

**Case Control Study of Multiple Myeloma Among Workers Exposed to
Ionizing Radiation and Other Physical and Chemical Agents
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Acknowledgments

Although we have been involved in epidemiological research studies of workers in Department of Energy nuclear facilities for over a decade, the Multiple Myeloma Study was our first experience with gathering documents and information directly from DOE sites. An experience it was.

We approached the issue of gaining access to sites with some trepidation. We were one of the first teams of NIOSH extramural researchers to have the responsibility for studying the health of DOE workers. Moreover, our study included workers from four different DOE sites. Although many difficulties were encountered along the way, we for the most part were able to obtain the information that we sought, including personnel files, occupational health records, and information on exposures to radiation and chemical hazards. Our work was facilitated by the cooperation and assistance of a host of persons from the four DOE sites, the Oak Ridge National Laboratory, the Savannah River Site, the Hanford Site and the Los Alamos National Laboratory; by staff members from both the Department of Energy Headquarters in Germantown, Maryland and their operations offices at Oak Ridge, Richland, Savannah River, Albuquerque and Los Alamos; and by our research partners from the Health-Related Energy Research Branch at the NIOSH. In recognition of their efforts we will attempt to mention by name all of those persons who assisted us in our work. If we fail to include anyone, please accept our apologies for this forgetfulness. We are grateful to each person who pulled records from old dusty boxes, set up microfiche readers, explained monitoring programs, searched for old databases, and generally provided us with the information that we needed to complete this study.

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requests for data and willingly shared their knowledge of DOE sites and their experience with data collection from DOE facility records.

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Sue Wolf
Steve Wing

Chapel Hill, NC
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Study of Multiple Myeloma Among Workers Exposed to Ionizing Radiation and Other Physical and Chemical Agents

I. INTRODUCTION

The National Institute for Occupational Safety and Health (NIOSH) contracted with the University of North Carolina to conduct a case-control study of multiple myeloma among workers at Department of Energy nuclear facilities. The basic design and data to be used for the study were specified by NIOSH. The overall objective of this research was to evaluate occupational exposures to ionizing radiation and other biological, physical and chemical hazards as risk factors for multiple myeloma.

Although increased rates of multiple myeloma and other hematological malignancies have been observed in relation to higher doses of ionizing radiation among A-bomb survivors and some medically exposed groups (BEIR V, 1990), epidemiological studies of low dose, low dose rate exposures in the range encountered in occupational settings are less clear (Gilbert et al., 1989a), although suggestive of an increased risk (Wilkinson, 1991). The ambiguity of results of such studies derives from the low magnitude of potential excess risks to be detected at low doses, the rareness of the disease, difficulties in correctly classifying worker exposures over long time periods, and the potential for confounding or modifying effects of other occupational exposures. Of the various Department of Energy (DOE) worker cohorts for which epidemiological findings have been reported, only Hanford has shown an increase in multiple myeloma risk with increasing doses of external radiation, a finding based on a handful of cases in the higher dose groups (Mancuso et al, 1977; Gilbert et al., 1989b). This association of external radiation and multiple myeloma continued to be observed in more recent follow-up of the Hanford population (Gilbert et al., 1993a). A weaker association was reported for a combined analysis of Hanford, Rocky Flats, and Oak Ridge National Laboratory populations (Gilbert et al., 1993b).

In addition to ionizing radiation, a number of other exposures have been considered as risk factors for multiple myeloma. These include chronic immune stimulation, employment in agriculture, family history of multiple myeloma and other diseases (Olshan, 1991), consumption of various foods, and use of alcohol and tobacco (Herrinton et al., 1996). A recent review of published epidemiological studies found that 17 of 18 studies showed agricultural workers to be at excess risk of multiple myeloma, and that 6 of 7 studies showed painters to be at excess risk (Herrinton et al., 1996). Evidence of excess risks in other occupational groups is less clear. Benzene is among specific agents clearly implicated, and there are findings suggestive for other solvents, pesticide exposures, and other select chemical agents (Herrinton et al., 1996; Reidel et al, 1991; and Heineman et al, 1992).

The population for this study was assembled from five cohorts of workers from four DOE nuclear facilities: the Oak Ridge National Laboratory (ORNL), the Savannah River Site (SRS), the Hanford Site (Operations Workers), the Los Alamos National Laboratory (LANL)-University of California, and LANL-the Zia Company. The study compares demographic characteristics, prior work history, and occupational exposures of workers who died as a result of multiple myeloma to a group of workers, selected from the combined cohort from the five facilities, who lived to be as old as the cases. The primary quantifiable occupational exposure is external penetrating ionizing radiation. Information on exposures to internally deposited radionuclides, chemical agents, and

occupational medical x-rays are also considered. Prior work history, security clearances, smoking, health status during employment and are also explored as potential confounders.

II. BACKGROUND AND STUDY FACILITIES

IIA. Selection Of DOE Facilities And Worker Cohort

Several methods were used to select DOE facilities for inclusion in the study. A literature review determined the availability of computerized rosters and the characteristics of the cohorts including size, vital status follow-up and death certificate ascertainment. Informal interviews with epidemiologists, statisticians, and health physicists who research on DOE populations were conducted to learn about historical exposures and exposure monitoring at these facilities. Documentation from existing data sets of DOE populations was also reviewed. The Comprehensive Epidemiologic Data Resource (CEDR) and the Center for Epidemiologic Research of the Oak Ridge Associated Universities (ORAU/CER) were primary sources of data. Finally, a computerized bibliographic search was conducted of energy-related literature, technical reports, and other published documents in order to determine the availability, accessibility, and quality of data among DOE worker cohorts.

Guidelines were developed to assist in the process of selecting facilities for inclusion. The following factors were considered:

- the availability of a computerized roster of the workforce
- the potential for external radiation exposure
- primary radiation exposure not from uranium dusts
- vital status follow-up completed at least through 1986
- the quality and quantity of the radiation monitoring data

A computerized roster of all workers employed at each facility from its inception until its closure, or until 1978 in the case of facilities that are still in operation, was available for over 20 DOE facilities. These included: Fernald, Hanford Operations, Idaho National Engineering Laboratory (INEL), Lawrence Livermore National Laboratory, Linde, Los Alamos National Laboratory (LANL), Mallinckrodt Chemical-St. Louis, Mound Laboratory, Oak Ridge Gaseous Diffusion Plant (K-25), Oak Ridge National Laboratory (ORNL), Paducah Gaseous Diffusion Plant, Pantex, Pinellas, Portsmouth Gaseous Diffusion Plant, Rocky Flats, Sandia, Savannah River Plant, TEC, Y-12, and Zia Company/LANL.

Facilities where the primary activity was the production and milling of uranium were excluded. Workers at many DOE facilities had the potential for contamination with radionuclides through inhalation, ingestion, and wounds. Internal exposures could be stratified in the analysis. By excluding those facilities where the primary radiation exposure results from dust inhalation, analytical problems associated with distinguishing outcomes associated with both the physical and chemical properties of the dusts were reduced. For these reasons, the Fernald Feed Materials Plant, TEC, Y-12, Linde and the Mallinckrodt Chemical Company were excluded.

Three gaseous diffusion plants among DOE operations were excluded. The Oak Ridge Gaseous Diffusion Plant, K-25, had a relatively large but not unexpected number of cases of multiple

myeloma available (n=74) for study. K-25 workers represented a large cohort of approximately 44,000, over half of whom were first hired during the WW II era. Since 40% of the cohort was deceased as of 1990, it was not unexpected that a substantial number of multiple myeloma cases would be identified from this cohort. The number of cases available for study at K-25, however, did not outweigh concerns about including K-25 in this study. First, the exposures at K-25 were primarily internal, resulting from the escape of uranium hexafluoride from the cascade. External radiation exposures were relatively low (Galloway, 1992) and confined to select areas in the plant (Watkins & West, 1990). Second, 70% of the 74 multiple myeloma cases had neither internal nor external radiation monitoring data in the existing computerized files. Eleven cases have external radiation monitoring data; 20 cases had bioassay data. The Paducah and the Portsmouth Gaseous Diffusion Plants were excluded for similar reasons.

The roster for Idaho National Engineering Laboratory (INEL) and the follow-up of vital status were incomplete at the inception of this study. In addition, it was not feasible to include the Lawrence Livermore National Laboratory (LLNL) or the Sandia Laboratories in Albuquerque, NM because data from prior studies were not archived in CEDR. The Pantex Plant could not be included because the roster of workers was limited to white males and follow-up of vital status was available only through 1978. Moreover, external radiation monitoring data were limited to persons employed after 1963.

Cohorts from other DOE facilities were not considered for this study for various reasons. A roster of employees at the Pinellas Plant (Florida) was available, however, there was no documented evidence of radiation exposures at this facility (Cragle, 1993). A roster of workers from the Mound Laboratory in Ohio was available in CEDR, but this population was small compared with other facilities and had a maximum of two documented cases of multiple myeloma. Lastly, vital status follow-up of the Rocky Flats Plant has completed through 12-31-83 with a single identified case of multiple myeloma.

After careful consideration of all of the potential DOE worker populations, five cohorts representing workers employed at four DOE facilities were selected for inclusion in this case control study: The Hanford Site-Operations Workers¹, The Oak Ridge National Laboratory (ORNL), The Savannah River Site (SRS), The Los Alamos National Laboratory (LANL) and The Zia Company which provided maintenance services at LANL. In addition to having complete computerized rosters of their workers, adequate vital status follow-up and cause of death ascertainment, these populations have been the focus of epidemiological studies by a variety of epidemiologists and statisticians. As such, the data used in these studies have been well scrutinized and their strengths and their weaknesses identified. This was recognized as an important benefit to this study.

¹ Construction workers were another other large group of workers at the Hanford Site. The roster of these workers was constructed separately from the Operations Workers and was not available for this study.

II.B. Facility Descriptions

This section presents an overview of historical operations and activities at the study facilities. The diversity of highly specialized research and production at these facilities is indicative of the complexity of worker exposures.

Oak Ridge National Laboratory

Construction of the Clinton Laboratories at the X-10 site was begun in 1943 by Du Pont de Nemours and Co. The site was initially operated by the University of Chicago, which relinquished control to the Monsanto Chemical Company in 1945. The site was renamed the Clinton National Laboratory in 1947 and the Oak Ridge National Laboratory in 1948. Union Carbide Corporation's Carbide and Carbon Chemical Company (C&CCC) took over operation of the laboratory in 1948. Martin Marietta Corporation replaced Union Carbide Corporation as the prime contractor for the site in 1984.

The primary mission of the laboratory in 1943 was the production of nuclear weapons material. The site was designed as a pilot plant for the development of plutonium production and chemical separation processes. The mission of the Laboratory following WW II included the following research areas: 1) the production of other radioisotopes (1943-present), 2) research and development of chemical separation methods for other radionuclides from irradiated fuel elements (1943-present), 3) nuclear reactor development (1943-present), 4) research and development of chemical plant systems for processing nuclear materials, 5) research and development of thermonuclear fusion for the production of nuclear power, 6) research, development and fabrication of nuclear fuel elements and other nuclear reactor components, 7) research, development and fabrication of analytical devices and instruments for metallurgical research, 8) research and development in pure and applied (reactor) nuclear physics including the evaluation of the atomic structure, interaction of radiation with matter and development of alternative reactor designs, 9) research on the effects and mechanisms of radiation damage in materials used in nuclear systems, 10) investigation of biological mechanisms of radiation damage, 11) research and development of alternative energy technologies including coal gasification.

The Oak Ridge site produced and separated plutonium from 1943 through 1945 by nuclear fission of uranium at the Clinton pile, a graphite-moderated reactor. The site began producing large quantities of radioactive lanthanum by nuclear fission of barium-140 in 1945 for Los Alamos. The site ceased plutonium production at the Clinton pile in 1945 but continued pilot plant development of plutonium (REDOX and PUREX), thorium (THOREX) and other chemical separation processes for Hanford and Savannah River.

ORNL expanded its activities in the production and separation of radioisotopes to include research and development of methods, materials and equipment to produce and separate a variety of stable radioisotopes for research and nuclear medicine applications. This work included the development of remote source fabrication techniques, the preparation of target materials for radioisotope production, and continued research and development in the separation of radioisotopes by electromagnetic fields. By 1950, the site was distributing more than fifty different radioisotopes. The site continues to produce and distribute radioisotopes.

Nuclear reactor research and development activities at ORNL began with the design, construction and operation of the Clinton pile in 1943. Subsequently, reactors were designed, constructed, and tested for a variety of applications. Examples of these applications are the aircraft nuclear propulsion reactor (1954), the high neutron flux materials testing reactor, the tower shielding facility reactor (1953), the bulk shielding reactor, the Low Intensity Test Reactor (1949), the swimming pool reactors (1950), the homogeneous reactors (1956-61), the high performance research reactor (1958), the molten salt reactor (1958), the Army package reactor, and the submarine thermal reactor (1958-63)). These activities continued through 1994

Metallurgy and materials science research and development activities have been conducted since 1943 to support the design and manufacture of nuclear fuel elements, nuclear reactor components, analytical devices and instruments. These activities have also included the development of procedures and equipment for high temperature metal and ceramic/metal material fabrication, powder metallurgy, and non-destructive testing.

Particle research programs began at ORNL in 1946 and have expanded over the years to include research and development programs in pure, and applied, nuclear physics including the evaluation of atomic structure and the interaction of radiation with matter. These research activities have relied on a variety of accelerators and related equipment including calutrons, cyclotrons, Van de Graaff electron accelerators, the Cockroft-Walton accelerator, magnetic spectrographs, focusing collimeter, scintillation spectrometer, spectrophotometer, molecular beam, coulomb excitation, neutron time-of-flight chopper, high energy accelerator and combined cyclotron/synchrotron (Johnson and Schaffer, 1994).

Fundamental research on the formation and motion of ions in electric fields was conducted by the ORNL Electronuclear Division using various cyclotrons, electrostatic machines and related equipment. During the late 1940s and early 1950s, the Oak Ridge Y-12 site built three cyclotrons to study properties of compound nuclei and heavy particle reactions. Additional cyclotrons constructed at the site included the isochronous (variable energy) cyclotron in 1962 and a electron linear accelerator at the Hollifield heavy ion research facility completed in 1980.

Thermonuclear fusion research and development activities at Oak Ridge began in 1957. The research program involved the creation and containment of a plasma within a magnetic field. Specific experiments and equipment associated with the project included the direct current experiment (DCX), a magnetic fusion device producing a deuterium plasma in a particle accelerator. Other fusion research devices were constructed and added to the site including a second direct current experiment and steady-state fusion device, and tokamak fusion device constructed in the late 1960s and early 1970s; and a fusion reactor (stellarator advanced toroidal facility) and radiofrequency facility for heating fusion plasmas constructed in the late 1980s. A large magnetic coil facility was constructed in the 1980s to test superconducting magnets used in fusion research.

Biological science research activities at ORNL began in 1946 with *in vitro* and *in vivo* studies of the genetic and physical effects of radiation. Early research activities included the development of radioisotope techniques for biological sciences. By 1949 the site maintained laboratory animal facilities to

support research in the biological sciences. The site continues to conduct research in the radiobiology and biology, genetics, toxicology and pharmacology.

Oak Ridge National Laboratory has maintained an active industrial hygiene program since inception. However few reports describing exposure assessment activities for specific buildings, processes or agents were identified in the published literature. Additional information describing site operations was identified in published histories of the site (Johnson and Schaffer, 1994 (X191); Jolley et al., 1994 (ORNL/M-2733/R1); Kerr et al., 1992 (ORNL/M-2108)).

Savannah River Site

The primary mission of the Savannah River Site is the production of nuclear materials for the military. Major plant facilities were constructed during 1950-1955 and include: 1) nuclear reactors (100 Area), 2) two separations areas for processing irradiated materials (200-F and -H Area), 3) heavy water extraction and recovery plant (400 Area), 4) fuel and target fabrication facility (300-M Area), 5) Savannah River Laboratory (700 Area), 6) administrative facilities, and 7) non-nuclear facilities to support plant operations.

Specific activities at SRS have included: 1) the production of plutonium and tritium isotopes by neutron absorption (100 Area); 2) the separation of plutonium, uranium, neptunium and tritium isotopes from irradiated fuel elements and target assemblies (F- and H-Area); 3) the fabrication of extruded enriched uranium-aluminum alloy fuel and canned depleted uranium metal targets for irradiation in SRS reactors (M-Area); 4) the separation and purification of heavy water (D₂O) and repurification of degraded reactor D₂O coolant (D-Area); 5) research and development in chemical separations of nuclear materials, fabrication of fuel elements, targets and radioisotope sources.

Area 100 includes five large reactors designed primarily for the production of plutonium and tritium. Each reactor includes a purification area, a pump and heat exchanger area, and a reactor room. There are three main operations performed at each reactor: 1) fuel and target assembly, test repair and charging, 2) reactor operations, and 3) spent fuel and target handling. Work activities and locations for the reactor areas were defined by Hickey and Cragle (1985).

Plutonium, uranium, neptunium and tritium isotopes are separated from irradiated fuel elements and target assemblies in the 200-F and -H Areas. The -F and -H Areas are comprised of the following facilities: 1) 221-F canyon building (Plutonium Processing), 2) 221-H canyon building (Uranium, Neptunium, Plutonium and special processing), 3) 232-H, 234-H, 238-H Buildings (tritium processing), 4) Receiving Basin for Offsite Fuels (RBOF in 244-H Building), 5) Resin Regeneration Facility (RRF in 245-H Building), 6) Metallurgy Building (235-F), 7) analytical laboratory (772-F), 8) uranium oxide processing (211-F support facility for 221-F building), and 9) support facilities (Laundry, F-Area).

The Fuel and Target Fabrication area (300-M Area) fabricates and tests fuel elements and metal targets. The following activities are conducted in the M Area: 1) fabricated reactor elements are tested in the low power and subcritical test reactors (305-M); 2) fuel and target elements containing natural, depleted and slightly enriched uranium ²³⁵U are bonded in aluminum cans in 313-M; 3) lithium-aluminum tubes for the production of tritium are fabricated by extrusion in 320-M; 4) tubular fuel and target

elements irradiated at SRP (mainly enriched uranium, with some plutonium and neptunium cores, dispersed in an aluminum matrix) are manufactured by coextrusion of a composite billet in 321-M; and 5) materials and products fabricated in the 300 Area are inspected and tested in the metallurgical laboratory (322-M).

The 400-D Area separates and purifies heavy water (D₂O) from Savannah River water and repurifies degraded reactor D₂O coolant. The 400-D Area is comprised of: 1) the 412-D Extraction Plant that separates naturally occurring D₂O from raw water using a dual-temperature process with countercurrent extraction of heavy water by H₂S gas and purification by distillation (GS Process); 2) the 420-D Rework Unit where water that has accumulated in the D₂O coolant used in the reactors is removed by distillation; and 3) the 420-D Distillation Plant (DW Process) concentrates the heavy water product from the Extraction Plant (GS Process, 412-D). Support facilities for this area include the 421- and 422-D Drum (Heavy Water) Cleaning, 772-D Analytical Laboratory, 484-D Power Plant (four coal-fired boilers provide steam and electrical power).

The Savannah River Laboratory conducts research and development activities in support of fuel element, target and radioisotope source fabrication and separations activities conducted at SRS. The Main Laboratory Building (773-A) contains facilities for: 1) the fabrication of fuel element prototypes of natural and enriched uranium from metal, alloy and oxide materials (Section D); 2) the fabrication of americium and curium targets (Section F); 3) the fabrication, testing and packaging of various types of radioisotope sources (²⁵²Cf, ²³⁸Pu) encapsulated in platinum, palladium, Zircaloy, or stainless steel (Section F); and 4) laboratory and pilot scale development and testing of separations processes including the handling of irradiated fuel and targets to the packaging of final product (Sections B, C, E).

Other facilities comprising the Savannah River Laboratory include: 1) the Environmental Sciences Laboratory (735-A); 2) the ⁶⁰Cobalt Irradiation Facility (774-A); 3) the Heat Transfer Laboratory (786-A) which tests the behavior of thermally heated reactor fuel elements under various cooling conditions; 4) the Reactor Hydraulic Test Facility (786-A) which is a reactor mockup for studying steam injection, transport and quenching; 5) the Liquid Waste Disposal Facility (776-A); 6) the Manipulator Repair Facility (779-A) which receives, decontaminates, and repairs contaminated master-slave manipulators from the shielded facilities in the main laboratory and other SRP production areas; 7) the Experimental Physics Laboratory (777-M) which evaluates fuel assemblies and lattice arrangements in heavy water reactors; 8) the TNX-CMX Semiworks (678-, 679-G) which investigates chemical processing problems and tests production-scale equipment using non-radioactive materials or natural uranium; and 9) the Steam Power Plant (700-A and CMX-TNX Powerhouses).

Savannah River has maintained an active industrial hygiene program since inception. However few reports describing exposure assessment activities for specific buildings, processes or agents were identified in the published literature. Potential exposures to a variety of chemical and physical agents were identified from a review of process flow sheets, process descriptions, chemical inventories, environmental impact statements and other published documents. Additional information describing site operations was identified in environmental assessments and environmental impact statements describing the site operations (U.S. Department of Energy, 1979 (S116-F)) and waste management operations (U.S. Department of Energy, 1977 (S117-F); Looney et al., 1987 (S124)).

Hanford Site

Operations at the Hanford Site began in 1943 with a mission to produce radioactive materials (^{239}Pu and others) for use in nuclear weapons (Gerber, 1992) and nuclear research. This mission involved the production of irradiated nuclear fuel containing the desired radionuclides in on site nuclear reactors and the separation of these radionuclides from the irradiated fuel using chemical methods.

The facility was designated as the Hanford Site in 1977 by the U. S. Department of Energy (Gerber, 1992). Prior to this time, the facility was identified as Site W, the Gable Project, the Hanford Engineer Works (HEW) (1947), the Hanford Atomic Product Operation (HAPO) (1953) under prime contractor General Electric Co. and the Hanford Reservation (1975). Over the years, there have been numerous contractors working on the site. The following represents only the prime contractors for operations: E.I. Du Pont de Nemours, The General Electric Company, Battelle-Columbus, Pacific Northwest Laboratory, Hanford Environmental Health Foundation, Westinghouse, Douglas United Nuclear, Isochem, ITT Services, and The Boeing Company. In addition, there were numerous construction contractors who employed workers on the site. Construction employees were not included in this study.

Construction of the Hanford site was started in 1943 to provide a remote facility for the production and purification of plutonium for the Manhattan Project. Nine nuclear reactors were eventually constructed in the 100 Area along the Columbia River to provide irradiated nuclear fuel for the plutonium separation and purification process.

Chemical processing, waste treatment, storage and disposal facilities were constructed in the 200 Area (East and West). Chemical separation processes and unit operations used at Hanford were initially developed and tested at the semi-works pilot plant at the Oak Ridge National Laboratory and Hanford C plant (not semi-works plant) and subsequently implemented in full scale production at Hanford. Chemical separation at Hanford involved a succession of processes that increased production yields and production capacity. Early processes generated large quantities of contaminated liquid wastes. Process changes were made which reduced waste volume, recovered radionuclides in the waste streams (e. g. uranium, neptunium, strontium, cesium) and recycled process chemicals. The early chemical separation of plutonium from irradiated fuel elements used a bismuth phosphate process to remove ^{239}Pu . The process was replaced by a more efficient reduction oxidation (REDOX) process in 1952 and eventually by the PUREX process in 1955. Additional new construction and renovation of existing facilities occurred from 1950-1955 due to increased production demands and improvements in process operations. These changes included improvements in chemical separation processes and waste management. Peak production of nuclear materials occurred from 1956 to 1963.

Pilot plant facilities, metallurgical facilities, laboratories, reactors and other test facilities were constructed in the 300 Area. Other facilities at the site include the fast flux test facility (Area 400), administrative and services areas (1100 Area bus lot, 700 Area and 3000 Area) and nuclear power stations operated by the Washington Public Power Supply System. Multiple support buildings, facilities, laboratories and offices were also constructed at the site by 1945.

Work at the Hanford site also included research and development programs to support the production activities and included: 1) the design and testing of nuclear reactors, 2) the fabrication of nuclear fuel elements, 3) the development of treatment methods for removal and recovery of other radionuclides from liquid and gaseous waste streams, 4) the evaluation of potential biological effects of plutonium, 5) the evaluation of alternative nuclear fuels, fuel element designs and fabrication methods, 6) the production of radioisotopes for research uses, and 7) the evaluation of radiation damage on materials.

Service activities that supported the primary laboratory mission included: 1) treatment and disposal of solid and liquid wastes contaminated with radioactive materials, 2) monitoring of worker exposures and environmental contamination to ionizing radiation and radionuclides, 3) evaluation of the biological effects of radiation (*in vivo* and *in vitro* studies), 4) operation of site utilities including electric power/process steam plant and process water filtration and treatment plant, 5) construction and renovation of production facilities, storage tanks and waste handling systems, 6) operation of central shops providing drafting, machining, welding, painting, carpentry, glass blowing and related services. Basic community services (transportation, housing, schools, health care, recreation facilities) were also provided and operated by the Hanford facility due to the remote location of the site.

Hanford has maintained an active industrial hygiene and health physics program since inception. Several reports describe exposure assessment activities for specific buildings and processes at the facility since the 1950s. Exposures to uranium oxide in the Melt Plant (Building 314) were reported by several investigators (Adley et al. 1952; Ingalls and Sanborn, 1956). Exposures to other chemical agents identified in the published literature include: 1) nitrogen oxide exposures from calcining uranium nitrate hexahydrate in the 224-U Bulk Reduction Building (Ingalls and Sanborn, 1956), 2) nitrogen oxide and nitric acid exposures from metal fabrication (pickling) of reactor fuel rods in Building 313 (Adley, 1949a, b), 3) bio-assay monitoring of workers exposed to benzene (Adley, 1950), 4) nitrogen oxide exposures from the PUREX process (Pajunen and Dirkes, 1978), 5) nitrogen oxide exposures during the fabrication of uranium fuel elements in 313 Metal Fabrication Building (Adley, 1949a, 1949b).

Research and production activities involved potential exposures to a variety of chemical and physical agents identified from process flow sheets, process descriptions, chemical inventories, environmental impact statements and other published documents. An inventory of chemical agents prepared by Klem (1990) (H183-F) for waste management and decommissioning activities at selected Hanford site facilities provided a list of agents by building and date. Additional information describing site operations was identified in environmental impact statements describing the operation of the PUREX plant, uranium oxide plant and other production and waste management operations (U. S. Energy Research and Development Administration, 1975 (H186); Pajunen and Dirkes, 1978 (H149); Strachan et al. 1993 (H152); U. S. Department of Energy, 1982 (H-101-F); Raab and Schmidt, 1978 (H184-F)).

Los Alamos National Laboratory

The laboratory was originally identified as Project Y of Site Y under the Manhattan Project and subsequently as the Los Alamos Scientific Laboratory (LASL). In 1981 it was granted the status of a national laboratory. The primary mission of Los Alamos National Laboratory (LANL) encompasses military activities involving the research, development and testing of nuclear and thermonuclear weapons. LANL started operations in 1943 with a mission to develop and test a nuclear fission (atomic) weapon.

The success of the device resulted in subsequent research and development of thermonuclear (fusion) weapons beginning in the late 1940s that continues to the present (LASL, 1978a). The scope of the Laboratory's research activities expanded over the years to encompass military, energy, biomedical and environmental, and physical research in nuclear and non-nuclear technologies including directed energy weapons, defensive lasers, conventional defense systems, space technology, nuclear reactors, and superconductor technology for storage and transmission of energy.

Since the beginning of operations at the Laboratory, the University of California has been the prime contractor, responsible for the overall operation of the site. Maintenance work was done by the Zia Company until 1986 followed by the PAN AM Company and Johnson Controls Inc. (JCI).

The initial work of LANL in the early 1940s involved research and development of a nuclear fission weapon. These early activities required the development of processing and manufacturing methods for the fabrication (e.g. nuclear core, metal and explosive components), manufacture and assembly of nuclear weapons components. The laboratory operated machine shops to fabricate components, instrumentation shops to manufacture radiation monitoring equipment, facilities for the assembly of nuclear components, chemical laboratories for the separation of nuclear materials, and facilities for the fabrication and testing of high explosives. The laboratory also maintained medical care and health research facilities to evaluate radiation exposures and health effects in workers and animals.

The laboratory accelerated development of the first thermonuclear (fusion) weapon in the 1950's, testing the first thermonuclear bomb at the Pacific Proving Ground. During this time the laboratory also conducted research, development, manufacture, and testing of the first aqueous homogeneous reactor (water boiler) and the first mercury cooled plutonium fast reactor (Clementine). The Omega West research reactor was constructed in 1956. The Laboratory conducted controlled thermonuclear reaction (CTR) research with a series of experiments in plasma confinement technology, leading to the CTR theta- and Z-pinch research programs. Scylla and Scylla II, magnetic confinement devices used in CTR research, began operation in 1957 and 1959, respectively.

During the 1960's the Laboratory conducted a series of applied research programs on the uses of nuclear energy, including space applications, power reactor programs, CTR, radiobiology and medicine. These research programs included the Los Alamos Power Reactor Experiments; the Los Alamos Molten Plutonium Reactor Experiment; the helium-cooled Ultra-high Temperature Reactor Experiment; high temperature fuel and materials technology research; and the design and development of the Kiwi series of nuclear reactors for the Rover Program (a joint National Aeronautics and Space Administration-Atomic Energy Commission nuclear rocket program).

Research and development activities in the 1970's expanded to include astrophysics, earth sciences, energy resources, nuclear fuel safeguards and laser research. The Clinton P. Anderson meson physics facility, an 800 MeV proton accelerator for medium energy physics research, was constructed in 1972. Other research and development activities during this time included laser fusion and laser isotope separation, solar energy, superconducting electrical storage and transmission systems, and hydrogen fuel technology.

Approximately 85 percent of the laboratory's research was military-related in 1979, with primary research areas described as: 1) nuclear weapons technology; 2) energy research; 3) medium energy physics; 4) nuclear safeguards and accountability; 5) plutonium technology; 6) satellite-borne detection systems; 7) health, biological, and environmental research; 8) stable isotope research; and 9) basic research in nuclear science, computer science, space physics, astrophysics and cosmology, chemistry, nuclear chemistry, materials science and metallurgy, low temperature physics, explosives and shock hydrodynamics, and electronics (LASL, 1979).

The Laboratory research activities through the 1980's were concentrated in nuclear weapons design, applied and theoretical nuclear physics, and nuclear fusion. This research utilized a variety of unique devices, installations, and systems. These experimental devices and facilities included several linear accelerator systems, inertial confinement laser fusion systems, and magnetically-confined high-temperature high-pressure plasma fusion systems (LANL, 1990).

By 1989, approximately 75 percent of the laboratory's research was military-related, with primary research programs described as: 1) nuclear weapons technology; 2) non-nuclear defense technology; 3) energy and related technologies; 4) chemistry and materials science; and 5) basic sciences (LANL, 1990). These programs included a variety of technical activities encompassing research in nuclear physics, computer sciences, thermonuclear fusion, neutral particle beam (NPB) physics, free-electron lasers (FEL), explosives, nuclear fission reactor safety, metallurgy and ceramics, high-temperature super-conductivity, materials chemistry, condensed matter physics, radiochemistry, analytical, physical, nuclear and environmental chemistry, radioisotope production and other activities.

The Laboratory also operates dedicated facilities for research and development of plutonium-based nuclear fuels, fuel fabrication and testing methods and radioisotope production. The physical facilities are presently designed as controlled isolation and containment environments using glove boxes, shielding and remote control devices to handle plutonium-based fuels and radioisotopes. Additional Laboratory facilities exist for biomedical research, nuclear chemistry, photochemistry and instrumentation research and development for nondestructive assay of nuclear materials. The Laboratory maintains technical libraries, central computing facilities, administrative offices, printing and photographic production facilities and operates a small research reactor.

The Laboratory presently maintains several interdisciplinary research centers that utilize the physical resources of the site to conduct research in geoscience, nonlinear studies, materials science, national security, human genetics, high-temperature superconductivity (exploratory research and development), meson physics, neutron scattering center (LANSCE) and an advanced computing laboratory (LANL, 1990). Laboratory personnel also conduct research activities at explosives and munitions test sites at the Laboratory, at sites near the facility, and at remote locations (e.g., nuclear underground testing at the Nevada Test Site).

Several types of shop facilities support the research and development activities of the Laboratory. A central shop and smaller branch shops located throughout the site provide capabilities to fabricate components from precious metals, ceramics, ceramic-metals, graphite and radioactive, toxic and pyrophoric materials using a variety of processing methods and equipment. Other Laboratory shops

manufacture electrical components and circuits using processing methods common to semiconductor fabrication and electronic component manufacturing and assembly.

These research activities appear to present potential for exposure to a diverse group of physical agents including microwave and radiofrequency radiation, extremely low frequency electromagnetic fields, static magnetic fields, lasers (visible and ultraviolet) and ionizing radiation. Research activities have also involved work with a variety of chemical agents including: 1) metals such as arsenic, thallium, uranium, lead, niobium, beryllium, lanthanum, thorium, tantalum with nuclear properties needed for the production of nuclear weapons; 2) organic solvents; 3) lubricating and machining oils; 4) explosives; 5) various other agents used in completion of the laboratory mission (adhesives, inorganic solvents, acids); and 6) agents used in the measurement of radiation, such as chemical dosimeters measuring energy absorption or as phosphors used in scintillation counters.

Los Alamos has maintained an active industrial hygiene and health physics program since inception. Several reports describe exposure assessment activities for specific buildings/processes at the facility since the 1950s. A review of general information on activities and potential occupational hazards at the Laboratory identified a variety of chemical agents including: 1) fluorine and hydrogen fluoride (Winburn, 1976; Maraman et al., 1975); 2) arsenic, barium nitrate, niobium, lanthanum, tantalum, thallium, chloromaleic anhydride, tributyl phosphate (Hyatt and Milligan, 1953); 3) alkali metals, zirconium, titanium, magnesium and other metals in the form of turnings, dusts, oxides, hydrides and alloys (Stout, 1958); 4) potassium carbonate, lithium carbonate, asphalt-base oil, metal pickling and electropolishing agents (sulfuric and chromic acid) (Stearns, 1956; Duncan et al. 1957); and 5) carbon tetrachloride, diethyl ether, ethyl alcohol, freon (Maraman et al. 1975). Additional information describing site operations was identified in environmental assessments, environmental impact statements and related documents (U.S. Department of Energy, 1979 (L140-F); Los Alamos Scientific Laboratory, 1978; U. S. Department of Energy (1978)).

The Zia Company

The Zia Company was founded in April 1, 1946 as a municipal organization to provide services to Site Y (Los Alamos) of the Manhattan Project. The Company took over maintenance, construction and support services handled by the U. S. Army Corps of Engineers (Force Account) during WW II. Civilian personnel formerly engaged in these duties were transferred to Zia. The company was responsible for maintenance and construction support in technical areas of the laboratory, and provided municipal services to the Los Alamos community. The Zia Company operated the hospital, schools, transportation, housing, utilities, cafeterias, fire department, power and steam plants, and provided maintenance, construction and other service functions to technical areas of the laboratory. During the mid-1960s, the responsibilities for these community services were taken over by the county government or were transferred to the private sector.

By 1950 most of the workers were unionized and consisted of laborers and skilled trades drawn from the surrounding communities. Hispanics and Native Americans from the surrounding area of northern New Mexico were an important component of this workforce.

Throughout the late 1950's through the mid 1980's the Zia Company personnel provided construction support, maintenance, and skilled labor. The Zia Company continued to be the support services contractor until July 1, 1986 when Pan American World Services took over the contract. Pan Am World Services was purchased by Johnson Controls, Inc. in 1989.

II.C. DOE Facility Comparison Study

Review of existing DOE cohort data bases indicated that some DOE facilities with large numbers of MM cases were not chosen for inclusion in the case control study. Following submission of the MM study feasibility report, which was prepared as the first phase of this research, we were asked by NIOSH to evaluate whether we had excluded DOE cohorts with markedly elevated MM rates from the study. Three DOE populations from the Oak Ridge Reservation were of particular interest because their size, old age, and adequacy of vital status follow-up: the Tennessee Eastman Corporation (TEC), Y-12 and K-25 cohorts. These facilities were not chosen for inclusion in the case control study because their work environments are dissimilar to the chosen facilities, and/or their historical radiation dosimetry data are relatively lacking. However, it was recognized that a case control study using one or more of those cohorts might be justified if the MM rates were considerably higher than the rates in the chosen populations, taking into account workers' time periods of birth and ages of follow-up. On request from NIOSH, we undertook a cohort comparison study of multiple myeloma death among the five chosen cohorts as well as the other three Oak Ridge cohorts.

The data required to enumerate the cohorts for a comparison of death rates from multiple myeloma were previously collected for DOE epidemiological studies. The individual data elements required for this analysis were minimal and included: an identifier assigned by the Center for Epidemiological Research at ORAU (CERID) that is unique for any individual enumerated on any DOE facility roster that has been loaded into their master data base; date of birth; dates of hire at the respective DOE facilities; vital status; date of last observation; and cause of death (underlying and any cancer contributing cause) for decedents. Data were acquired from three sources: ORAU/CER, PNL, and CEDR. While the information needed for each worker was limited, the overall volume of data assembled to conduct this investigation was staggering and required the resources of the mainframe computer. Following is a description of the data sources for each of the eight facilities included in the facility comparison analyses.

ORNL and Savannah River. All information (master roster, employment dates, vital status and cause of death) was received directly from ORAU/CER. Theoretically, it was the same information available from CEDR except for variables that were truncated for confidentiality reasons in the CEDR database. These variables appeared in their original form in our data base. For ORNL and Savannah River vital status was determined by a computer algorithm developed at UNC using the "submission" and the "death" files and the employment dates. The "submission file" was the composite of all types of vital status searches done for each member of the cohort.

Hanford. The secondary data source utilized for construction of the Hanford cohort was an analysis file (IARC89) at UNC that was obtained directly from PNL in 1992. The Hanford cohort was recently updated from a later version of this analysis file that was available through CEDR.

LANL and Zia. Both the LANL and the Zia cohorts were constructed from working files available through CEDR. At our request, additional information concerning the vital status of these cohorts was made available through CEDR by the Epidemiology Division at LANL.

Y-12. All data used to construct the Y-12 cohort had already been obtained from ORAU/CER because of an ongoing study of this population by investigators at this institution.

TEC and K-25. For these two cohorts, information on demographics and employment dates was obtained from CEDR and vital status information was provided by CER/ORAU.

For inclusion in any of the facility rosters, an individual had to be first hired prior to 1-1-79; have a valid year of birth before 1963 and a minimum age at hire of 15 years; and have a hire year within valid ranges for the facility of first hire (the index facility). The rosters for ORNL, TEC, Y-12, K-25 and SRP identified all DOE facilities at which an individual was known to have been employed. The rosters for LANL, Zia and Hanford did not provide this information so employment dates at all of the facilities were compared to identify individuals who worked at more than one facility. Cases of multiple myeloma (ICDA 203) were classified as either an underlying or a contributing cause of death case.

Persons who worked at more than one facility were counted only once in the cohort comparison analysis. Persons were not excluded if they had a missing or out-of-range hire date at a second facility. A date of hire at the second facility was assigned which was consistent with the term date at the index facility. The end of the follow-up period was 12-31-90 for all cohorts except Hanford, which was 12-31-86. If a person worked at more than one facility, the vital status with the most recent follow-up was used.

For analytical purposes three analysis files were constructed: the first consisted of the five cohorts selected for inclusion in the case-control study and counted only underlying cause MM deaths. The second file consisted of all eight cohorts. The third file included the six facilities for which contributory cause cancer deaths were routinely coded. The LANL and Zia cohorts were excluded because non-underlying cause cancers were not consistently coded for all years during the period of observation of this study.

Many workers in the DOE cohorts were employed at more than one facility, especially at the Oak Ridge reservation. We therefore treated facility of employment as a time-dependent variable. Each worker entered the study on their first-facility date of hire, contributing person-time to that facility. Single-facility workers contribute all person-time and deaths to a single facility. Workers that were employed at more than one facility began contributing person-time to the "multiple facility" category at their first hire date at a second facility. Under a zero lag assumption (used in all analyses presented here), all deaths occurring in multiple facility workers are counted in the multiple facility category.

Age and birth cohort specific person-years and MM deaths were counted using the method of Pearce and Checkoway (1988). A SAS program was written to calculate standardized mortality

ratios directly adjusted for age (in five-year intervals) and birth year (<1905, 1905-14, 1915-24, 1925+) for each facility using the total population person-year distribution as a standard. Therefore, in each analysis, an SRR of 1.0 indicates that a facility's adjusted rate is equal to the average rate for all cohorts combined for that analysis.

Results of the facility comparison analysis are shown in tables 2.1-2.4. Table 2.1 shows the number of workers, vital status, and the number of MM cases found in each of the eight cohorts. In Table 1, workers and deaths are counted in each cohort of employment. Of the facilities studied, SRP is the only one that began operations after 1950, and has the smallest number of workers and lowest proportion of decedents, 16.8%. TEC is the oldest and largest cohort, having employed over 46 thousand workers before closing in 1947, and it has the highest proportion of decedents, 46.3%. In the LANL and Zia cohorts, workers were not classified as dead unless a death certificate had been obtained. Among the other cohorts, the proportion of decedents for whom death certificates had not been retrieved ranged from 1.7% for Y-12 to 4.5% for TEC (data not shown). The available Hanford data indicate that no worker has an unknown vital status. The proportion of workers with unknown vital status in other cohorts ranges from 0.7% in TEC and K-25 to 11.0% at Zia.

Numbers of MM deaths range from nine at SRP to 103 at TEC (Table 2.1). Most occurrences of MM appeared as the underlying cause of death. There were no contributory MM deaths at Zia, presumably in part due to the lack of contributory cancer cause coding there. Among the remaining facilities, the proportion of all MM deaths that appeared as a contributory cause was approximately 10% at Hanford, LANL, TEC and SRP and 20% at ORNL, Y-12 and K-25.

Table 2.2 presents SRRs for MM as an underlying cause of death among the five facilities chosen for the case-control study. Table 2.2 also give the numbers of person-years of follow-up and numbers of underlying cause MM deaths for each cohort and for the multiple facility group. The numbers of person-years and MM deaths is largest for Hanford. Only four underlying cause MM deaths occurred among workers employed in more than one of these five cohorts. The SRR for Zia is lowest, 0.78, and the other groups vary between 0.93 and 1.08.

Table 2.3 presents the same analysis for all eight cohorts. Due to the inclusion of three cohorts from the Oak Ridge Reservation additional to ORNL, the multiple facility category is considerably expanded over the five-cohort analysis. Comparison of Tables 2.1 and 2.3 shows that out of the 14 underlying cause MM deaths observed among ORNL workers, only six occurred among ORNL workers that were never employed in another one of these eight cohorts. Over half of the Y-12 underlying cause MM deaths occurred among multiple facility workers as well. SRRs vary from 0.50 at ORNL to 1.26 among multiple facility workers. TEC is the only specific facility with an SRR above 1.0.

Table 2.4 includes both underlying and contributory cause MM deaths in comparison of the six facilities for which contributory cause coding was routine. The SRR for ORNL is again the lowest, 0.71, followed by Y-12 at 0.78 and SRP at 0.83. The multiple facility category is most clearly elevated in this analysis, with an SRR of 1.29.

We concluded from these comparisons that the numbers of MM deaths in the Oak Ridge facilities *not* selected for inclusion in the case control study were large primarily due to the size and age of the populations rather than to high age-cohort specific MM death rates.

Other specific findings were of potential secondary interest. The cohort construction process highlighted a number of differences between the cohorts in vital status ascertainment, death certificate retrieval, and coding of contributory cause information. The relatively low SRRs for the Zia cohort in Tables 2.2 and 2.3 may have been due, in part, to lower access to medical care and high rates of coding to ill-defined conditions that have been reported for Hispanics in New Mexico (Becker et al., 1990). Death rates for ill-defined conditions have been high for the Oak Ridge populations as well (Cragle and Fetcher, 1992). Variation between the cohorts was also noted in the proportion of all MM deaths that appeared as an underlying vs. contributory cause.

III. MATERIAL AND METHODS

III.A. Enumeration and Description of the Five Study Cohorts

In order to enumerate all workers who were members of the five study cohorts, determine their vital status, and ascertain their causes of death, all available computerized employee rosters containing unique identifiers and demographic characteristics, vital status follow-up information, work histories, and radiation monitoring data, were obtained for each of the five worker cohorts selected for study from the Center for Epidemiological Research (ORAU/CER) at Oak Ridge, Tennessee, and the Comprehensive Epidemiological Data Resource (CEDR) at the Lawrence Berkeley Laboratory, Berkeley, California. A single multi-facility roster was constructed, and consisted of the 119,922 workers who were ever a member of one of the five worker cohorts prior to 1-1-79. Workers hired at later times were excluded because rosters of three of the five cohorts were incomplete after 1978. For the purposes of case identification and control selection, a worker belonging to more than one cohort was counted in the first or index cohort as of the date of first hire. After removing duplicate records for persons who were members of more than one cohort, and records for persons with missing birth dates, dates of first hire, or vital status information, 115,143 persons were eligible for inclusion in the combined facility cohort.

Table 3.1 presents an overview of the characteristics of the five DOE cohorts selected for study. Race is missing for virtually all of the LANL population and 48.9% of Zia workers. Gender is also missing for a substantial portion of the Zia workers (24.5%). Since these attributes were not considered as matching criteria it was unnecessary to eliminate any worker for reasons of missing race or gender. Additional interesting information about these populations is also presented in Table 3.1. The Zia cohort tends to have more older members than any of the other four cohorts, with approximately 33% born before 1915 and only 9% born after 1945. The percentage of workers born after 1945 in the other four cohorts range from 17-20%. The older age of the Zia cohort is further evidenced by the increased proportion of confirmed deaths in this population (34.6%) as compared with 19.8% at ORNL, 15.8% at SRP, and 17.4% at LANL. The Hanford cohort has 21.8% reported deceased, but follow-up for this cohort is only through 12-31-86. The number of hires is reasonably consistent over time at ORNL, Hanford and LANL. At SRP, however, 72% of the cohort was hired between 1952, when the facility opened, and 1959. A similar pattern appears in the Zia cohort,

where 64% of the workers were hired during the first few years of the operation of LANL. Age at death is not consistent among the five worker cohorts. SRP has the highest proportion of deaths in the under age 60 group (52%); Zia had the lowest with 29.6%. However, it is difficult to determine the effect that the relatively large number of workers lost to follow-up in the Zia cohort has on the distribution of age at death.

III.B. Follow-Up of Vital Status

Information on the vital status follow-up was available for four of the five cohorts through 12-31-90. Follow-up of the Hanford cohorts was only complete through the end of 1986. Further follow-up of the study cohorts was not undertaken for this study. Vital status at the end of the study was known for more than 94% for all cohorts, except Zia, where 11% of the workers were lost to follow-up. Follow-up of the Hanford cohort was reported by the PNL investigators (Gilbert et al., 1993a) as 100% because they assumed a worker was alive at the end of the study, in this case as of 12-31-86, when there was no death indication. At other facilities, the status of workers was counted as unknown after the date of last known vital status, usually termination of employment, if no confirmation of alive status could be obtained. Death certificate ascertainment was above 95% for ORNL, SRS and Hanford. Because of insufficient data for LANL and Zia workers concerning dates of death for persons with death indications not confirmed by death certificates, only verified deaths were considered deceased, hence death certificate ascertainment was reported at 100%. For the LANL and Zia cohorts, workers who had a death indication but no estimated date of death were considered unknown and withdrawn from the study as of the date last known to be alive.

III.C. Case Identification and Control Selection

Cases of multiple myeloma were identified from the combined five cohort roster when the International Classification of Disease Code (ICDA) 203 was determined to be the underlying cause of death, or the secondary cause of death, or a significant condition, on the death certificate. For the LANL and Zia workers, only the underlying cause of death had been coded consistently for prior epidemiological studies of these cohorts. To complete case ascertainment, all death certificates for the LANL and Zia cohorts were reviewed at LANL to determine all occurrences of multiple myeloma. Controls were randomly sampled from the combined five cohort roster using an incidence density matching technique described by Beaumont et al. (1989). Controls were matched only on age at risk. Four matched controls were selected for each case.

III.D. Data collection

Data were collected by the principal investigator, co-investigators, project manager and research assistants of the project. A bibliographic data base was developed and maintained to organize numerous published journal articles, published and unpublished technical reports, industrial hygiene reports, and other relevant documents that were collected for this study. Procite software was chosen for this purpose. A copy of the bibliography of reference materials collected for this study is included in Appendix I.

DOE public reading rooms, technical libraries at LANL and ORNL, two libraries serving as repositories for federal documents, and archived records at the individual sites were excellent resources for providing general descriptive information about the four study sites, for identifying potential radiation and chemical hazards, and for providing descriptions of the radiation and industrial hygiene programs. A variety of methods were employed to identify relevant materials from these resources. Listings of the holdings of DOE Reading Rooms at Hanford and at ORNL were obtained in electronic form, and a printed list was obtained from the LANL Public Reading Room. A computerized search of energy-related literature was also conducted to identify relevant materials available from government sources including NTIS, the DOE Office of Scientific and Technical Information, and the published literature. The Radiological Assessments Corporation in Neeses, South Carolina, who is conducting the dose reconstruction project for the Savannah River Site, provided us with copies of inventories of documents retrieved for these projects. This data base was instrumental for locating important documents relevant to the chemical hazards assessment archived at the Savannah River Site. Mr. Till was also interviewed about the availability of similar documents for the Hanford Site.

Demographic information, employment dates, job titles, departments, and internal and external radiation monitoring data were acquired from CEDR and from ORAU/CER, a DOE contractor which has conducted prior epidemiological studies of ORNL and SRS. These data were used either as the sole source of data or as a means of verifying data collected from hard copy records. Since it was not an objective of this study to verify data available in electronic form with the original source documents, a comparison of the two data sources was not incorporated into our research plan. However, computerized records were used to ascertain the completeness of the hard copy records that were made available to us. In a number of instances, with both work history and radiation monitoring data, we were able to determine that we did not have available records.

Hard copy records were reviewed at each of the four DOE facilities under study and also at ORAU/CER. Assessment of exposures resulting from situations outside of employment at any of the four study facilities, with the exception of information pertaining to prior occupational history included in personnel records at the study facilities, was not undertaken for this study. This includes work at DOE facilities, other than the four study sites. The design of the study involved no contact with any subjects, either in person or by proxy.

III.D.1 Facility information and organizational structures

Valuable information describing the four study sites was obtained from documents found in DOE public reading rooms at Oak Ridge, TN; Richland, WA; Los Alamos, NM; and Aiken, SC. The Davis Library at the University of North Carolina at Chapel Hill, which serves as a repository for federal documents, and the Hill Library at North Carolina State University in Raleigh, provided documents required for this study. Contacts at the DOE sites assisted us in identifying resource materials. At ORNL, materials assembled for the human experimentation investigation were catalogued in an electronic data base which permitted us to easily identify relevant materials from their central files. At LANL, we reviewed the documents from the industrial hygiene group that were stored in the Laboratory archives. At Hanford, a group of boxes were identified from archives

that contained materials from the Health and Mortality Studies. The contents of these boxes were examined, as well as four boxes of archived industrial hygiene materials..

In addition to materials describing the organizational structure of each individual site, we sought: historical site maps; detailed descriptions of individual areas and activities and potential exposures in those areas; processes, systems, tools and equipment used; potential exposures to chemical and physical agents; building names; and possible associations between departments, locations and buildings.

Because specific information on organizational structures and department titles was so vital to our research, particularly the chemical hazards assessment, the information that we gathered for each site is next described in more detail.

Oak Ridge National Laboratory. An electronic file of department titles assembled by research staff at ORAU/CER was available to us and was used to identify the names of departments for ORNL workers. Departments were also identified by code and by title in the personnel records of individual workers. These were recorded. Information about the major divisions at ORNL from 1945 to the present was obtained from old telephone lists that were fortuitously kept by a former director in the Personnel Office. Also available to help us understand the Laboratory's work and the workforce were building lists and a history of the ORNL (Johnson and Shaffer, 1994).

Savannah River Site. At the Savannah River Site, the departments of the workers were considered proprietary and we were not successful in obtaining any organizational information. Fortunately, departments were identified by name in the personnel file of the individual worker, which allowed us to have a general understanding of the work of the department.

Hanford Site. An organizational coding system was developed at the Hanford site which identifies both the contractor and the organization, the latter being analogous to department at other sites. Several sources were utilized in order to associate a name with the organization codes for each of the workers in the Hanford portion of the study: 1) an electronic file of organization titles from 1944-1968 which was compiled by HEHF for the DOE Health and Mortality Studies; 2) copies of the source documents used by HEHF to compile an electronic file of the organizational titles from 1968 to the mid 1980's; and 3) organization titles that were found along with organization codes to which a person was assigned in individual work histories. HEHF source documents included Isochem, Douglas United Nuclear, Battelle/PNL, and the Westinghouse Company from 1978-1986. Source documents were missing for the Westinghouse Company from 1969-1977, and, most unfortunately, the electronic version of the organizational title file created by HEHF in the 1980's was never located for our use.

Los Alamos National Laboratory. Staff at LANL, had prepared a genealogy of the organizational structure of the laboratory from its inception. We copied the genealogy from the primary source and used it, together with a history of the Laboratory (Hawkins, 1983), to identify the titles of divisions and groups for workers employed by the University of California.

the Zia Company. Little information was available describing the way the Zia Company was organized for work at the LANL site except for the documentation for the external radiation monitoring data which contained an overview of the structure of the Zia Company in the mid 1960's. Unfortunately, departmental titles rather than numerical codes were used to assign workers to departments or cost centers. This allowed us to create a framework sufficient for completing the chemical hazards assessment.

D.2 Personnel and work history information

In addition to verifying the demographic characteristics of each worker from cohort files, personnel records were reviewed to obtain the following information: (1) birthplace; (2) years of formal school completed; (3) military service; (4) prior farm residence; (5) prior work history; and (6) security clearances. Personnel records also routinely contained hire and rehire dates, dates of paid consultant periods at the site, reasons and dates of termination, dates and names of assignment to organizational units, pay codes, job titles, and an occasional job description. This information from personnel records was used to construct work histories for the workers in the study. All available personnel records were reviewed for each worker.

Except for workers at the SRS and a few workers at ORNL, payroll records were not routinely used, and the personnel record was relied upon to complete the work histories. In retrospect, the payroll records would have been easier in reconstructing a person's work history since all of the jobs and departments are listed in sequential order by date. Personnel records contain the forms used to initiate the hire or termination of an employee or change the payroll status of a worker, including department and job title. This information is usually recorded on a single, standard 8 1/2 by 11 inch sheet of paper and found scattered throughout the personnel record. Moreover, an individual form kept in this manner is easily misplaced or misfiled.

Medical records were also used to complete the collection of personnel and work history information for workers at each of the four sites. Medical records proved to be a valuable source of information for estimating hire and termination dates, and for determining job titles and departments for workers with missing personnel records. For most workers, medical records were also the single best source of information for identifying work locations i.e., area and building.

The data collection instruments designed for recording personnel information and work histories are included in Appendix II, Exhibits A and B, respectively. Guidelines for abstracting personnel and work history data are included in Appendix III and Appendix IV. Although the forms designed to collect work histories at each site contain the same basic information, forms were tailored to each individual facility to facilitate data collection. Before data collection began at each of the four sites a work history was prepared for each worker based on information from existing computerized records. For ORNL and Hanford, existing computerized work histories were relatively complete. Work histories for SRS workers consisted only of employment dates and for the LANL and Zia workers, only employment dates and first and last job titles. Nevertheless, having this information on hand as the research staff attempted to reconstruct a work history and determine work locations increased the efficiency and reliability of the data collection effort. This was

particularly true at ORNL and Hanford where the computerized work histories were relatively complete.

ORNL. All personnel records that could be located for the ORNL workers in the study population were reviewed. A locator file consisting of small 2" x 4" card has been maintained for anyone ever employed at ORNL. This system was still active and used to verify the employment dates of each worker with a missing personnel record. The cards also contained some information on departments and job titles. Payroll records or wage packets which are separate from the personnel records and stored in the Personnel Department at the Y-12 site were reviewed for persons missing personnel records. The personnel records that could not be located were primarily for persons employed solely by Du Pont between 1943 and 1945. These original records were transferred to the Du Pont Hall of Records in Wilmington, Delaware when Du Pont left ORNL at the end of WW II. The data collection team for the early DOE Health and Mortality Studies apparently retrieved these records from Du Pont. For these workers, work histories from the electronic files in CEDR were utilized.

Savannah River Site. Personnel and work history information was initially retrieved for SRS workers from records at ORAU/CER. SRS employment records were received at ORAU/CER in the Autumn of 1989 and consisted of records for both hourly and salaried personnel, active and terminated, as of 3-31-89. Records for hourly workers included an employee data sheet consisting of department information but without a corresponding effective date and a payroll card containing job titles and corresponding effective dates but no department information. Available records for salaried workers consisted of an employee data sheet and a payroll record which included information on educational background and prior employment in addition to job titles and effective dates. Neither hourly or salaried workers had an employment application or security clearance information that would normally be contained in a personnel record.

The records at ORAU/CER were stored in various places depending on the employment status of the worker and the type of record. Records were available in both paper copy and in microfilm. Employment records in all locations were reviewed, and all records pertaining to workers in the multiple myeloma study were photocopied.

All personnel records available for SRS workers were reviewed by the UNC research staff in offices of the SRS Medical Division. The records were brought to the Medical Division offices there by a staff member of the Westinghouse Personnel Department. Many records had been permanently stored in the Federal Records Center in Atlanta, Georgia. An employee data sheet, the same as that found at ORAU/CER, was available for four workers whose personnel records could not be located. Relevant personnel and work history information was abstracted from the personnel files using standardized data collection forms. Medical records were reviewed for persons with missing personnel records to glean pertinent personnel or work history information. As was our experience with the other DOE facilities in our study, occupational health records were found to be a rich source of information about jobs, departments and the actual physical location of the work performed at the site. Payroll records were not accessed for SRS workers at the Savannah River Site.

Hanford Site. All available personnel records for the Hanford workers were reviewed in Records Holding Area (RHA) at the Federal Complex in Richland. Since most of the workers in the study had terminated many years ago their personnel records were stored at the Federal Records Center in Seattle and had to be transferred to the RHA for our review. Copies of personnel records for employees of Battelle/PNL were turned over to the DOE Operations Office by Battelle who then transferred them to us.

Personnel records only included computerized information for the prime operations contractors at Hanford. We did not have access to the personnel records of the construction contractors nor did we obtain the Occupational Health History (OHH) File for construction workers. Consequently, we attempted to complete the work histories for all workers for all employment periods on the Hanford Site from occupational health records. This was possible because the General Electric Company and more recently the Hanford Environmental Health Foundation (HEHF) provided occupational health services for all Hanford site personnel. We were able to augment work histories with a rather rich supply of work history information in the occupational health records including work areas and buildings embedded.

For several prime contractors, such as Isochem Inc., we had to rely solely on the information in the computerized work history (OHH) file, since original personnel records were not always available for verification. Records for the Westinghouse Company were also missing from the files of some workers who were employed by both GE and Westinghouse. Other minor operations contractors that provided services to the Hanford site never had their rosters or work histories computerized for the Health and Mortality Studies. We were able to identify these work histories from occupational health records.

As was the case at ORNL, records were not available for persons employed solely by Du Pont who terminated before General Electric assumed responsibility as the prime contractor at the Hanford Site. The personnel files for these early Du Pont workers are stored in Wilmington, Delaware at the Du Pont Company corporate headquarters. Comprehensive computerized work histories (OHH File) for all Hanford operations workers constructed by the data collection and management team for the Health and Mortality Studies (HMS) were made available to us. These records were utilized to construct the work histories for the early Du Pont workers. They were verified from microfiche records of the Health and Mortality Studies (HMS) that we reviewed in the Records Holdings Area. The microfiche records consisted of the original HMS master data coding sheets and, for some workers, copies of original forms from personnel records. For reference, there also exists in microfiche, a copy of a computer printout of Du Pont Company employees which includes name, date of birth, date of hire, birthplace, citizenship and security clearance. It appears that these records were the output of computerized files constructed for the HMS, and, while not an original data source, this information was useful for a select group of workers who were only employed during the early days at the Hanford site.

LANL. Personnel files for University of California employees at LANL were made available to us in the Personnel Department. Since the majority of the records were available only on microfiche, we were given access to equipment necessary to make paper copies from the microfiche. All personal identifying information was redacted from the copied records before they were sent to

UNC-CH. The computerized work history information available from prior epidemiological studies of LANL workers was limited so it was necessary to construct work histories exclusively from the personnel records. Information on educational background, types of security clearances, and prior work history was also abstracted from the personnel records. Duplicate microfiche copies of the LANL personnel records were also available in the Epidemiology area, but there was no working equipment available either to copy the microfiche or make paper copies of forms on the fiche.

The Zia Company. As was the case with the LANL cohort, work history information available in electronic form from prior epidemiological studies for the Zia workers was limited to employment dates and first and last job title. A search for personnel records for Zia workers was made in microfiche files residing in the LANL Epidemiology area and also in the archived personnel records of the Zia Company presently maintained by Johnson Controls, Inc. in the records storage area. The majority of records located for Zia workers were microfiche records. Paper copies of the records were made and the copies were redacted and sent to UNC-CH. Work histories were constructed and personnel information was abstracted directly from the Zia personnel records.

Additional job title information, more detailed than what was available in the existing computerized records for Zia workers, was located in the Epidemiology area on microfiche copies of hire-term cards. All employment dates and job title information were abstracted for Zia workers. As a final attempt to reconstruct complete work histories for Zia workers, medical records were also reviewed for work history and personnel information.

III.D.3 Occupational health data

In addition to the use of occupational health records for work history information, these records were reviewed for their unique purposes. Radiation exposures from medical sources, both diagnostic (x-ray) and therapeutic, were recorded, as were smoking habits; evidence of medical surveillance for workplace hazards; exposures to non-radiological hazards; health problems or health procedures indicative of exposure to radiation or chemical exposures, e.g., a history of chelation therapy); a history of cancer; and all internal radiation monitoring data. The form used for collection of occupational health information is included in Appendix II, Exhibit C and the guidelines developed for record abstraction are included in Appendix V. Special forms were also designed and used to abstract bioassay results from radiological and non-radiological sources from occupational health records. (See Appendix II, Exhibit E).

Oak Ridge National Laboratory. The Medical Division at ORNL is responsible for providing occupational health services for ORNL employees. Their records were reviewed in offices of the Medical Division and all relevant information was abstracted. As was the case with personnel records, medical records were not available for the early Du Pont employees who terminated before 1946.

Savannah River Site. Occupational health records were obtained and reviewed for workers from the Savannah River Site in the offices of the Medical Division. All occupational health records are stored in the Medical Division, usually in microfiche in the case of older records. Most of the

information was abstracted from the records using our abstraction forms. However, pertinent work history and exposure information was photocopied for our records.

Hanford Site. Occupational health services were provided by Du Pont and General Electric when they were primary contractors at the Hanford Site. However, when General Electric left the site, the Hanford Environmental Health Foundation (HEHF) was incorporated to take over the function of providing occupational health services. As with the personnel records, occupational health records were reviewed in the Records Holding Area at the Federal complex in Richland. Because so many of the workers in this study terminated many years ago, most of the records for the workers were transferred from permanent storage at the Federal Records Center in Seattle. Early records included information on hospitalizations at the local Kadlec Hospital.

Like their predecessors, HEHF provided services for the employees of all of the contractors on the Hanford site. For several reasons this was an immense benefit to the study. From the occupational health records we were able to verify existing computerized work histories for contractors for whom we were not able to recover personnel records for review. Likewise, we could identify employment on the site at times where we had no indication of employment. Occupational health records were also used to inform the work histories of the locations and buildings of the workers.

Los Alamos National Laboratory/ The Zia Company. The Medical Division at LANL provided occupational health services for both University of California (UC) and Zia Company employees. The records were reviewed at the Medical Division offices, and all relevant information was abstracted. Even more than at other DOE sites, the occupational health records at LANL were a rich source of both internal and external radiation monitoring data for workers during the early years of operation. All radiation monitoring information that was not already recorded from other sources or available in existing computerized files was also abstracted.

III.D.4 Radiation monitoring data

A questionnaire about health physics programs was developed in conjunction with investigators from the University of Texas Medical Branch at Galveston who are conducting a study of female employees at multiple DOE facilities. The questionnaire is based primarily on Procedures for Assessing Occupational Radiation Monitoring Data for Use in Epidemiologic Studies (Crawford-Brown et al, 1989), and from the DOE Office of Health Physics and Industrial Hygiene Questionnaire. This composite questionnaire was sent to health physics personnel at the four DOE sites prior to our initial site visit. We were not successful in getting the questionnaire completed prior to our visits, but our health physics co-investigator used the questionnaire as a guide during interviews with the health physics personnel at the sites and was able to complete the questionnaire during each visit.

External Radiation Monitoring Data

For each of the five worker cohorts, computerized dosimetry files for external whole body exposures were available from either ORAU/CER or CEDR. These files were retrieved and a file

containing only records for the cases and controls in this study was created. The information in the electronic files was supplemented by a review of all hard-copy radiation records that we were able to recover for each worker. Where we were able to obtain copies of original records, we abstracted information which was considered most important for exposure assessment. From the two major sources of external radiation monitoring data, electronic and hard copy, we constructed a radiation exposure history file for external whole body radiation. Records of radiation exposures at DOE facilities other than the study facilities were not collected.

The information that was considered most important for exposure assessment included:

- (1) The period of time covered by the record.
- (2) The exact date on which the measurement device was read; otherwise estimates were made. For example, end of quarters were coded 3-31, 6-30, etc.
- (3) The method used for monitoring: pocket chamber, film badges, TLDs, track etch, and activation foil.
- (4) The kind of radiation monitored. Two broad classes were made: total penetrating and total non-penetrating radiation. Sub-classes of penetrating radiation were defined as: gamma/X-rays, fast neutrons, and high energy betas (10 MeV lower energy cut-off). Sub-categories of non-penetrating radiation included: soft X-rays, slow or thermal neutrons, betas, and alphas.
- (5) The type of result indicating whether the result was routine, a special reading from knowledge of an unanticipated exposure, or a "dummy" reading intended only for calibration and quality assurance tests.
- (6) The location of the monitor. This information typically concerns the location of the dosimeter on the body (helping to distinguish whole-body doses from, for example, extremity doses).
- (7) The result and the units of the measurement.

Collection of external radiation monitoring data at each of the four sites varied greatly. Generic forms were designed to include the elements that were considered essential for exposure assessment. (See Appendix II, Exhibit D). In practice, data collection forms and methodology were adapted to fit the information that was available at each site.

Our experiences with data collection and the variations in the forms of the data collected at each of the four study sites are described below.

Oak Ridge National Laboratory. The radiation protection staff at ORNL responsible for the radiation exposure records recently collated all available original radiation records for each worker in individual files. These records were made available to us to photocopy and all records for

workers in the MM study were copied and sent to UNC-CH. As was our experience with other data at ORNL, radiation records for the early Du Pont workers were not available. Consequently, computerized records retrieved from CEDR and ORAU/CER were relied upon for the exposure histories for these workers. For the time period 1943-45, the computerized records consisted of annual whole body doses.

Over 8,600 individual film badge readings were entered from the paper records retrieved for the ORNL workers in this study. The results for more than 18,000 pocket dosimeter readings were also entered into electronic files and were used to estimate dose equivalents only when film badge results were not available in the years prior to 1948. Neutron monitoring results were entered into a separate electronic file.

Savannah River Site. Dosimetry records for SRS employees were available at two locations: ORAU/CER and SRS. Twenty-eight rolls of microfilm copies of computer printouts of detailed (weekly, quarterly) external dosimetry records beginning in 1958 and ending in 1977 were located at CER. Individual monitoring results were ordered on the microfilm by badge number within each quarter and year. Four other sets of microfilm records were found which contained copies of radiation monitoring folders for each worker. Each of the four sets was arranged alphabetically by termination date. These records contained external radiation monitoring data prior to 1958 and internal dosimetry records. All information from the microfilm for the SRS workers in this study was photocopied. Abstraction of the external radiation dosimetry data from 1958-77 microfilms was not undertaken.

As part of the documentation of the radiation exposure data available for SRS, all of the materials at ORAU/CER were reviewed, and copies of relevant documents were made for our records to be used in the assessment of the radiation dosimetry data for the SRS workers.

Radiation monitoring data were also obtained directly from the Radiation Protection Group at SRS. External radiation data were supplied in two formats. Copies of original daily, weekly and quarterly data cards on which external doses were recorded were provided for all workers. Additionally, workers employed at SRS since 1979 had all of their external radiation monitoring data computerized in an annual summary file called HPAREH. A printed output of HPAREH was included in each of their radiation files.

A significant gap in the external radiation data that were supplied by SRS was identified by comparing the original monitoring records with data for SRS workers in the CEDR database and with individual workers' employment dates at the site. The radiation folders were missing results after the second quarter of 1958 for those workers who were not employed in 1979 and included in the HPAREH file. These data could be retrieved from the microfilm records at ORAU/CER that were described above or from the computerized CEDR data set. In the interest of time, we captured the missing radiation monitoring records from the computerized CEDR files.

Hanford Site. External radiation dosimetry data for this study were purchased from the Radiation Dosimetry Group at Battelle-Pacific Northwest Laboratory. They provided to us printed copies of each worker's annual whole body radiation doses from PNL's computerized data base. A

comparison of these data with annual external doses for each worker in the CEDR data base was made and all discrepancies were reconciled. In cases where the reason for the difference was not apparent to us, personnel at PNL provided us with the assistance necessary to resolve the differences. Because detailed radiation dosimetry records were not provided to us for all workers in the study, hard copy detailed records were received for a sample of ten workers to permit a limited validity check of the annual recorded doses.²

Los Alamos National Laboratory/The Zia Company. Radiation protection activities for all of the workers at the Laboratory, including the employees of the University of California (UC) and Zia, have been the responsibility of the radiation monitoring group employed by UC. External radiation doses available in the CEDR files for both LANL and Zia workers were expressed only as a whole body dose, i.e. gamma, neutron, beta and tritium doses were not reported separately. Hard copy records were available to us which allowed us to abstract both annual radiation doses and the detailed monitoring results for time periods ranging from weekly to quarterly. All radiation records were abstracted from printouts of computerized data. However, because the electronic radiation data were stored in numerous, inaccessible files, the cost to retrieve these data was prohibitively expensive. Therefore, it was decided to abstract the data for study subjects from the hard copy printouts. The original laboratory notebooks containing all of the historical external dosimetry data, the source of the detailed computer files, were available to us for reference and validity checking. The notebooks were maintained by area or location where the monitoring was done. The source laboratory notebook, however, was identified in the detailed files so an individual record could be traced back to its original source.

Internal Radiation Monitoring Data

As with external radiation monitoring data, bioassay results and *in vivo* measurements for internal radiation contamination were gathered in a variety of ways depending on the state of historical radiation records at each of the four DOE sites. In addition to seeking out sources of radiation monitoring within the radiation protection groups, we also reviewed and abstracted any radiation measurements contained in medical records. A standard data collection form was developed which could accommodate all radionuclides and all types of internal data. Plutonium, uranium, strontium and tritium results were entered into separate site specific files. All other radionuclides were entered into a single site specific file.

The primary information for internal exposure assessment was:

- (1) The date on which the measurement was taken and the date on which it was read.
- (2) The method used for monitoring: urine analysis; whole body counts; fecal analysis; blood analysis; tissue analysis; nasal swipes.
- (3) The type of result: routine, a special reading from knowledge of an unanticipated exposure, or a control sample (used for calibration and quality assurance tests).

² Hanford was the only study facility where it was not possible for us to arrange access to detailed external dosimetry records.

- (4) The kind of radionuclide monitored. The element and the isotope were recorded where available.
- (5) Any information on the solubility classification for the radionuclide.
- (6) The result itself and the units of the measurement.

Oak Ridge National Laboratory. All bioassay and *in vivo* measurements of internal contaminants were included in the radiation monitoring files photocopied at ORNL. The information was converted to machine readable form by UNC research staff.

Savannah River Site. Copies of the source documents containing bioassay and whole body counts were provided by the SRS Radiation Protection Group.

Hanford Site. The common radiation report purchased from PNL contained bioassay as well as *in vivo* results in addition to the annual external radiation dosimetry data. These data were entered into computer files for analysis.

Los Alamos National Laboratory/The Zia Company. Plutonium urine bioassay results were available in computerized format from CEDR. Tritium bioassay results converted to whole body doses were available from the external radiation monitoring data that we abstracted at the Laboratory. The results of other bioassay measurements were not available except for those abstracted from occupational health records, and these data were only available for early years. Consequently, we had incomplete information for uranium, a radioactive material that was one of the primary radionuclides that we had planned to include in our exposure analysis.

In response to a request for all bioassay data in as close to the original form as possible, staff of the LANL Radiation Protection Division (ESH-12) suggested that we review the laboratory notebooks where the results of the bioassays were originally recorded. The notebooks are stored in the LANL Records Storage area. Select laboratory notebooks were reviewed to ascertain the feasibility of collecting the bioassay data in this manner, and it was determined that our project did not have sufficient resources to do so.

To obtain all of the bioassay data for the LANL and Zia workers in the MM Study four strategies were proposed by LANL staff: 1) LANL staff provide bioassay in electronic form. This option was prohibitively expensive because the work required writing new computer programs or queries to search individually archived annual files specific for each radionuclide for workers in the MM Study; 2) revamping the entire data storage and retrieval system for bioassay data. This work was definitely beyond the scope of this research project although it would facilitate access for future researchers; 3) constructing dose histories for the workers in the MM Study from bioassay results; and 4) attempting to figure out who would have any bioassay data and then abstracting the data from the lab notebooks. None of these options were tenable and the decision was made to rely on the

bioassay data from two sources: the plutonium data in the CEDR data set and the bioassay data that we abstracted from the medical records.³

Early *in vivo* monitoring done at LANL was in the form of chest counts using a scintillation counter called HUMCO. The consensus of opinion, including that of Jim Lawrence, a physicist who has worked in the radiation protection program at LANL for many years, was that results from the HUMCO System have limited utility except as an indicator that a person was monitored. Whole body and chest counts done with later technologies using sodium or cesium iodide crystals or phoswich detectors would be useful for the study. These data are relatively accessible and arrangements were made to have a retired Laboratory employee collect *in vivo* data for the study. Since the early 1970's, all data have been computerized but are also available in the original hard copy records in file cabinets. Data before the 1970's may be indexed on the computer data base. Hard copy records from the early years of the program were destroyed in a flood.

III.D.5 Industrial Hygiene

Site visits were conducted at each facility to obtain copies of relevant documents that provide information used in assigning exposures. Industrial hygiene personnel at each study site were contacted to identify information resources that may be used to evaluate historical exposures to the agents of interest. Additional information resources were identified and retrieved from Department of Energy Reading Rooms at each study site.

Historical information resources for all study sites were initially identified using printed and electronic bibliographic information resources covering U. S. Government Documents from 1940 through 1990 and included: 1) the printed monthly catalog of the Superintendent of Documents (prior to 1976), 2) the government documents electronic database (1976 and beyond), 3) the National Technical Information Service database, and 4) Nuclear Science Abstracts (1948-1975). Site specific information identifying historical information on industrial hygiene monitoring reports, agent inventories, descriptive site information, safety analysis reports, incident reports, operating procedures, process histories, and organization information is described below.

The information obtained from all sources was summarized in electronic database files using Paradox Version 5.0 software to allow query and retrieval of pertinent information for the exposure assessment. Database files that were created included: 1) a chemical and physical agents file, 2) a building/location file, 3) an industrial hygiene file, 4) an agent inventory file, 5) an organization/department file, and 6) a reference file.

Los Alamos National Laboratory. Industrial hygiene and records management personnel from the Los Alamos National Laboratory were contacted to identify historical industrial hygiene information resources. Relevant documents were identified from records transfer request forms used by the Industrial Hygiene group to transfer and store records. These documents included: 1) biological monitoring results for chemical agents, 2) monthly, quarterly and annual industrial hygiene, health physics and engineering development group reports, 3) safety analysis reports, 4) incident

³ LANL was the only study facility where it was not possible for us to arrange access to detailed bioassay dosimetry records.

reports, 5) air sampling data sheets, and 6) special investigations. Documents were located through searches of storage areas of the Industrial Hygiene group and copies of pertinent documents were obtained. Additional exposure information resources, including computer databases and industrial hygiene files which inventory non-ionizing radiation sources, asbestos and other chemical agents, were reviewed with LANL industrial hygienists.

Holdings of the DOE Public Reading Room at Los Alamos were also reviewed to identify historical documents describing operations, organization and history of the site. Relevant documents included environmental restoration program operable units reports, comprehensive environmental assessment and response program (CEARP) reports, solid waste management units (SWMU) reports, safety analysis reports, and environmental assessments for hazardous waste sites at LANL. These documents also contained information linking organizations with physical locations, and identified chemical agents encountered at each location.

Oak Ridge National Laboratory. Industrial hygiene and records management personnel from the Oak Ridge National Laboratory were contacted to identify historical industrial hygiene information resources. The following documents and resources were obtained: 1) historical industrial hygiene monitoring reports from ORNL Central Files covering the period 1947 to 1965; 2) electronic files containing industrial hygiene monitoring records for the period 1970 through 1990; 3) an inventory of radiofrequency and microwave radiation sources (1995); and 4) division and department directories covering the period 1947 through 1995. The documents were abstracted and added to the exposure assessment database for ORNL.

Three database files containing historical information relevant to the study were identified and reviewed. Historical industrial hygiene monitoring data after 1970 was contained in a single database constructed from multiple databases by ORNL staff. The database file contains information from the industrial hygiene workplace sampling data sheets (green sheets) covering the period 1970 through 1990. A copy of the electronic file without personal identifiers was obtained from ORNL industrial hygiene staff.

Public reading room holdings at the U. S. Department of Energy, Oak Ridge Operations Office, Oak Ridge, TN, were reviewed for historical information on chemical and physical agent exposures, agent inventories, organization information and related facility information. Copies of relevant documents were obtained and the information was abstracted and added to the ORNL exposure assessment database.

Savannah River Site. Industrial hygiene personnel from Savannah River Site were contacted to identify historical industrial hygiene information resources. Relevant industrial hygiene documents were initially identified using the Environmental Monitoring System database developed by Radiological Assessments Corporation as part of the Centers for Disease Control dose reconstruction project at the Savannah River Site. Documents were reviewed at the SRS Records Management Center and copies of pertinent documents were obtained. Additional exposure information resources, including computer databases and SRS Industrial Hygiene Group files, were reviewed with SRS industrial hygienists. An electronic hazard assessment database (Personal Environment Record System or PERS) containing historical information describing work activities,

work locations, chemical and physical agents and related information was identified but could not be retrieved for the present study. Completed PERS data entry forms were identified but not retrieved for this study.

U. S. Department of Energy public reading room holdings at the University of South Carolina-Aiken were reviewed to identify documents containing historical information on chemical and physical agent exposures, agent inventories, organization information and related facility information. Copies of relevant documents were obtained during the site visit including industrial hygiene monitoring reports, descriptive site information, safety analysis reports, incident reports, operating procedures and process histories.

Historical records and documents used by Dr. John Hickey in completion of the chemical exposure assessment at the Savannah River plant (Hickey and Cragle, 1985) were also reviewed at ORAU/CER, Oak Ridge, TN. Pertinent documents included: 1) memo reports describing the industrial hygiene monitoring activities at the Savannah River plant and laboratory from 1952 through 1986, 2) walk-through survey notes of the Savannah River Plant (1985) by Dr. John Hickey, and 3) various standard operating procedures for Savannah River Plant operations.

Hanford Site. Hanford has maintained an active industrial hygiene and health physics program since inception. Reports describing exposure assessment activities for specific buildings and processes at the facility since the 1950s were identified in the government documents collections of repository libraries. Process flow sheets, process descriptions, chemical inventories, environmental impact statements and other published documents were obtained.

Industrial hygiene personnel from Westinghouse, Battelle PNL and HEHF at the Hanford site were contacted to identify historical industrial hygiene information resources. However, only limited information was obtained from the site, including descriptions by area, printout and documentation of the industrial hygiene database file (New HEX file) for the period 1978 to 1983, and a printout of the qualitative exposure assessment database (old HEX file). Four boxes of industrial hygiene data and boxes of materials from the Hanford Health and Mortality Studies were reviewed.

U. S. Department of Energy public reading room holdings at Richland, WA were reviewed to identify documents containing historical information on chemical and physical agent exposures, agent inventories, organization information and related facility information. Copies of relevant documents were obtained during the site visit.

III.E Completeness of Record Retrieval

Table 3.2 presents the numbers and percents of records retrieved for five types of records (personnel, occupational health, external radiation dosimetry, bioassay and *in vivo* measurements) at the DOE study facilities. LANL employees (UC) had the highest percentage of personnel records available for review (97.3%; n=110); Zia workers had the lowest (20.4%; n=19). Personnel records were located for 50 (65.8%) workers at ORNL, 33 (63.5%) workers at SRS, and 131 (74.9%) workers at the Hanford Site. Occupational health records were retrieved for 100% of SRS workers

(n=52), 97.1% (n=170) of Hanford workers, 83.2% (n=110) of LANL employees, 81.5% of ORNL workers (n=62) and 45.2% of Zia workers (n=42).

Personnel records were located for 68.4% of the cases (n=67) and 70.6% (n=276) of the controls (Table 3.3). Retrieval of occupational health records was also very similar for cases and controls, 80.6% (n=79) and 83.3% (n=326) respectively (Table 3.3).

As noted previously, personnel records and occupational health records were not available for early Du Pont workers at ORNL and the Hanford Site who terminated before 1947. Records for these workers were transferred to Wilmington, Delaware in the late 1940's and this is the primary explanation for missing personnel and occupational health records at ORNL and Hanford. Retrieval of both personnel and occupational health records was poorest for Zia workers. According to reports from LANL Epidemiology staff, many Zia records, particularly for the 1940's, were either destroyed or damaged due to flooding in the record storage area. It is unclear if Zia workers were missing occupational health records because their records were lost or because they were never seen by the Occupational Health Group. All but three of LANL workers had a personnel file, and the majority of LANL workers who did not have occupational health records were not located at the Los Alamos site. These workers were located, for example, at the New York or Los Angeles purchasing offices.

All of the occupational health records were available for SRS workers, however, we have not found a reasonable explanation for the relatively large number of SRS workers with missing personnel records. A review of their work histories did not suggest that their records were purged from the personnel files because the employees were not vested in the retirement system. Most of the workers with missing personnel records were employed for over ten years, and some as long as 30 years.

External radiation monitoring records were retrieved at the four DOE sites, although individual workers records were not always complete. 88.5% (n=46) of SRS workers had external radiation records on site as did 76.3% (n=58) of ORNL workers and 68.0% (n=119) of Hanford workers (Table 3.2). Ten ORNL and eighteen Hanford workers who were employed by Du Pont during the mid 1940's did not have radiation monitoring records available on site because the records were transferred to the Du Pont corporate offices. Significantly lower percentages of LANL and Zia workers had external radiation monitoring records, 47.8% (n=54) and 25.8% (n=24) respectively (Table 3.2), because of a policy consistent throughout the history of the site, of monitoring only potentially exposed workers.

The majority of SRS workers (76.9%; n=40) (Table 3.2) had bioassay monitoring for internal contamination with radionuclides, primarily tritium. Of the Hanford workers 54.3% (n=95) had bioassay data; of ORNL workers 26.3% (n=20) had bioassay data. For LANL and Zia workers, the majority of the bioassay data that were utilized in this study were captured from CEDR files. Relatively few bioassay records were retrieved directly from the LANL site and the data that were feasible to collect were abstracted from occupational health records. Bioassay results and nose counts were obtained for 29 of 196 workers ever employed by either LANL or the Zia Company.

The results of *in vivo* measurements, whole body or chest counts, were available for a small fraction of the workers (Table 3.2). At SRS, where termination *in vivo* measurements were taken, 32 workers (61.5%) had at least one count. Fifty Hanford workers (28.6%) and 13 ORNL workers (17.1%) had *in vivo* counts. Twelve LANL workers (10.6%) and two Zia workers (2.1%) had available *in vivo* measurements done by reliable techniques. LANL did *in vivo* monitoring during the very early history of the laboratory using the HUMCO system, a techniques that was not considered very reliable or sensitive. For this reason, and for reasons of accessibility, data were not captured.

III.F Definition of Analysis Variables

Data assembled from the records collected at the study facilities were used to develop classifications that allowed workers to be assigned to exposure categories. In many cases these classifications are routine (gender, age, birth year) or easily explained during the presentation of results (smoking). This section describes the creation of variables that required more detailed evaluation.

III.F.1 Prior work history

The contract for this study required evaluation of exposures outside of employment at the study facilities. Little such information was available from records. However, employment histories were routinely requested as part of the employment application at these sites. The description of employment, where available, was used to classify each worker as having a prior work history that included work in certain industries that have either been associated with MM in past studies, or that may entail exposure to agents of interest. The mention or absence of a history of work in the following industries was noted when employment forms were available: farm, military, other DOE facilities, other nuclear industry, painting, and industries involving exposure to non-ionizing radiation.

All employment applications were used to define work history. For workers hired only once, this means that work history reflects only employment prior to work at a study facility. For workers who terminated employment at a facility and were re-hired later, or who worked at more than one study facility, work history includes interim time periods of employment. Workers without employment applications or with inadequate information (i.e., more than a two-year gap between end of schooling and hire date) were classified as unknown.

The procedures for assigning prior work history occupation, employment and potential for exposure to ionizing radiation and other chemical and physical agents are described in Appendix III (Guidelines for Data Abstraction, Personnel Record). Completed job applications, resumes, personnel records, work histories and job descriptions were reviewed by the study industrial hygienist to determine if the study subject was ever employed at other nuclear facilities, was ever employed in an occupation involving farm work, or ever had potential exposure to paints and paint solvents, nonionizing radiation (NIR), and ionizing radiation.

Prior work involving farming was based on the job title, work activity, work location and/or industry for the period of prior work history of the study subject. Work activities or job titles must

have specifically referenced plant farming or animal farming occupations. Industries must have specifically referenced plant farming or animal farming. Prior work at other nuclear facilities was based on employment at a nuclear facility, including any Manhattan Engineering District, US Atomic Energy Commission, US Energy Research and Development Administration, and US Department of Energy (DOE) facilities and sites, and any nuclear power plants including Nuclear Regulatory Commission (NRC) -regulated facilities.

The potential for exposures to ionizing radiation was evaluated for employment at other nuclear facilities described above and for employment at non-nuclear facilities such as medical, metallurgy, mining and other industries not designated as nuclear facilities. Job titles and work activities with potential exposure to ionizing radiation must have specifically referenced ionizing radiation (α , β , γ , x-ray, 'cosmic ray'), or included job titles with a reasonable likelihood of exposure to ionizing radiation sources (x-ray technicians, miners). Work locations must have specifically referenced ionizing radiation or radiation sources and involved work activities with a reasonable likelihood of exposure.

Potential exposures to paints and paint solvents must have included work activity and/or industry with a reasonable likelihood of exposure to paints or paint solvents (organic). Work activities or job titles must have specifically referenced paints, varnishes or similar surface coating materials and involved a reasonable likelihood of exposure. Industries must have specifically referenced paints, varnishes or similar surface coating materials, and included work activities with a reasonable likelihood of exposure.

Potential exposures to NIR (static magnetic fields, extremely low frequency electromagnetic fields, radiofrequency and microwave radiation) must have included a job title, work activity, work location and/or industry with a reasonable likelihood of exposure to NIR. Work in industries involving NIR sources, job titles involving routine work with NIR, or work activities that identify specific NIR sources were considered as evidence of potential exposure.

III.F.2 Occupational health variables

Although occupational health records were used for multiple purposes, including as a source of work history and occupational exposure information, certain variables were constructed solely or primarily from occupational medicine records. These included medical sources of ionizing radiation, medical work restrictions, and cigarette smoking.

Diagnostic x-rays were used for a wide variety of reasons. However, medical departments at some sites provided comprehensive medical care, while departments at other sites served more as occupational medicine clinics that were used in addition to primary practitioners. Thus, there was substantial variation between sites in the recording of non-occupational x-rays. X-rays records were categorized, and it was clear that most common type was the chest x-ray used for annual screening at each site. Because they were uniformly in the records for all facilities, the variable for medical x-rays included only these screening chest x-rays. Information was not available that would have allowed determination of the dose delivered by specific equipment in use over time at each facility.

We considered using health status ratings given by the occupational medicine departments as a basis for evaluating health-related selection of workers for jobs involving greater exposure to hazards. Although ratings were routinely available, there was much variation in their use at different facilities and over time. Changes in health ratings were noted for only 26 workers in the study, and 96 workers were missing information on this variable. Therefore, this information was not used to construct a variable that would indicate health-related selection.

Smoking was recorded from health records where available. Due to variation in the kinds of questions asked about smoking, it was decided that only a yes vs. no determination could be made. This indicated whether the worker had ever, or never, been a smoker. Data on this variable are presented below.

III.F.3 Chemical and physical hazards

Exposures to chemical and physical agents that are potential risk factors for multiple myeloma were evaluated using a qualitative rating that considered the potential for exposure and the confidence in the exposure estimate. Exposure potential was evaluated for the following agents: 1) aromatic hydrocarbons such as benzene, toluene and trinitrotoluene, 2) halogenated hydrocarbons such as carbon tetrachloride, methylene chloride, perchloroethylene, 3) metals such as beryllium, cadmium, lead, mercury, nickel, uranium and welding fumes, 4) asbestos, and 5) non-ionizing radiation including radiofrequency and microwave (RF/MW) radiation, extremely low frequency electromagnetic fields (ELF EMF), and static magnetic fields. The procedures for assigning potential exposures to chemical and physical agents are described in Appendix VI (Guidelines for Assessment of Chemical and Physical Agent Exposures).

The potential for exposure to the study agents was based on a review of the work history, including job title, department and physical location reported for each study subject. The assessment involved the following steps: 1) pertinent work history information was recorded on the coding sheets (CERID, Division or Department number and name, job titles, dates and building numbers), 2) radiation monitoring reports were reviewed for evidence of internal and external monitoring, 3) occupational health coding sheets were reviewed for evidence of exposures to the study agents included in the worker's occupational health records at the site, 4) industrial hygiene, building and inventory databases were reviewed for evidence of exposure to the study agents for the departments, buildings or job titles indicated in the work history, 5) job descriptions from personnel records (when available) were reviewed for evidence of potential exposures to the study agents, 6) facility summary documents were reviewed for evidence of potential exposures to the study agents, 7) published information resources (books, technical papers, facility news articles, and other resources) were reviewed for evidence of potential exposures to the study agents, 8) industrial hygiene databases were queried using search strings related to the study subject (job title, department or division, building, work activity). Standardized guidelines for assigning exposures were developed for specific job titles, departments and/or locations when the potential for exposure was likely to be consistent within a job, or associated with a specific department or location at the study site based on the available information resources (see Appendix VI: Guidelines for Assessment of Chemical and Physical Agent Exposures).

The confidence assigned to the exposure rating was based on the strength of the evidence available in making the assignment. The criteria used to assign confidence estimates in the exposure rating are summarized below.

High confidence, positive exposure - Agent was identified in an inventory for building, department or process, linked by work history to an individual; potential for exposure was confirmed by industrial hygiene data or health records; description of the job title and department was sufficient to determine that the agent is normally associated with the job title and department; biological monitoring results for the agent of interest, its metabolite or characteristic reversible biochemical change induced by the agent were identified for the study subject; the study subject participated in a biological monitoring or medical surveillance program specifically designed for the agent of interest.

Moderate confidence, positive exposure - Agent was identified in inventory for building or process, linked by work history to an individual; and potential for exposure exists based on knowledge of the process, operation, job or work location; industrial hygiene data or occupational health records confirming exposures were not available; description of either the job title or department was sufficient to determine that the agent was normally associated with the job title or department; biological monitoring results for the agent of interest, its metabolite or characteristic reversible biochemical change induced by the agent, or participation in a biological monitoring or medical surveillance program specifically designed for the agent of interest, was identified for individuals from the same department, work location or job title.

Low confidence, positive exposure - Agent was not identified in inventory for building or process; work history was not able to link an individual to a building or department; potential for exposure was based on knowledge of the process, operation, job or work location; industrial hygiene data or occupational health records confirming exposures were not available; description of both the job title and department was insufficient to determine that the agent was normally associated with the job title and department.

High confidence, negative exposure - Agent was not identified in inventory for building, department or process, linked by work history to an individual; no potential for exposure was confirmed by industrial hygiene data or health records; description of the job title and department was sufficient to determine that the agent was not normally associated with the job title and department.

Moderate confidence, negative exposure - Agent was not identified in inventory for building or process, linked by work history to an individual; potential for exposure did not exist based on knowledge of the process, operation, job or work location; description of either the job title or department was sufficient to determine that the agent is not normally associated with the job title or department.

Low confidence, negative exposure - Agent was not identified in the inventory for building or process; work history was not able to link an individual to a building or department; potential for exposure did not exist based on knowledge of the process, operation, job or work location;

description of both the job title and department was insufficient to determine that the agent was not normally associated with the job title and department.

Potential exposures were assigned High confidence if the agents were identified in the building or department associated with the individual's work history, or if the job title was identified in monitoring results for a specific agent (e.g. electricians repairing electrical converters containing mercury). Confidence was also assigned High for job titles exposed to agents typically associated with the job, where industrial hygiene or agent inventory information identified the agent in use throughout the facility (e.g. Hanford millwright exposures to halogenated hydrocarbons).

Potential exposures were assigned Medium confidence if the agents were normally associated with a job, although monitoring results or inventory data did not identify the agent (e.g. wood dust exposures in carpenters, asbestos exposures in machinists and foundry workers), or if the agent was identified in a building or department and the job may involve work activities resulting in exposure to the agent (e.g. metal exposures to an associate scientist in metallurgy department).

Potential exposures were assigned Low confidence if the agent may be associated with the department or building, but was not specifically identified in monitoring results or agent inventories. Confidence was also assigned Low if the agent was identified in the department or building of the individual, but the job title would not normally be associated with exposure to the agent (e.g. clerk typist exposures to metals and halogenated hydrocarbons in explosives group) or if evidence from other jobs in the building or department indicate potential exposures (e.g. exposures of janitors to halogenated solvents and metals based on descriptions of spill cleanup, or janitors identified for participation in a beryllium medical surveillance program at other buildings or departments).

Exposures to chemical and physical agents for each study subject were evaluated for the period of employment at the study site using a qualitative rating based on the potential for exposure and the confidence in the exposure assignment. Exposures after the index age were not counted. The exposure and confidence ratings were used to group individuals into three exposure groups for subsequent analysis: 1) an exposed group consisting of individuals with potential exposure to the agent of interest and a moderate or high level of confidence, 2) an unexposed group consisting of individuals not exposed to the agent of interest and a moderate or high level of confidence, and 3) an uncertain exposure group consisting of exposed and unexposed individuals with a low level of confidence in the exposure estimate. The exposure and confidence ratings were assigned as a single rating for the individual during their work history at the study site. Changes in exposure potential that may have occurred over time were not considered in assigning the exposure or confidence ratings due to incomplete information for the time period of interest.

III.F.4 Radiation hazards

Cumulative external radiation dose equivalents for individual workers were constructed by summing annual whole body dose equivalents including inorganic tritium and neutrons. Although tritium provides an internal radiation exposure, it was treated in the dosimetry files at the DOE facilities as a whole-body exposure; it was treated similarly in this study. Neutron doses were included using quality factors employed at the facilities, which varied from 8 to 20. External doses

were counted taking into account 5, 10 and 20-year lags (latency assumptions) from the index age. Cumulative doses were counted for all ages, and separately for ages below 45, and ages 45 and above.

Variables were created for internal radionuclide contamination which indicated whether the worker had ever been monitored with bioassay for each specific radionuclide, and whether there had been any monitoring for any radionuclide by bioassay or whole body counting. This variable was considered with a lag from the index age that was set equal to the lag for external cumulative radiation dose being used in a specific analysis.

Doses were calculated for plutonium. However, these calculations entailed very large uncertainties in bone marrow dose estimates due to lack of information about chemical and physical properties of the radionuclides and route of contamination (respiration, ingestion, absorption). Given the high level of uncertainty as well as the relatively small numbers of workers who were monitored for plutonium (see Results), plutonium doses were not used in the analysis.

III.G. Statistical Analysis

All variables were checked and screened for inconsistent values. Distributions of final analytical variables were evaluated with respect to case or control status, and this information was used to form categories for analysis.

Variables for analysis were selected on the basis of the reason they were measured and on the basis of the quality of the data. Some variables were not of primary interest in this study of occupational exposures to physical and chemical agents, and were treated as confounding factors. These included a number of variables that were measured accurately, such as age, gender, birth year, and period of hire. Other variables that were not of primary interest, but would have been candidates for inclusion in the analysis as possible confounding factors if they had been measured uniformly and well, were excluded (e.g., some of the variables based on medical records).

Occupational exposure variables included history of prior work in specific industries, number of screening chest x-rays, exposures to specific chemical and physical hazards, and the estimated dose from external whole body radiation. When the primary reasons for missing data were very short duration of employment or very low exposure potential, missing values were categorized as zero. When this was not the case, a separate category for "missing data" or "uncertain" was created.

Exposure differences between cases and controls were evaluated using odds ratios calculated from conditional logistic regression using the SAS PHREG procedure (SAS Institute, Inc., 1991). This method maintains the matched case control sets. Crude odds ratios for each occupational hazard variable were calculated from conditional logistic regression, and adjusted odds ratios were calculated using race, gender, birth cohort and facility as control variables. Based on these initial analyses, a final model was constructed as a basis for evaluating external penetrating radiation. The final model included WW II hire and internal radionuclide monitoring in addition to the basic control variables.

IV. RESULTS

The results of our data collection are presented in two parts. First we present information about the primary variables that were collected, including those for which the proportion of missing data (and assumptions that would be necessary to make these variables more useful) was too great to permit risk analyses. We also describe the distribution of some variables in more detail than could be presented in analyses. We then report results of analyses evaluating exposure differences between cases and controls. Associations are presented in terms of odds ratios, which are estimates of the risk of dying with MM among exposed compared to unexposed workers.

IV.A. Characteristics of Cases and Controls

Table 4.1 shows the numbers of cases and controls in groups defined by the index age for the matched sets of cases and controls. Following the logic of the cohort study from which cases and controls are drawn, this variable is called "age at risk," which refers to the age of death for cases. The distribution of cases and controls is the same for this variable because of the matching. Approximately two thirds of the study population has an index age of between 55 and 74, and about one fifth have an index age of 75 or greater.

Table 4.2 shows the information on race that was obtained for cases and controls. Most (92%) were classified as White. There are notable case-control differences in the proportions classified as African American and unknown. Race for most workers could be ascertained from employment records. The primary reason for the discrepancy in the proportions of workers with unknown race between cases and controls is due to the use of death certificate information to obtain race information when race was missing from employment records. Because death certificate information was available for all cases but not all controls, the completeness of this variable is greater for cases. Race is considered later as an analytical variable classified as Black and non-Black, a decision that was made based on both the literature on MM, which shows greater risk among Black Americans compared to Americans of other races, as well as on the small numbers of workers that were non-Black and non-White. The larger proportion of unknown race for controls than for cases might be interpreted as a reason for the higher proportion of cases (5.1%) than controls (1.3%) classified as African American. However, most workers with unknown race were from the Zia cohort, where the proportion of Black workers was very low. Most of the workers with unknown race are probably Hispanic or non-Hispanic whites or Native American. We do not expect this differential quality of information between cases and controls to affect the evaluation of the risk in Blacks compared to non-Blacks.

The distribution of year of hire at the index facility is given in Table 4.3. Over half of the workers were hired during the W.W.II era, before 1948. Approximately one third were hired during the next seven years, 1948-54. This distribution reflects both the large numbers of workers hired during the Manhattan Project effort to build the first atomic weapons, and the higher death rate among workers hired in the early years.

Length of employment of cases and controls is shown in Table 4.4. About one quarter of the workers in the study were employed for less than one year. Cases and controls are distributed similarly with respect to the length of employment categories.

Information on the number of years of school completed by cases and controls is presented in Table 4.5. This information was not available for approximately one third of cases and controls; we decided that this was too incomplete to use as an analytical variable. Among those workers with information on numbers of years of school completed, the large proportion with at least some college, and with graduate degrees, is noteworthy. These are high levels of schooling for workers hired in this time period, which reflects the scientific backgrounds that were required of workers in the research and development aspects of this industry, as well as the greater amount of information on schooling available from employment records of professional staff.

Smoking history obtained from medical records was unavailable for 298 workers (Table 4.6). This lack of information reflects the lack of medical attention given to smoking during the 1940's and 1950's. Among those workers for whom smoking data were obtained, 134 were classified as having smoked, and 57 were classified as never having smoked.

Security clearance records were collected in order to evaluate whether this information could be used to evaluate selection factors within the worker population that might lead to presence of more highly screened workers for jobs with greater exposure potential. There was little variability, however, in the types of security clearances and termination of clearances within this population. We found evidence that five workers had special security clearances, and that eight workers had a security clearance terminated. This led us to conclude that the data would not be useful for evaluating selection factors.

Occupational medicine records included indications of whether workers were ever denied a job for health reasons. This information was evaluated as a potential source of indicator of selection factors within the worker population that would have led to differences in occupational exposures between workers with different baseline health status. However, ninety-four workers were missing such information in the medical records, and among those with information, only four had ever been denied a job for health related reasons (table not shown). Based on the frequency of missing data and low proportion of positive findings, we concluded that this classification would not be used as a control variable when evaluating exposure-disease associations.

Table 4.7 shows the frequency of screening chest x-rays for cases and controls at a time five years prior to the age at risk. These x-rays were generally given annually and are highly correlated with the number of years of employment. Among workers with one or more x-rays (N=384), the correlation between number of x-rays and years of employment is 0.84. Most workers with no medical records were employed for less than two years, so, in Table 4.7, these workers are counted in the category of 0-1 x-rays. The distribution of number of x-rays is very similar for cases and controls.

The detailed ratings for physical and chemical hazards are given in Table 4.8. By using a cross-classification of exposure status (exposed or unexposed) with level of confidence (low,

medium or high), each worker was assigned to a category for every agent. The classifications refer to any exposure during employment at any study facility. The proportion exposed at any confidence level ranged from 20.2% for microwaves to 47.9% for halogenated hydrocarbons. Exposed classifications were mostly made with low or high confidence; the modal level of confidence for unexposed was medium for all hazards. These results were used to define three categories for further analysis of exposure-disease associations. In regression analyses reported below, workers rated with medium or high confidence were classified as either exposed or unexposed, and those rated with low confidence were classified as uncertain.

The frequency of bioassay monitoring for contamination by specific radionuclides is given separately for each study facility in Table 4.9. Monitoring indicates only that bioassay data were collected at least once during employment at a particular study facility, not that the result was positive. Workers employed at more than one facility are counted in each facility of employment. Among the specific radionuclides in this study, workers were most frequently monitored for plutonium. Internal monitoring for radionuclides other than strontium was most common at SRS and least common at Zia. Strontium was monitored primarily at ORNL. Other radionuclides include thorium, cesium, americium, gross alpha radiation, and fission counts.

Approximately one fifth of workers were monitored for internal radionuclide contamination by whole body counting (Table 4.10). Whole body counting was conducted most frequently among SRS workers (61.5%) and least among Zia workers (2.2%). Whole body counting was conducted for the following radionuclides: ^{241}Am , ^{144}Ce , ^{137}Ce , ^{60}Co , ^{131}I , ^{238}Pu , ^{239}Pu , ^{106}Ru , ^{90}Sr , ^{235}U , natural uranium, fission products, ^{40}K , ^{22}Na , ^{141}Ce , ^{58}Co , ^{24}Na , ^{103}Ru , ^{234}Th , and ^{134}Cs .

Whole body dose data for external penetrating radiation were not available for one third of workers in the study (Table 4.11). The proportion of cases and controls with no data was similar. Table 4.11 also shows that monitoring for neutron radiation was conducted for 16.2% of workers. Original dose records were not available for all Hanford and some LANL and Zia workers, therefore neutron dose equivalent values calculated by health physics staff at each facility were used to combine neutron with other whole body dose data.

Table 4.12 shows the proportion of work years with external monitoring data separately for each facility. External radiation monitoring data were most complete for ORNL, followed by SRS, Hanford, and LANL/Zia. Cases and controls had similar levels of completeness of monitoring for external radiation. Data for LANL and Zia, which were served by the same health physics program, are combined in this table.

Cumulative external radiation dose was calculated under a variety of assumptions about age differences in sensitivity to radiation and latency between exposure and death. Table 4.13 shows the distribution of total cumulative dose over all ages, assuming a five-year lag, for cases and controls. In order to avoid excluding the one third of workers with no external dose data from analyses of external penetrating radiation, cumulative doses for unmonitored workers were estimated to be zero. Compared to monitored workers, who had a median duration of employment of over 10 years, workers with no external dose data had shorter durations of employment (median less than one year), and some of them were workers assigned to jobs far from the main facility (school teachers, shipping

and receiving clerks) where there was no exposure potential. The cumulative dose distribution is highly skewed, with 47.9% of workers estimated to have had zero dose and 30.3% less than 10 mSv. Forty-two workers (8.6%) had doses over 50 mSv. The highest two cumulative doses, both controls, were 441 and 975 mSv. Under longer lag assumptions, the distribution of cumulative doses shifts to lower values.

Table 4.14 shows separately the sum of cumulative whole body doses received before and after age 45. The proportion of workers with zero doses in each of these age ranges is larger than the proportion with zero dose for all ages, and the distribution is shifted to lower doses. Only one control received a dose above 400 mSv below age 45, and none received more than this amount after age 45.

B. Analysis of Exposure-Disease Associations

Exposure-disease associations were evaluated using odds ratios. The odds ratio is an estimate of the ratio of the MM death rate in exposed compared to the rate in unexposed workers. Odds ratios have been calculated using conditional logistic regression to account for the matching of cases and controls based on age. Two groups of variables were defined. The first group represents social, demographic and employment factors that are not of primary interest, but which could affect the evaluation of occupational exposures, and are therefore considered as controlling factors. The second group of variables includes prior work history, chemical and physical hazards, and radiation exposures. Odds ratios for each of these occupational exposure variables are presented with and without adjustment for the variables in the first group.

Associations are first given for the controlling factors. A larger proportion of cases than controls were African American (Table 4.15). The odds ratio for African American compared to other race (including race unknown) is 4.00; this rises to 5.76 with adjustment for birth cohort, facility and gender. A larger proportion of cases were men than women; the odds ratio for male vs. female gender considering only age is 1.99, and is 2.20 with adjustment for birth cohort, facility and race (Table 4.16).

Year of birth was categorized in three groups, workers born before 1905 (25.1%) between 1905 and 1915 (31.5%), and after 1915 (43.4%). Table 4.17 shows that odds ratios for the oldest cohort compared to the youngest were about unity, and were a little below unity for the middle birth cohort, with and without adjustment for race, gender and facility.

The relationship between facility of employment and MM was considered in three ways. Workers were classified according to whether or not they were ever employed at a facility; according to whether they worked only at each of the facilities or at multiple facilities; and according to their longest facility of employment. In the first approach, separate models were constructed to compare workers who had ever been employed at each facility to those who had never been employed at that facility (Table 4.18). In the second approach, one model was used to compare workers who had been employed at only each facility or at multiple facilities with each other (Table 4.19). In the third approach workers were compared according to their longest facility of employment (Table 4.20). Odds ratios for ORNL were above unity, and odds ratios for SRS and multiple facility workers were

below unity, considering Hanford as the referent. However, in no case were there any odds ratios, either adjusted for age only or adjusted for age, race, gender and birth cohort, that differed significantly from unity. Because facility of longest employment allowed each worker to be assigned to one facility without creating an additional category of multiple facility workers, we chose that variable to use as a control variable for subsequent Model 2 results.

We also considered hire during the W.W.II era as a risk factor. This variable has been of interest in past studies of DOE workers because many healthy men were in the military during W.W.II, which may have resulted in the hiring of workers who would have higher death rates regardless of their occupational exposures. Without adjustment for this variable, risks might be attributed to occupational exposures (which were often high during the war) that were really due to the selective hire of less healthy workers. The W.W.II era may also have been characterized at some facilities by poorer measurement of exposures. We therefore compared the cases and controls according to their period of hire, before or after 1948 (Table 4.21). Sixty-one percent of cases and 48.6 percent of controls were hired before 1948. The odds ratio for age matched case-control sets for hire prior to 1948 was 1.68, and was 1.89 after adjustment for race, gender, facility and birth cohort. Based on these observations and the *a priori* interest in this variable, hire before 1948 was added to the list of control variables for analysis of occupational exposures.

Another employment-related variable that has been of interest in past studies is length of employment. In some studies it has been argued that short-term workers have different employment patterns and living conditions that impact their mortality rates irrespective of their occupational exposures, which tend to be low in industries where higher exposure levels are generally reached through longer employment. However, when higher exposures are primarily reached through longer employment, and exposure measures are poor, length of employment may be a proxy for exposure and it could be inappropriate to control for this variable. In this study, the odds ratio for short-term employment (less than one year) compared to longer-term employment was 0.91, and 1.00 with adjustment for race, gender, facility and birth cohort (data not shown). Therefore, length of employment was not considered further.

Prior work history was evaluated with respect to work in industries that have been associated with increased risk of MM in previous studies. Odds ratios for prior employment in farming, military service, DOE facilities, other nuclear work, painting, and non-ionizing radiation, are presented in Table 4.22. In this table, workers with prior history in each of these types of industries are compared to those workers whose work histories did not indicate any such employment. Workers classified as unknown due to inadequate work history information are also compared to those whose records did not indicate employment in each industry. The only category for which prior work history was suggestive of an increased risk was non-ionizing radiation (panel F); 14.3% of cases and 6.9% of controls had records of prior employment in jobs that may have involved exposure to non-ionizing radiation. The odds ratio for prior employment with potential for exposure to non-ionizing radiation was 2.32, and 1.98 with adjustment for race, gender, facility and birth cohort (Table 4.22). This evaluation was based solely on industry and occupation, not on any exposure measurements.

Odds ratios for numbers of chest x-rays comparing 2-9 and 10+ x-ray groups to the 0-1 group are shown in Table 4.23, counting the number of x-rays up to 5, 10 or 20 years prior to the