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Rachel P. Leiton, Director
Division of Energy Employees Occupational Illness Compensation
Office of Workers' Compensation Programs
U.S. Department of Labor, Room C-3321
200 Constitution Avenue NW
Washington, DC 20210

Dear Ms. Leiton:

We are writing this letter to express our concern that some Department of Energy workers with beryllium sensitization and chronic beryllium disease are not currently being recognized by the Department of Labor under the current definition of beryllium sensitivity, defined as an "abnormal beryllium lymphocyte proliferation result (BeLPT) performed on blood or lung lavage cells". Based on several lines of research, it is our medical opinion that the combination of three borderline BeLPTs is also evidence of an immune response consistent with sensitization to beryllium. This opinion is recognized in medical guidelines and by experts in the medical community. Several government agencies have already included 3 borderline BeLPTs as evidence of an immune response to be beryllium, consistent with beryllium sensitivity. Below, we outline the evidence that supports our strong recommendation that the combination of three borderline BeLPTs be added to the Department of Labor definition of beryllium sensitivity.

Dan Middleton, MD from the Agency for Toxic Substances and Disease Registry (ATSDR) published a paper in 2011 examining the predictive value of abnormal and borderline test combinations (Middleton et al, 2011). Dr. Middleton used the data that Oak Ridge Associated Universities had compiled from the DOE former worker programs. His manuscript concluded that, based on modeling, three borderline results predicted BeS (91% positive predictive value, at a population prevalence of 2%) which was similar to the predictive value of an abnormal and borderline test result combination. Middleton and authors concluded, based on this 2011 paper and a previous paper from 2008, that the definition of "confirmed positive" should include two abnormal results, an abnormal and a borderline test result, and/or three borderline tests. This recommendation is based on the studies which showed that these other two combinations (AB/BL and BL/BL/BL) result in a positive predictive value (PPV) similar to two abnormal test results and are an equal predictor of BeS. At a 2% prevalence of BeS/CBD in the population, test result combinations predicted BeS as follows: (a) 1 AB (55%); (b) 3 BL (91%); (c) 1 AB + 1 BL (94%); (d) 2 AB (98%); (e) 1 AB + 2 BL (99%); (f) 2 AB + 1 BL (100%); and (g) 3 AB (100%).

As a result, once a person has three borderlines, we recommend that they be afforded the same follow up for others with beryllium sensitivity as per the DOL. Based on the results of the two Middleton studies, the combination of three borderline results is acknowledged as BeS and is an indication for referral for clinical evaluation for CBD by physician groups and government agencies.

- The Energy Facility Contractors Group (EFCOG) included 3 borderline results in their 2008 BeLPT algorithm for DOE site occupational medicine directors as a criterion for CBD clinical evaluation.
- The ATS statement on beryllium acknowledged that three borderline BeLPTs may indicate BeS (Balmes et al, 2014).
- Washington State Department of Labor and Industries uses three borderline tests as evidence of BeS (L&I, 2015).
- The revised Occupational Safety and Health (OSHA) beryllium rule passed in 2017 also acknowledges three borderline tests as beryllium sensitization (OSHA 2017). Using the Middleton 2011 study, OSHA reasoned as follows:

“This study further demonstrates the value of borderline results in predicting beryllium sensitization using the BeLPT. OSHA finds that multiple, consistent borderline BeLPT results (as found with three borderline results) recognize a change in a person’s immune system to beryllium exposure” (p 2501). OSHA defined a confirmed positive BeLPT as follows: “Confirmed positive means the person tested has beryllium sensitization, as indicated by two (either consecutive or non-consecutive) abnormal BeLPT test results, an abnormal and borderline test result, or three borderline test results” (p 2736).

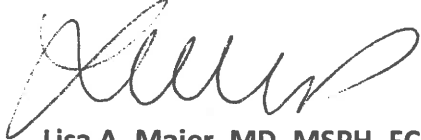
To evaluate the clinical relevance of 3 borderline BeLPTs, we performed a retrospective study of patients who presented to National Jewish Health for diagnostic evaluation with a history of three borderline and no abnormal BeLPTs. This was published in an abstract and presented at the 2012 American Thoracic Society (ATS) international conference (Mayer et al, 2012). We identified eight patients who were evaluated due to three borderline BeLPTs. Five of eight had evidence of sensitization or disease: 1 had CBD (granulomas on biopsy and abnormal BAL BeLPT); 2 had confirmed BeS (abnormal blood/BAL BeLPT); 2 had granulomas on biopsy (probable CBD); and 3 had no abnormal findings on clinical evaluation. Importantly, it should be noted that the combination of three borderline BeLPTs is rare, both in our clinical experience as noted above, as well as in a large former worker screening program. Over the course of screening greater than 14,000 workers over 10 years, only 7 were found to have this unusual combination, less than 0.2%.

The Department of Labor has appropriately cast a wide net, by recognizing beryllium sensitivity, defined currently as a single abnormal BeLPT. Based on the data above, we strongly recommend that Department of Labor recognize the combination of 3 borderline BeLPTs in addition. This is not only medically appropriate, but also consistent with the definition implemented already by national and international medical groups: American Thoracic Society (ATS); Energy Facility Contractors Group (EFCOG); Washington State Department of Labor and

Industries; and the Occupational Safety and Health Administration (OSHA) in the 2017 beryllium rule. We strongly recommend the Department of Labor update its definition of beryllium sensitivity to include the combination of 3 borderline BeLPTs. Most importantly, these individuals need to be provided coverage for long term follow up to determine if they progress to CBD, and medical treatment for CBD once they do.

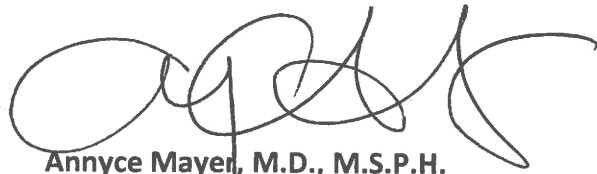
Please let us know if we can provide you any additional information or data regarding this important issue.

Sincerely,

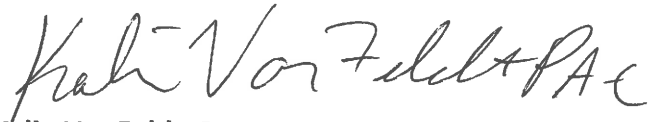


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