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**CENTRIFUGE WORKERS STUDY  
PHASE II  
COMPLETION REPORT**

H. D. Wooten

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ORNL-6822

**CENTRIFUGE WORKERS STUDY  
PHASE II  
COMPLETION REPORT**

H. D. Wooten

Date Published — September 1994

Prepared by  
Engineering Technology Division  
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**MARTIN MARIETTA ENERGY SYSTEMS, INC.**  
for the  
**U.S. DEPARTMENT OF ENERGY**  
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## SUMMARY

This report has been developed to satisfy, in-part, the fiscal year 1994 Phase II closeout requirements for the program HR-Epidemiologic Activities, Field Work Proposal Number EHHR001, Centrifuge Workers Study.

The Phase I study efforts were completed in August 1989. Results from this phase indicated that the centrifuge workers had greater than a seven-fold increase in risk for developing bladder cancer compared with the risk of the general population. These results were considered to be inconclusive because only a portion of the former centrifuge workers were surveyed during the Phase I study.

Interviews for Phase II of the Centrifuge Workers Study, a health survey, began in January 1990. Results of the Phase II study did not confirm the increase in bladder cancer found in Phase I. However, the participants in both phases reported an excess of temporary symptoms related to working with solvents. In addition to those symptoms, temporary skin rashes related to working with epoxy resin systems were reported. To date, no causative agent has been identified as being related to the bladder cancers reported in the Phase I survey.

During the latter part of May 1994, the Phase II results were mailed to Phase I participants, whose health and work histories were updated during Phase II, and to the Phase II survey participants. In addition, the Phase II results were presented at three meetings held at the Oak Ridge K-25 Site, Oak Ridge, Tennessee, during the month of June 1994. These meetings were open to all former K-25 Site centrifuge workers as well as other interested employees. The results of the Phase II follow-up study were also mailed to former centrifuge manufacturers that may have current or former employees who have concerns relative to possible exposure while they were working on the Centrifuge Development Project. A listing of the former centrifuge manufacturers is in Appendix A.

Any additional or follow-up health study activities will be directed by the Department of Energy (DOE) and the National Institute of Occupational Safety and Health.

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## 1. BACKGROUND

Phase II of the Centrifuge Workers Study was a follow-up to the Phase I efforts. The Phase I results had indicated a higher risk than expected among centrifuge workers for developing bladder cancer when compared with the risk in the general population for developing this same type of cancer. However, no specific agent could be identified as the causative agent for these bladder cancers. As the Phase II Report states, "Phase I had been limited to workers who had the greatest potential for exposure to substances used in the centrifuge process. Phase II was designed to expand the survey to evaluate the health of all employees who had ever worked in Centrifuge Program Departments 1330-1339 but who had not been interviewed in Phase I. Employees in analytical laboratories and maintenance departments who provided support services for the Centrifuge Program were also included in Phase II" (see Appendix C, p. C-3, Phase II Report).

In December 1989, the Oak Ridge Associated Universities (ORAU), now known as Oak Ridge Institute for Science and Education (ORISE), was contracted to conduct a follow-up study (Phase II). Phase II of the Centrifuge Workers Study expanded the survey to include all former centrifuge workers who were not included in Phase I. ORISE was chosen because they had performed the Phase I tasks and summarized the corresponding survey data therefrom.

## 2. PURPOSE

The purpose of this report is to formally transmit the Phase II results of the epidemiology study of employees who formerly worked in the Gas Centrifuge Enrichment Program. This report deals mainly with the Phase II activities; however, the Phase I documented results have been included to provide continuity for the entire Centrifuge Workers Health Study.

Both Phase I and Phase II of the Centrifuge Workers Study were performed by ORISE under subcontract to Martin Marietta Energy Systems. The results of Phase I are contained in Appendix B, and the Phase II results are in Appendix C.

Over a period of approximately twenty years that began in the mid 1960s, several cases of cancer among personnel who had worked in the Centrifuge Program were reported to the leadership of the Oil, Chemical, and Atomic Workers Union. Those reports of cancer heightened the concern of other former centrifuge workers relative to an increased risk of developing cancer. That concern prompted the request that DOE fund a health study of former centrifuge workers to determine the validity of the concern. DOE approved funding for the health study, and ORISE began the study in mid 1987.

### 3. APPROACH

The methods utilized by ORAU (now known as ORISE) in conducting the Centrifuge Workers Health Survey are documented in the Fact Sheet and Executive Summary information submitted by ORISE at the completion of Phases I and II. The Phase I documents are contained in Appendix B, and the Phase II documents are in Appendix C.

The general Phase I approach, as stated in the Phase I Fact Sheet, was that "ORAU conducted telephone interviews with workers who worked close to any aspect of (i.e., maintenance, component assembly, centrifuge operation) the centrifuge program and an equal number of comparison workers who were employed at K-25 but never worked in the centrifuge area. This allowed us to compare the number of illnesses reported by the two groups and to attempt to determine whether working in the centrifuge process had any relationship to these illnesses."

The Phase II study included all former centrifuge workers except those included in Phase I. The general approach for Phase II, as stated in the Phase II Fact Sheet, was that "ORISE conducted telephone interviews with these individuals and an equal number of comparison workers who were employed at K-25 but who never worked in the centrifuge areas. The number of illnesses reported by the two groups was compared to determine whether working in the centrifuge process had any relationship to these illnesses. The medical histories of centrifuge workers and comparison workers interviewed in Phase I were also updated. In addition, more detailed exposure histories were obtained."

#### 4. COST

The Centrifuge Workers Study was funded by DOE. The project cost is given in the following table.

<b>Activity</b>	<b>Cost</b>
Phase I subcontract	\$145.4K
Phase II subcontract	\$450.2K
Phase II subcontract administration and report preparation	\$ 44.0K
<b>TOTAL</b>	<b>\$639.6K</b>

## 5. RESULTS OF EPIDEMIOLOGY STUDIES

### 5.1 PHASE I

The results of the Phase I survey as reported by ORISE are contained in Appendix B. The statistically significant increases in disease or symptoms are restated here: "Among the centrifuge workers, the rate of bladder cancer was greater than 7 times that which was expected in the general population as estimated from national statistics (1.38 per 1000 person-years when 0.18 was expected). Others for this group were temporary skin rashes: four times greater than expected (3.98); dizziness: almost twice what is expected; insomnia (difficulty in sleeping): twice that expected (2.21)\*; numb/tingling limbs: one-and-a-half times that expected (1.68); and kidney stones: three-and-a-half that expected (3.50).

"The wreck workers experienced more than six-and-a-half times more cases of stomach ulcers than the control group (12.11 per 1000 person-years; the control group had none).

"\*Note that the insomnia cases increased in 1986, after the centrifuge process was virtually discontinued and were, therefore, not likely to be related to the process."

### 5.2 PHASE II

The results of the Phase II survey as reported by ORISE are in Appendix C. The statistically significant symptoms are restated here: "During the time that centrifuge workers were working in the Centrifuge Program, they reported significantly more emphysema and numb and tingling limbs than their comparison group. Maintenance workers reported significantly more urinary tract infections; rashes; growths; dizziness; and bone, muscle, and joint diseases. Numb and tingling limbs, rashes, dizziness are temporary symptoms that go away when individuals stop working with solvents and epoxy resin systems.

"Phase II involved all workers from centrifuge departments even though their potential for exposure to process chemicals was lower. The results of the Phase II survey indicate that these workers are not at increased risk of developing bladder cancer. Phase I included only workers who had the greatest potential for exposure to chemicals and substances used in the centrifuge process. Results of Phase I and the medical history updates showed a significant excess of bladder cancer among this group. After an extensive review of work histories and monitoring data, we have not been able to identify a specific occupational exposure or causative agent for these cancers. In general, smokers are at greater risk for developing bladder cancer. Most of the individuals who reported having bladder cancer are current or former smokers."

## 6. CONCLUSIONS

The conclusions below are restated from the Phase II Executive Summary contained in Appendix C: "In comparing the results of the two phases of the survey, the increase in bladder cancer noted in Phase I was not evident in Phase II. In both phases, the potentially exposed groups reported an excess of temporary symptoms" [Temporary symptoms tend to disappear when one *is* no longer working with the causative agent(s).] "related to working with solvents. These included rashes, dizziness, and numb and tingling limbs. Temporary skin rashes are also related to working with epoxy resin systems.

"Due to the significant bladder cancer increase and excess of the specific symptoms found in Phase I, it is recommended that educational material concerning the signs and symptoms of bladder cancer be made available to interested individuals. To date no causative agent has been identified as being related to the bladder cancers from the Phase I study."

**Appendix A**

**LIST OF FORMER CENTRIFUGE MANUFACTURERS**

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**Allied Signal (AirResearch Casting Company)**

Attention: Public Affairs  
2525 West 190th Street  
Torrance, California 90504

**ALSO:**

**Technical Services Corporation**  
NASA Lewis Research Center  
2100 Apollo Drive  
Brook Park, Ohio 44142

**Aerospace Division**  
3000 Presidential Drive  
Suite 300  
Fairborne, Ohio 45324

**Aerospace Division**  
7550 Lucerne Drive  
Suite 203  
Middleburg Heights, Ohio 44130

**Boeing Engineering Company Southeast, Inc.**

Attention: Mr. O. R. Sanders  
767 Boeing Road  
Oak Ridge, Tennessee 37830

**Environmental Services Company (ENSCO)**

Attention: Frank Virginia  
333 Executive Court  
Little Rock, Arkansas 72205

**Exxon Corporation**

Attention: Public Affairs  
225 East John W. Carpenter Freeway  
Irving, Texas 75062

**Goodyear Aerospace Corporation**  
Centrifuge Equipment Division, Plant D

Attention: Mr. J. N. Apisa  
1210 Massillon Road  
Akron, Ohio 44315

**Rollins Environmental Services**

Post Office Box 609  
2027 Battle Ground Road  
Deer Park, Texas 77536

**ALSO:**

13351 Service Highway  
Baton Rouge, Louisiana 70807

**University of Virginia**

Research Laboratories for the Engineering Sciences  
Attention: Dr. J. E. Scott  
Post Office Box 3366  
University Station  
Charlottesville, Virginia 22903

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**Appendix B**

**CENTRIFUGE WORKERS STUDY  
PHASE I RESULTS**

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**FACT SHEET  
CENTRIFUGE WORKER STUDY RESULTS**

**Why and when was the study begun?** The Oil, Chemical, and Atomic Workers Union (OCAW) leaders had been given a list of several of the former centrifuge workers who had developed cancer. Some of the other employees who had worked in those areas were concerned that they might be at increased risk of developing cancer. The union leadership requested that Martin Marietta review the information that had been obtained to determine if the plant management agreed that further investigation was needed. The study began in June 1987, when Martin Marietta requested Oak Ridge Associated Universities (ORAU) assistance in developing a health survey of centrifuge workers.

**Why was ORAU selected to do the study?** ORAU maintains confidential work history and identifying data for all Oak Ridge plant workers. This is part of ORAU's work for the Department of Energy's Health and Mortality Study pertaining to illness and death rates of workers at both active and inactive DOE sites. Thus, ORAU would be able to complete a thorough study quickly. Also, some epidemiologists and other research staff at ORAU are Q-cleared and therefore could have access to all information about the centrifuge process and materials.

**Who paid for the study?** Martin Marietta Energy Systems

**What was the role of management and labor in the study?** Management and labor representatives participated in all phases of the study. The OCAW scientific consultant, Dr. Kenneth Miller, reviewed and accepted the study protocol and interview questionnaire as did Energy Systems.

**How was the study conducted?** ORAU conducted telephone interviews with workers who worked close to any aspect of (i.e., maintenance, component assembly, centrifuge operation) the centrifuge program and an equal number of comparison workers who were employed at K-25 but never worked in the centrifuge area. This allowed us to compare the number of illnesses reported by the two groups and to attempt to determine whether working in the centrifuge process had any relationship to these illnesses.

**What were the possible chemical exposures that MMES and OCAW were concerned about?**

MDA (4,4-Methylenedianiline)  
mPDA (m-Phenylenediamine)  
BECPE (bis (2,3-Epoxypropyl) ether)  
DGEBA (Diglycidyl Ether of Bisphenol A)

These were the substances that made up the epoxy resin systems used in the centrifuge process and were suspected of being carcinogenic in animals; solvent exposure was also a concern.

What kinds of diseases did the study cover? Since animal studies previously indicated epoxy resin exposure as a potential risk factor in cancers of the lung, kidney, liver, small intestine, and bladder, as well as leukemias, reticulum cell sarcoma, lymphoma, skin tumors, and skin rashes, questions were asked concerning those diseases. Other questions related to solvent exposure included occurrence of blurred vision, dizziness, tremors, irregular heartbeat, insomnia, persistent cough, wheezing, numbness and tingling of limbs, ringing of the ears, dark colored urine, and difficulty swallowing. The questionnaire also contained questions to determine the effects of resin exposure on fertility. Only information on diseases reported as occurring after beginning work in the centrifuge program was included in the study.

How were exposure profiles developed? In order to develop exposure profiles, the Health, Safety and Environmental Division at ORGDP supplied ORAU with department numbers, job titles, and medical surveillance lists of names of workers involved in the centrifuge program. There were 10 designated centrifuge departments, however, personnel from several other departments were involved in various aspects of the centrifuge process. Workers in department 1016, the Resident Development Maintenance Department, were in charge of centrifuge maintenance; workers in department 1785, the Chemical Operations Administration, were in charge of cleaning up following "wrecks." Many of the craft persons, including refrigeration mechanics, laborers, janitors, and carpenters, who worked in these areas were from other plant maintenance departments. Unfortunately, organization charts along with department numbers for this group were not available, therefore, they could not be included in the study.

The only unique job title for the centrifuge area was "component assembler." The other job titles were the same as those used in other areas of the plant. This made it impossible to identify the study group using job title alone, we had to develop a method which combined job title and department code.

The medical surveillance list included the names of employees who were under medical surveillance because they had the potential for exposure to the substances which made up the resins used in the centrifuge process. Since these substances were suspected of being carcinogenic in animals, and affecting fertility, Martin Marietta and the union were particularly concerned about the effects that exposure to them might have had.

In addition to considering job titles, department numbers, and the medical surveillance list, representatives of ORAU met with several individuals who were managers or supervisors in the centrifuge program or who were responsible for activities, like industrial hygiene, that were related to the centrifuge process. Also, members of the ORAU research staff reviewed the scientific literature to obtain information on the substances of interest.

Which workers were included in the study? The study population included persons of all races and sexes who worked at K-25 in centrifuge departments for at least 5 years during the late 60s to the mid 80s, the years that the centrifuge program was operational. Also, some workers in the Resident Development Maintenance Department and "wreck cleanup workers" in the Chemical Operations Administration were included.

How were workers within this group chosen to participate? Representatives from the Union and Martin Marietta who were knowledgeable about the centrifuge program and the manner in which the materials were handled ranked job titles for the departments in one of the following exposure categories:

- 0 - Job titles whose responsibilities and lack of access to materials and certain processes provided minimal or no likelihood of exposure to certain industrial types or quantities of toxic materials.
- 1 - Job titles with responsibilities which would ordinarily be expected to provide opportunity for at least intermittent exposure to industrial types and quantities of toxic materials.
- 2 - Job titles and responsibilities which would very likely provide routine exposure to selected industrial materials and processes.

A list of more than 500 centrifuge workers was compiled according to the number of days of exposure in category 2 or routine exposure centrifuge process jobs. Two hundred and fifty-one centrifuge workers and 49 wreck cleanup workers with the greatest number of days of exposure were chosen to be interviewed. This brought the total number of study subjects to 300.

How was the comparison group chosen? An equivalent number of workers who never worked in the departments of interest, but were employed at the plant during the period of time that the centrifuge process was operational, were chosen as a comparison group. Each centrifuge worker was matched with a comparison person who was the same sex, race, and age as the centrifuge worker. The comparison subject had to have started working at K-25 at the same time as the centrifuge worker, and had to be present at K-25 on the day that the centrifuge worker began working in the program. This matching procedure helps us to choose, by computer, workers who are similar to the centrifuge workers. A study like this cannot reach good conclusions without a comparison group of unexposed workers.

What happened if someone did not want to participate? We contacted the next person on the list of centrifuge workers. This list had been sorted by length of exposure in routine exposure areas.

What kind of questions were asked in the questionnaire? The questionnaire asked for some basic information like age, race, and sex. There were also questions concerning the study participant's medical history, including the incidence of several types of cancer, educational and occupational history, and tobacco and alcohol use. Other questions asked pertained to the occurrence of the specific symptoms mentioned in question #5 that might be related to solvent exposure. After the questionnaire was developed, it was reviewed by representatives of the Martin Marietta medical staff, Martin Marietta management, Union representatives, and the Union medical consultant, so we could get their suggestions or address any concerns that they might have.

How were study subjects contacted? Two contact letters were mailed to each of the potential study participants. The first letter was a joint letter of support for the study from Martin Marietta and the Union. A few days later, ORAU followed-up with an additional letter requesting their participation. Individuals agreeing to participate were asked to sign and mail back a consent card stating that they understood the purpose of the study and the procedures involved.

When were the interviews conducted? We started interviewing in August 1988 and had completed 610 interviews by April 1989. The 610 interviews comprised 263 centrifuge workers, 271 centrifuge comparison workers, 38 wreck cleanup workers, and 38 wreck comparison workers.

How were the rights of study participants protected? According to the guidelines established by the National Institutes of Health for any studies in the United States that involve people. These guidelines require study plans to be reviewed and approved by the Institutional Review Board of the researchers' organization; in Oak Ridge this is the ORAU/ORNL Committee on Human Studies. The Committee is made up of physicians and other scientists from ORAU and ORNL, an employee representative and several members of the public including a lawyer, and a clergyman who represent the persons who will be included in a study. The Committee is responsible for reviewing the study plans and all related documents such as contact letters and questionnaires to assure that the participants are not being put at risk and that their rights to privacy and confidentiality are adequately protected. A study plan must be approved by all the Committee members before any study involving people can begin. The plans for the Centrifuge Worker Study were reviewed and approved by the ORAU/ORNL Committee on Human Studies.

How many persons were interviewed and what was the makeup of the group? Three hundred and one of the persons interviewed were in the centrifuge group and 309 were in the comparison group. In the centrifuge group there were 4 black females, 25 black males, 15 white females and 257 white males adding up to a total of 301 persons. The comparison group had 309 persons in 3 of the categories. This occurred when the first potential participant we tried to contact did not respond within a given period of time. After unsuccessfully trying to obtain a new address for that person or to make contact by phone, we would go on to the next possible participant on the list. In a few instances the original person we had tried to contact responded and was interviewed after a replacement had been chosen and interviewed. So, several persons in the centrifuge group have two comparison subjects which is acceptable.

Did most of the workers you tried to contact respond to the request? Yes, the response rate was 92% for the centrifuge workers and 86% for the comparison group. The 6% higher response rate in the centrifuge workers was expected since they had a vested interest in the study.

What similarities were found between the centrifuge workers and the control groups? The groups were similar in religious background, marital status, military service, current employment status, and tobacco and alcohol consumption. The control group for the centrifuge workers had slightly more years of education than the centrifuge workers.

What were the major results of the study? There was no difference in fertility rates, miscarriage, or stillbirths between the centrifuge workers or their spouses and the comparison group.

There were 12 cases of cancer among the centrifuge workers and 7 in the centrifuge comparison group. The wreck workers reported one case of cancer (of the lung) while the wreck comparisons reported two (one prostate; one vocal cord). The breakdown of cancer occurrences among the centrifuge workers and the comparisons is as follows:

	Workers	Comparisons
Bladder	5	0
Breast	1	1
Chest cavity	0	1
Colon	0	2
Kidney	1	0
Lung	1	0
Lung/Liver	0	1
Lymphoma	2	1
Melanoma	1	0
Prostate	1	1
Vocal cord	0	0

Were any of the increases in disease or symptoms statistically significant? Yes. Among the centrifuge workers, the rate of bladder cancer was greater than 7 times that which was expected in the general population as estimated from national statistics (1.38 per 1000 person-years when 0.18 was expected). Others for this group were temporary skin rashes: four times greater than expected (3.98); dizziness: almost twice what is expected; insomnia (difficulty in sleeping): twice that expected (2.21)\*; numb/tingling limbs: one-and-a-half times that expected (1.68); and kidney stones: three-and-a-half that expected (3.50).

The wreck workers experienced more than six-and-a-half times more cases of stomach ulcers than the control group (12.11 per 1000 person-years; the control group had none).

\*Note that the insomnia cases increased in 1986, after the centrifuge process was virtually discontinued and were, therefore not likely to be related to the process.

HEALTH STUDY OF ORGDP CENTRIFUGE WORKERS  
EXECUTIVE SUMMARY

Prepared by Oak Ridge Associated Universities  
Medical Sciences Division  
Center for Epidemiologic Research  
August 15, 1989

Early in 1987, officials of the Oil, Chemical, and Atomic Workers Union (OCAWU) approached the management of Martin Marietta Energy Systems (MMES), the Department of Energy (DOE) contractor in charge of operations at Oak Ridge Gaseous Diffusion Plant (ORGDP), with concerns about the health of group of employees who had worked in the gas centrifuge process. The union leadership had become aware of at least nine cases of cancer among these workers. Some of the other former centrifuge workers were concerned that they were at increased risk of developing cancer. The union leadership requested that MMES review the information that had been obtained to determine if MMES agreed that further study was necessary.

In June 1987, MMES management requested the assistance of Oak Ridge Associated Universities (ORAU) in developing a special study to evaluate the health status of this group or cohort of employees. ORAU agreed to develop a plan (protocol) that would describe the type of study that might be done to examine the health of the cohort of centrifuge workers in terms of illness experience and cause of death. A protocol was written and MMES decided to sponsor ORAU to conduct the study. ORAU involved representatives of MMES and ORGDP management and the OCAWU in all phases of the study.

ORAU maintains computerized work history, vital status, and identifying data for all Oak Ridge workers as part of their work mission for the Department of Energy (DOE) to maintain health surveillance on

populations of workers at active and defunct DOE sites. Use of these existing data systems expedited the start of the study.

In order to develop exposure criteria, the Health, Safety and Environmental Division at ORGDP supplied ORAU with department numbers, job titles, and lists consisting of names of workers who were medically monitored because of their association with the centrifuge process. The names of contact persons familiar with the centrifuge process and information regarding materials used were also furnished.

There were 10 designated centrifuge departments, however, personnel from several other departments were involved in various aspects of the centrifuge process. The Resident Development Maintenance Department was in charge of centrifuge maintenance and the Chemical Operations Administration was in charge of cleaning up following centrifuge malfunctions or "wrecks". Many craft personnel, including refrigeration mechanics, laborers, janitors, and carpenters, who worked in the centrifuge areas were from other ORGDP maintenance departments. However, organization charts along with department numbers for this group were not available so it was impossible to identify them for inclusion in the study.

The only unique job title for the centrifuge area was the hourly worker title of "component assembler". The other job titles were those used throughout ORGDP for hourly, weekly, and monthly employees. Since it was not possible to identify the study cohort on the basis of job title alone, a method was devised which combined job title and department code.

Lists maintained by the Medical Department identified employees who were under medical surveillance due to their potential for exposure to 4,4-Methylenedianiline (MDA), m-Phenylenediamine (MPDA),

bis(2,3-Epoxypropyl)ether (BECPE), and Diglycidyl Ether of Bisphenol A (DGEBA), the substances which made up the resin systems used in the centrifuge process. Since these substances were suspected of being carcinogenic in animals, MMES and OCAWU were particularly concerned about the effects that exposure to them might have had on the centrifuge workers. The potential for exposure to high levels of solvents was also of concern.

In order to determine whether the centrifuge workers were different with respect to mortality (cause of death), the original study protocol called for the comparison of mortality among the centrifuge cohort with mortality in the general U.S. population and with a comparison group of other ORGDP workers. However, after the group of all centrifuge workers was identified from the ORAU data base (irrespective of level of exposure) it was determined that there was not a sufficient number of deaths in this group to do a meaningful mortality study. Although no formal statistical analysis could be performed, the causes of death are enumerated in the full version of this report.

ORAU defined the study population as all race/sex groups of employees who worked at ORGDP in centrifuge departments during the period of operation of the centrifuge process, that is the late 1960s to the mid 1980s. Also, workers in the Resident Development Maintenance Department and "wreck cleanup workers" in the Chemical Operations Administration would be included. There was some debate about whether the "wreck cleanup workers" should be part of the study population since they were exposed to a fully cured, and presumably inert, physical form of the substances of interest. After further discussion between ORAU, MMES, and OCAWU, it was agreed that their exposures were important and these workers should be included.

Representatives from OCAWU and MMES, who are knowledgeable about the centrifuge process and the manner in which process materials were handled, ranked process job titles for the centrifuge departments in one of the following exposure categories:

- 0 - Job titles whose responsibilities and lack of access to materials and certain processes provide minimal or no likelihood of exposure to industrial types or quantities of toxic materials.
- 1 - Job titles with responsibilities which would ordinarily be expected to provide opportunity for at least intermittent exposure to industrial types and quantities of toxic materials.
- 2 - Job titles with responsibilities which would very likely provide routine exposure to industrial types and quantities of toxic materials.

A list of more than 500 centrifuge workers who ever worked in a job that was categorized as a level 2 job was compiled. The list was sorted according to the number of days of exposure in category 2 or routine exposure centrifuge process jobs. Two hundred and fifty-one workers with the greatest number of days of exposure were chosen to be interviewed. It was decided that 49 wreck cleanup workers should also be interviewed. This brought the total number of study subjects to 300. An equivalent number of workers who never worked in the departments of interest but were employed at the plant during the period of time that the centrifuge process was operational were chosen as a comparison group. These comparison workers were individually matched to the centrifuge workers according to date of birth, race, sex, date of facility hire, and presence at ORGDP on the day that the exposed worker began working in the centrifuge process.

A questionnaire was developed to collect specific demographic data and information concerning the participant's medical history, including the

incidence of several types of cancer, educational and occupational history and information on tobacco and alcohol use. The questionnaire was reviewed by representatives of the MMES medical staff, MMES management, OCAWU representatives, and the OCAWU scientific consultant.

An Application for the Use of Humans as Experimental Subjects was submitted to and approved by the ORAU/ORNL Committee on Human Studies as is required by the National Institutes of Health and DOE for all studies involving humans. Along with the application, copies of the following documents were required: an overall study protocol, a protocol for contacting study subjects, the contact letter from OCAWU and MMES, the contact letter from ORAU, an information statement concerning the Privacy Act of 1974 which was included with the contact letter from ORAU, the study participation card and the proposed questionnaire.

The morbidity (or illness) phase of the investigation utilized telephone interviews with workers in the more highly exposed category and an equal number of matched controls from the ORGDP population. This phase addressed the question of whether the centrifuge workers had a similar incidence of cancer and attempted to determine whether the exposures had any effect on fertility. Cancers of specific interest prior to the start of the study (based on the scientific literature) included: liver cancer, kidney cancer, lung cancer, leukemias, reticulum cell sarcoma, lymphoma, skin tumors, cancer of the small intestine, and bladder cancer. Questions related to solvent exposure effects included the occurrence of blurred vision, dizziness, tremors, irregular heartbeat, insomnia, persistent cough, wheezing, numbness or tingling of limbs, ringing of the ears, dark colored urine and difficulty swallowing.

Following the approval of the questionnaire by the Committee on Human Studies, two contact letters were mailed to each of the potential study participants. The first letter was a joint letter of support for the study from MMES and OCAWU. A few days later, ORAU followed-up with an additional letter requesting the worker's participation. Individuals agreeing to participate in the study were asked to sign a consent form stating that they understood the purpose of the study and the procedures involved. In the event that a centrifuge worker chosen to be interviewed refused to participate in the study, we contacted the next person on a list of centrifuge workers which had been sorted by length of employment in the high exposure areas. In all circumstances, the rights of the study subjects and potential study subjects were protected and their privacy was maintained.

Interviews began in August 1988 and 610 interviews were completed by April, 1989. The interview group comprised 263 centrifuge workers (CW), 271 centrifuge comparison workers (CCW), 38 'wreck' workers (WW), and 38 'wreck' comparison workers (WCW).

The exposed and comparison workers proved to be closely matched with a median year of birth of 1944 for the CW, CCW, WW, and WCW groups. The median year of hire at ORGDP was 1974 from the CW and CCW groups with a range from 1944 to 1980. The median year of hire at ORGDP for the WW and WCW groups was 1971 with a range from 1944 to 1976.

The groups showed no difference for the following demographic variables: religious background, marital status, military service, current employment status, tobacco history (including cigarettes, pipe, cigars, chewing tobacco, and snuff), and alcohol consumption history. The CCW

group had more education than the CW group with 33.6% of the group having a college education or greater compared to 17.5% for the CW group.

There did not appear to be any difference between the groups with regard to the questions related to fertility. The groups had similar distributions with respect to number of children born before entering the centrifuge program and after first exposure to the program. The number of miscarriages experienced before and after the centrifuge work experience were similar for exposed and comparison workers. Also, there was no difference in the number of stillbirths between the groups. The number of workers reporting experiencing trouble conceiving was similar between the exposed and comparison groups.

Incidence rates for all symptoms or specific diseases were calculated in each group from the date of first work in the centrifuge process until the end of the study. Each comparison worker was assigned the date of entry of the centrifuge worker to whom he/she was matched. All diseases or symptoms reported before this 'centrifuge date' were disregarded since it would be impossible for the disease or symptom to be related to an exposure that had not yet occurred.

The total number of cancers reported in each group after the beginning of work in the centrifuge process, by cancer type, is displayed in Table 1.

Table 1. Incident Cancers in the Study Groups

Cancer	Centrifuge Worker	Centrifuge Comparison Worker	Wreck Worker	Wreck Comparison Worker
Bladder	5	0	0	0
Breast	1	1	0	0
Chest cavity	0	1	0	0
Colon	0	2	0	0
Kidney	1	0	0	0
Lung	1	0	1	0
Lung/liver	0	1	0	0
Lymphoma	2	1	0	0
Melanoma	1	0	0	0
Prostate	1	1	0	1
Vocal cord	0	0	0	1
TOTAL	12	7	1	2

A total of 12 cancers was reported by centrifuge workers versus 7 reported by centrifuge comparison workers. One cancer was reported by a wreck worker versus 2 in the wreck comparison group. The difference in total cancer incidence between the exposed and the comparison groups was not statistically significant.

Looking at the cancers on a site by site basis, the largest difference between the groups appears to be the incidence of bladder cancer. Five bladder cancers were reported in the CW group and none in the CCW group. The rate in the CW group is 1.38 per 1000 person years. The rate in the CCW group cannot be calculated because there were no reported cases. Using available statistics for age specific bladder cancer incidence rates in the general population, an expected rate for bladder cancer in the CCW group was calculated to be 0.18 per 1000 person years. Thus, the CW have greater than a seven-fold increase in risk for developing bladder cancer compared to the general population.



the CW did not appear until 1986 and after, which makes it less likely that this particular symptom was truly related to the centrifuge process since the process was virtually discontinued by that time.

Skin rashes have long been noted to be a symptom related to exposure to epoxy resin systems. The finding of a 4-fold increase is not, therefore, unexpected. The other symptoms that are increased in the CW are those that are related to high solvent exposure. These include blurred vision, dizziness, and numb and tingling limbs. Therefore, since solvent exposure was also a concern at the outset of this study, an increase in these symptoms could also serve as a confirmation of these exposures.

The finding of an increase in kidney stones in the CW group was unexpected and at this time has not been correlated with any specific centrifuge materials. More in depth analysis of the job titles and duties of these workers may reveal a biologically plausible mechanism which would explain this increase.

The bladder cancer increase needed further examination and characterization. Bladder cancer was one of the cancers of interest identified at the beginning of the study based on results of animals exposed to one of the materials utilized in the centrifuge program.

Examination of personal characteristics of the 5 workers with bladder cancer revealed that they were all smokers at one time; smoking is a known risk factor for bladder cancer, conferring a 2-fold increase in risk to present smokers. There does not appear to be any common previous exposure to known bladder carcinogens with the exception of one individual who was briefly employed in the rubber industry more than 30 years before his bladder cancer was diagnosed.

With the permission of the individuals concerned, we sought and have received histologic confirmation from hospital medical records for all of the primary bladder cancer cases.

Other factors found to be significantly correlated to the development of bladder cancer in this study included: previous military service (N=5), diabetes (N=2), and work with trichloroethylene before employment at ORGDP (N=4). These factors are not known to be risk factors for bladder cancer.

Each of the 5 bladder cancer cases agreed to be interviewed in order to determine exact job duties and plant areas of work. The interviews were conducted between August 4, 1989 and August 10, 1989. None of the five workers had any job that required routine, 'hands-on' work with any of the epoxy resin materials (MDA, MPDA, BECPE, or DGEBA). Three of the bladder cancer cases had the opportunity to pass through T-Lab although they were not routinely assigned to that area and did not come in direct contact with materials used there. Three of the workers helped with decontamination and cleanup following centrifuge malfunctions. Four workers were in close proximity to centrifuge operation areas during the time of centrifuge malfunctions.

At this time it is not possible to identify one specific agent or process that could be labeled as the causative factor for these bladder cancers.

This work was sponsored by Martin Marietta Energy Systems and performed by Oak Ridge Associated Universities under Contract No. DE-AC05-76OR00033 between the Department of Energy, Office of Energy Research and Oak Ridge Associated Universities.

**Appendix C**

**CENTRIFUGE WORKERS STUDY  
PHASE II RESULTS**

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## **CENTRIFUGE WORKER HEALTH SURVEY PHASE II FACT SHEET**

The results of Phase I of the Centrifuge Worker Health Survey, which was completed in April 1989, indicated an increased risk of bladder cancer among centrifuge workers. Phase I was limited to workers who had the greatest potential for exposure to substances used in the centrifuge process. Phase II was designed to expand the survey to evaluate the health of all employees who were ever assigned to the Centrifuge Program but who were not interviewed in Phase I. The results of Phase II show no increased rate of bladder cancer among the 855 potentially exposed workers included in the survey.

### **When and why was Phase I of the Centrifuge Worker Health Survey conducted?**

The initial survey, Phase I, began in August 1987, and was completed in April 1989. Concerned Oil, Chemical, and Atomic Workers Union (OCAW) members had given OCAW leaders a list of names of several former centrifuge workers who had developed cancer. Other employees who had worked in those areas were concerned that they might be at increased risk of developing cancer. Union leaders met with representatives of Martin Marietta Energy Systems, Inc. (Energy Systems) to review the list and decide what action should be taken. Since representatives of both Energy Systems and OCAW concluded that further investigation was needed, Energy Systems requested that Oak Ridge Institute for Science and Education (ORISE) develop a survey to assess the health status of former centrifuge workers, and particularly to assess whether former centrifuge workers appeared to be at increased risk of developing cancer.

### **Why was Phase II of the Centrifuge Worker Health Survey necessary and how was it conducted?**

The results of Phase I indicated that the rate of bladder cancer among the centrifuge workers was higher than what would have been expected in the general population. Five cases of bladder cancer were reported and less than one would have been expected. Centrifuge workers also reported more episodes of symptoms related to solvent exposure than the comparison group. These symptoms included rashes, dizziness, and numb and tingling limbs. Rashes are also known to be highly associated with exposure to epoxy resin systems. The symptoms are temporary and go away when individuals stop working with solvents and epoxy resin systems. Phase I had been limited to workers who had the greatest potential for exposure to substances used in the centrifuge process. Phase II was designed to expand the survey to evaluate the health of all employees who had ever worked in Centrifuge Program Departments 1330-1339 but who had not been interviewed in Phase I. Employees in analytical laboratories and maintenance departments who provided support

services for the Centrifuge Program were also included in Phase II. ORISE conducted telephone interviews with these individuals and an equal number of comparison workers who were employed at K-25 but who never worked in the centrifuge areas. The number of illnesses reported by the two groups was compared to determine whether working in the centrifuge process had any relationship to these illnesses. The medical histories of centrifuge workers and comparison workers interviewed in Phase I were also updated. In addition, more detailed exposure histories were obtained.

**Who sponsored the survey?**

It was sponsored by the Department of Energy (DOE) with Energy Systems as the managing contractor.

**Why was ORISE selected to do the survey?**

ORISE maintains certain confidential work history and identifying data for DOE contractor employees at three Oak Ridge facilities. This information was collected for the Health and Mortality Study of DOE contractor workers that ORISE conducted for DOE from 1977-1991. This was a study of illness and death rates among workers at both active and inactive DOE sites. These studies are now being conducted by the National Institute for Occupational Safety and Health.

**What were the roles of management and labor?**

Management and labor representatives participated in developing both phases of the survey. OCAW's medical consultant, Dr. Kenneth Miller, reviewed and approved the survey protocol and interview questionnaire, as did Energy Systems.

**How were the rights of survey participants protected?**

Rights were protected according to the guidelines established by the National Institutes of Health for any study involving people conducted in the United States. These guidelines require that study plans be reviewed and approved by the Institutional Review Board of the researchers' organization; in Oak Ridge this is the ORAU/ORNL Committee on Human Studies. The Committee is made up of physicians and other scientists from ORISE and ORNL; an employee representative; and several members of the public, including minority group representatives and a lawyer who represent persons included in a study. The Committee is responsible for reviewing study plans and all related documents such as the contact letters and questionnaires. This is to assure that the participants are not being put at risk and that their rights to privacy and confidentiality are adequately protected.

A study plan must be approved by all the Committee members before any study involving people can begin. The plans for the Centrifuge Worker Health Survey were reviewed and approved by the ORISE/ORNL Committee on Human Studies.

**What were the possible chemical exposures that Energy Systems and OCAW were concerned about?**

MDA (4,4-Methylenedianiline)  
mPDA (m-Phenylenediamine)  
BECPE (bis (2,3-Epoxypropyl) ether)  
DGEBA (Diglycidyl Ether of Bisphenol A)

These were the substances that made up the epoxy resin systems used in the centrifuge process and were suspected of causing cancer in animals. Solvent exposure was also a concern. Published studies have shown that working with MDA may possibly increase the risk of developing bladder cancer; however, none of the individuals in the previous survey or this survey who reported having bladder cancer routinely had hands-on exposure to MDA.

**What kinds of diseases did the survey cover?**

The medical history section of the survey included questions about cancers of the lung, kidney, liver, small intestine, and bladder; leukemia; reticulum cell sarcoma; lymphoma; skin tumors; and skin rashes. A review of animal studies indicated epoxy resin exposure as a potential risk factor for these diseases. Questions were also asked about the occurrence of symptoms related to solvent exposure, such as blurred vision, dizziness, tremors, irregular heartbeat, insomnia, persistent cough, wheezing, numbness and tingling of limbs, ringing of the ears, dark colored urine, and difficulty swallowing. Only information for diseases and symptoms reported as occurring after participants began working in the Centrifuge Program was included in the survey.

**What other kinds of questions were asked in the questionnaire?**

The questionnaire asked for some basic information such as age, race, and gender. There were also questions concerning educational background, occupational history, and tobacco and alcohol use. After the questionnaire was developed, it was reviewed by Energy Systems' medical staff and management, OCAW representatives, and OCAW's medical consultant so ORISE could get their suggestions or address any concerns they might have. This input was used to improve the usefulness and effectiveness of the questionnaire.

**When were the interviews conducted?**

Interviews began in January 1990 and continued through June 1992.

**How many people were interviewed?**

Interviews were conducted with 1,737 individuals who met the criteria for survey participation. This group included 627 centrifuge workers, 646 centrifuge comparison workers, 228 maintenance workers, and 236 maintenance comparison workers. The numbers of both comparison groups were greater than the numbers of centrifuge workers and maintenance workers. Several persons in the centrifuge and maintenance groups had two comparison subjects, which is acceptable.

**How many men and women were in each group and what race were they?**

Among the centrifuge worker group there were 9 African-American females, 23 African-American males, 132 white females, and 463 white males. The maintenance worker group included 2 African-American females, 16 African-American males, 1 white female, and 209 white males. In the combined comparison groups there were 13 African-American females, 41 African-American males, 134 white females, and 694 white males.

**What percentage of the workers contacted chose to be interviewed?**

Of the workers who were contacted and met the requirements to participate in the study, 78.5% agreed to be interviewed.

**What were the major results of the Phase II?**

During the time that centrifuge workers were working in the Centrifuge Program, they reported significantly more emphysema and numb and tingling limbs than their comparison group. Maintenance workers reported significantly more urinary tract infections; rashes; growths; dizziness; and bone, muscle, and joint diseases. Numb and tingling limbs, rashes, dizziness are temporary symptoms that go away when individuals stop working with solvents and epoxy resin systems.

Seventy-two cases of cancer were reported by centrifuge workers and 69 reported by their comparison group. The maintenance workers reported 21 cases of cancer and their comparison group reported 25. Six cases of bladder cancer were evenly distributed between the centrifuge and maintenance workers and their comparison groups. Bladder cancer was reported by one centrifuge worker and one centrifuge comparison worker, as well as two

maintenance worker and two maintenance comparison workers. Other types of cancer were also evenly distributed between the centrifuge and maintenance workers and the comparison groups.

Phase II involved all workers from centrifuge departments even though their potential for exposure to process chemicals was lower. The results of the Phase II survey indicate that these workers are not at increased risk of developing bladder cancer. Phase I included only workers who had the greatest potential for exposure to chemicals and substances used in the centrifuge process. Results of Phase I and the medical history updates showed a significant excess of bladder cancer among this group. After an extensive review of work histories and monitoring data, we have not been able to identify a specific occupational exposure or causative agent for these cancers. In general, smokers are at greater risk for developing bladder cancer. Most of the individuals who reported having bladder cancer are current or former smokers.

If you have questions about the signs and symptoms of bladder cancer, please contact the K-25 Health Service Center. Educational information will be available upon request.

## Centrifuge Worker Health Survey, Phase II

### Executive Summary

In June 1987, Martin Marietta Energy Systems, Inc. (Energy Systems), the Department of Energy (DOE) contractor in charge of operations at the K-25 Site (Oak Ridge Gaseous Diffusion Plant), asked Oak Ridge Associated Universities (ORAU), now known as the Oak Ridge Institute for Science and Education (ORISE), to develop a survey for evaluating the health of a group of employees who worked in the gas centrifuge process at the Site. The Centrifuge Program was in operation from the mid-sixties to the mid-eighties. Nine cases of cancer among employees who had worked in the program were reported to leaders of the Oil, Chemical, and Atomic Workers Union (OCAW), causing other former centrifuge workers to be concerned that they were at an increased risk of developing cancer. With the full support and involvement of Energy Systems and OCAW, ORISE created a telephone interview health survey to assess the occurrence of illness. The survey focused on cancer incidence and symptoms related to solvent exposure in these workers. Due to the results of the initial Centrifuge Worker Health Survey, the investigation evolved in two distinct phases.

The Phase I survey population included individuals of all race and gender groups judged to have the greatest exposure potential to substances used in the centrifuge process. These substances included 4,4-methylenedianiline (MDA), m-phenylenediamine (mPDA), bis(2,3-epoxycyclopentyl)ether (BECPE), and diglycidyl ether of bisphenol A (DGEBA), the

chemicals that made up the resin systems used in rotor fabrication. The potential for exposure to high levels of solvents was also of concern.

Representatives of OCAW and Energy Systems ranked exposure potential using a method based on job title and department code. They evaluated job titles from the ten designated centrifuge departments, the Resident Development Maintenance Department, and the Chemical Operations Administration. The Resident Development Maintenance Department was in charge of centrifuge maintenance, and the Chemical Operations Administration cleaned up following centrifuge malfunctions or "wrecks." Workers from other craft and maintenance departments were assigned to the Centrifuge Program; however, since organizational charts and department numbers for these individuals were not available, it was impossible to include these workers in the survey.

Two hundred and sixty-three centrifuge workers who had the greatest number of days of potential exposure and agreed to participate in the survey were interviewed. Thirty-eight wreck cleanup workers were also interviewed bringing the total number of centrifuge survey subjects to 301. An equal number of workers were chosen as an internal comparison group. Individuals in this group had to be employed in other areas of the plant during the time the centrifuge process was in operation.

Data analysis for Phase I was completed in August 1989, and the results indicated that the most noteworthy difference between the groups appeared to be in the incidence of bladder cancer. Five bladder cancers were reported and confirmed among the centrifuge workers while none were reported among the comparison workers. Since there were no reported cases among the comparison workers, no bladder cancer rate could be calculated

to compare with the bladder cancer rate among the centrifuge workers. Therefore, the rate of bladder cancer among the centrifuge workers had to be compared with available statistics for age-specific bladder cancer incidence rates in the general population. The comparison indicated that the rate of bladder cancer among centrifuge workers was higher than what would have been expected in the general population. However, no causative agent for the bladder cancers was identified because each of the cases worked in a different area of the process and had different responsibilities. Published studies have shown that exposure to MDA may increase the risk of developing bladder cancer; however, none of the individuals in this survey who reported having bladder cancer routinely had hands-on exposure to MDA.

Other diseases or conditions showing a statistically significant increase among the centrifuge workers were skin rashes, dizziness, numb and/or tingling limbs, kidney stones, and insomnia. Skin rashes, dizziness, numb and/or tingling limbs, and insomnia are temporary symptoms that disappear when individuals stop working with solvents and epoxy resin systems. There was no difference in self-reported fertility rates, miscarriages, or stillbirths between the centrifuge workers or their spouses and the comparison group.

After reviewing the results, Energy Systems instituted a screening program for current and former employees. It was also requested that ORISE expand the interview survey to involve a larger number of workers and to update the medical histories of centrifuge workers and comparison subjects interviewed in Phase I. In addition, a more detailed exposure history was obtained. Phase II of the Centrifuge Worker Health Survey was designed to expand the survey and assess the health status of all persons who had ever worked in Centrifuge Program Departments 1330-1339 but who had not been interviewed in Phase I.

Employees in analytical laboratories and maintenance departments who provided support services for the Program and had potential exposure to the materials used in the centrifuge process were also included in the survey. An equal number of workers employed at K-25 while the centrifuge process was in operation but who never worked in the Centrifuge Program were chosen as an internal comparison group. Each centrifuge and maintenance worker was individually matched with a comparison worker by date of birth, race, gender, and date of hire. In addition, the comparison worker had to be employed at the plant when the matched centrifuge or maintenance worker began working in the Centrifuge Program.

To identify maintenance workers for inclusion in the survey, a questionnaire was designed to collect information regarding years of employment, specific areas or buildings, and job duties in the Centrifuge Program. Data pertaining to potential chemical exposures were also collected. OCAW supplied a list of names of individuals who worked in maintenance department 1016 or were assigned to the Centrifuge Program but were not in departments 1330 through 1339. Questionnaires were sent to these individuals. Workers responding who indicated that they had worked in centrifuge areas were included in the survey.

For the first phase of the survey, a telephone interview questionnaire was developed to collect specific demographic data, medical histories, educational and occupational histories, and information on tobacco and alcohol use. The medical histories included questions about occurrences of kidney, lung, and bladder cancers; leukemias; reticulum cell sarcoma; lymphoma; and cancer of the small intestine. Other questions pertained to symptoms of solvent exposure such as dizziness, numb and tingling limbs, insomnia, skin

rashes, persistent cough, wheezing, dark colored urine, and difficulty swallowing. For the second phase of the survey, specific questions about potential centrifuge process exposures were added to the original questionnaire. Questions were phrased so that exposure categories assigned by industrial hygienists could be validated by self reported exposure information obtained from the questionnaires. This allowed exposure potential to be judged more accurately.

The ORISE/Oak Ridge National Laboratory (ORNL) Committee on Human Studies reviews proposed research protocols to ensure that the rights and privacy of participants in research projects are being protected. Before beginning the Centrifuge Worker Health Survey, an Application for the Use of Humans as Experimental Subjects was submitted to the Committee for approval. The application contained the survey protocol, the participant contact letters, the proposed questionnaire, a survey participation consent form, and information regarding privacy and confidentiality. The application was approved before any survey participants were contacted.

Phase II of the Centrifuge Workers Health Survey began in January 1990. As in Phase I, a joint letter of introduction and support for the Phase II health follow-up survey was sent from Energy Systems and OCAW to potential participants. Approximately three days later, ORISE sent a letter to them explaining the purpose of the survey and requesting participation in a telephone interview. Workers agreeing to be interviewed were asked to sign survey participation consent and plant medical records release forms and return them in self-addressed, postage-paid envelopes provided by ORISE.

From January 1990 through June 1992, 1,737 individuals who met the criteria for survey participation were interviewed. This group included 627 centrifuge workers (CW), 646 centrifuge comparison workers (CCW), 228 maintenance workers (MW), and 236 maintenance comparison workers (MCW). Among the centrifuge group there were 9 African-American females, 23 African-American males, 132 white females, and 463 white males. The maintenance worker group included 2 African-American females, 16 African-American males, 1 white female, and 209 white males. In the combined comparison groups there were 13 African-American females, 41 African-American males, 134 white females, and 694 white males.

The data collected during the interviews were analyzed. Demographic data indicated that the median year of birth for the centrifuge workers and their comparison group was 1944 with a range of 1909 to 1964. For the maintenance workers and their comparison group, the median was 1942 with a range of 1909 to 1957. According to work history information, the median year of hire in the Centrifuge Program was 1978 (range = 1962-1985) for the centrifuge workers. For the maintenance workers, the median year of assignment to the Program was 1975 (range = 1962-1985).

Incidence rates in each group were calculated for all symptoms or specific diseases reported from centrifuge date, the first workday in the centrifuge process, until the end of the survey. To calculate these rates, each comparison worker was assigned the centrifuge date of the centrifuge worker with whom he/she was matched. All diseases or symptoms reported before this date were disregarded. Any disease or symptom reported before the

centrifuge date could not have been related to chemicals or substances used in the centrifuge process, since those potential exposures had not yet occurred.

Incident cancers in the Phase II survey group are presented in Table 1. Centrifuge workers reported 11 basal cell carcinomas (skin tumors that are not usually metastatic but may cause local invasion) and their comparison group reported six. However, this type of cancer was more prevalent among centrifuge workers before they worked in the Program, indicating that centrifuge process exposures were not responsible for the increase. Three centrifuge workers, one maintenance worker, and one comparison worker previously had basal cell cancer. One centrifuge worker had basal cell cancer the same year that he began working in the centrifuge process. The centrifuge comparison group reported having lung cancer four times as frequently as centrifuge workers. No lung cancers were reported by maintenance workers or their comparison group.

New cases of bladder cancer were evenly distributed throughout the subgroups. One centrifuge worker and one centrifuge comparison worker reported having bladder cancer. Two maintenance workers and two maintenance comparison workers also reported having bladder cancer.

Table 1. Incident Cancers in the Phase II Survey Groups

Cancer Type	Centrifuge Worker	Centrifuge Comparison Worker	Maintenance Worker	Maintenance Comparison Worker
Bladder	1	1	2	2
Brain	1	0	0	0
Breast	3	1	0	0
Cervix/Uterus	2	0	0	0
Colon	2	1	0	1
Hodgkin's disease	1	0	0	0
Kidney	3	2	2	0
Leukemia	2	0	0	0
Lung	1	4	0	0
Lymphoma	1	1	1	0
Melanoma	5	3	1	1
Ovarian	0	2	0	0
Pancreas	0	0	1	0
Prostate	1	4	1	2
Skin cancer	33	42	11	17
Basal cell	11	6	0	0
Squamous cell	2	0	0	0
Testicle	0	0	0	1
Throat	1	0	0	0
Thyroid	0	2	1	0
Vocal cord/Larynx	1	0	1	1
Unknown source	1	0	0	0
Total	72	69	21	25

Table 2 presents the diseases or symptoms that showed significant increases in the centrifuge and maintenance workers relative to their comparison groups. The centrifuge workers reported significantly more emphysema and numb and tingling limbs than their comparison group since the year they began working in the Centrifuge Program. Urinary tract infections, blood diseases, and melanomas were increased in the centrifuge workers; however, the increase was not significant. Centrifuge workers reported having anemia, insomnia, skin rashes, and basal cell carcinoma more frequently before working in the Program than their comparison group. After becoming centrifuge workers they continued to report a higher occurrence of these diseases and symptoms.

From the year of assignment to the Centrifuge Program, the maintenance workers reported significantly more urinary tract infections, rashes, growths, dizziness, and bone, muscle, and joint diseases. They also reported more bronchitis, emphysema, asbestosis, blurred vision, tremors, insomnia, and dark colored urine; however, the increase in these symptoms or diseases was not statistically significant.

In Phase II, causes of death were reported for 34 deceased centrifuge and maintenance workers; 18 were known to be dead before the survey began. Data for these individuals were collected from interviews with close family members who agreed to participate as proxies. Sixteen additional deaths have been reported among this group from the beginning of the second phase of the survey to the present. Information gathered from death certificates indicated that lung cancer was recorded as the underlying cause of death for two centrifuge workers and two maintenance workers. This was the most frequently reported type of cancer.

Table 2. Diseases or Symptoms that Appeared to be Increased in the Centrifuge or Maintenance Worker Groups					
Centrifuge Workers					
Disease/Symptom	CW Rate/1000PY	N	CCW Rate/1000PY	N	Incidence Ratio* (95% CI)
Emphysema	1.77	16	0.75	7	2.35(1.00,5.57)
Urinary tract infection	3.78	33	2.21	20	1.70(0.98,2.94)
Blood diseases	2.12	19	1.34	12	1.64(0.80,3.35)
Melanoma	0.55	5	0.32	3	1.72(0.42,7.07)
Numb/tingling limbs	11.73	99	7.76	69	1.51(1.11,2.05)
Maintenance Workers					
Disease/Symptom	MW Rate/1000PY	N	MCW Rate/1000PY	N	Incidence Ratio* (95% CI)
Bronchitis	2.71	10	1.06	4	2.56(0.84,7.83)
Emphysema	2.39	9	0.76	3	3.15(0.91,10.84)
Asbestosis	1.57	6	0.50	2	3.12(0.68,14.22)
Urinary tract infection	2.96	11	0.77	3	3.86(1.18,12.61)
Bone, muscle & joint disease	6.91	25	2.84	11	2.43(1.23,4.83)
Kidney cancer	0.52	2		0	
Growths	12.41	44	4.68	18	2.65(1.57,4.49)
Blurred vision	6.08	22	3.64	14	1.67(0.86,3.24)
Dizziness	7.80	28	4.10	16	1.90(1.04,3.48)
Tremors	2.38	9	1.28	5	1.86(0.64,5.47)
Insomnia	4.26	16	2.55	10	1.67(0.77,3.65)
Skin rashes	7.42	27	3.97	15	1.87(1.01,3.48)
Dark colored urine	2.10	8	1.01	4	2.09(0.65,6.74)

\*95% confidence interval is contained in parentheses. The incidence ratio is the rate of disease in the exposed group (CW or MW) divided by the rate of disease in the respective group (CCW or MCW).

Phase II also included contacting Phase I participants to request that they complete an additional telephone interview to update their medical histories. Eleven cases of various types of cancer were reported by individuals participating in the update; however, five were skin cancers. No cases of bladder cancer were reported during the health updates. Incident cancers reported from the time of completion of the Phase I interview until the time of the

health update interviews are shown in Table 3. The four types of cancer reported by centrifuge workers included breast (one), prostate (one), skin (three), and stomach (one). Among the comparison subjects, the four types of cancer found were breast (one), kidney (one), lung (one), and skin (two). No cases of bladder cancer were reported during the update; however, after the cutoff date for the interview component of the survey, one individual informed ORISE that he had been diagnosed with bladder cancer.

Cancer Type	Reported by Centrifuge Worker	Reported by Comparison Subject
Breast	1	1
Kidney	0	1
Lung	0	1
Prostate	1	0
Skin	3	2
Stomach	1	0
Total	6	5

As previously stated, centrifuge workers participating in Phase I of the health survey were individuals judged to have the greatest potential for exposure to substances and materials used in the Centrifuge Program. Phase II included all employees who worked in Program departments and chose to participate. The individuals were identified using plant work history records. A sample of maintenance workers and laboratory personnel from departments associated with the Program were also included.

In comparing the results of the two phases of the survey, the increase in bladder cancer noted in Phase I was not evident in Phase II. In both phases, the potentially exposed groups reported an excess of temporary symptoms related to working with solvents. These included rashes, dizziness, and numb and tingling limbs. Temporary skin rashes are also related to working with epoxy resin systems.

Due to the significant bladder cancer increase and excess of the specific symptoms found in Phase I, it is recommended that educational material concerning the signs and symptoms of bladder cancer be made available to interested individuals. To date, no causative agent has been identified as being related to the bladder cancers from the Phase I survey.

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