PROTOCOL:
DOE FORMER BERYLLIUM WORKER
MEDICAL SURVEILLANCE PROGRAM (BMSP)

MANAGED BY
OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION (ORISE)
OAK RIDGE, TENNESSEE

ABSTRACT

The DOE BMSP (managed for DOE by Oak Ridge Institute for Science and Education [ORISE]) is composed of five interrelated tasks and includes the identification, notification, scheduling, initial testing, and retesting of former employees of DOE sites who believe they were exposed to beryllium during their employment. Rosters of former employees from DOE sites under the BMSP will be obtained and appropriate BMSP notification letters and participation forms will be sent to persons on these rosters. Individuals indicating a desire to participate in the BMSP are tested for sensitivity to beryllium, and may also be given a chest x-ray if they report respiratory symptoms compatible with chronic beryllium disease (CBD). All persons who show sensitivity to beryllium on the first test are scheduled for a second test to confirm the positive finding. Further medical evaluation to determine the presence of CBD is offered to those identified as beryllium sensitized (two positive tests) or who have suspicious lung pathology on chest x-ray examination. Retesting is offered once every three years to former employees who are found to have normal test results. In addition, retesting is offered every year to former employees who have a single positive blood test for sensitivity to beryllium that was not confirmed by the second test or who had an abnormal chest x-ray possibly associated with CBD.

1. PURPOSE

The main purpose of the program is to control CBD through early detection and treatment. Results from the program provide information that may help DOE identify and offer screening to other workers who may be at risk of getting CBD. Information from this program may also help evaluate the effectiveness of DOE health protection programs by revealing the number of former workers affected at each site.

The program is designed to: 1) identify former employees who were exposed to beryllium while employed at DOE sites and have subsequently developed an allergic sensitization to beryllium; 2) offer a detailed medical evaluation to former workers who are found to be sensitized or who have chest x-ray changes suggestive of CBD, for the purpose of diagnosing CBD; and 3) provide ongoing medical surveillance to former employees of DOE sites who were exposed to beryllium while employed at these sites.

2. IDENTIFICATION OF BERYLLIUM-EXPOSED FORMER EMPLOYEES

ORISE will work with DOE site Medical, Industrial Hygiene and Personnel Departments to determine the best method to identify those individuals who may have been exposed to beryllium. Deceased workers will be removed from the lists by matching Social Security Number (SSN) and or name to files maintained by Pension Benefit Information (PBI). The PBI files contain death notifications from the Death Master File of the Social Security Administration (SSA), the Railroad Retirement Board, the Office of Personnel Management (OPM), the Department of Defense, a number of state death indexes, and several proprietary sources. The PBI data base is updated monthly. Address searches will be performed for former employees not found to be deceased by matching against files maintained by Trans Union, a large credit agency. The agency provides last known address, but does not provide any credit information.

Notification letters and participation forms will be mailed to all individuals not found to be deceased for whom we obtain an address. Self-addressed, stamped return envelopes are provided to the potential participants for use in returning their participation forms. The notification letter contains information about whom to contact (an 800 number to contact the ORISE physician or project manager) if the participant has questions before returning the form. The former workers may choose one of the following levels of participation: 1) I want to participate in the BMSP for former employees, 2) I do not want to participate, but keep me on the mailing list, or 3) I do not want to be contacted at any time about this subject. Individuals requesting participation will be called to schedule a beryllium clinic visit at a location close to their home. The consent form, questionnaire, information brochures, map to the testing site, and a letter confirming the appointment will be sent to the home address after the participant has been scheduled. A BMSP staff member will call persons who provide incomplete information (no level of participation chosen) or who provide conflicting information (more than one level of participation chosen) to clarify their desired participation in the program.

3. DIAGNOSTIC TESTING

When the participant arrives at the testing location, they are greeted by an ORISE staff member who discusses the consent form, answers any questions, and witnesses their signature of the consent document. The consent document describes the purpose of the program, the Be-LPT, what will happen to medical records generated in the program, privacy and confidentiality of records, and the Beryllium Registry (which is described in Section 8 of this protocol). After consent is given, the ORISE staff member reviews the questionnaire with the participant to make sure that it has been filled-out and to obtain additional information where appropriate. Information from the questionnaire is entered into a database at a later date. A computer-generated questionnaire is provided to the participant at each subsequent testing appointment. The participant reviews the information previously provided on the questionnaire and updates information that has changed.

Participants are provided a Be-LPT through the collection of 30 ml of blood. A posterior/anterior chest x-ray with B-reader evaluation will be offered to those participants who report shortness of breath or any respiratory symptom known to be related to CBD.

A participant is considered to be sensitized if two consecutive positive Be-LPTs have been identified by the original laboratory or if two positive Be-LPTs are identified in two separate labs. This condition must exist before an individual is considered to be beryllium sensitized and is offered referral for a medical evaluation for CBD. Retesting to confirm initial positive Be-LPTs greatly diminishes the likelihood of falsely identifying individuals as being beryllium sensitized when they are not.

One-Year/Three-Year Retesting

After the initial Be-LPT is performed and if the results of this initial test are negative, a Be-LPT is offered to participants every three years (as funding is available).

More frequent testing will be offered in the following cases:

- An individual develops symptoms suggestive of CBD (participants are instructed to call anytime if they experience symptoms of CBD).

- Participants who have an abnormal x-ray possibly associated with CBD and decline further clinical evaluation will be offered a repeat Be-LPT and chest x-ray in the year following the original abnormal chest x-ray finding. If the repeat Be-LPT is normal and no changes have occurred in the chest x-ray, the individual will return to a three-year retest schedule.

- Individuals with unconfirmed positive Be-LPT results will be retested one year following the anniversary date of the positive Be-LPT. If the one-year Be-LPT result is negative the individual will return to a three-year retest schedule.

Be-LPT Quality Control Program

A quality control program will monitor the results of the Be-LPTs performed at the ORISE Beryllium Testing Laboratory and the three Be-LPT laboratories under contract. BMSP participants are selected on a random basis to assist in the quality control program by allowing extra blood to be drawn so testing can be performed in two or three labs and the results compared. Participants who volunteer to assist in this effort will have 30 or 60 ml of blood drawn in addition to the 30 ml required for one test. Blood is sent to two or three labs for all persons requiring a second test (i.e., positive, borderline positive, or uninterpretable results on the first test). The Be-LPT laboratories under subcontract have participated in the DOE-Beryllium Industry Scientific Advisory Committee (BISAC) study examining standardization of the Be-LPT.

4. RADIOGRAPHIC EXAMINATIONS

All chest x-rays taken as part of the BMSP are evaluated by board certified B-reader radiologists. Following B-reader evaluation the x-rays are returned to the BMSP physician for review and classification into three broad categories (normal or minor abnormalities not requiring medical follow-up -" A"; abnormal requiring medical follow-up, not CBD related -"B"; and abnormal,

possibly CBD related -"C"). Individuals with chest x-rays in category B, needing further medical evaluation are contacted by the BMSP physician who recommends that the individual contact their private physician(s) regarding the findings. Notification regarding the availability of additional medical services for the determination of CBD is sent by the BMSP physician, to individuals with chest x-rays in category C (possibly related to CBD).

5. CBD MEDICAL EVALUATIONS

Referrals for CBD medical evaluations are made for any of the following reasons: 1) beryllium sensitized - Be-LPT positive on two separate test dates or one test date by two laboratories; 2) borderline Be-LPT positive on three test dates; 3) single Be-LPT positive (positive only on one day at one beryllium concentration) at one or more laboratories on three test dates; 4) chest x-ray with small opacity profusion of 1/0 or greater; and 5) clinical symptoms consistent with CBD without other explanations (results from Be-LPT and chest x-ray previously found negative).

The plan for the medical evaluation will be decided by the physician who examines the participant after reviewing the preliminary test results, medical history, and after discussing options with the patient. The patient is encouraged to share the information with his/her primary care physician and family before deciding to have the evaluation. The evaluation may include: physical examination, blood work, chest x-ray, chest CT, pulmonary function tests, exercise tolerance tests, or bronchoscopy with lavage and/or biopsy.

The physician who performs the additional diagnostic tests provides a report to the referring ORISE physician based on the CBD medical evaluation findings offering an opinion of whether the participant has CBD. The BMSP provides repeat CBD medical evaluations for all sensitized participants until the diagnostic criteria for CBD for Workers' Compensation liability has been established. The medical evidence required to qualify for Workers' Compensation varies from state to state. Former workers will be referred to their site benefits office for assistance in determining eligibility for Workers' Compensation.

6. BMSP REPEAT CLINICAL EVALUATIONS

Cases of beryllium sensitization who do not qualify for Workers' Compensation are medically evaluated every 2 years unless symptoms occur before the re-evaluation date. Physicians at the medical centers under subcontract to ORISE for the diagnosis of CBD have recommended that individuals with probable cases of CBD receive annual or semi-annual repeat clinical evaluations to measure the progress of the disease and/or confirm the CBD diagnosis. The BMSP physician reviews cases on an individual basis for appropriate medical follow-up interval.

7. DATA BASE MANAGEMENT AND MEASURES TO ENSURE CONFIDENTIALITY OF PERSONALLY IDENTIFIED MEDICAL DATA

Data with attached individual identifiers is necessary to conduct the medical surveillance program so that participants may be contacted, scheduled, tested, and advised of the results of their testing. The intent to offer repeat tests at regular intervals makes it necessary to maintain the identifying information indefinitely. All medical information will be treated as confidential medical information. ORISE employees are instructed in procedures to assure the safety, security, and confidentiality of personally sensitive data. Reproduction, transmission, and/or disclosure of identifying information is prohibited. Hardcopy records containing identifying information are stored in secure areas and cabinets that are locked at the close of working hours.

ORISE personnel are briefed at the time of first employment and periodically, that any data, results, or information they may view while performing their job is not to be discussed outside the workplace. Anyone violating this rule is subject to disciplinary action up to and including dismissal. All employees sign a confidentiality agreement. Computer security receives constant attention and ORISE personnel are periodically reminded of the security policies in effect. Security items such as password protection, not leaving terminals unattended with a session in progress, password protected screen savers, etc., are discussed periodically.

Information collected for this surveillance program can be used or disclosed only as required by the Americans with Disabilities Act, the Privacy Act of 1974, or as required by court order or under another law. It would be available as the Freedom of Information or Privacy Act allows, such as to Congress, or to a second individual showing compelling circumstances affecting the health and safety of an individual. In addition, if the participant applies for a job or for insurance, they may be requested to release the records to a future employer or an insurance company.

All records collected for this surveillance program are DOE-owned records. All records that contain identifiable information are maintained within the appropriate DOE System of Records. Access to information within these systems of records is limited by the Privacy Act of 1974. Medical information is maintained in DOE-33, Personnel Medical Records. Routine uses of the identified information within this system of records includes health hazard evaluations, epidemiologic studies or public health activities performed by the Department of Health and Human Services, and health studies by federal, state and local health agencies and collaborating researchers. Use of this information for research by such agencies requires appropriate Institutional Review Board (IRB) approvals and must comply with 10 CFR 745, or where appropriate, 45 CFR part 46.

8. DOE BERYLLIUM REGISTRY

The DOE has established a Beryllium Registry to collect and maintain information on all current and former workers who are known or suspected to have been exposed to beryllium. Information to be collected includes basic facts such as month and year of birth, gender, employment dates, dates and types of exposures to beryllium, beryllium jobs, dates and results of medical tests such

as the Be-LPT or other studies recommended by physicians, and causes of death. The Registry will not contain any personally identifiable information such as names, addresses, phone numbers, or SSNs. A unique identifier will be assigned to each worker's records by the ORISE Beryllium Registry staff. The unique identifier will be used on all records sent to the Beryllium Registry. Only the ORISE physician and the Registry database administrator will be able to link the unique identifier to the worker.

The Registry was developed to help DOE understand, conduct, and improve its environmental, safety, and health responsibilities regarding past, present and future beryllium exposure effects and more effectively prevent or control future disease. Information in the Registry will assist DOE in understanding the effectiveness of its efforts to reduce exposures and related health problems by providing information on workers who were exposed to beryllium, the work environment, specific job tasks and subsequent medical problems. Information in the Registry will allow an evaluation of the health effects related to beryllium disease. For example, physicians and scientists need to learn more about CBD and the factors in the work environment that may influence the risk of developing the disease. The Registry may also be useful for studies to better understand the nature of beryllium disease. However, use of information in the Registry for studies can only occur after review and approval by the appropriate IRB(s). Researchers who are given permission to conduct studies using the information in the Registry, will not have access to personally identified information, because the Registry contains no names or similar identifiers.

9. REPORTS AND PUBLICATIONS

Summary information on the number of participants, examinations, and cases found will be used to prepare monthly progress reports. De-identified health risk information could be published in reports or submitted to peer reviewed journals for publication. Any use of data for research will conform to the requirements of the Federal Regulation 10 CFR 745, Protection of Human Subjects. Project participants will be provided summary health risk information in periodic newsletters and other formats.

ADDITIONAL INFORMATION

DEFINITIONS

Abnormal Chest X-ray (possibly associated with CBD) - Posterior/anterior chest x-rays are evaluated according to the International Labor Organization (ILO) classification system for radiographs of pneumoconioses by board certified radiologists who are certified B-readers. The presence of noncaseating granulomas and/or mononuclear infiltrates is consistent with CBD. The profusion of small opacities is used to determine individuals who might have noncaseating granulomas. The abnormal profusion of small opacities is defined as profusion greater than or equal to 1/0 by the ILO classification.

Beryllium Sensitized - Sensitization is determined by the following criteria: Blood Be-LPT confirmed positive (a "confirmed" positive requires the blood Beryllium Lymphocyte Proliferation Test (Be-LPT) to be positive at 2 different laboratories from the same blood draw or at the same laboratory on consecutive blood draws); blood Be-LPT unconfirmed positive with more than one additional borderline or single positive result; multiple (more than 2) unconfirmed blood Be-LPT positives; or the beryllium skin patch test positive.

Chronic Beryllium Disease - CBD is a chronic granulomatous disorder of the lungs following the inhalation of beryllium in which a specific cell-mediated immune response plays a central role. The pathogenesis of CBD is believed to be a cell-mediated hypersensitivity reaction to beryllium bound to tissue proteins.

In the DOE BMSP, the following diagnostic criteria have been established.

Chronic Beryllium Disease, C - Blood Be-LPT confirmed positive, lung Be-LPT positive, and lung biopsy shows granulomas. Exceptions: Other criteria met, but biopsy shows single granuloma or micro granuloma. Lung Be-LPT negative, but biopsy shows granulomas and disease has progressed sufficiently that treatment is required, with no other explanation for the lung findings.

Chronic Beryllium Disease, B - Positive blood and lung Be-LPTs, plus evidence of lung pathology that cannot be explained by another disease process after thorough clinical evaluation. The evidence of lung pathology may include: 1) biopsy shows a lymphocytic process consistent with CBD; 2) computerized axial tomography (CT) scan shows changes consistent with CBD; or 3) pulmonary function or exercise testing shows pulmonary deficits consistent with CBD. Blood and lung Be-LPT negative, but patch test positive and biopsy shows granulomas or biopsy shows other findings consistent with CBD; with additional pulmonary findings not explained by another disease process. Blood Be-LPT positive, lung Be-LPT negative, biopsy shows granulomas, and other pulmonary findings are present not explained by another disease after thorough evaluation.

Chronic Beryllium Disease, A - Blood Be-LPT confirmed positive, lung Be-LPT positive, and biopsy: 1) not done; 2) negative; or 3) explained by another pulmonary condition. Positive blood Be-LPT, negative lung Be-LPT, and biopsy showing granulomas or other findings consistent with CBD, but without other pulmonary findings (unless explained by another disease).

Medical Evaluation Referrals for Chronic Beryllium Disease - Referrals for CBD medical evaluations are made for any of the following reasons: 1) beryllium sensitization - Be-LPT positive on two separate test dates or on a single test date by two laboratories; 2) borderline Be-LPT positive on three test dates; 3) single Be-LPT positive (positive only on one day at one beryllium concentration) at one or more laboratories on three test dates; 4) chest x-ray with small opacity profusion of 1/0 or greater; and 5) clinical symptoms consistent with CBD in a patient with no other explanation for the symptoms, even if results from Be-LPT and chest x-ray previously found negative.