Adverse Reproductive Outcomes among Females Employed at Department of Energy Facilities:

The Feasibility of Epidemiologic Studies

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Health-Related Energy Research Branch
Division of Surveillance, Hazard Evaluations, and Field Studies
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Introduction

Under a Memorandum of Understanding (MOU) between the Department of Energy (DOE) and the Department of Health and Human Services (HHS), HHS is conducting analytic epidemiologic studies relating to past and present DOE activities. Within HHS, the National Institute for Occupational Safety and Health (NIOSH) is responsible for performing occupational studies of the DOE workforce. The Health-Related Energy Research Branch (HERB) has been tasked with assessing the need for and feasibility of conducting epidemiologic studies related to specific populations and outcomes.

Among the goals of the HERB research agenda are to evaluate outcomes other than cancer, and to expand the populations studied beyond white males. The DOE has requested that female worker populations be the focus of future epidemiologic work. As a result, HERB has undertaken this report in order to address the following questions:

- Is it feasible to conduct an epidemiologic study to determine whether there is an increased risk of adverse reproductive outcomes among females employed at DOE facilities?

- If such a study is feasible, what resources would be required to organize and implement it?

In order to collect the data needed to conduct this assessment, HERB sought reports from the Center for Epidemiologic Research at the Oak Ridge Associated Universities (ORAU) about female worker populations at DOE facilities. The female populations were characterized using three data sources: the Center for Epidemiologic Research (CER); the Comprehensive Epidemiologic Data Resource (CEDR); and other sources. The sites in the CER group are those for which CER has access to the in-house data. The sites in the CEDR group are those for which epidemiologic studies have been done by a group other than CER and the data has been sent to CEDR. The group of "other" sites are those for which epidemiologic efforts have been minimal or the data from an epidemiologic study are not available from CER or CEDR. For these sites, the facility was contacted to gather information about the female workforce. For the Portsmouth Gaseous Diffusion Plant, NIOSH was contacted to provide information about the female workers. The sites in each group are as follows:

CER: Oak Ridge National Laboratory, Oak Ridge Y-12 Facility, Oak Ridge Y-12 Facility (TEC), Oak Ridge K-25 Site, Savannah River Site, Fernald Environmental Management Project, Mallinckrodt Chemical Works, and Linde;

CEDR: Hanford Site, E G & G Mound Applied Technologies, Los Alamos National Laboratory, Rocky Flats Nuclear Weapons Plant, Zia Company, and Pantex Amarillo Plant;

Other: Portsmouth and Paducah Gaseous Diffusion Plants, Lawrence Livermore National Laboratory, Pinellas Plant, Kansas City Plant, and Nevada Test Site.

Using these sources ORAU collected information on demographic characteristics, employment dates, crude job descriptions, exposures, radiation monitoring, and vital status for all females employed by the sites. With this information, summary reports were prepared and contained the following:

summary of the facility history including years of operation;

source of information presented in the summary;

number of female workers ever employed at the facility;

vital status distribution of female workers by race;

average length of employment (mean, median, and range);

number of female workers ever monitored for external radiation, with annual dose distributions where data are available;

number of female workers ever monitored for internal radiation, with annual dose distributions where data are available; and,

number of production versus non-production female workers.

In evaluating these data, many issues arose which are similar to those considered in a report on the feasibility of conducting epidemiologic studies of adverse reproductive outcomes in families of atomic veterans (IOM, 1995). The format of this report therefore loosely follows that of the Institute of Medicine report. In order to answer the questions posed above, this report will first contain a review of adverse reproductive outcomes, their relative frequency in the general population, and how they are measured. Following this, a discussion of whether these outcomes have been related to female radiation exposure will ensue. The feasibility of conducting an epidemiologic study depends largely on four issues: selection of an appropriate study population; a valid case definition and means of ascertainment; exposure to the agent(s) in question, and sufficient data to characterize such exposure(s); and, adequate sample size to demonstrate an effect. Each of these subjects will be treated in depth.

Adverse Reproductive Outcomes

An adverse reproductive outcome is any number of morbidities and mortalities that may occur during the course of human reproduction and development. Depending on the stage of life at which an agent (biologic, chemical, or physical) acts, it can be classified as a reproductive toxicant, i.e., an agent that affects post-pubertal reproductive or sexual function; or, a developmental toxicant, i.e., an agent that affects growth, development, or acquisition of normal organ function between conception and puberty (NIOSH, 1988). According to these definitions, teratogenic agents cause one form of developmental toxicity while carcinogenic and mutagenic agents are capable of causing both reproductive and developmental toxicity.

Human reproduction is complex, involving the central nervous system, endocrine system and gonads. In females, reproductive processes include:

hormonal function (age at menarche and menopause, ovulatory function);

fecundability (capacity for fertilization and implantation);

fertility (capacity to conceive and to carry a viable offspring);

the delivery of normal progeny; and,

lactation.

In males, reproductive system disorders can be considered in terms of fecundity (sexuality and semen quality), fertility, and effects on progeny (Hatch and Stein, 1988). Reproductive toxicants can act on the mother, father, or offspring, and can result in adverse outcomes at any point during the reproductive process.

Given the susceptibility of the process, the end-points of adverse outcomes are many, and varied. They include: sexual dysfunction, sperm abnormalities, and infertility, (which collectively can be manifest as a low birth rate), illness during pregnancy, early fetal loss/spontaneous abortion (gestational age $<$ 28 weeks), late fetal loss/stillbirth (gestational age $\geq$ 28 weeks), intrapartum death, death in first week, low birth weight, altered gestational age (prematurity or postmaturity), altered sex ratio, multiple births, contaminated breast milk, birth defects, chromosomal abnormalities, infant death, childhood morbidity, developmental disabilities, behavioral disorders, childhood cancer, and age at menopause (Bloom, 1981; Sever and Hessol, 1984; Monson, 1990).

Due to the large number of biological processes that may be affected and the numerous endpoints, data on the relative frequencies of these events in the population are incomplete. Table I shows the rates of occurrence, type of rate, and units of rate for selected outcomes that have been quantified. It should be noted that these events are not rare in the general population. Given the approximate 95,000 female DOE workers (see table II), and their expected 226,000 offspring (based on 2.4 children per female), it would not be unusual to see 6,800 major congenital malformations occurring in the absence of any effects of radiation. This probably represents the highest estimate since it assumes that all children affected would have been born during or after the women worked at the facility. Other effects that are known to cause these outcomes include inherited defects, environmental agents, smoking, alcohol use, maternal illness, and poor nutrition. These many causes make it difficult to design a valid study of radiation exposure and congenital malformations.

<u>Infertility and Sterility</u>
Infertility and sterility resulting from exposure to post-pubertal ionizing radiation are the result of a direct effect on the germinal cells. In women, the effects are dependent on the dose, the dose rate, and the age at exposure. Once exposed, the damaged oocyte may repair, or may be destroyed by phagocytosis. Populations of women exposed by pelvic radiotherapy and atomic bomb blasts have shown that a single dose to the ovary may be more damaging than fractionated doses (Ogilvy-Stuart and Shalet, 1993). A dose of 0.65-1.5 sievert (Sv) has been found to temporarily impair fertility. However, fractionated doses on the order of 6-20 Sv may be well tolerated (BEIR V, 1990). Mature oocytes are the most radiosensitive, with a dose of 4 Sv leading to a 30% increase in sterility in women 40 years old and younger, while the same dose would lead to a 100% increase in sterility in women over 40 years of age (BEIR V, 1990; Ogilvy-Stuart and Shalet, 1993).

<u>Spontaneous Abortion</u>
Spontaneous abortion is defined as "the non-deliberate interruption of intra-uterine pregnancy

before 28 weeks [based on the last menstrual period] in which the embryo or fetus is dead when delivered" (WHO, 1970). In many technically advanced countries, a cut-off of 22 weeks gestational age is used to differentiate between spontaneous abortion and stillbirth (Bracken, 1984).

The highest risk period for spontaneous abortions is early pregnancy, with most occurring before pregnancy is recognized (see table I). Most sources cite rates between 30-35% of all pregnancies end in spontaneous abortion, while others believe up to 80% are lost in the early period. Once clinically recognized, 15% will terminate due to spontaneous abortion, with approximately 1-3% of these occurring during the second trimester.

There are many causes of spontaneous abortion. It is probably best to consider the loss of aneuploid and euploid embryos and fetuses separately. Many if not all of the aneuploid embryos and fetuses are spontaneously aborted due to their genetic anomalies, and a resulting incompatibility with life. These losses generally occur early in the pregnancy. Of euploid embryos and fetuses, the causes are varied. One group of risk factors related to maternal uterine factors include fibroid tumors, a prolapsed or retroverted uterus, cervical erosion, or a septate uterus. Repeat spontaneous abortions are thought to be related to very early or very late menarche.

Lifestyle factors which are though to contribute to the risk of spontaneous abortion include maternal smoking, alcohol, caffeine, and recreational drug use. Various maternal infections increase the risk substantially. Occupational exposures of risk for spontaneous abortion include antineoplastic drugs, vinyl chloride, lead, and solvents. The frequency of spontaneous abortion was studied among atomic bomb survivors, but the data were internally inconsistent (Neel and Schull, 1991). Data on spontaneous abortion presented in a paper on perinatal loss and neurological abnormalities of children of the atomic bomb show a rate of 10.0 per 100 pregnancies, which does not differ from the background rate (Yamazaki and Schull, 1990). A study of occupational exposure to antineoplastic drugs and fetal loss among nurses also examined exposure to X-rays (Selevan et al., 1985). An odds ratio of 2.27, with a 95% confidence interval of 0.94-5.47 was found for exposure to X-rays.

Congenital Malformations

Congenital malformations, or birth defects, are conditions present at birth that interfere with normal physical and/or mental development. Table I shows the prevalence of congenital malformations among live births. They can be classified into two groups according to their severity. Major defects are those that are either incompatible with life, are life-threatening, or prevent normal functioning in society. Although the dividing line is unclear, the remainder of conditions are considered to be minor. Birth defects can also be further defined as those that occur as a result of a genetic or chromosomal defect, and those that lead to developmental defects in an individual with normal genotype. The two will be discussed separately in this report.

Chromosomal abnormalities or hereditary genetic defects are thought to occur as a linear, non-threshold function of dose (BEIR V, 1990). Most research in this area is based on the mouse and *Drosophila* models. Extrapolating from studies of the mouse, one Sv of low dose-rate, high LET (linear energy transfer) radiation is thought to be required to double the background mutation rate. This model ignores the fact that most diseases are of complex genetic origin, and may require more than one single defect, or are the result of co-existing genetic and environmental factors. A repair mechanism is also known to exist when one member of a base pair is unaffected. Table I shows the prevalence rate of chromosomal abnormalities in three populations: women experiencing early spontaneous abortions, amniocentesis specimens, and live births.

Epidemiologic studies have shown the absence of a statistically significant increase of chromosomal abnormalities in children exposed to the atomic bomb in utero (BEIR V, 1990). This is not unexpected given that the mean dose level was <0.5 Sv, and the population exposed at that level was limited in size. A study of Hanford workers, primarily males, showed no convincing evidence that parental radiation exposure or work at the facility increased the risk of chromosomal defects (including Down syndrome) in offspring (Sever et al., 1988). To date, there has been no unequivocal demonstration of radiation-induced genetic effects in studies of humans.

Developmental abnormalities may be physical and/or functional in nature, and may range from being barely detectable to completely disabling. Several hundred birth defects are recognized and have been characterized by Bracken (1983). Table I shows the prevalence of physical and functional disorders in infants less than one year of age. Less than half of infants with a major congenital anomaly will be diagnosed at birth, the remainder will be diagnosed sometime before age 10 (IOM, 1995). This makes complete ascertainment difficult before this age. A subgroup of physical abnormalities exist, called deformational, where the organ system develops normally, but a secondary deformity is incurred later (IOM, 1995). One common example of this is congenital hip dislocation which occurs as a result of uterine molding.

In the study of Hanford workers, congenital hip dislocation and tracheoesophageal fistula were found to be related to work at the facility, but not to parental radiation exposure (Sever et al., 1988). Studies of the Hiroshima and Nagasaki survivors have found neurological abnormalities among children exposed in utero. Mental retardation, microencephaly, seizures, and poor performance on conventional tests of intelligence and in school were the outcomes found to be increased (Yamazaki and Schull, 1990). The most sensitive period for exposure was found to be 8-15 weeks after conception, which corresponds to a rapid increase in the number of neurons, migration to the developmental sites, and loss of the capacity to divide. A 4% probability of effect is associated with every 0.1 Sv during the critical period (BEIR V, 1990). The nature of the dose-response curve is not known; however, little if any threshold appears to exist (BEIR V, 1990).

<u>Perinatal Loss</u>

The term "perinatal loss" refers to both stillbirths (fetal deaths occurring at or after 28 weeks gestation) and early neonatal deaths (deaths of infants less than 7 days of age) since both share many common causes, and differ from deaths of older infants (IOM, 1995). Higher perinatal mortality rates are seen in lower socio-economic status (SES) families, but the exact cause of this is unknown. Most experts agree that SES serves as a marker for another "true" risk factor, which may relate to social, environmental, or behavioral conditions, but is at this point undefined. Health factors relating to increased risk of perinatal mortality includes maternal illnesses, such as diabetes, renal disease, preeclampsia, uterine infection, and Rh incompatibility. Other factors include pregnancy complications such as placenta previa or abruptio; umbilical cord prolapse; difficult, or prolonged labor, malpresentation; and, fetal complications. Increased maternal age is also associated with perinatal loss. When studying these outcomes, all these risk factors need to be taken into account. Studies of atomic bomb survivors found no increases in perinatal loss related to radiation exposures (IOM, 1995).

Feasibility of an Epidemiologic Study

Study Populations

In order to evaluate the effect of external radiation received during employment at a DOE facility on reproductive outcome, it would be necessary to identify a representative sample of exposed female workers and their families. The reports prepared by ORAU have identified females who were employed at most of the major DOE sites, in varying numbers. The total female workforce over the history of the facilities combined is greater than 95,000, although some women may have been counted more than once if they worked at more that one facility. The largest numbers of women were employed at the Oak Ridge Y-12 facility (under the Tennessee Eastman Corporation), the Oak Ridge K-25 site, Hanford, and Nevada Test site (see table II). In recent years, however, several of these facilities have undergone dramatic downsizing. Far fewer women are now employed at the facilities (see table III), and of those, even fewer are of reproductive age (defined as 45 years of age or younger). Of the total female workforce, a certain percentage will now be deceased, and follow-up through the National Death Index, Social Security Administration, or other sources should be possible. Actively employed individuals, although a small percentage of the total, could be located through the individual facilities. The most difficult group to locate are retired or otherwise terminated employees. Many may have moved out of the area and no central organization exists which could locate these individuals. In addition, while information such as vital status may be more easily obtainable on such a population, no record system exists which would include reproductive histories in the detail needed for a study of this type.

Case Definition and Ascertainment

To conduct a sound epidemiologic study of reproductive outcomes, one would need to identify normal as well as abnormal outcomes in an unbiased fashion. However, this presents several difficulties with regard to the nature of the data to be collected and the time frame during which these events would have occurred.

Three options exist in order to ascertain the outcome of interest. The first is a record-based system. Many reproductive outcomes are not included in a standard medical record, and the event may in fact not be known even to the woman (i.e., early fetal loss or chromosomal abnormalities). This may be especially true for events that had taken place 15-50 years ago, during the reproductive period for many of the females employed by DOE, due to the limits of medical technology at that time. Occupational health records vary in the amount of information they contain about reproductive events, and are usually available only in hard copy. Abstracting any information present would be a very labor intensive effort.

The second option is collecting questionnaire or interview data directly from the woman. In this population this option would be difficult, because of the problems in locating the population, and the amount of time that has passed since the events would have occurred. In addition, recall bias might be a significant problem due to the real or perceived risk associated with the exposure, and emotional issues surrounding adverse reproductive events.

The third option involves the use of existing registries, such as birth defect registries. The DOE facilities evaluated for this report are/were located in fourteen states: California, Colorado, Florida, Idaho, Kentucky, Missouri, Nevada, New Mexico, New York, Ohio, South Carolina, Tennessee, Texas, and Washington. Of these, six states have birth defects registries currently operating. Their systems are described below, and summarized in table IV.

California began its program in 1983, when it covered the entire state, but has since limited the number of counties included in the registry to fourteen of a total of 58 in the state. The system involves an active surveillance of hospital medical records for infants with congenital malformations, and biochemical or genetic defects diagnosed up to one year of age. DOE has one site in California, the Lawrence Livermore National Laboratory, currently employing 2,400 females.

The Colorado Registry for Children with Special Needs began in 1989, and collects information on all birth defects, genetic diseases, and developmental disabilities in children up to age three. This active surveillance system covers the entire state, and relies on multiple sources of data including birth and death certificates; hospital discharge data; physician reports; and, special child health registries. All diagnoses are validated before inclusion in the system. The Rocky Flats Weapons Plant is the only DOE facility located in Colorado, and has employed 1,564 females.

Kentucky is in the process of developing a state-wide passive surveillance system. Data collection began in late 1994, and includes congenital malformations, genetic diseases, fetal alcohol syndrome and other drug-induced conditions, low birth weight, and failure to thrive. The Paducah Gaseous Diffusion Plant is the only DOE facility located in Kentucky. A roster of employees has not yet been developed, therefore, the number of female employees is unknown.

Missouri passively collects reports on children through age three with one or more of the following conditions: birth defect, genetic disease, infant mortality, fetal death, and low birth weight. Coverage is state-wide and population-based, with data available from 1982. Two DOE facilities are located in Missouri: the Kansas City Plant, which has employed 5,896 females, and the Mallinckrodt Chemical Works, which has employed 543 females.

The Tennessee Birth Defects Registry is a population-based, state-wide hybrid design surveillance system. Cases of all adverse reproductive outcomes (birth defects, genetic diseases, infant mortality, fetal death, low birth weight, and developmental disabilities) are passively reported, but actively verified. Data collection began in 1991. Tennessee has several DOE facilities: the Oak Ridge Y-12 facility, which employed 20,423 females under the Tennessee Eastman Corporation, and more recently has employed 4,494 females; the Oak Ridge K-25 Site which has employed 11,763 females; and, the Oak Ridge National Laboratory, which has employed 7,323 females.

The Washington State Birth Defects Monitoring Program began in 1987 as a state-wide active surveillance system of hospital medical records. Data on adverse reproductive events included birth defects, fetal deaths >20 weeks gestation, infant mortality, low birth weight, cerebral palsy, mental retardation, childhood cancer, and congenital infections. These data are available through 1992. Since then, the program lost funding and the data quality has diminished significantly. In addition, written consent is required from every subject before their data can be released. Washington state is the site of the Hanford facility, which has employed 11,471 females.

Given that registries exist in only six of the states with DOE facilities, and their data are available for recent years only, it would be difficult to conduct a study based on registries at this point in time.

Exposure Assessment and Dosimetry

To demonstrate a dose-response relationship between exposure to external ionizing radiation and adverse reproductive outcomes, it is necessary to have a sufficiently exposed population, and the ability to characterize that exposure. Table II shows the number and percent of female DOE workers with recorded external monitoring data. For most facilities only a portion of the female workers were routinely monitored. However, at the Hanford Site and the Nevada Test Site all workers were routinely monitored.

Table V shows the cumulative external radiation dose received by female DOE workers at sites with available monitoring data. Overall, the doses are very low, with the vast majority (57%) having received a cumulative dose less than one cSv; and 39% having received no measurable dose. Only 4% of the entire female population received one cSv or more. Because most of the higher doses were received during non-routine (accidental) exposures, the median value represents the best measure of central tendency. Cumulative median doses range from zero to 0.380 cSv. This extremely low level of exposure presents problems in planning an epidemiologic study. Background radiation from all sources (cosmic, medical, radon, etc.) amounts to 0.36 cSv per year on the average (NCRP, 1987). The dose from a chest X-ray is typically 0.06-0.10 mSv today, but ranged from 0.30-1.0 mSv during the 1950-1970s. The dose from a lumbar spine radiograph was 10-35 mSv historically (Kumamoto, 1985; NCRP, 1989; Norwood, 1972). Any health effects are typically seen at 20 cSv. Therefore, it is unlikely that any excess adverse reproductive outcomes would occur at exposures of the magnitude received by this population. If such a study were attempted, common exposures such as medical X-rays and procedures, and residential history would need to be considered as strong potential confounders.

Table VI shows the past and present female DOE workers monitored for internal radiation, and the type of monitoring performed. Fewer than 8,000 total women were ever monitored for internal deposition. Those facilities with the highest percentage of the female workforce monitored were the Fernald Environmental Management Project (89.7%), EG&G Mound Applied Technologies (86.4%) and the Oak Ridge Y-12 Facility (54.6%). Most monitoring consisted of urinalysis sampling and whole body counts.

Personal and area monitoring practices for chemicals are shown in table VII, along with the availability of complete job title and/or department data. At only five percent of the facilities were workers monitored using personal sampling for chemical hazards. At thirty-seven percent partial personal sampling was done. Area monitoring was conducted at twenty-one percent of the facilities, with twenty-six percent having partial data. Complete job title and/or department information is available at seventy-four percent of the facilities. The most common form is computerized data, although five facilities have either microfilm or hard copy data. At four facilities the availability of these data are unknown.

Sample Size

Adequate sample size and statistical power are necessary in order to detect an association if one exists, between occupational exposure to external ionizing radiation and adverse reproductive events. Table VIII shows the sample sizes required to detect a range of relative risks for the highest dose category (>10 cSv) in a test for trend in the proposed study of atomic veterans (IOM, 1995). The sample size is affected by several parameters: the frequency of the outcome in an unexposed population, the strength of the association to be detected, and the variance in the exposures received. The total sample of females DOE workers available for study is approximately 95,000, with external monitoring data recorded for 32,110 of those. The females who received a non-zero external dose number approximately 20,000. Given the size of this population, and the overall low dose received, it would be nearly impossible to detect a statistically significant relationship, if one exists, between exposure to external ionizing radiation and adverse reproductive outcomes.

Conclusions

The purpose of this report was to answer the two following questions:

- **Is it feasible to conduct an epidemiologic study to determine whether there is an increased risk of adverse reproductive outcomes among females employed at DOE facilities?**

There are a large number of difficulties associated with locating an adequate sample of exposed females workers; in detecting an extremely small potential excess risk; in determining and documenting adverse reproductive outcomes that may have occurred many years in the past, and over a long interval; and, reliably documenting other exposures that might confound the relationship of interest. When considering outcomes that directly impacted the offspring of these women, the difficulties mentioned above become further problematic.

Some commonly used study designs would be impossible to employ with this population. Birth defects registries do not cover a long enough time period, nor a large enough group of exposed women. Retrospective studies of spontaneous abortion are best conducted during recent time periods (previous 4-5 years) and the age distribution of this population would prohibit this. Prospective studies of early fetal loss require a large number of currently exposed women of reproductive age, and this population is not available. As a result, the opportunity for an epidemiologically sound study is not present at this time.

- **If such a study is feasible, what resources would be required to organize and implement it?**

Since it is not believed that such a study is feasible, consideration was not given to the time and financial resources that would be required.

Table I. Reproductive Outcomes and Measures of Frequency

me	Rate	Type of Rate	Units of Rate*
ity	10-15	Prevalence	N/100 couples/year†
aneous abortion	10-25	Attack	N/100 pregnancies‡
etal loss	67-75	Attack	N/100 pregnancies
osomal abnormalities	30-50	Prevalence	N/100 early spontaneous abortions
			N/100 amniocentesis specime
osomal abnormalities	2	Prevalence	N/100 live births
osomal abnormalities	0.2	Prevalence	N/100 full term pregnancies
th	2-4	Attack	N/100 live births
nital malformations	2-4	Prevalence	N/100 live births
irth weight£	7-15	Prevalence	N/100 infants <1 year
al/functional disorders	6-15	Incidence	

umber †unprotected intercourse ‡recognized pregnancies §in women <35 years £<2500 g

, 1981; Monson, 1990; Office of Technology Assessment, 1985; Beckman, 1986; Carr, 1983; Fabro 1985

Table II. Past and Present Female DOE Workers and Percent Monitored for External Rad

Facility	N	N with External Data	Pe
Oak Ridge Y-12 Facility (TEC)	20423	N/A	
Oak Ridge K-25 Site	11763	3054	2
Hanford Site	11471	11471	1
Nevada Test Site	>10000	>10000	1
Oak Ridge National Laboratory	7323	6233	8
Los Alamos National Laboratory	6800	1684	2
Kansas City Plant	5896	N/A	
Oak Ridge Y-12 Facility	4494	3050	6
Savannah River Site	4154	3528	8
Lawrence Livermore National Laboratory	>2400	N/A	
EG & G Mound Applied Technologies	1789	671	3
Portsmouth Gaseous Diffusion Plant	1771	1273	7
Rocky Flats Weapons Plant	1564	1352	8
Zia Company	1504	439	2
Pantex Amarillo Plant	1222	120	
Fernald Environmental Management Project	1167	797	6
Pinellas Plant	566	N/A	
Mallinckrodt Chemical Works	543	67	1
Linde	301	N/A	

N/A = data not available

Table III. Current Female DOE Workers and Those of Reproductive Age (<45 year

Facility	Year*	N	n <45 years	F
Oak Ridge K-25 Site	1992	2040	1554	
Savannah River Site	1989	1915	1538	
Oak Ridge Y-12 Facility	1992	1266	760	
Rocky Flats Weapons Plant	1979	440	287	
Fernald Environmental Management Project	1992	295	182	
Pantex Amarillo Plant	1982	196	166	
Hanford Site	1988	249	140	
Zia Company	1986	96	40	
Oak Ridge National Laboratory	1993	1	1	
Los Alamos National Laboratory	1980	2	0	
Lawrence Livermore National Laboratory	1994	2197	N/A	
Kansas City Plant	1994	855	N/A	
Pinellas Plant	1994	310	N/A	

*Latest year for which data are available   N/A = data not available

Table IV. Birth Defect Registries in States with DOE Facilities

e	Surveillance	Years	Coverage	Outcomes	Facilities
nia	Active	1983-present	14 counties	CM,GD	Lawrence Livermore Nation Laboratory
do	Active	1989-present	State-wide	CM,GD,DD	Rocky Flats Weapons Plant
ky	Passive	1994-present	State-wide	CM,GD,DD LBW,CP,GR	Paducah Gaseous Diffusion Pl
uri	Passive	1982-present	State-wide	CM,GD,IM,FL LBW	Kansas City Plant Mallinckrodt Chemical Work
see	Hybrid	1991-present	State-wide	CM,GD,IM,FL LBW,DD	Oak Ridge Y-12 Facility Oak Ridge K-25 Site Oak Ridge National Laborato
gton	Active	1987-92	State-wide	CM,FL,IM LBW,CP,DD CC,CI	Hanford Site

congenital malformations GD=genetic diseases DD=developmental disabilities LBW=low birth wei
P=cerebral palsy GR=growth retardation IM=infant mortality FL=fetal loss CC=childhood cancer
CI=congenital infections

Table V. Female DOE Workers and Cumulative External Radiation Dose*

Facility	D† = 0 (%)	0 < D < 1 (%)	D ≥ 1 (%)
Mallinckrodt Chemical Works	0 (-)	48 (0.3)	19 (1.4)
Pantex Amarillo Plant	20 (0.2)	82 (0.4)	18 (1.3)
EG & G Mound Applied Technologies	143 (1.1)	458 (2.5)	70 (5.2)
Savannah River Site	1170 (9.4)	1787 (9.8)	571 (42.3)
Oak Ridge Y-12 Facility	1184 (9.5)	1701 (9.3)	155 (11.5)
Rocky Flats Weapons Plant	595 (4.8)	688 (3.8)	69 (5.1)
Zia Company	194 (1.6)	228 (1.2)	17 (1.3)
Hanford Site	2235 (17.9)	9145 (50.1)	91 (6.7)
Oak Ridge K-25 Site	1512 (12.1)	1528 (8.4)	14 (1.0)
Oak Ridge National Laboratory	4078 (32.6)	1963 (10.8)	192 (14.2)
Los Alamos National Laboratory	874 (7.0)	676 (3.7)	134 (9.9)
Fernald Environmental Management Project	489 (3.9)	308 (1.7)	0 (-)
Total	12504	18256	1350

*Data no available for the following facilities: Nevada Test Site, Kansas City Plant, Lawrence L National Laboratory, Linde, Oak Ridge Y-12 Facility (TEC), Pinellas Plant, Portsmouth Gaseous Plant, and Paducah Gaseous Diffusion Plant

†D = Cumulative external radiation dose measured in cSv

Table VI. Past and Present Female DOE Workers Monitored for Internal Radiation and Type of

Facility	N with Internal Data	Percent	Type of
EG & G Mound Applied Technologies	1546	86.4	
Oak Ridge National Laboratory	1252	17.1	UA,W
Fernald Environmental Management Project	1047	89.7	UA,
Portsmouth Gaseous Diffusion Plant	827	46.7	
Oak Ridge Y-12 Facility	813	54.6	UA,
Rocky Flats Weapons Plant	785	50.2	
Oak Ridge K-25 Site	619	5.3	UA,
Los Alamos National Laboratory	532	7.8	
Mallinckrodt Chemical Works	218	40.1	UA, br
Zia Company	149	9.9	UA,
Savannah River Site	90	2.2	UA,
Hanford Site	45	0.4	
Nevada Test Site	30	<3.0	UA,W
Lawrence Livermore National Laboratory	30	<1.3	N
Pinellas Plant	10	1.8	

UA = urinalysis WBC = whole body count N/A = data not available

Table VII. Personal and Area Monitoring for Chemicals and Job title/Department Data

ty	Personal	Area	Job title/ Departme
Ridge Y-12 Facility (TEC)	No	Partial	Yes*
Ridge K-25 Site	Partial	Yes	Yes*
ord Site	No	No	Yes*
da Test Site	Yes	No	Unknown
Ridge National Laboratory	Partial	Partial	Yes*
lamos National Laboratory	No	No	No
as City Plant	Partial	Partial	Unknown
Ridge Y-12 Facility	Partial	Partial	Yes*
nnah River Site	No	No	Yes†
ence Livermore National Laboratory	Partial	Yes	Unknown
G Mound Applied Technologies	No	No	Yes*
mouth Gaseous Diffusion Plant	Partial	Yes	Yes*
y Flats Weapons Plant	Partial	Partial	Yes†
ompany	No	No	Yes‡
x Amarillo Plant	No	No	Yes‡
ld Environmental Management Project	No	No	Yes*
las Plant	No	Yes	Unknown
nckrodt Chemical Works	No	No	Yes†
	No	No	Yes*

omputerized †=hard copy ‡=microfilm

Table VIII. Sample Sizes Required to Detect a Range of Relative Risks for the Highest Dose Category >100mSv (>10cSv) in a Test for Trend*

	Sample Size for Relative Risk of:			
Frequency of Outcome (%)	1.5	2.0	3.0	4.0
0.1	2816000	868000	329000	180000
0.5	580000	182000	64000	36000
2.0	148000	47000	16000	9000
3.0†	100000	32000	11000	6000

*The estimated sample sizes were calculated for those in the highest dose category (>10cSv) with type 1 and type 2 errors of 10 and 20, respectively. The sample sizes have been rounded to the nearest thousand to avoid an undue perception of accuracy.
†Frequency of major congenital defects in the general (unexposed) population

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