). Generally, the dose at intermediate dose rates is additive and results in a leukemic response at a certain dose regardless of dose rate (Tom Seed, ANL, personal communication). At ANL, beagles are being exposed to ^{60}Co irradiation at low dose rates (.1 rad/day to 2.5 rads/day). Results to date at 2.5 rads/day have shown the induction of leukemia at a predictable cumulative dose (Tom Fritz, ANL, personal communication).

In the beagles irradiated with ^{60}CO irradiation, the induction of leukemia is accompanied by characteristic cellular changes detectable at the onset of exposure (Tolle et al., 1982). These cellular changes may be exploited in further investigations of the mechanisms of induction of myeloproliferative disorders (Tom Fritz, Doug Grahn and Tom Seed, ANL, personal communications). Studies on the response of hematopoietic stem cells from several species, including human, to neutron and gamma radiation have been initiated (Tom Seed, ANL, personal communication). These studies may lend insight into the mechanisms for interspecies differences in radiosensitivity.

The studies of ^{60}Co irradiation in the ANL beagle population have provided evidence for a radiosensitive subpopulation. At dose rates of 5 to 10 rads/day, some of these dogs died of aplastic anemia early in the radiation exposures. Other dogs are more radioresistant and die of leukemia at higher cumulative doses.

A program to investigate the age-dependence of radiosensitivity is ongoing at CSU under Steve Benjamin. This program is currently sponsored by National Cancer Institute (NCI) and Federal Drug Administration (FDA) through October 1982. As a major part of this study, 1680 beagles were exposed to 16 rads or 83 rads of ^{60}Co irradiation in utero or immediately after birth (Benjamin, 1980). Results to date indicate an increased radiosensitivity in the perinatal period (time surrounding birth) (Benjamin, 1980a,b) and may confirm similar epidemiological findings in man (Stewart, 1956). This beagle population is aging, but a number of animals, especially those exposed to 16 rads, are still alive. Therefore, much information on dose-response to low dose perinatal irradiation is potentially available from this unique population. Such information could have a major impact on the scientific community which may be reluctant to accept epidemiological findings in the absence of laboratory confirmation. Continuation of this program will require a new source of funding.

2.4 Genetic Effects of Ionizing Radiation

The majority of the research on the genetic effects of ionizing radiation is done at ORNL. Much of this work currently involves the genetic effects of external irradiation at low doses. Most of the recent results support the conclusions of the BEIR III committee (Lea Russell, ORNL, personal communication).

Less information is available on the genetic risk from internal emitters than from external irradiation. Studies are ongoing at ORNL of mutations in mice which were sired by males injected with 10 Ci/kg ^{239}Pu citrate (Paul Selby, ORNL, personal communication).

Other ongoing or proposed research at ORNL will study the rate of mutations at low dose rates of external irradiation (.005 rads/minute) and the induction of mutations in oocytes (Paul Selby, ORNL, personal communication).

ORNL is facing potential funding reductions of 25% of the current budget (Lea Russell, ORNL, personal communication). Because of the labor-intensive nature of these studies, such funding cuts will hamper the conduction of the planned studies.

2.5 Environmental Mobility of the Actinides

DOE is funding a number of studies on actinide behavior in the environment. These studies appear to be securely funded over the near future. Current research on actinides in soil concerns the degree of vertical movement within soil, the degree of root uptake, the relative contribution to the actinide content of plants of surface deposition as compared to root uptake and the degree of concentration of incorporated actinides in edible parts of plants. In addition, studies have been initiated to determine the uptake of actinides incorporated into plants through the GI tract of grazing animals.

At PNL, Gene Schreckhise is conducting studies on actinide uptake by crop plants. Recent findings include: (1) uptake is dependent on the crop--i.e., legumes take up a factor of 10 times more material than do grain crops, (2) Np is 1000 times more available for uptake by plants than is Pu and 100-200 times more available than is Am or Cm (Schreckhise and Cline, 1980), and (3) the content of actinides in seeds is lower than in other above-ground parts (Schreckhise and Cline, 1980). Future studies will address crop uptake of Np, Am, Cm and U during several growth cycles (Gene Schreckhise, PNL, personal communication).

Ray Wildung (PNL) has initiated studies of gut absorption by grazing animals of actinides, including Pu, Am, Np and Tc, incorporated into plants. In preliminary studies, the incorporation of actinides into plants enhanced the gut absorption of the actinide (Ray Wildung, PNL, personal communication). A study on gut

absorption of plant incorporated actinides has also been proposed by Ray Bondiette (ORNL, personal communication) and is under consideration by NRC. This study will characterize gut absorption of actinides following intake in goats grazed on a contaminated floodplain, and the transport of actinides to milk.

Crop uptake of ^{238}Pu and other actinides has been studied at the Savannah River Laboratory in areas contaminated with effluent from a nuclear fuel reprocessing plant. Studies are ongoing on Np, Cm, and Pu uptake in crops and in trees (John Corey, Savannah River Laboratory, personal communication). A recent publication (Corey et al., 1982b) discussed dosimetry considerations for hypothetical individuals living and farming in the area near the plant. Deposition on the plant surface accounts for the majority of the Pu found associated with crops (Corey et al., 1982a). Therefore, the main dose to man from the agricultural use of contaminated land would be due to resuspension of surface-deposited material and subsequent inhalation during soil tillage (Corey et al., 1982a,b).

Results from studies at Savannah River Laboratory and Los Alamos National Laboratories have traced the movement of environmental releases of actinides. These studies support the conclusion that physical processes (e.g. wind, erosion, water) predominate in the transport of actinides, with biological processes (e.g. plant uptake) playing a relatively minor role (Corey et al., 1982.a;. Tom Hakonson, LANL, personal communication).

DOE is funding a number of studies on the behavior of actinides in fresh water and marine systems. Topics under current investigation include uptake of actinides by water biota, the effect of chemical form on sedimentation rate, and the evidence for actinide solubilization after sedimentation.

In a recent report (Bohen and Livingston, 1979) evidence was presented for resolubilization of sedimented Pu in the Atlantic Ocean. This finding has been substantiated by more recent studies (Vaughn Bohen, Woods Hole, personal communication). Similar evidence for Pu resolubilization has been reported by

Vic Noshkin (LLNL, personal communication) in studies of the water near the Marshall Islands. However, studies by Tom Beasley (OSU) on the continental shelf of the Western US have failed to yield any evidence for Pu resolubilization (Tom Beasley, OSU, personal communication).

The work of Don Nelson and Robert Larsen at ANL have brought into focus the importance of the oxidation state of Pu on distribution coefficients between sedimented and suspended states and on potential biological uptake. The relationship of oxidation state to limnological parameters such as organic composition of the water is the subject of current research (Don Nelson, ANL, personal communication). As a part of this program, a study has been proposed for determining actinide content in fish from waters of different organic composition. In a similar study, Tom Beasley (OSU) has proposed the characterization of actinide remobilization by uptake in the biota of the Columbia River (Tom Beasley, OSU, personal communication).

A large research effort is ongoing to investigate actinide behavior in marine and fresh water systems (Vaughn Bohen, Woods Hole; Martha Scott, Texas A&M, personal communications). Research is ongoing on actinide inventories in offshore marine areas, better characterization of actinide behavior, and particulate behavior in general, in near shore environments, and better characterization of actinide adsorption and particulate behavior in fresh water systems.

The above discussion is intended as a broad summary of the DOE research program on issues which relate to dosimetry. A much more detailed research review is included in section 4.4.

3.0 COMMENTS OF INTERVIEWEES ON ICRP30

Recent information concerning dosimetry with radioactive materials is under review by several NCRP Task Groups. Among these is an NCRP Task Group which is reviewing lung modeling (Bruce Boecker, ITRI, personal communication), and an NCRP Task Group on hematopoietic parameters of radiation injury (Tom Fritz, ANL, personal communication). The latter group is reviewing myeloproliferative disorders, including myelogenous leukemia, induced by ^{60}Co and by low level ^{90}Sr feeding in dogs. This group will evaluate dose response to internal emitters as compared to external radiation. Also, an NCRP Task Group is concerned with liver dosimetry.

A Task Group of Committee II of ICRP is reviewing ICRP Publication 19 on actinide metabolism. David Taylor of the Institut für Genetek and für Toxikologie of West Germany is heading this group. According to Taylor (personal communication), the work of this Task Group has just been initiated. Recent results on actinide metabolism in experimental animals will be reviewed and a consensus reached as to how to extrapolate to man. Among probable changes discussed by Taylor (personal communication) is an increase in the f_1 (for fraction absorbed across the gut mucosa) for most actinides. Of particular note is the current f_1 (gut absorption) for Np which is too high and will be brought into line with Pu. According to John Stather of the NRPB of England, who serves on this Task Group, Np should be reduced by a factor of 2 to 3 from the current recommendations by the ICRP. The Task Group may recommend the use of f_1 gut absorption values as a "physiological factor" and include a mechanism for using a "reasonable safety factor" for workers who have been exposed to a known compound (John Stather, NRPB, personal communication). No change is anticipated by Taylor in the liver and bone distribution ratios for the actinides but the report will emphasize the wide variability in these metabolic parameters. The Task Group is currently reviewing liver retention times outlined in ICRP19 for the actinides; a 50% decrease is not considered unreasonable (David Taylor, personal communication).

John Stather's group of the NRPB of England, in collaboration with Ray Masse of the CEA in France, is responsible for the section in the report by the ICRP Committee II Task Group on actinide metabolism after inhalation. The mission of this group is to describe the metabolism of inhaled actinides in man. Limitations of the 1966 Task Group on Lung Dynamics (TGLD) model, which is used by ICRP19, will be delineated. John Stather (personal communication) described the TGLD model as "adequate for planning purposes" but hindered by some major drawbacks. There are a number of industrially produced actinide compounds which do not conform to the TGLD model. Information on such compounds is difficult to input into the TGLD model because most of the overall clearance times in the model are based on experimental data from rats, which may be very different from those in man. Furthermore, the TGLD proposed a three compartment model of the respiratory tract and clearance characteristics were described for each compartment. The clearance processes from the various compartments, such as mucociliary clearance from the upper respiratory tract and blood translocation from the lower respiratory tract, are actually competing. Newer models, such as the "mechanistic" model proposed by Richard Cuddihy of ITRI, consider competition between clearance processes and allow easier extrapolation to man (John Stather, NRPB, personal communication). Finally, the behavior of mixed dusts is not addressed by ICRP30. Inhalation of mixed dusts such as Pu containing dusts from fast breeder fuels may be more relevant to an industrial situation than inhalation of pure compounds (John Stather, NRPB, personal communication). Future model development to describe the metabolism of inhaled actinides will need to consider the information that is now available on mixed compounds.

Keith Eckerman (ORNL, personal communication) is currently involved in some skeletal modeling efforts which extend beyond ICRP30 by considering energy deposition and dose to bone surfaces and bone marrow. Parameters for retention of actinides in the skeleton may involve some future Task Groups of the ICRP and may be subject to modification in the near future, but no major changes in bone risk are immediately forthcoming (Keith Eckerman, ORNL, personal communication).

Most of the individuals who were interviewed were aware of the limitations of ICRP30, but opinions as to its relative merit were varied. Individuals who served on Committee II tended to compare ICRP30 favorably with ICRP2. Charles Mays (University of Utah, personal communication) indicated that some of the reluctance to accept ICRP30 may be attributable to the introduction of several new concepts (e.g., new units of measure, and the concept of effective dose) in ICRP Publications 26 and 30. William Bair (PNL) pointed out that ICRP30 was prepared with the objective of protecting the worker, and, in the interest of objectivity, the committee did not consider the potential controversy which might surround a given decision, such as the choice for f_1 for Np. In Bair's opinion, no one on the committee anticipated the controversy which has subsequently arisen concerning the adoption of ICRP30. Roy Thompson (PNL, personal communication) said that ICRP30 was based on the best information which was available at the time and Keith Eckerman (ORNL, personal communication) strongly asserted that ICRP30 should be adopted because existing standards based on ICRP2 do not reflect the current knowledge of radioisotope metabolism.

Keith Eckerman (ORNL, personal communication) indicated that ICRP is a guideline document concerned with the protection of the radiation worker. A distinction should be made by the technical community between dosimetry for setting guidelines for radiation protection and dose assessment for an exposed individual in a working environment. In the latter situation, only the most current concepts should be applied. For environmental exposures, ICRP30 may not be applicable, because little information is available on the metabolism of radioactive contaminants which are in the chemical forms likely to be encountered in the environment.

Modifications in methods of risk assessment in ICRP30 have met resistance in the health physics community. For example, some individuals feel that the Annual Limitations on Intake (ALI) are restrictive. ICRP Publication 2 allowed 1/50th of the total permissible dose per year, but no provisions were made for the fact that actual exposures tend to be acute

rather than continuous. However, the ALI considers the total committed dose equivalent integrated over 50 years. (Charles Mays, University of Utah, personal communication).

The concept of "critical organs" presented by ICRP2 is apparently better accepted by the health physics community than is the effective dose equivalent concept of ICRP30. The major limitation of the "critical organ" system is the growing evidence that a number of organs are at risk from neoplastic disease (cancer). Also, the "critical organ" concept is dependent upon a threshold, which may not be accurate (Keith Eckerman, ORNL, personal communication). Some individuals advocate a third "additive risk" system, which could consider variables such as age at exposure and dose rate (John Storer, ORNL, personal communication). The failure of ICRP30 to consider dose rate is of major concern to some investigators (Marvin Goldman, UC Davis, personal communication).

Most American members of Committee II expect changes in future documents from ICRP. William Bair (PNL) and Charles Mays (University of Utah) explained (personal communication) that ICRP30 was prepared with the objective of protecting the worker. In some cases, realistic models were not available, which necessitated arbitrary decisions about what was incorporated. An effort was made to err on the conservative side which has resulted in some unrealistic dosimetry. Charles Mays (University of Utah, personal communication) believes that ICRP30 will have to be redone with an emphasis on numbers that actually estimate doses. Parameters which obviously overemphasize dose, such as estimated endosteal dose for Pu, will have to be revamped based on new experimental evidence.

A revision of ICRP30 could incorporate recent experimental data. However, Keith Eckerman (ORNL, personal communication) disagrees with updates on single parameters because ICRP30 presents an integrated model which should provide some consistency over time. William Bair (PNL) also disagrees with adoption of a partial, rather than a total ICRP system. Even assuming a consensus concerning needed changes in dosimetry, Roy Thompson's words at the National Health Physics

Society Meeting in Las Vegas, June 27 to July 1, 1982, were probably prophetic in that "ICRP never moves very quickly."

4.0 RESEARCH REVIEW

Research funded by DOE on radioactive material dosimetry may be divided into four major areas: (1) internal emitters, especially factors affecting dosimetry from actinide exposure, (2) somatic effects of ionizing radiation, (3) genetic effects of ionizing radiation and (4) environmental behavior of transuranic elements, with emphasis on factors which affect risk estimates from accidental releases or from high level waste management. Discussion of each category is divided into two broad sections, one of which describes recent findings which impact dosimetric and dose response relationships and the second summarizes ongoing and proposed research.

4.1 Internal Emitters

The DOE funded research on internal emitters includes ongoing efforts on gut absorption, organ distribution and retention, and dose-response relationships. Recent results from this research program suggest the need for major changes in modeling assumptions for risk assessment. Examples of areas where major changes may be forthcoming are gut absorption parameters and dosimetry for bone seekers.

4.1.1 Recent Results

4.1.1.1 Gut Absorption

In the dosimetric models for the gastrointestinal tract, both ICRP2 and ICRP30 described a parameter (f_1) for the fraction of a stable element which reaches body fluids following ingestion. This parameter was considerably revised in ICRP30 from ICRP2 for some radionuclides. For example, for Np, a combination of a high gut uptake fraction (f_1 of 10^{-2} (ICRP30) as compared to an f_1 of 10^{-4} (ICRP2)), and a high environmental mobility may render Np a major isotope of concern for high level waste management (HLWM) (Cohen, 1982, Hill et al., 1980). Recent estimates based on ICRP30 indicate that Np may be the most hazardous material remaining in HLW from 10,000 years to 30 million years after disposal (Thompson, 1982a).

Recent studies have indicated that the high gut absorption (f_1) for Np proposed by ICRP30 is inaccurate. ICRP30 proposed an f_1, or fraction absorbed from the gut, of 10^{-2}. Roy Thompson, PNL (1982a; personal communication), concluded that the studies reporting high Np gut absorptions were affected by the chemical toxicity to the GI tract of the large quantities of Np. These early studies utilized ^{237}Np in large masses. Maurice Sullivan (PNL) has found that, at lower, "environmentally relevant" masses in adult mice, the absorption of Np is 5×10^{-4}, which is almost two orders of magnitude lower than ICRP30 (Sullivan, Miller and Ryan, 1982). However, newborns exhibited a 10^{-2} to 3×10^{-2} absorption (Maurice Sullivan, PNL, personal communication). In similar studies, Marica Bhattacharyya and Robert Larsen of ANL (1981) reported that, in mice, absorption increased about 10 fold from levels of about 3×10^{-4} absorbed in fed animals to 10^{-3} when animals were fasted.

In his recent review, Thompson (1982a) suggested that lower fraction absorbed from the gut (f_1) for Np may be appropriate to very low exposure levels such as would occur from environmentally dispersed Np, but an f_1 of 0.01, as proposed by ICRP30, might be a reasonable value for protection of radiation workers. In a later correspondence (1982b), Roy Thompson was influenced by the results of Sullivan and Bhattacharyya to conclude that an f_1 of 10^{-2} for Np is an artifact of high mass feeding experiments and is too high by at least a factor of 10. At a National Health Physics Society meeting in Las Vegas, Nevada, June 27 to July 1, 1982, Roy Thompson presented recent findings to confirm a gut absorption value of 10^{-3} for all forms of Np. In ICRP30, a caveat indicated that Np uptake may be lower for forms that have incurred environmental interactions. Roy Thompson removed this caveat and said that 10^{-3} is the appropriate gut uptake for all forms of Np. This will decrease the hazard of Np by an order of magnitude and may reduce the ranking from a waste management standpoint. When questioned as to when ICRP will incorporate the 10^{-3} value, Thompson indicated that ICRP "never moves quickly and that several years may elapse before this value is adopted".

Harrison and Stather (1982) of the NRPB in England reported values for gut absorption of Np in hamsters which were tenfold lower than those found by Maurice Sullivan (PNL) in rats. This discrepancy was attributed by Maurice Sullivan (PNL, personal communication) to species variation. However, in a personal communication, John Stather (NRPB) described gut absorption of Np in hamsters as on the order of 5×10^{-4} fraction absorbed, in agreement with Sullivan's findings.

There is mounting evidence, therefore, that the gut absorption of Np at low masses is more accurately described by an f_1 of 10^{-3} rather than 10^{-2}, as stated by ICRP30. Some important studies have been initiated in primates by Robert Larsen of ANL and Norman Cohen of NYU as described in section 4.1.2. These studies will potentially corroborate the lower gut absorption reported in rodents.

GI tract absorption values for Pu are also receiving scrutiny. While the ICRP30 f_1 values for Np now appear too high, there are indications that the ICRP30 f_1 values for Pu may be too low (Roy Thompson, PNL, and Maurice Sullivan, PNL, personal communication). Plutonium gut absorption values were increased from the ICRP2 value of 3×10^{-5} to 1×10^{-4} in ICRP30. According to recent experimental findings, the increase may not have been enough.

Low values for Pu gut absorption reported in earlier studies (Katz, Kornberg and Parker, 1955, Weeks et al., 1956) may have been affected by the large quantities of plutonium which were administered (Robert Larsen, ANL, personal communication). Mass effects on gut absorption of Pu are opposite to mass effects of Np. Whereas high masses of Np result in increased gut absorptions because of chemical toxicity to the mucosa, high masses of Pu decrease gut absorption, due to increased degree of polymerization of the Pu (Larsen et al., 1981).

At low mass quantities, f_1's for Np and Pu may be similar. Larsen et al., (1982) obtained values for Pu retention from drinking water of 2×10^{-3} in fasted mice and 3×10^{-3} in fasted rats. Sullivan et al., (1982) found absorption of Pu to be an order of

magnitude higher than the ICRP value of 10^{-4} in adult rats.

Plutonium absorption at low masses is not altered by relatively small changes in administered dose. Robert Larsen (ANL, personal communication) has administered Pu to mice in three different concentrations--at the maximal permissible concentration (MPC) for Pu in drinking water, at 100 times less than the MPC, and at 100 times greater than the MPC. Retention was 3×10^{-2} in all cases. In another study Maurice Sullivan (1981) used graded mass quantities of Pu, and absorption was inversely related to the administered dose. At high concentrations, the gut absorption of plutonium is greater for Pu citrate than for Pu nitrate, but at lower concentrations, absorption is not dependent upon the chemical form (Maurice Sullivan, PNL, personal communication).

Absorption has been reported to increase in fasted animals when compared to animals fed a normal diet. Bhattacharyya and Larsen (1981) found that a fraction of 2×10^{-3} of the administered Pu was absorbed in fasted mice and that the absorbed fraction decreased 13 fold in fed mice. Larsen et al., (1982) discussed the need to use absorption values in fasted animals for extrapolation to the human situation, in view of the fact that drinking water is frequently consumed in the absence of food.

Plutonium absorption is probably higher than the ICRP30 value. Maurice Sullivan, PNL, (personal communication) speculated that newer data on Pu may generate as much controversy as did values for gut absorption of Np. Roy Thompson (1982a) indicated that the f_1 should be increased by a factor of 10 for trace quantities, such as may be found in the environment, and, in private conversation, expressed concern that such an increase may not be enough. Larsen et al., (1982) stated that the true f_1 for Pu is surely greater than 1×10^{-3} and may be as high as 2×10^{-1}, based on analogy with uranium. John Stather of the NRPB (personal communication) indicated that absorption values of 10^{-4} for soluble Pu and 10^{-5} for the oxide are adequate for occupational exposure

but should be higher for Pu that has encountered environmental interactions. Much of the data on gut absorption of Pu at low mass levels have been obtained from rodents, and without complementary data on other species, extrapolation to man is tenuous.

4.1.1.2 Inhalation Exposures

Dosimetry from inhalation exposures to radioisotopes has been evaluated at PNL and at ITRI. Results generally support the model of the 1966 Task Group on Lung Dynamics (ICRP 1966) which was adopted in ICRP30 (Bruce Boecker, ITRI, personal communication). However, improved computer models have recently been developed that stress "mechanistic" concepts and take into account such physical parameters as the particle size of the inhaled aerosol (Mewhinney, Diel and Muggenburg, 1981). These models are discussed under an earlier section of this review.

One major shortcoming to the inhalation parameters given in ICRP30 is the failure to consider dusts of mixed composition (Bruce Boecker, ITRI, and John Stather, NRPB, personal communications), such as Pu-U mixed oxides and Pu containing dusts generated from a fast breeder reactor. The behavior of mixed dusts may differ markedly from the pure compound (John Stather, NRPB, personal communication). For example, at LASL, Pu aerosols containing ZrO_2 have caused lung cancers in hamsters, whereas the pure PuO_2 compounds do not (Thomas and Sullivan, 1979). The induction of lung cancer in hamsters is poorly understood, but serves to demonstrate the effects of dust mixtures on dose response. No further Pu exposures in hamsters are planned and much of the health effects research at LASL is now done at the cellular level (Robert Thomas, LASL, personal communication).

4.1.1.3 Organ Distribution and Retention of Actinides

The estimates of dose commitments from internal emitters depend heavily on parameters of organ distribution and retention times. For all the actinides, estimates of organ distribution are difficult because of wide interspecies variability among experimental

animals and the uncertainty of extrapolating results in experimental animals to man.

According to ICRP30, for all actinides, .45 of the blood-borne material enters bone and .45 enters liver, with retention half-times of 100 years and 40 years, respectively.

The estimation of appropriate liver retention times for the human is extremely difficult because of the dramatic differences in liver retention times among various species of laboratory animals. Retention times of actinides in rodents are extremely short (weeks) and retentions in other laboratory species vary from months (baboons) to years (beagles) (Norman Cohen, NYU, personal communication).

Liver retention times for actinides in humans has not been resolved. The liver retention is an important consideration for estimating the dose to liver and estimating the risk of developing liver cancer. There is recent evidence that the 40 year biological lives retention time proposed by ICRP30 for actinides is too long. For example, a model has been recently developed by Griffith et al., (1980-1981) for estimating distribution of ^{241}Am in the body from excretion analysis. Human data were used to validate the results from the model and liver retention times from 0.5 to 3 years for ^{241}Am were calculated.

Risk assessment for cancer from bone-seeking radionuclides in humans is based on analogy with radium. A large data base is available for humans exposed to radium from industrial or medical uses. Dosimetry to bone is determined by the amount of radiation delivered by incorporated radionuclides to surface endosteal cells. ICRP30 classifies plutonium and the other actinides as "surface seekers" which are uniformly distributed at the radiosensitive endosteal surface. By contrast, radium is "volume distributed," throughout the bone. Therefore, much of the radiation from radium is delivered to nonradiosensitive areas.

At the University of Utah, accurate microdistribution of Pu in bone and subsequent dose to endosteal tissue is studied. Recent findings include: (1) Pu is

not uniformly distributed throughout the bone but seeks highly vascularized bones with hematopoietic (red) marrow, (2) surface deposited Pu is subject to processes of bone remodeling which result in burial of substantial amounts of material within the interior of the bone, and (3) the rate of bone turnover is an important parameter in the tendency of a given burden of Pu to induce osteosarcomas (Webster Jee, University of Utah, personal communication). The data supporting these conclusions and the implications of these findings on dose response are discussed below.

Autoradiographic techniques from the bones of beagle dogs exposed to Ra and Pu have been used to verify the burial of surface Pu by remodeling processes (Wronski et al., 1980). These data are currently being used in a simulation model of remodeling processes and burial of Pu in bone (Webster Jee, 1982).

The newest data on Pu metabolism in bone will improve current understanding of the factors influencing genesis of Pu-induced osteosarcomas. For example, Ra gives rise to osteogenic sarcomas not related to high bone turnover sites. In contrast, Pu gives rise to osteogenic sarcomas related to high bone turnover sites (Webster Jee, University of Utah, personal communication). These conclusions are substantiated by a recent publication (Wronski et al., 1981) which suggests that the relative degree of ^{239}Pu deposition on trabecular bone surfaces and the rate of bone turnover plays a role in induction of osteosarcomas.

The data from the University of Utah studies indicate that the assumptions presented by ICRP30 for estimates of bone dosimetry of the actinides are inaccurate because no provision is made for the burial of surface-seeking radioactive materials (Webster Jee, University of Utah, personal communication and Charles Mays, 1982) and for the rate of bone growth (Webster Jee, University of Utah, personal communication). Also, the concept of average endosteal dose introduces major inaccuracies because it presents endosteal cells as a single, static population uniformly distributed over all bone surfaces (Webster Jee, 1982). Several investigators have recently emphasized that realistic models for burial and redeposition of plutonium in human bone are

needed in order to describe accurate dose-response relationships (Webster Jee, personal communication; Mays, 1982 and Priest, 1979).

Bone metabolism for actinides other than Pu are poorly characterized. Roy Thompson (1982a) reported that the ICRP30 values of .45 for retention of Np in bone corresponds to the average values reported in rats. However, some investigators have reported higher retention values (cited in Thompson, 1982a) and these may be more appropriate for conservative estimates. Because the microdistribution for Np as well as other actinides is poorly characterized, there are no clear data which support the assignment of Np as a volume or a surface seeker.

Chemical toxicity has largely been ignored in setting standards for actinide exposure. However, at least in the case for U and Np, chemical toxicity is clearly a concern when estimating potential health effects. For example, there is some evidence (discussed by Thompson, 1982a) that Np may represent an increased risk for carcinogenicity if the effects of chemical toxicity are considered.

4.1.1.4 Dose-Response for Internal Emitters

Recent results on dose-response relationships for internal emitters include induction of cancer by bone seeking radionuclides generated at the University of Utah and UC Davis and the dose response from inhaled radionuclides of various types studied at PNL and ITRI.

A large data base exists for the induction of bone cancer in humans from individuals exposed to radium as a result of industrial exposure (e.g., radium dial painters) and from German patients treated for spinal tuberculosis (BEIR III, John Rundo, ANL, personal communication). Risk estimates for all bone-seekers are based on analogy to radium with modifying factors for β-emitters and for surface seekers (ICRP30). The calculations of accurate RBE's for bone-seeking radionuclides relative to radium have been the subject of extensive research.

At UC Davis, a large number of beagles have been fed ^{90}Sr beginning *in utero* to the 540th day of life. Dose-response relations for the ^{90}Sr have been described and compared to dose-response from ^{226}Ra administered by injection (Book et al., 1980). The RBE of the ^{90}Sr relative to radium was dose rate dependent and decreased at lower dose rates (Raabe et al., 1981a).

Eighty percent of the premature deaths from ^{226}Ra were due to primary bone cancer. Causes of death due to ^{90}Sr ingestion included cancers of the soft tissue surrounding bone, leukemia and primary bone cancer (Raabe et al., 1981a). At dose rates greater than 1 rad per day bone dose, many animals incurred leukemia at cumulative doses of 1000 to 5000 rads. Animals which survived the 1000 to 5000 rad "window" for leukemia died later of bone cancer. Within the range of doses above 1 rad per day, the total cumulative doses resulting in bone cancers were lower for the lower dose rates (Raabe et al., 1980). For doses from .1 rad to 1 rad per day, carcinomas of soft tissue adjacent to bone, especially gingiva, were observed (Raabe et al., 1981b). No obvious life shortening was observed for an average dose rate to skeleton of less than .1 rad per day for ^{90}Sr and .05 rad per day for ^{226}Ra (Raabe et al., 1981b).

The high rate of leukemia induction reported in these studies could have an impact on risk assessment from ^{90}Sr exposure. Induction of leukemia in the UC Davis studies required protracted exposure of the bone cells (Raabe et al., 1981a). After feeding of the ^{90}Sr was ceased, ^{90}Sr was preferentially lost from the trabecular bone, resulting in a rapid reduction in dose to the bone marrow and a decreased incidence of leukemia (Raabe, 1981a). The occurrence of leukemias is rare after acute exposures to ^{90}Sr, even at high doses (Snipes et al., 1981).

The dose-response from beagles after ^{226}Ra exposure has been compared with the response in industrially-exposed humans. At similar dose rates, humans exposed to ^{226}Ra required 3.6 times longer to develop bone tumors when compared to tumor development in beagles (Raabe et al., 1981b). The latency period for tumor induction correlates with life expectancy.

Otto Raabe (UC Davis) has suggested that a "practical threshold" for bone cancer exists, which, in humans, occurs at about a cumulative dose of about 80 rads. Below this dose, induction times for tumor development exceed the human life span (Raabe et al., 1980).

Longevity studies are nearing completion at ITRI in beagles which have inhaled $^{90}SrCl_2$, $^{144}CeCl_3$, $^{91}YCl_3$, $^{137}CsCl$; and ^{90}Y, ^{91}Y, ^{144}Ce and ^{90}Sr which were bound to insoluble clay (fused aluminosilicate) particles (Hahn et al., 1981). With soluble aerosols (inhaled chlorides), all organs in which the radioisotopes were retained were susceptible to cancer. With insoluble aerosols (fused clay), cancers developed in organs receiving indirect radiation, such as the heart, and in organs receiving no appreciable radiation exposure. The latter observation indicates a systemic or whole-animal effect of the deposited radiation. For example, the radiation exposure may cause a general immunosuppression and predispose the animal to neoplasia throughout the body. These observations are difficult to reconcile with a "critical organ" concept which was utilized in ICRP2 for risk evaluation.

4.1.2 Ongoing and Proposed Research on Internal Emitters

The research which is ongoing or proposed is considered in several broad categories: (1) studies on GI tract absorption of actinides in experimental animals, (2) biokinetics and dosimetry of plutonium, (3) biokinetics and dosimetry of the other internal emitters, and (4) epidemiological studies of actinides in man.

4.1.2.1 GI Tract Absorption of Actinides

Studies on GI tract absorption and subsequent biokinetics, i.e., organ deposition and retention, and excretion patterns, of actinides are being conducted by Maurice Sullivan, PNL, Robert Larsen, ANL, Marica Bhattacharyya, ANL, and Norman Cohen at NYU. The proposed studies will potentially expand the current knowledge on gut metabolism of actinides. Of particular interest are characteristics associated with the exposed animal that may affect the experimental findings, including age, species, diet, and the chemical

form of the actinide. The four investigators appear to communicate well with one another and to share intermediate results.

Maurice Sullivan, PNL, has generated most of the recent data on Np and has planned further studies in rats to clarify the pathological effect of a high concentration of Np on the GI tract and the potential effects on the kidney (Maurice Sullivan, PNL, personal communication). Sullivan is currently evaluating data defining the effect of fractionated administration on gut absorption of NP. These studies should enhance the understanding of the chemical toxicity of Np but will require additional funding by DOE (Maurice Sullivan, PNL, personal communication).

Robert Larsen, ANL, and Norman Cohen, NYU, (personal communication) have initiated a joint study in adult baboons on the metabolism of Np and of other actinides following GI tract absorption. These studies would provide important data for the extrapolation of the actinide data from experimental animals to the human. Factors to be investigated include the effect of nutritional status of the animal and the chemical form of the ingested isotope on GI tract absorption. This project was initially sponsored by DOE and subsequently went under contract with NRC. Currently, no additional funding is forthcoming from NRC. Some baboon exposures are underway with the citrate form of Np (Norman Cohen, NYU, personal communication). If funds are available, baboons will also be exposed to Np bicarbonate. Also, Norman Cohen (NYU, personal communication) plans studies on chelation therapy for the removal of internal Np. These would employ several types of chelators, since DTPA is relatively ineffective for Np (Norman Cohen, NYU, personal communication; Thompson, 1982).

Robert Larsen (ANL, personal communication) discussed other studies which he would like to perform on GI absorption of Am, Th, Pa and U, with emphasis on intragastric behavior. Norman Cohen and Robert Larsen were extremely enthusiastic about the potential value of their results, but were uncertain about the funding status of these studies.

4.1.2.2 Plutonium Metabolism

4.1.2.2.1 Injected Plutonium Comparison to Radium

Most of the studies on the RBE of plutonium relative to radium are underway at the University of Utah. Ongoing studies include: (1) toxicity of ^{239}Pu and ^{226}Ra in young adult beagles, (2) toxicity of ^{239}Pu and ^{226}Ra in juvenile and mature beagles, (3) development of mathematical models to describe the comparative toxicity of the actinides, and (4) toxicity of ^{239}Pu and ^{226}Ra in St. Bernards. These studies focus on dose-response relationships, especially neoplasia induction as related to endosteal cell dose. Most of the information on these studies, which are discussed below, is contained in the current budget submission.

A study on toxicity of injected ^{239}Pu and ^{226}Ra in young adult beagles, will yield (1) dose-response relationships and (2) data on bone-turnover. Preliminary data have been incorporated into a mathematical model by E. Krimmel (1982) which allows extrapolation of risk estimates to man. The model describes plasma and skeletal retention and emphasizes liver and bone toxicity. Data for bone turnover of beagles and humans were provided by in vivo prebiopsy labeling with tetracycline.

Because of the relationship between bone turnover rate and dose-response (Wronski et al., 1981), a second study was designed to determine the effect of age on the dose-response to Pu. Plutonium-239 and ^{226}Ra were injected into juvenile (3 months) and mature (5 years) beagles. This study has included dogs sacrificed at early times after injection for determination of retention over time as a function of age, and dogs maintained for long-term observations for dose-response relationships. A pilot study has been completed and all animals on line for this study have been injected.

A study is ongoing in which ^{239}Pu and ^{226}Ra at graded dose ranges were injected in St. Bernards. This study was initiated because of the high natural sensitivity of St. Bernards (185 times more sensitive than man - Glen Taylor; University of Utah, personal communication) to bone cancer. Data from this study will

yield the relationship between natural susceptibility to bone cancer and susceptibility to radiation-induced bone cancer. Preliminary information indicates that the St. Bernards are 5 times more sensitive to radiation-induced bone cancer than is man (Taylor, 1982).

Charles Mays (University of Utah, 1982; personal communication) is heading a project which would clarify comparative toxicity of ^{224}Ra in mice, beagles and humans. The human aspect is based on followup of German patients treated for spinal tuberculosis with Ra injections. The group proposes the injection of 36 beagle pups (3 months old) with ^{224}Ra. Some of these animals would receive ^{224}Ra in combination with a colloidal platinum and eosin. This therapeutic regimen, of ^{224}Ra and the colloidal substance, is directly analogous to the therapy used on the German patients.

The large body of information generated by the University of Utah project is utilized by a group headed by Webster Jee (University of Utah) in the development of skeletal risk simulation models (Jee, 1982). These models correlate microdosimetry, tumor site and incidence, and parameters of skeletal turnover in beagles, St. Bernards, mice, rabbits and man. A computer simulation of adult structural bone turn-over and interaction of ^{239}Pu with the bone remodeling system has been constructed. Information on ^{241}Am microdistribution has been incorporated into this model. Other factors affecting skeletal risk are under study, including various aspects of bone physiology, such as osteoporosis, pregnancy and Vitamin D deficiencies. Bone microdosimetry studies are ongoing, under the direction of Webster Jee, for ^{239}Pu nitrate, ^{239}Pu oxide, ^{238}Pu oxide, ^{244}Cm and ^{241}Am. Many of the samples have been generated by inhalation exposure of beagles to actinides at other laboratories, especially PNL and ITRI.

In summary, the studies at the University of Utah are providing data on dose-response relationships at low doses and differences in dose response in populations of different ages and of different radiosensitivities. The development of skeletal microdosimetry models will contribute to dosimetric considerations in

health protection and to an understanding of the mechanisms of radiation-induced carcinogenesis.

4.1.2.2.2 Other Metabolism Parameters and Dose-Response Relationships for Plutonium

Studies of the metabolism of inhaled Pu are ongoing at UC Davis, PNL and ITRI. At PNL, studies are in progress in dogs that have inhaled various plutonium compounds (Park, 1982). Plutonium oxide studies were initiated in 1972, 1973 and a significant number of unexposed controls and low level exposed dogs are still living (Roy Thompson, PNL, personal communication). These studies should yield dose-response relationships for low exposure levels in the near future. Dogs were exposed at PNL to $^{239}Pu\ (NO_3)_4$ in 1976 and 1977 (Dagle, 1982), and most of these dogs are still living.

A number of studies on the effect of inhaled Pu in rats are ongoing at PNL. Rats have been exposed to small amounts of PuO_2 resulting in life span radiation doses of 2 to 100 rads (Sanders, 1982). These animals are being held for life-span observations.

A project on toxicity of Pu in prenatal and juvenile rats is underway at PNL (Sikov, 1982). Preliminary data indicate age-related differences in ^{239}Pu microdosimetry and concentration among skeletal components which result in variations in the anatomic distribution of the bone tumors. Late gestation has been identified as a relatively radiosensitive period for exposure to Pu. Additional data on ^{239}Pu distribution and dosimetry with exposure at different ages will be forthcoming from these studies.

Several studies at PNL are investigating potential synergistic effects of compounds inhaled in conjunction with Pu. For example, rodents have been exposed to Pu together with sodium, which could be released from a liquid metal fast breeder reactor (Hackett, 1982). Also, dogs and rats have been used in studies on the effect of cigarette smoking on plutonium metabolism (Filipy, 1982).

A program to investigate the metabolism of actinides, including Pu, administered by intratracheal

instillation in beagles and nonhuman primates has been proposed by Otto Raabe at UC Davis (personal communication).

At ITRI, a number of studies are being conducted which address dosimetry and dose-response to inhaled Pu under a variety of exposure conditions. These include studies with both $^{238}PuO_2$ and $^{239}PuO_2$ in beagles (Muggenburg et al., 1981). Preliminary data from the $^{238}PuO_2$ animals have been used in the development of a "mechanistic simulation" model which includes kinetics of transfer and retention in several intralung compartments as well as in blood and other organs (Mewhinney et al., 1981). Life-span studies with $^{238}PuO_2$ in young adult beagles and $^{239}PuO_2$ in young adults, immature and aged beagles are ongoing (Muggenburg et al., 1981). In these studies, animals were exposed to several sizes of monodisperse aerosols and achieved a graded range of lung burdens. The aged dogs to date have died earlier and at slightly lower body burdens than have younger dogs. A sacrifice study has been performed in Cynomolgus monkeys, mature and immature, with inhaled $^{239}Pu(NO_3)_4$ (Brooks et al., 1981). A study is in progress on the toxicity of $^{239}PuO_2$ in Fisher (344) rats. This study will yield information on the dose-response to low amounts of inhaled plutonium and on the effect of repeated inhalation exposures. In preliminary observations, slightly decreased survivability has been seen at the lowest lung burden of 0.012 Ci ^{239}Pu/kg body weight (Redman et al., 1981).

In summary, the metabolism, dosimetry and dose response to Pu are studied under several DOE contracts. The program at the University of Utah will establish more accurate RBE's for Pu relative to Ra, following IV injection in beagles. PNL and ITRI are looking at dose response after inhalation exposure in rats and beagles. All of the above mentioned laboratories have ongoing studies which address the question of the age-dependence of radiosensitivity. Studies of GI absorption and subsequent metabolism of Pu have been proposed by Norman Cohen of NYU and Robert Larsen of ANL, as discussed in the previous section, and Otto Raabe of UC Davis has proposed intratracheal instillation of ^{241}Pu in non-human primates. ITRI also is

proposing some non-human primate studies, although details in the personal communications were scanty. The funding climate is such that few new lifespar studies have been proposed in large animals. For example, studies of longevity in beagles at PNL after inhalation of $^{238}Pu(NO_3)_4$ have not been initiated as planned and may be abandoned (Roy Thompson, PNL, personal com- munication). For the future, the majority of studies will probably be short-term, with a focus on such vari- ables as age and nutritional status of the experimental animal.

4.1.2.2.3 Internal Emitters Other Than Plutonium

Several ongoing and proposed studies address the metabolism and toxicity of other actinides, besides Pu, and of other internal emitters. In the future, new dose-response studies based on longevity in large animals are unlikely because of the funding considerations discussed above. However, an ambitious program on actinide toxicity is underway at the University of Utah. Also, several short term metabolism studies and longevity studies in laboratory rodents are being conducted at PNL, ITRI and University of Utah. Lifespan studies on inhaled fission products in beagles, initiated previously at ITRI, are nearing completion. These studies are discussed below.

At PNL, inhalation toxicity of actinides in rodents is being studied. These studies include pulmonary and skeletal carcinogenesis with inhaled $^{241}AmO_2$ and with fractionated exposures to $^{244}CmO_2$. In preliminary results, these fractionated exposures of $^{244}CmO_2$ have led to an increased yield of lung and bone tumors as compared to an earlier study with a single exposure to $^{244}CmO_2$ (Sanders et al., 1978). At PNL, a study in which dogs inhaled $^{241}AmO_2$ is complete. The studies of actinides have been funded until completion, but some ancillary studies may be eliminated due to reduced funding (Roy Thompson, PNL, personal communication).

Studies are also being performed in rodents at PNL on the inhalation hazards encountered by uranium miners. These studies include the roles of unattached radon daughter products and of daughter product

disequilibrium in the inhalation hazards. Also, beagle dogs are on study to determine the pathology with chronic inhalation exposures to carnolite uranium ore dust, with and without exposure to radon daughter products.

A major project at PNL investigates the biological hazards associated with uranium-thorium breeder fuels and fuel recycle process solutions (Ballou, 1982). These studies include a study of long term pulmonary retention of inhaled $^{233}UO_2(NO_3)_2$ and $^{232}UO_2(NO_3)_2$ in rats. Male rats have been exposed to graded doses of ^{231}Pa citrate aerosols.

At ITRI, a relatively small number of studies are underway on actinides other than Pu. Rats have inhaled $^{244}CmO_x$ and are being held for life-span observations (Guilmette et al, 1981). From previous studies in which beagle dogs inhaled monodisperse or polydis- perse aerosols of $^{241}AmO_2$, a simulation model has been developed for prediction of organ retention after Am exposure (Griffith et al., 1981).

Studies have been proposed by Otto Raabe (UC Davis, personal communication) for intratracheal instillation in beagles and non-human primates of Cm, Am and breeder fuel, as well as ^{241}Pu. These studies will locus on metabolic parameters, but a study on dose effects is also being proposed.

At the University of Utah, studies on the metabolism and toxicity of a number of actinides in beagles and rodents are underway. As a control for the beagle studies on actinide metabolism, the background concentration of actinides on beagles is being determined (Narayani Singh, University of Utah, personal communication). Tissues have been obtained from unexposed dogs at ITRI and at UC Davis as well as from the colony at the University of Utah.

As part of the comprehensive program on actinide toxicity at the University of Utah, beagles have been injected with ^{244}Am, ^{249}Cf and ^{252}Cf and are being held for lifespan observations. Also, short term studies with ^{233}U, ^{249}Cf, ^{252}Cf, ^{241}Am, $^{243/244}Cm$ and ^{253}Es have been completed. The metabolism of

these actinides is being studied especially as relates to dosimetry, and the effectiveness, compared to Pu, in producing osteosarcomas is being estimated. Bone microdosimetry for Cm^{244} and Am^{241} is being incorporated into "skeletal risk" models (Jee, 1982).

Data from previous studies in which animals were injected with ^{228}Th, ^{232}U, and ^{228}Ra are being analyzed to estimate potential risk from these radionuclides in humans (Wrenn, 1982a). The data collected from the studies of the comparative toxicity of the actinides in beagles is being compiled by Ed Wrenn and Narayani Singh into mathematical models which describe time-dependent organ and tissue concentrations. This project includes a summary of accepted human dosimetric models and an analysis of human data available from sources such as in uranium miners (discussed below) (Wrenn, 1982a).

An experiment is underway at the University of Utah under Glenn Taylor (1982; Glenn Taylor, University of Utah, personal communication) in which the toxicity of a number of actinides is being compared in laboratory mice, Deer mice (Peromyscus maniculatus) and Grasshopper mice (Onychonys leucogaster). Metabolic studies have shown that the non-laboratory mouse species have prolonged retention of Pu and Am in liver and skeleton. These longer retentions may render the wild mice species more suitable than laboratory mice for dose response studies. This study was initiated because of widespread concern that the current risk estimates for liver cancer with actinides are inaccurate (C. Mays, 1982, Glenn Taylor, University of Utah, personal communication). Risk estimates in humans are based on human epidemiological data, derived from patients which were injected with thorotrast. The carcinogenicity of thorotrast may be enhanced compared to other actinide compounds by chemical toxicity. Existing experimental data on laboratory animals, on the other hand, may not be appropriate for extrapolation to man because the liver retention times for actinides is so short for laboratory rodents and because the susceptibility to bone cancer in beagles may override liver carcinogenicity of actinides in this species.

The above project under Glenn Taylor, University of Utah, also includes a study which will compare liver carcinogenicity of ^{241}Am directly with that of thorotrast. ^{241}Am is less likely to induce bone cancer than is Pu. Therefore, liver carcinogenicity is more likely to be detected with ^{241}Am than with Pu. The premise of the study is as follows:

$$\left[\frac{Am^{241}}{\text{Thorotrast}}\right]_{\text{Animal}} = \left[\frac{Am^{241}}{\text{Thorotrast}}\right]_{\text{Man}}$$

Accordingly, Deer and Grasshopper mice, which avidly retain actinides in the liver, have been injected with overlapping doses of ^{241}Am and thorotrast. Charles Mays discussed the importance of the forthcoming dose response data in a recent publication (1982).

At UC Davis, the 20 year project in which dogs ingested ^{90}Sr is "nearing completion" (Marvin Goldman, UC Davis, personal communication). However, according to a recent paper (Raabe et al., 1981b) there are several hundred living dogs. These dogs will provide additional data on the response to the low doses of ^{90}Sr measured as a decrease in longevity. Also, this study may yield computer models of metabolism and dosimetry of bone-seeking radionuclides at a cellular level (Raabe et al., 1981a). The UC Davis program has recently experienced a 10-20% funding cut from DOE (Marvin Goldman, UC Davis, personal communication). Ten percent of the total funding is from the NRC.

ITRI is nearing completion on several long-standing studies of longevity following inhalation of fission products in beagle dogs. These studies include $^{90}SrCl_2$, $^{144}CeCl_3$, $^{91}YCl_3$, $^{137}CsCl$ and ^{90}Y, ^{91}Y, ^{144}Ce and ^{90}Sr which were bound to insoluble clay (fused aluminosilicate) particles. Some dogs exposed to low levels of radioactive materials remain, and further dose-response relationships at low levels are expected.

4.1.2.2.4 Actinide Metabolism in Man

Data on actinide metabolism in humans are invaluable in the extrapolation of dose response information from experimental animals to man. Such data are collected at the University of Utah and at PNL. At the University of Utah, the Department of Defense is funding a study, headed by Narayani Singh, on actinide content of autopsy tissues from residents of Southern Utah, who were exposed to heavy fallout from nuclear weapons tests, as compared to tissue from residents of Northern Utah (Narayani Singh, University of Utah, personal communication). Also at the University of Utah, an NRC funded project is ongoing on the actinide content of lungs from uranium miners. Results to date were summarized in a recent report (Singh, 1981). Organ distribution values in the uranium miners agreed with ICRP30 predictions. At ANL an ongoing study is headed by John Rundo on populations exposed to radium from industrial applications (John Rundo, ANL, personal communication). This study is funded by the NRC. A proposal to determine actinide content of autopsy tissues from the general population has been submitted to DOE by Ed Wrenn of the University of Utah (Wrenn, 1982b).

In summary, the metabolism and dose-response to actinides other than Pu are under study by several DOE-funded laboratories. Beagle dogs have been exposed to aerosols of $^{241}AmO_2$, various uranium aerosols and have received injections of a number of actinides. Many studies of actinides are being conducted in rodents. Some studies on non-human primates have been proposed at NYU and at UC Davis. With funding of the non-human primate studies and with completion of the rodent studies, the metabolism of a number of actinides will be more completely characterized than is now possible.

4.2 Somatic Effects of Ionizing Radiation

Most research on the somatic effects of ionizing radiation concentrates on the induction of cancer. Current data indicate that ionizing radiation shortens life primarily by neoplastic disease (BEIR III). Several issues are at the forefront of research on the

induction of cancer by ionizing radiation: (1) the shape of the dose response curve at low doses and dose rates, (2) the effect of fractionated doses as compared to acute exposure, (3) the effect of age on the radiosensitivity of exposed populations, (4) the RBE of neutrons compared to gamma external radiation and (5) the possibility of a radiosensitive subpopulation which may warrant special consideration in risk assessment.

4.2.1 Recent Results

4.2.1.1 Dose-Response

Research has been conducted at ORNL on the carcinogenicity of ionizing radiation in large numbers of mice. The effects of low dose rates, radiation quality (gamma vs. neutron) and natural incidence of cancer in the exposed animal population have been studied. In experiments to date, which encompass approximately 40,000 mice of different strains, the dose response to gamma radiation has been described as complex. No simple model describes the dose-response relationship over the entire dose range (Storer et al., 1979) and the shape of the dose-response curve is affected by a number of factors. Dose-response is affected by the sex of the exposed animal, strain of mice and the end point selected for response (Storer et al., 1979). If the induction of a particular type of tumor is assessed, the dose response curve depends on the tumor (Ullrich and Storer, 1979, Ullrich, 1980).

At ORNL, the relative effect of gamma and neutron radiation has been compared. The RBEs for neutrons relative to gamma radiation for life shortening (Storer et al., 1979) and for induction of lung tumors (Ullrich, 1980b) increased with increasing dose. That is, the ratio of the incidence of a given effect, for example cancer induction, induced by neutron radiation to the incidence of the same effect induced by gamma radiation depends on the doses of the two types of radiation. The ratio is lower if both gamma and neutron doses are high than if both gamma and neutron doses are low. Neutron irradiation is more damaging, compared to gamma irradiation, at low doses.

The effects of fractionation of dose on dose-response are different for neutron exposure when compared to effects from gamma exposure. Fractionating doses had no effect on the induction of lung tumors by a total cumulative dose of neutron irradiation although the fractionation of gamma doses at higher dose rates decreased the tumorigenicity of a given dose (Ullrich, 1980b).

R. Ullrich has recently reported (1982a,b) that the dose response to neutrons "bends over" in the 10 to 20 rad dose range. That is, the dose response curve becomes convex rather than decreasing linearly with decreasing dose. These results are important because they indicate that linear extrapolation from data above 50 rads could result in an underestimation of risk. Indirect evidence was presented which supported linear response at low doses (below 10R) rather than a continuation of the convex curve (Ullrich, 1982b).

In a comparison of studies on different strains of mice and species of rodents at ANL, Fry et al., (1982) concluded that the relative risk of cancer induction by radiation derived from these studies may be extrapolated directly to man because the incidence of radiation-induced cancer is a direct function of the natural susceptibility to cancer.

ANL is conducting studies similar to ORNL using mice to investigate RBEs of neutrons relative to gamma radiation and the biological effects of low doses of ionizing radiation. Studies at ANL include the induction of myeloproliferative disorders (leukemia) by ^{60}Co irradiation of beagles. A large number of mice are also under study, and the program includes studies of cell transformation <u>in vitro</u>.

A high incidence (45%) of nonlymphatic leukemia occurs in dogs which are exposed continuously until death at dose rates of 5 and 10 rads per day of whole body ^{60}Co radiation (Tolle et al., 1982). Results from ^{60}Co irradiation in beagles have yielded dose response curves for induction of myeloproliferative disorders similar to the dose relationships derived in the ^{90}Sr feeding experiments at UC Davis (Tom Fritz, ANL, personal communication). Data suggest that the

induction of neoplastic disease ("leukemogenic event") occurs at about 2000R total accumulated dose, although leukemia is not detected clinically until later.

The dogs at ANL exposed to intermediate doses of 5 to 10 rads per day ^{60}Co radiation, responded in one of two ways. Some of the dogs incurred an immediate depression of all types of circulating blood cells, from which they never recovered. These dogs died of aplastic anemia at 200 to 300 days after the initiation of exposure. The remaining dogs also developed a depression of circulating blood cells at the initiation of exposure, but the hematopoietic system of these latter dogs rebounded to pre-exposure levels. Although the hematopoietic system appeared to develop resistance to the radiation, these dogs died later of leukemia. The early death of some of the dogs with intermediate doses of ionizing radiation is considered evidence for the existence of a radiosensitive subpopulation (Tom Fritz, ANL, personal communication, Tolle et al., 1982). Definitive evidence for such a radiosensitive population among humans could have a major impact on risk assessment (BEIR III).

The effects of lower dose rates of ^{60}Co radiation have not been resolved. In preliminary results from dogs exposed to 2.5 rad/day, no pattern of depression of circulating blood cells has been observed, but some dogs incur leukemia at a cumulative dose of approximately 2000 rads (Tolle et al., 1982). The latter observation indicates the importance of cumulative dose in the induction of myeloproliferative disorders. However, if the exposures are terminated at 200 to 300 days (at cumulative doses of 1000 to 3000 rads), the incidence of leukemia decreases (Tom Seed, ANL, personal communication).

Tom Fritz, Tom Seed, and Doug Grahn (ANL, personal communications) expressed an interest in the physiological events which precede the development of myeloproliferative disorders. Recently, dogs exposed to very low dose rates (0.3 rads per day) were observed to incur a subclinical leukocyto-platelet depression (Tom Fritz, ANL, personal communication). The leukocyto-platelet depression is an important physiological observation for indicating pathological effect of low

dose rates. In the future, comparison of physiological parameters associated with gamma vs. neutron irradiation may provide insight into the mechanisms of the induction of leukemia (Tom Fritz, ANL, personal communication).

The investigators involved in the ANL studies are optimistic that this work will yield basic information on cancer induction by radiation. Theoretically, the sequel of events leading to leukemia induction by gamma radiation reflects hematopoietic damage followed by activation of repair mechanisms. These repair mechanisms temporarily restore hematopoetic function to resistant animal populations. Leukemia ultimately results because the mechanisms are error-prone and lead to proliferative disorders (Tom Fritz, ANL, personal communication). Following exposure to neutrons, repair mechanisms are evidently not activated. Such repair mechanisms would result in decreased effectiveness of fractionated exposures. However, an ameliorating effect of fractionation of neutron exposures is not observed. Because repair mechanisms are not activated, fewer leukemias and increased soft tissue tumors would be expected from neutron exposures when compared to gamma exposures. This hypothesis, of leukemia arising from error-prone repair mechanisms, may receive support from the current re-evaluation of the role of neutrons in dose response in Hiroshima-Nagasaki survivors (Tom Fritz, ANL, personal communication).

The effect of ^{60}Co irradiation in beagles is also studied at UC Davis (Stitzel et al., 1981). Irradiation at dose rates up to 11 Roentgen per day was initiated in utero. These animals have survived much higher cumulative doses than have animals in which exposures were begun postnatally (after birth). These studies demonstrate the ability of an exposed animal to develop radioresistance, presumably through activation of repair mechanisms.

The effects of external gamma or neutron irradiation of 40,000 mice have been studied at ANL since 1971 (Thomson et al., 1982a). These studies have been summarized in a series of articles by Thomson et al., (1982a,b, 1981a,b). Several differences have been observed between the effects of neutron vs. ^{60}Co

gamma radiation. As reported in the studies at ORNL, fractionation of a given dose of neutrons did not affect the response, but fractionation decreased the effectiveness of a given dose of gamma. Neutrons were more likely than gammas to induce lung tumors and less likely than gammas to induce lymphoreticular tumors. As in the studies at ORNL, the effectiveness of a given dose of neutrons in producing tumors or life-shortening increased at low doses relative to gammas (Doug Grahn, ANL, personal communication). Studies are ongoing which determine the RBE's of neutrons relative to gamma at doses below 20 rads (Doug Grahn, ANL, personal communication). In preliminary observations, the RBEs of neutrons compared to gamma have been observed to continue to increase at very low dose rates (Doug Grahn, ANL, personal communication).

Grahn et al., (1978) summarized the mortality findings from mice of different sex and genotype exposed to different dose rates of gamma radiation. The life shortening per rad was dependent on cumulative dose and was independent of the above factors. The authors de-emphasized the importance of natural sensitivity to radiation induced cancers and indicated that percentage life-shortening per rad could be extrapolated directly between species. If data on life shortening in mice can be extrapolated directly to man, the current maximum permissible dose (ICRP30) accumulated over a lifetime could have a significant impact on longevity in humans.

In cell cultures exposed to gamma or X-irradiation, fractionation of doses increased cell survival rates and decreased transformation frequency. Results indicated that subeffective transformation damage is repaired during low dose-rate irradiation (Han, Hill and Elkend, 1980). However, with neutrons, reduced dose rates resulted in increased transformation frequency. The investigators concluded that neutrons don't induce repair or increase the net error-prone component of repair (Hill et al., 1982). In an unpublished study (Han, unpublished summary) neutrons were more effective at transforming cells when delivered at reduced dose rates compared to high dose rates. Han expressed concern (unpublished summary) that the risk of cancer induction due to work-related exposure in the

nuclear power industry may be greater than predicted from linear extrapolation to low doses from high dose exposure.

4.2.1.2 Age-Dependence of Radiosensitivity

The effect of age at the time of exposure on the response to radiation is studied at the Radiological Health Laboratory at CSU under S. Benjamin. This project was initiated to investigate epidemiological findings of increased childhood cancers in individuals who received X-irradiation in utero (Stewart, 1956). The program at CSU is currently sponsored by the National Cancer Institute (NCI) and Federal Drug Administration (FDA) through October, 1982. The continuation of this project will depend on a new source of funding.

The research at CSU may be divided into 5 major sections. The first has characterized prenatal (prebirth) development and short-term prenatal radiosensitivity, with particular emphasis on malformation, growth retardation and pre- and neonatal mortality. The second study has investigated delayed effects within a few years following exposure to the LD_{50} dose level. The third, largest study, is looking at effects on longevity of perinatal (time period surrounding birth) irradiation at relatively low doses. A fourth study is designed to characterize disease incidence among 72 environmental control dogs. The fifth study examined radiosensitivity of 50 aging dogs.

In the perinatal radiosensitivity study a total of 1680 beagles were exposed to 16 or 83 rads of ^{60}Co gamma radiation at either 8, 28 or 55 days post-coitus (conception) or at 2, 70 or 365 days post partum (after birth). Of these, 93 dogs have developed neoplasias, including 81 malignancies. Four dogs died under the age of two of malignancies, a rare event in unexposed dogs. Results to date demonstrate an increased sensitivity to radiation carcinogenesis in late prenatal and early neonatal life (Benjamin, 1980b).

The mean age of dogs from the CSU study is 10 years. The investigators expect to see increased mortality due to malignancy in the irradiated animals as the dogs grow older. There is also a possible

increased incidence of renal disease in these exposed dogs (Benjamin, 1980b). Because many of the animals exposed perinatally to 16 rads remain alive, funding of this project is crucial for collection of further dose-response data available from this animal population.

Studies to determine the dose-response to internal emitters, especially actinides, on immature and aged animals at ITRI and University of Utah indicate that both old and very young individuals may be more radiosensitive than young adults (Muggenburg et al., 1981; Park, 1981).

In summary of somatic effects of ionizing radiation, studies at ORNL and ANL show that the RBE of neutrons relative to gamma radiation increases at decreasing dose rates. Also, some recent results from mice exposed at low dose rates at ORNL and in cell culture at ANL indicate that the dose response curve for neutrons may actually be convex at low doses. Therefore, the concern exists that linear extrapolation of the dose response curve may underestimate the health risk from neutron exposure at low doses. Contributing to this concern is the evidence that very little repair of neutron-induced damage occurs with fractionated exposures.

Also potentially important to risk assessment from external ionizing radiation are the studies at ANL for leukemia induction by ^{60}Co exposures in beagles. These studies indicate the importance of cumulative dose in dose response. Also, the development of fatal aplastic anemia in some of these animals may indicate the existence of a radiosensitive subpopulation. BEIR III discussed the potential impact that the demonstration of a radiosensitive population in humans could have on risk assessment.

Age at exposure affects radiosensitivity. The experiments at the Radiological Health Laboratory at CSU have confirmed the epidemiological findings of Alice Stewart (1956) that the perinatal period is highly radiosensitive. In a recent report (1980a), Steve Benjamin (CSU) concluded that the findings of radiation carcinogenesis at single doses of 16 rads and 83 rads in a small number of experimental animals

exposed perinatally indicates a potential hazard for smaller doses to larger populations.

4.2.2 Ongoing and Proposed Research on the Somatic Effects of Ionizing Radiation

Several studies in progress at ANL are examining the induction of leukemia by ^{60}Co radiation at low dose rates in dogs and the relative effects of gamma and neutron radiation in mice. Dogs are being exposed to 0.4, 1.0 and 2.5 rads per day of ^{60}Co radiation. In preliminary observations, leukemia has been observed at a predictable cumulative dose in dogs exposed to 2.5 rads per day (Tolle et al., 1982). Therefore, these studies potentially will confirm the "additivity" (i.e., dose rate independent) effect of low dose ionizing radiation in dogs and will be useful in extrapolating the data to human exposures (Tom Fritz, ANL, personal communication).

At ANL, the NRC is funding studies on neutron and gamma radiation in large numbers of mice to predict the dose response and life shortening of very low doses of radiation (Thomson ,1982b). These studies are about 40% complete and preliminary results indicate that the dose response is linear at low doses (Doug Grahn, ANL, personal communication). A study is in progress which compares the effect of ionizing radiation in laboratory mice compared to the effect of a longer-lived wild rodent, the white-footed deer mouse. Preliminary results indicate that both species of mice incur the same degree of risk, expressed as percentage life-shortening. Also, a large study has been initiated in which mice are administered 24 weeks of gamma radiation at low dose rates of 1 to 10 millrads per minute to examine the dose-response to protracted doses.

Tom Seed (ANL, personal communication) has proposed a study in collaboration with Dr. Flüdener at the University of Ulm in West Germany. This study would compare the response to gamma and neutron irradiation of hematopoietic stem cells taken from mice, dogs and men. Such a study would provide baseline information for the use of stem cells as biological dosimeters, as well as for information on interspecies variability in radiosensitivity.

In the future, Doug Grahn (ANL, personal communication) would like to pursue studies on the mechanisms of radiation injury. Such studies would examine the differences in response with neutron vs. gamma radiation. Tom Seed and Tom Fritz (ANL, personal communication) emphasized the value of pursuing the mechanisms of induction of myeloproliferative disorders in whole animal systems. The hope is that study of hematopoietic response to low dose radiation will yield pivotal information on the primary radiation-induced lesion.

4.3 Genetic Effects of Ionizing Radiation

4.3.1 Recent Results

The majority of the research on the genetic effects of ionizing radiation is conducted at ORNL by a group under the direction of Lea and William Russell. The technique used by BEIR III for estimating the induction of mutation by ionizing radiation was developed by Paul Selby of this group. This system quantitates mutations on a per gamete (i.e., per sperm or oocyte) basis based on the detection of dominant skeletal mutations (DSM). Earlier risk estimates (BEIR I) were based on specific locus mutations (SLM) which described mutations on a per gene basis. Most of the ongoing research in mouse mutations supports the conclusions of the BEIR III committee (Lea Russell, ORNL, personal communication).

A recent publication (Russell and Kelly, 1982) described the effects of low dose rates on specific locus mutations (SLM). There were no statistically significant differences between mutations obtained with 300 rads of external gamma irradiation delivered at 0.005 rads/minute and 0.0007 rads/minute compared to radiation delivered at 0.8 rads/minute. This supports the earlier hypothesis that, below approximately 0.8 rads/minute, the frequency of mutation is independent of dose rate and is linearly related to dose. This assumption has been used by national and international committees concerned with risk estimation (Russell and Kelly, 1982).

The amount of information forthcoming from the ORNL mouse experiments is limited by the labor-

intensive nature of the research and the probability of funding cuts (Lea Russell, Paul Selby, ORNL, personal communications). Nonetheless, ambitious future research has been planned.

4.3.2 Ongoing and Proposed Research

Mutation damage induced by internally deposited plutonium is being investigated (Lea Russell and Walderico Generoso, ORNL, personal communications). A study is in progress at ORNL to determine the induction of DSMs and SLMs in mice which were sired by males injected IV with 10 Ci per kg of ^{239}Pu citrate. In preliminary studies, the rate of induction of mutations by Pu was higher at 6 months than at 1 year (Walderico Generoso, ORNL, personal communication).

Some work has been done at ITRI (Brooks et al., 1981b) to establish the RBE of Pu, relative to ^{137}Cs, for induction of mutations in Chinese hamster liver cells, *in vivo*. A RBE for Pu of 15 was estimated, and is comparable to the RBE of 13 used by the BEIR III committee.

Paul Selby, ORNL, (1982a,b) has developed methods for detection of mutations in the first generation of offspring without further breeding. In the original studies, animals were bred in painstaking experiments to trace the development and transmission of a mutation. The use of the new "non-breeding" clinical tests greatly expedites studies of the induction of mutations.

These "non-breeding" methods are being used in a study on mutations induced at low dose rates (.005 R/minute) of ionizing radiation. Also, the induction of DSMs in gonial (in the stem cells producing sperm) vs. post-gonial (in the sperm themselves) tissue has been investigated. Early results indicate that, unlike SLMs, DSMs are gonial rather than post-gonial. This finding is significant because post-gonial mutations are eliminated with time but the genetic damage persists in gonial mutations, because they occur in the stem cells of the reproductive organs.

Paul Selby of ORNL has also proposed a study to examine the induction of mutations in females, because

the radiosensitivity of the oocyte is relatively poorly characterized. The funding for such a study is uncertain. Selby indicated that the development of non-breeding tests for DSM may permit the investigation of "irregularly inheritable disorders." These disorders account for the majority of human genetic disease (Paul Selby, ORNL, personal communication). The irregularly inheritable disorders are passed as dominant traits, but due to incomplete penetrance, the trait may or may not be expressed in the individual. These disorders are adequately modeled by the DSM system. Previous studies in which multigenerations of mice were exposed to low doses of ionizing radiation have indicated that the mutational component in irregularly inheritable disorders is negligible. However, the earlier studies monitored longevity of the population as an end-point, which could be masked by the large population variability in longevity. The use of DSM in studies of the inheritance of these disorders may uncover important evidence concerning the overall genetic risk from ionizing radiation.

4.4 Actinides in the Environment

4.4.1 Recent Results

4.4.1.1 Soil Mobility and Plant Uptake

A number of studies characterize the behavior of actinides within contaminated soil. Among the subjects studied are the degree of vertical movement of the radioisotopes within the contaminated soil, the degree of root uptake in contaminated soil, the relative contribution of surface deposition as compared to root uptake following atmospheric releases, and the degree of concentration of the contaminant in edible parts of the plant. These studies appear to be securely funded over the near future.

Gene Schreckhise (PNL) is studying uptake of ^{239}Pu in the oxide vs. nitrate form in various crops. The uptake of the oxide is 10 to 100 times less than the nitrate (Gene Schreckhise, PNL, personal communication). Gene Schreckhise has also studied soil mobility of Np. The mobility decreased with time, but the Np has remained highly mobile over 5 years of

study. Np is consistently a factor of 1000 more available for plant uptake than is Pu (Gene Schreckhise, PNL, personal communication).

In a study that compared the plant uptake of a number of actinides in the nitrate form, the following relative order of uptake in plants was established (assuming Pu=1) (Gene Schreckhise, 1982):

$$^{237}Np(2200 \text{ to } 45{,}000) > {}^{244}Cm = {}^{241}Am\ (10\text{-}20)$$

$$> {}^{239}Pu = {}^{238}Pu(1)$$

The number in parentheses represents the relative uptake of the radionuclide compared to Pu uptake. Therefore, in soil contaminated with material from spent Liquid Metal Fast Breeder Reactor Fuel, the concentration of other actinides in the biota would exceed that of ^{239}Pu. Other important observations from Schreckhise's studies included a high concentration in the legumes (10 times the concentration in the grasses) and a decreased actinide content of seeds as compared to concentration in parts of the plant above the ground (Gene Schreckhise, PNL, personal communication).

Also at PNL, Ray Wildung is conducting studies in which actinides are placed in soil and taken up by plants. These plants are fed to animals, and the subsequent transport across the gut is assessed. Preliminary observations (Ray Wildung, PNL, personal communication) indicate that the plant uptake of Pu and Cm are similar and are lower than Np by several orders of magnitude. These results are different from those of Schreckhise who is only studying plant uptake without animal consumption. When incorporated into plants, actinides are more available for uptake through the digestive tract of grazing animals by a factor of 10 to 20 times compared to unincorporated actinides (R. Wildung, PNL, personal communication).

Detailed studies on the radioisotopes released from nuclear fuel separation plants are conducted by a group headed by John Corey at Savannah River Laboratory in collaboration with the Savannah River Ecology Laboratory operated by the University of Georgia. A number of recent publications and preprints were avail-

number of recent publications and preprints were available from the group. Both geophysical and biological aspects of actinide behavior have been studied. The particles released from the fuel reprocessing plants have been found to consist of particles containing Pu, and other impurities (Horton and Gay, 1982). The deposition of these particles on soil and vegetation varies as the inverse of the distance from the release point (Horton and Gay, 1982). For crops planted in the immediate area of the reprocessing plants, the adherence of Pu-bearing particles to the external surfaces of carrots, turnips, red potatoes and sweet potatoes accounted for greater than 93% of the total Pu content (Corey et al., 1982a). Studies of released particle sizes (Gay and Watts, 1982), particle resuspension with soil disturbance (Shin, Homan and Gay, 1982) and plant uptake (Corey et al., 1982a) were considered as input data to theoretical dose calculations for individuals farming in the area (Corey et al., 1982b). From these calculations, the main dose to man from agricultural use of contaminated land would be due to the resuspension of surface-deposited Pu and subsequent inhalation during soil tillage operations (Corey et al., 1982b). These dose calculations depended on the assumption that all internally and externally deposited Pu was retained in food products. With this conservative assumption, 2% of the total dose resulted from internal ingestion and the remainder resulted from inhalation of suspended particles. The results from studies at the Savannah River Laboratory support the conclusions that the Pu-bearing particles move primarily by physical processes, with biological processes exerting a relatively minor impact (Corey et al, 1982b).

Studies on environmentally released actinides have also been conducted at LANL. These studies have led to similar conclusions to those reached from the Savannah River studies; that is, physical processes dominate the transport of actinides through the environment with little influence from chemical or biological transport (Tom Hakonson, LANL, personal communication). In the LASL studies, plant content was due mainly to surface deposition rather than root uptake. Also, sampling of wild fauna has revealed that the internal tissue content for Pu, Cs and Am is very low in animals that graze and hunt in the area (Tom Hakonson, LANL, personal communication). This indicates that the biological availability of the actinides is very low.

4.4.1.2 Water Systems

A number of studies of transport of actinides and other radioisotopes in aqueous systems are ongoing. Of primary interest are the factors which control the rate of sedimentation and the potential for resuspension of particle-adsorbed actinides. Characterization of actinide behavior is of interest because of the need for risk assessment for waterway contamination by accidentally-released actinides and also because the actinides may mimic the behavior of other chemical pollutants. Studies of actinide behavior may yield basic information about the particulate behavior in the ocean and other aqueous environments.

A research group under Vaughn Bohen at Woods Hole Oceanographic Institute has performed extensive studies on the behavior of Pu and Cs in the Atlantic and Pacific Oceans, the Arctic oceans and the Norwegian and Greenland Seas (Vaughn Bohen, Woods Hole, personal communication). This research has concentrated on man-made actinides, especially Am, Pu and some Cm. Neptunium has not been studied. Studies on U and Th are in progress. Major efforts have been directed to the characterization of the equilibrium between suspended and sinking particles and evidence to support the resolubilization of plutonium. An early paper (Livingston and Bowen, 1979) reported alterations in the Cs : Pu ratios with sediment depth. These authors interpreted their findings as evidence for Pu resolubilization. This interpretation has a significant impact on the risk assessment of environmental releases of Pu and has been disputed by other investigators (Tom Beasley, OSU, personal communication). Tom Beasley contended that the shift in Pu : Cs ratios could be readily explained by diffusion of the Cs (Beasley, Carpenter and Jennings, 1982; Tom Beasley, OSU, personal communication). However, subsequent research on the patterns of Pu distribution within the water column has indicated that Pu in sediments is subject to resolubilization (Vaughn Bohen, Woods Hole, personal communication).

Tom Beasley, OSU, has characterized the behavior of Pu released from reactors at Hanford to the Columbia River (Beasley, 1981). Similar studies on U and other

selected elements from Southeastern rivers have been performed by individuals at Savannah River Laboratories (Fay et al., 1982). In the studies by Tom Beasley, particulate matter within the river was observed to scavange and transport the Pu to downstream sediments or past the river mouth into the Pacific Ocean (Tom Beasley, OSU, personal communication). More recently, ^{238}Pu, ^{241}Am and ^{137}Cs inventories and vertical profiles in Washington and Oregon continental shelf sediments have been described (Beasley, Carpenter and Jennings, 1982). No separation of Pu from ^{137}Cs was observed with depth in the Pacific shelf sediments, as was observed by Vaughn Bohen's group in Atlantic costal sediments. The differences between the Atlantic and Pacific studies were attributed to differences between the water bodies in the diffusibility of Cs in sediments of varying porosities. No evidence was obtained for resolubilization of Pu within sediments in the Pacific studies at OSU. However, Vic Noshkin (LLNL, personal communication) cited evidence for Pu resolubilization in the waters near the Marshall Islands. Tom Beasley is confident that such resolubilization does not occur (OSU, personal communication) because studies by Beasley off the coast of Nova Scotia failed to show any evidence for the movement of Pu out of the sediments.

Robert Larsen and Don Nelson at ANL have studied the effect of various parameters, such as organic content of the water, on the oxidation state of suspended Pu. The effect of oxidation state on the distribution coefficient (K_d) of the Pu between solid and suspended state has also been studied. A pivotal finding, reported by Robert Larsen, ANL, (1978), was that Pu (IV) is oxidized to Pu (VI) by chlorine in water treatment plants and distribution systems. Larsen cited evidence that the GI tract absorption of Pu (VI) is increased in the oxidized state (Weeks, 1956). The oxidation state of Pu (VI) has a substantial impact, therefore, on potential biological availability.

Other factors may affect Pu remobilization. Several recent reports have been prepared by Don Nelson and his colleagues at ANL on the distribution coefficients (K_d's) of plutonium in various waters and the correlation of Pu removal with U-Th ratios (Nelson et

al., 1980, Nelson and Metta, 1981, Wahlgren and Orlandini, 1981). Uranium - Thorium ratios are of interest to this and similar research groups because U tends to remain suspended whereas the Th daughter product is absorbed onto particulates. Thorium removal rates may be used as an estimation of the rate of removal of the particles to which the Th is attached (Nelson and Metta, 1981). Uranium and Thorium, therefore, are natural analogues of Pu (IV) and Pu (VI), respectively (Wahlgren and Orlandini, 1981).

Plutonium distribution is affected by the content of dissolved organic carbon (Nelson, Karttunen and Mehloff, 1981). The reduced state (Pu(IV)) is favored in the presence of organic carbon because of the formation of soluble, reversible complexes with Pu(IV). Formation of these organic complexes keeps the associated Pu (IV) in suspension. If the carbon content of the water is low, the oxidized form of Pu (Pu(VI) is favored. Pu(VI) tends to remain in suspension because of a low particulate adsorption tendency. Because of the interplay of these factors, a fraction of the Pu tends to remain in suspension (Don Nelson, ANL, personal communication).

Other members of the ANL group (Wahlgren and Orlandini, 1981) have studied the geochemical behavior of fallout Pu in North American Lakes and found that the K_d's for Pu (IV) and Th were a linear function of dissolved organic carbon with no significant correlation with other limnological parameters. Similar findings have been reported in marine systems (Don Nelson, ANL, personal communication; Nelson and Lovett, 1978). These findings are significant because of the demonstration that Pu sedimentation rates may be modified by environmental factors in the water system.

A group at Texas A&M directed by Martha Scott has studied the Gulf of Mexico, including draining rivers and estuaries. This group (Martha Scott, Texas A&M, personal communication) has measured the natural U-Th series and also Pu and ^{137}Cs. The estuary constitutes a particularly complex system because the salinity gradient can cause both adsorption and desorption. Within the estuary, Pu in shallow water sediments is dominated by marine-contributed rather than fresh

water-contributed material. The fresh water particles tend to move laterally and deposit as a "bath tub ring" around the gulf (Martha Scott, Texas A&M, personal communication).

In recent review articles, Scott summarized existing information on actinide behavior in the Gulf of Mexico (Scott, 1981, 1982). Of particular note was the lack of general information about the behavior of chemical pollutants in the Gulf. The author proposed that the behavior of reactive elements, like Th and Pu, in coastal water masses may be useful homologues for the behavior of other chemically reactive pollutants.

A recent book edited by Wayne Hanson (1980) summarized much of the current data on the environmental behavior of radioactive materials. Although the text includes most DOE-funded research, a fair amount of relevant research was not included. Among the investigators whose studies were not part of this book were the effort at Woods Hole Oceanographic Institute and an estimated 35 to 40% of the available material on actinides (Vaughn Bohen, Woods Hole, personal communication).

The behavior of plutonium and other actinides in aqueous systems is the subject of a considerable amount of ongoing research. In the near future, the amount of information which is available on actinide behavior in the environment should increase accordingly. Of particular interest to risk assessment are the studies of the factors which affect the oxidation state of the Pu and subsequent biological availability and studies which are relevant to the question of Pu resolubilization after sedimentation.

4.4.2 Ongoing and Proposed Research - Environmental Mobility of Actinides

Field studies are underway at LANL on methods for prevention of actinide transport in High Level Waste Storage (Tom Hakonson, LANL, personal communication). Also modeling efforts are ongoing in collaboration with the Department of Agriculture, for hydrologic transport of radioactive materials, especially as related to erosion transport. Also, a study of Np is planned for

the fall which will include the introduction of Np into the ecosystem.

At ANL, Gene Schreckhise is engaged in ongoing studies with ^{232}U, $^{238,239}Pu$, ^{241}Am, ^{244}Cm and ^{237}Np. Uptake is being characterized in grass, barley, peas and alfalfa (personal communication). Uptake of ^{239}Pu nitrate compared to ^{239}Pu oxide has been studied (Schreckhise and Cline, 1980). This study may be repeated in the future with more advanced experimental techniques. The vertical redistribution and root uptake of ^{239}Pu and ^{233}U within a soil column is being studied during 4 growing cycles of crops. Gene Schreckhise is in the process of developing mathematical models which will describe vertical redistribution and root translocation (Gene Schreckhise, PNL, personal communication).

Studies are ongoing at Savannah River Laboratory under the direction of John Corey on biosphere interactions of $^{238,239}Pu$ from fuel reprocessing plants. Most of the previous work has been done with ^{238}Pu which is produced by one of the two plants at the Savannah River site. Corroborative work is underway for ^{239}Pu, which is released by the other plant (John Corey, Savannah River, personal communication). Neptunium and americium are also under study for uptake in crop plants. A corn crop grown in soil contaminated with Am has been harvested and is under analysis. Soybeans and wheat crops will be studied in 1983. Curium, Am, and Pu uptake has been studied in trees, and data collection for this study is complete. Tree uptake has been preliminarily characterized as consistent with literature values for crop plants. Work with Tc is under consideration (John Corey, personal communication).

Few results are available for uptake in animals of environmentally available forms of actinides (Ray Bondiette, ORNL, personal communication). The ongoing studies will increase the knowledge of the biological availability of actinides in contaminated soil. At PNL, Ray Wildung, (personal communication) is studying actinide uptake in grazing animals fed plants grown on contaminated soil. Studies of uptake of Pu and Am are nearing completion; studies on Np and Tc are underway.

Similar studies are proposed by Ray Bondiette (ORNL personal communication). Goats will be allowed to feed on a contaminated flood plain and the GI transport of actinides from the ingested plants will be characterized. This latter proposal has been submitted to the NRC.

Uptake of actinides by biota in aqueous systems is under investigation. Don Nelson of ANL outlined (personal communication) an ambitious program for the study of physicochemical behavior of actinides, especially Pu, as related to potential uptake in the biosphere. The work of Don Nelson and Robert Larsen of ANL have brought into focus the effect of the oxidation state of Pu on the distribution coefficients and on potential biological uptake. Plutonium oxidation state is affected by dissolved organic carbon, as described above. Don Nelson has submitted a proposal in which Pu content of fish from water of different organic composition would be assayed. If Pu tends to remain in an oxidized state in waters of low organic content and if the oxidized state is more readily available for uptake, fish in waters of low organic content should contain more Pu. Ray Bondiette (ORNL) (personal communication), is also involved in a study in which the uptake of actinides in fish is characterized. These fish are in a contaminated pond which contains Pu, Am and U at low levels and to which Np has been added. Tom Beasley (OSU) has also proposed a study of actinide remobilization in the biota of the Columbia river (Tom Beasley, personal communication).

Other studies by Don Nelson, ANL, would concentrate on the physicochemical aspects of Pu behavior. Studies have been initiated on U:Th ratios in fresh water (Don Nelson, personal communication). As discussed above, turnover of Th can be used to estimate particle sedimentation rates; and U and Th can be viewed as natural analogs of Pu (VI) and Pu (IV), respectively. Studies on U:Th ratios are more scarce in fresh water as compared to marine waters, where U concentrations are much higher. Initial characterization has been reported (Nelson & Metta, 1981) on the rate of removal of Th isotopes from Lake Michigan. Another study which is proposed by Nelson in the current budget submission (Don Nelson, ANL, personal communication)

would characterize Pu flux in low water sediments. This study was proposed because, in many lakes, Pu concentration appears to be related to concentration on the superficial sediments. This observation indicates that Pu may be remobilized from the sediments.

Another proposal in preparation by Don Nelson, ANL, (personal communication) would determine the effect of chemical form on the tendency of Pu to polymerize at low concentrations (near MPC). These studies are important in evaluating gut absorption of Pu at different masses because polymerized Pu is less likely to be absorbed.

Other studies of geochemical and physical behavior of actinides in river and marine environments are ongoing at a number of facilities. Tom Beasley (OSU) will extend current studies on the continental shelf of the coast of Oregon by coring of the abyssal plain for transuranics, ^{210}Pb, ^{137}Cs and trace elements. An overall scope for future research at ANL (Beasley et al., 1982) included studies on: (1) the relative contributions of the supply of reactive material to the water column as compared to scavanging reactions in determination of sedimentary inventories, (2) the biological vs inorganic scavanging reactions and (3) the potential remobilization of sedimented radionuclides.

Martha Scotts' group (Texas A & M) is concentrating on the Gulf of Mexico and contributing rivers. In a recent review, (1982) Scott cited the need for additional studies of the nearshore environment, especially of U-Th series nuclides and fallout nuclides. Especially important are reactions in the river water-sea water mixing zone. Ongoing research emphasizes U-Th concentrations in rivers and the behavior of U in estuaries, where the salinity gradient can affect absorption (Martha Scott, Texas A&M, personal communication). Members of John Corey's group at Savannah River have also studied U-Th ratios in rivers (Fay et al., 1982).

Among several ongoing studies at Woods Hole Oceanographic Institute is the characterization of Pu behavior in Crater Lake in Oregon. This study is unique because Crater Lake is a closed system and findings

therein might be relevant to water reservoirs. Resolubilization reactions of Pu in this system would be of interest because of the low ion-exchange capacity of the soil and the low organic content of the lake (Vaughn Bohen, Woods Hole, personal communication). The Woods Hole project is receiving funding by DOE, EPA and NOAA (National Ocean Atmospheric Administration) (Vaughn Bohen, Woods Hole, personal communication). The project at Woods Hole Oceanographic Institute is currently in a period of transition due to the retirement of Vaughn Bohen.

The research program conducted by Victor Noshkin, LLNL, is involved in studies of nuclear materials derived from nuclear facilities, testing sites, waste disposal regions and global fallout in the Pacific Ocean. Among specific sites under study are the Humboldt Power Station near Eureka, California and the Diablo Canyon Reactor in California. Results indicate that plutonium is mobilized from sedimentary deposits (Vic Noshkin, 1982, personal communication).

Ongoing research on environmental mobility of actinides will contribute to an overall understanding of potential risks from environmentally-released radioactive materials.

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6.0 NAMES AND AFFILIATIONS OF INTERVIEWEES

1. William J. Bair
   Manager of Environmental Health and Safety
   Research Program
   Batelle Pacific Northwest Laboratories
   P.O. Box 999
   Richland, Washington 99352

2. Thomas M. Beasley
   Professor of Oceanography
   Oregon State University Marine Science Center
   Newport, Oregon 97365

3. Steven A. Benjamin
   Director of Collaborative Radiological Health
   Laboratory
   Colorado State University
   Fort Collins, Colorado 80523

4. B. Bruce Boecker
   Assistant Director
   Inhalation Texicology Research Institute
   Lovelace Biomedical and Environmental Research
   Institute
   P.O. Box 5890
   Albuquerque, New Mexico 87185

5. Ray A. Bondiette
   Manager of Toxic Substances Program
   Oak Ridge National Laboratory
   P.O. Box X, Bldg 1505
   Oak Ridge, Tennessee 37830

6. Vaughn T. Bowen
   Senior Scientist
   Department of Chemistry
   Redfield 3
   Woodshole Oceonographic Institution
   Woodshole, Massachusetts 02543

7. Norman Cohen
   Assistant Director of Laboratory for Environmental
   Studies
   Institute of Environmental Medicine
   New York University Medical Center
   Sterling Lake
   Tuxedo, New York 10987

8. John C. Corey
Research Supervisor for Environmental Sciences Division
Savannah River Laboratory
Aiken, South Carolina 29808

9. Keith F. Eckerman
Group Leader for Metabolism & Dosimetry
Health & Safety Research Division
Oak Ridge National Laboratory
P.O. Box X, Bldg. 7509
Oak Ridge, Tennessee 37830

10. Thomas E. Fritz
Associate Division Director
Division of Biology and Medical Research
Argonne National Laboratory
9700 South Cass Ave.
Argonne, Illinois 60439

11. Walderico M Generoso
Staff Member
Mammalian Genetics & Teratotology Section
Biology Division
Oak Ridge National Laboratory
P.O. Box Y
Oak Ridge, Tennessee 37830

12. Marvin Goldman
Director
Laboratory for Energy - Related Health Research
University of California
Davis, California 95616

13. Douglas G. Grahn
Biologist
Division of Biological and Medical Research
Argonne National Laboratory
9700 South Cass Ave.
Argonne, Illinois 60439

14. Thomas E. Hakonson
Staff Member
Environmental Science Group (L56)
Los Alamos National Laboratories
Mail Stop K495
Los Alamos, New Mexico 87545

15. Webster S. Jee
Research Professor
Division of Radiobiology
Dept. of Pharmacology
University of Utah
Salt Lake City, Utah 84112

16. Robert P. Larsen
Chemist
Argonne National Laboratory
9700 South Cass Ave.
Argonne, Illinois 60439

17. Charles W. Mays
Research Professor
Division of Radiobiology
Dept. of Pharmacology
University of Utah
Salt Lake City, Utah 84112

18. Donald M. Nelson
Chemist
Argonne National Laboratory
9700 South Cass Ave.
Argonne, Illinois 60439

19. Victor E. Noshkin
Section Leader for Aquatic Sciences
Lawrence Livermore National Laboratory
L453
P.O. Box 5507
Livermore, California 94550

20. Otto G. Raabe
Adjunct Professor
Associate Director of Science
Laboratory for Energy - Related Health Research
University of California
Davis, California 95616

21. John Rundo
Senior Biophysicist
Center for Human Radiobiology
Argonne National Laboratory
9700 South Cass Ave.
Argonne, Illinois 60439

22. Lea B. Russell
Section Head
Mammalian Genetics and Teratotology Section
Biology Division
Oak Ridge National Laboratory
P.O. Box Y
Oak Ridge, Tennessee 37830

23. R. Gene Schreckhise
Associate Manager of Environment and Risk
Assessment Section
Radiological Sciences Department
Battelle Pacific Northwest Laboratories
P.O. Box 999
Richland, Washington 99352

24. Martha R. Scott
Associate Professor
Dept. of Oceanography
Texas A & M
College Station, Texas 77843

25. Thomas M. Seed
Biologist
Division of Biology and Medical Research
Argonne National Laboratory
9700 South Cass Ave.
Argonne, Illinois 60439

26. Paul B. Selby
Staff Member
Mammalian Genetics & Teratotology Section
Biology Division
Oak Ridge National Laboratory
P.O. Box Y
Oak Ridge, Tennessee 37830.

27. Narayoni P. Singh
Associate Professor
Division of Radiobiology
Dept. of Pharmacology
University of Utah
Salt Lake City, Utah 84112

28. John W. Stather
National Radiological Protection Board
Chilton Nerdidcot
Oxfordshire, England OX110RQ

29. John B. Storer
Senior Research Staff Member
Biology Division
Oak Ridge National Laboratory
P.O. Box Y, Bldg. 9207
Oak Ridge, Tennessee 37830

30. Maurice F. Sullivan
Staff Scientist
Biology and Chemistry Department
Battelle Pacific Northwest Laboratories
331 Bldg - 300 Area
Richland, Washington 99352

31. David M. Taylor
Co-director
Institut fur Genetek and fur Toxikologic of West Germany
Karlsurhe, Germany

32. Glenn W. Taylor
Professor
Division of Radiobiology
Dept. of Pharmacology
College of Medicine
University of Utah
Salt Lake City, Utah 84112

33. Robert G. Thomas
Staff Member
Health Division (HDO)
Los Alamos National Laboratories
Mail Stop P228
P.O. Box 1663
Los Alamos, New Mexico 87545

34. Roy C. Thompson
Staff Scientist
Biology and Chemistry Division
Battelle Pacific Northwest Laboratories
331 Bldg - 300 Area
Richland, Washington 99352

35. Ray E. Wildung
Associate Manager of environmental Sciences Department
Battelle Pacific Northwest Laboratories
P.O. Box 999
Richland, Washington 99352

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