

PROTOCOL
FORMER BERYLLIUM WORKERS MEDICAL SURVEILLANCE PROGRAM (BMSP)
OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION (ORISE)
OAK RIDGE, TENNESSEE

ABSTRACT

The ORISE BMSP is composed of five interrelated tasks and includes the identification, notification, scheduling, 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 falling under the ORISE BMSP will be obtained and appropriate ORISE BMSP notification letters and participation forms will be sent to former employees designated as having had the opportunity for exposure to beryllium. All individuals indicating a desire to participate in the ORISE BMSP are tested for sensitivity to beryllium, and given a chest x-ray. Further medical evaluation to determine the presence of Chronic Beryllium Disease (CBD) is offered to those identified as beryllium sensitized or who have suspicious lung pathology on chest x-ray B-Reader examination. Retesting is offered once every three years to former employees previously tested for sensitivity to beryllium who were found to have normal test results. In addition, retesting is offered every year to former employees who had a positive blood test for sensitivity to beryllium that was not confirmed or who had an abnormal chest x-ray possibly associated with CBD. A BMSP Registry will be maintained for all individuals tested under the ORISE BMSP. The BMSP Registry, a Microsoft Access 97 computer database, will contain relevant demographic information for each participant, along with the results of beryllium sensitivity screening and/or CBD medical evaluations, their occupational work histories, and other information pertinent to the analysis of health studies data.

1. PURPOSE

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 determine the prevalence of CBD in those individuals identified as sensitized to beryllium or who have changes in their chest x-ray suggestive of CBD; and 3) provide ongoing medical surveillance to former employees of DOE sites who were exposed to beryllium while employed at these sites.

2. 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, which 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 - Blood BeLPT confirmed positive (A “confirmed” positive requires the blood Beryllium Lymphocyte Proliferation Test (BeLPT) to be positive at 2 different laboratories from the same blood draw or at the same laboratory on consecutive blood draws.) Blood BeLPT unconfirmed positive with more than one additional borderline or single positive result. Multiple (more than 2) unconfirmed blood BeLPT positive. 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 ORISE BMSP, the following diagnostic criteria have been established.

Chronic Beryllium Disease, CONFIRMED - Blood BeLPT confirmed positive, lung BeLPT positive, and lung biopsy shows granulomas. Exceptions: Other criteria met, but biopsy shows single granuloma or micro granuloma. Lung BeLPT 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, PROBABLE - Positive blood and lung BeLPT's, 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 BeLPT 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 BeLPT positive, lung BeLPT negative, biopsy shows granulomas, and other pulmonary findings are present not explained by another disease after thorough evaluation.

Chronic Beryllium Disease, POSSIBLE - Blood BeLPT confirmed positive, lung BeLPT positive, and biopsy: 1) not done; 2) negative; or 3) explained by another pulmonary condition. Positive blood LPT, negative lung 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 - BeLPT positive on two separate test dates or on a single test date by two laboratories; 2) borderline BeLPT positive on three test dates; 3) single BeLPT 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 BeLPT and chest x-ray previously found negative.

3. IDENTIFICATION OF BERYLLIUM EXPOSED EMPLOYEES

ORISE will work with DOE site Medical, Industrial Hygiene and Personnel Departments to determine those individuals who may have had the opportunity for exposure to beryllium while employed. Vital status searches will be performed on all former employees so identified. Address searches will be performed for former employees thought to be alive. Notification letters and participation forms will be mailed to all of these individuals. Individuals requesting participation will be screened by the ORISE BMSP Project staff regarding their potential opportunity for exposure to beryllium while employed at DOE sites. For individuals having a questionable history of beryllium exposure the ORISE BMSP project manager will contact the individual to discuss their concern regarding beryllium exposure, and to resolve the need for health surveillance testing.

4. DIAGNOSTIC TESTING & CBD MEDICAL EVALUATIONS

Individuals participating in the ORISE BMSP are provided a BeLPT through the collection of 30 ml of blood (60 ml - 90 ml for quality assurance purposes), and a posterior/anterior chest x-ray with B-reader evaluation. After the initial BeLPT is performed and if the results of this initial test are negative, a BeLPT is offered every three years with the following exceptions: 1) current work activities have the potential for exposure to significant levels of beryllium, i.e., above ambient airborne levels; 2) individual develops symptoms suggestive of CBD; 3) individual has chest x-ray findings possibly associated with CBD for which no definitive diagnosis is reached; and 3) BeLPT positive or borderline results not confirmed by a confirmational BeLPT. For these three exceptions a BeLPT is offered annually.

Referrals for CBD medical evaluations are made for any of the following reasons: 1) beryllium sensitized - BeLPT positive on two separate test dates or one test date by two laboratories; 2) borderline BeLPT positive on three test dates; 3) single BeLPT

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 BeLPT and chest x-ray previously found negative).

BeLPT Quality Control Program

A quality control program was designed to monitor the results of the BeLPTs performed at ORISE Beryllium Laboratory and the three BeLPT laboratories under contract. ORISE BMSP participants are selected on a random basis to submit quality control blood specimens. Quality control blood specimens are drawn from ORISE BMSP participants selected on a random basis, and sent to two laboratories (60 ml of blood drawn) or three laboratories (90 ml of blood drawn). Confirmational blood specimens are drawn for individuals with an initial positive BeLPT, a borderline positive BeLPT, or an uninterpretable BeLPT are treated in the same manner as quality control specimen individuals and blood specimens are sent to either two or three laboratories.

The BeLPT laboratories under subcontract have participated in the DOE-Beryllium Industry Scientific Advisory Committee (BISAC) study examining standardization of the BeLPT. Work is continuing on laboratory procedure standardization, but a “standard” value for determining a positive BeLPT stimulation index value was established at 3.0 by the DOE-BISAC study. This should allow for comparison of BeLPT results between laboratories to be made more easily.

“False-Negative” BeLPTs

A false-negative BeLPT is defined (in the ORISE BMSP) as a BeLPT for which a confirming negative BeLPT result is not obtained by either the original BeLPT laboratory identifying the negative BeLPT result or by the quality control laboratory.

“False-Positive” BeLPTs

A false positive BeLPT is defined (in the ORISE BMSP) as a BeLPT for which a confirming positive BeLPT result is not obtained by either the original BeLPT laboratory identifying the positive BeLPT result or by the quality control laboratory.

The calculation of a false positive rate is based on the premise that a positive BeLPT is a “true” positive and that a negative BeLPT is a “true” negative. If the BeLPT result for an individual is negative it is assumed to be a “true” negative, and no confirming BeLPT is required to validate the negative result.

Because of the potential for false positive BeLPT results, a beryllium sensitized individual is identified as one in whom two consecutive positive BeLPTs have been identified by the original laboratory or a quality control laboratory. This condition must exist before an individual is considered to be beryllium sensitized and is referred for a medical evaluation for CBD. Retesting to confirm initial positive BeLPTs greatly diminishes the likelihood of falsely identifying individuals as being beryllium sensitized when they are not.

One-Year/Three-Year Retesting

A repeat BeLPT and a chest x-ray is offered to former employees who have previously had a negative BeLPT result and who have not been tested for three years or more. Retesting every three years will continue, as funding is available. Employees who have received an abnormal x-ray possibly associated with CBD and have declined clinical evaluation will be offered a repeat BeLPT and chest x-ray in the year following the original abnormal chest x-ray finding. If the repeat BeLPT 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 BeLPT results will be retested one year following the anniversary date of the positive BeLPT. If a negative BeLPT result is returned the individual will return to a three-year retest schedule

Beginning in November 1996, as instructed by the Department of Energy (EH-61), the ORISE BMSP will not routinely offer chest x-rays to all participants. Individuals who are first time participants will receive a chest x-ray with B-reader review. Individuals who have participated in the program previously and had no findings that would be possibly related to CBD will not be offered a chest x-ray as part of their three-year follow-up testing. However, individuals who have participated in the past and had a chest x-ray with findings possibly related CBD will continue to receive a chest x-ray on retesting. Likewise, individuals who have had single positive or borderline BeLPT results that were not confirmed will be offered a chest x-ray when they are retested. Individuals with new pulmonary symptoms will be offered a repeat chest x-ray.

5. RADIOGRAPHIC EXAMINATIONS

Radiology Review

All of the chest x-rays taken as part of the ORISE BMSP are evaluated by board certified B-reader radiologists. Following B-reader evaluation the x-rays are returned to the ORISE 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 after B-reader evaluation reported as having abnormal findings unrelated to CBD ("B"), but of a nature that

warranted further medical evaluation are contacted by the ORISE BMSP physician who recommends that the individual(s) contact their private physician(s) regarding their x-ray findings.

Notification regarding the availability of additional medical services for the determination of CBD is sent by the ORISE BMSP physician, for individuals with chest x-rays after B-reader evaluation reported as having abnormal findings ("C") possibly related to CBD.

6. ORISE BMSP REPEAT CLINICAL EVALUATIONS

Under the direction of DOE/EH-61 the ORISE BMSP provides repeat CBD medical evaluations for all probable cases of CBD until the diagnostic criteria for CBD for Workers' Compensation liability have been established. In general, to be admitted under Colorado Workers' Compensation for CBD, the following is required: 1) a work history with the potential for beryllium exposure; 2) evidence of beryllium sensitization; 3) a positive lung lavage BeLPT; 4) histologic evidence of pulmonary granulomatous disease; and 5) evidence of symptomatic disease and/or treatment for CBD.

Cases of beryllium sensitization are medically evaluated every 2 years. 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 ORISE BMSP physician for appropriate medical follow-up reviews cases on an individual basis.

7. BMSP REGISTRY

A BMSP Registry computer database of all individuals tested under the ORISE BMSP will be maintained. The Registry will contain relevant demographic information, test results, occupational work histories, and other information pertinent to the analysis of health studies data. In addition to the computer registry, hard copy files are maintained

8. PRIVACY AND CONFIDENTIALITY OF IDENTIFIED DATA

The confidentiality of identified information maintained by DOE in the Beryllium Registry is protected under the Privacy Act of 1974. Personal identifiers will not be published in any reports generated from the DOE Beryllium Registry. Although the privacy and confidentiality of the data will be protected under most circumstances,

access to or release of an individual's records could be required under court order or DOE directive. Also, if an individual is still working with beryllium but for medical reasons it is recommended that the individual be transferred to an area where there will be no contact with beryllium, the personnel department and supervisor will be notified. Specific test results will not be released, but because of the work area restrictions, they may assume that the individual is sensitized to beryllium or has CBD.

(revised 10/20/99)