

Peer Reviewer Comments
NIOSH Alert: Preventing Beryllium Sensitization and Chronic Beryllium Disease

- 1- Looks good. Small comments noted in document.
- 2- This Alert is needed because CBD remains a difficult occupational disease to prevent. The Alert is very well written, easy to understand, and provides valuable information to workers and employers about CBD. This is an excellent Alert and I look forward to seeing the release of the final version.
- 3- National Jewish supports NIOSH in its efforts to advise employers and workers of the risks of beryllium exposure. Reduction of exposures is currently the most effective means of reducing risk of sensitization and disease. More emphasis on industrial hygiene measures and the use of these measures to reduce risk is needed.
- 4- NIOSH should not be afraid to take a firm public health stand with respect to beryllium exposure; the scientific evidence supports it. The Alert should use authoritative language that indicates there is no known safe exposure limit for beryllium.
- 5- In the second column, the following bulleted statement is made: “Keep inhalation exposure ...” It is difficult to understand the concept that the recommended standard may not be sufficiently protective for all workers. Although I struggled with a better way to say this, I could think of no better way than what is stated.
- 6- Workers: Warning Box: Workers exposed to particles or fumes from beryllium containing materials ARE at risk for developing beryllium sensitization and chronic beryllium disease.
- 7- Add “wear eye protection” [Keep beryllium-containing dusts...].
- 8- Add “work related rash” [Seek medical attention for...].
- 9- Add another bullet: Workers should look for beryllium identification on all materials and should question any metals that are likely to have beryllium associated with them.
- 10- Employers: Bullet 1: Add: All beryllium or beryllium-containing materials should be labeled as beryllium material as soon as it enters the facility. The label should be conspicuous and easily identified by workers.
- 11- Should include much stronger wording. For example: Beryllium Safety Training Programs should be required. Bullet 4: INSERT: ‘beryllium-containing materials’, through specific training sessions and interim updates.
- 12- Bullet 5; INSERT: “and collect both process specific and personal exposure data to document levels of exposure to which workers are exposed during processing.”
- 13- : Also state the DOE limit of 0.2 ug/m³ in this bullet. Communicate that sensitization and disease has been reported to occur even below the REL (Kelleher, 2001; Henneberger, 2001). The NIOSH REL was not proposed as protective for CBD. We question whether it should be used in this document, as it is probably not protective for beryllium related health effects. We suggest that inhalational exposures should be kept below the DOE recommended exposure limit of 0.2 ug/m³.
- 14- Change to: “Protect workers’ lungs and skin...”
- 15- Add: As much as possible, the areas of the plant in which beryllium is used should be limited and marked. These areas should not be provided with compressed air and should be cleaned using dustless method. Add another bullet about cleaning: Any machinery in which beryllium is used should be marked as such and cleaning must be accomplished without the use of compressed air and in such a manner so as to reduce the production of dust during cleaning. Add a bullet which says to avoid cleaning with compressed air, dry sweeping, or other dust generating

methods. Add another bullet: Employers have a responsibility to monitor for beryllium exposure at regular intervals.

16- Conduct medical surveillance of all workers in beryllium-using facilities. Indicate that medical monitoring should rely on the BeLPT. This final bullet should also include: “link medical surveillance data to industrial hygiene data to identify areas of high risk”. Add more explanation in the final bullet to explain that the breadth of an at-risk group should include direct, and indirect (bystanders) and incidentally exposed groups [e.g. construction trades, dust disturbers.] This bullet should be the first of this section, not the last. Last bullet: Add to the end... “as well as those who may be exposed to beryllium in the ambient air.”

17- In some workplaces the workers will need to be more proactive about PPE. “When advised to do so” will not be enough in this setting.

18- Not just any gloves will provide adequate protection. Note that up front here. Details latter or use website reference.

19- How do you do this? Need a website ref. For lessons learned at Brush or Speedwell for example (Quebec?)

20- What is medical surveillance? This needs at least a reference to DOE Rule or some other acceptable program using the LPT. Is there a NIOSH website where this is outlined?

21- Employers, 8th bullet: Not just any gloves will provide adequate protection. Note that up front here. Detail latter or use website reference.

22- Employer, 12th bullet: What is medical surveillance? This needs at least a reference to DOE Rule or some other acceptable program using the LPT. Is there a NIOSH website where this is outlined? Give guidance on frequency. Our work supports 3 yr interval (Judd N, Griffith W, Takaro TK and Faustman EM. A Model for Optimization of Biomarker Testing Frequency to Minimize Disease and Cost: Example of Beryllium Sensitization Testing. Risk Analysis 23: 1211-1220, 2004).

23- Change sentence structure: “Development of sensitization and disease requires exposure to beryllium and is affected by both job tasks and, in some workers, by genetic factors. Some jobs or tasks involve exposures that increase the risk of sensitization and disease. Some people have inherited genes that make them more likely to become sensitized or to develop chronic beryllium disease when exposed. Significant risks exist for not only those who work directly around beryllium (machinists), but also for those with bystander or brief, incidental exposures, such as managers, and construction trades workers.” NOTE: *Genetic factors should not precede exposure as that would overstate the importance of genetics and may lead people to think that exposure control is ineffective in reducing disease.*

24- Add business contacts, beryllium distributors and the press to the list of information providers.

25- It is noted that all beryllium-containing materials are associated with CBD. Is this true for beryllium ores as well? If so, then it might be mentioned.

26- The following sentence is wordy and difficult to understand: The risk for workers in other...” How about simplifying to “The risk for workers in other industries depends on potential exposure of their lungs and skin to dust particles, fumes, and beryllium-containing solutions and suspensions.”

27- The small amount of clinical published literature on skin exposure does not support the emphasis and amount of information presented in the document.

28- Page 1, Bullet 4 [An alloy or mixture...] should be moved up in to just beneath bullet 1 [Extraction compounds...] A comment should be added to indicate that work with alloys

represents the vast majority of exposures in the USA. Also include specific examples of the alloys including Be-aluminum, Be-cu, Be-Ni, Be-Mg.

29- Page 2, 1st paragraph: line 6 and 7 – We recommend strengthening the statement about risk by removing the “might.” Consider changing the sentence to “...but health risks exist if beryllium-containing material...”: Would also add a sentence to end: “Even some exposures to low percentage alloys can cause beryllium sensitization and chronic beryllium disease.”

30- Page 2, 3rd paragraph: Consider changing the first sentence to read: “Workers who machine, refine, and prepare beryllium and beryllium-containing materials are at greatest risk for developing disease”. NOTE: (*Rates in alloy-using operations can be just as high and are a more important public health issue.*) Last sentence: REMOVE beryllium-containing solutions and skin from last sentence. Again, this seems to be an overemphasis of the skin issue.

31- 4th paragraph, 1st sentence: “Some production jobs” INSERT [e.g. machining] have high rates of beryllium disease. Add construction trades workers to the list of incidentally exposed workers who develop disease.

32- 5th paragraph: The first sentence is reasonable. However, lack of clinical peer review published literature confirming the skin data or directly linking it to sensitization makes such detailed description of the findings inappropriate at this time. The following 14 lines should be removed (mice and corpse skin data). This paragraph should conclude with “Although research is continuing, we suggest that workers lessen the risk of sensitization by preventing tiny beryllium particles or solutions containing beryllium from contacting the skin...”

33- Page 2, column 2, line 14 which reads “...we suggest that workers lessen the risk...” Change to read: “...we recommend that employers implement steps to lessen workers’ risk of sensitization by preventing tiny beryllium particles...”

34- Some chemical test kits (e.g. swimming pools) have BeSO₄ in liquid concentrations up to 5%.

35- Add after located, “and where the disease process can begin (see below).”

36- Marked paragraphs 2 and 4 and wrote “include BeLPT on lavage cells?”

37- The sentence “In addition to exposure...” is redundant with the sentence “Recent research at NIOSH suggests that sensitization ...” at the bottom of column 1 on page 2. Perhaps one of these should be deleted.

38- I have several very small but very significant edits on page 3. I do not believe current data allow prediction that most sensitized workers develop CBD. More to the point, it is not evident how often “CBD” diagnosed in asymptomatic people actually progresses!!

39- Last paragraph, 1st sentence: change “whether all” to “what fraction of.”

40- Last paragraph, 2nd sentence: change “many” to “some.”

41- Move up sentence three [The risk of sensitization...] to start off the paragraph.

42- REMOVE the sentence beginning with “A person’s immune system.” This suggests that the worker is responsible for sensitization, not the exposure.

43- Consider removing sentence beginning with “In addition to exposure to beryllium by breathing, recent research...” due to the paucity of published data in this area.

44- Page 3, 2nd paragraph, 2nd sentence: Sentence should be changed to read: “However, a person must first be sensitized to develop the lung scars (called granulomas) of chronic beryllium disease.”

45- Page 3, 3rd paragraph: Consider moving the section about lung biopsy to the section on Chronic Beryllium Disease.

46- Page 3, 3rd paragraph: Add to end of paragraph: “Other tests can also help make the diagnosis.”

47- These sections give no context or perspective as to the likelihood of progression from exposure to sensitization to subclinical CBD to clinical CBD. This is what most folks want to know. Instead, it gives the reader the impression that even touching a product with beryllium in it will likely cause disease. This simplistic ‘rote algorithmic determination,’ i.e., the 100% inevitable, direct progression of exposure to a molecule of beryllium to clinical disease, is neither accurate nor fair to the worker. In fact, most of those who test positive do not progress to clinical CBD, but this important contextual information is not related whatsoever in the document. If I were a concerned worker, I would most certainly want this information to both contextualize my BeLPT results and to give me perspective in regard to my personal chances of getting the disease. Thus, in my opinion these sections, ‘as is,’ are overly alarmist and lack context and perspective. The sections lack even a basic discussion of the limitations of medical surveillance (I am assuming the use of the BeLPT). To serve that document’s purpose of ‘informed consent,’ the worker deserves to know the whole story. There is available information known about these statements which could be used to better qualify them for the reader. Please refer to the report by Steven H. Woolf, MD, MPH, particularly in regard to sensitization, the use of the BeLPT, and its limitations. In addition, the document neglects to even mention that the invasive follow-up testing advocated, based on results of the ‘iffy’ BeLPT, a lung biopsy, has inherent risks which albeit are rare, but certainly not benign—bronchospasm, hemorrhage, pneumonia, pneumothorax. Again, to serve the document’s purpose of ‘informed consent,’ the worker deserves to know the whole story. The document glosses over entirely that medical testing and the results may have a real impact and even cause negative repercussions on their job and ability to retain medical insurance, as well as real risks to privacy and confidentiality. In the interest of better serving the worker with a more complete disclosure of the significant benefits, risks, and potential harms of medical testing and surveillance, I suggest that the “Case Reports” be eliminated and a section devoted to this be substituted.

48- Last paragraph, change “usually” in second line to “verify”

49- 3rd paragraph, 3rd sentence: change “when” to “if” and insert “may” before “cause chronic chest...”

50- Last paragraph, first sentence: Delete the first word “The.”

51- 1st paragraph: After first sentence, INSERT a frequency of disease or risk of developing disease such as: “The risk of developing chronic beryllium disease is 1/100 to 20/100 depending on the circumstances of exposure.”

52- 3rd paragraph, first sentence, REMOVE: very. The range of progression varies from months to years.

54- 3rd paragraph, after second sentence ending “. . . has lung disease.” INSERT: “Doctors may mistake CBD for other lung conditions that imitate CBD, such as sarcoidosis, lung fibrosis, or asthma.”

55- 4th paragraph, first sentence, INSERT “CBD is an incurable illness, however”, the symptoms and lung function abnormalities usually respond . . .

56- 4th paragraph, last sentence INSERT after ...progressive lung damage, “or slow the rate of clinical deterioration. Despite available treatment, workers today still die from this disease.”

Line 3, Change to read: “This research ~~can be used~~ may help to develop exposure standards to protect all workers, to study laboratory animals...”

58- Although genetics is a contributing factor to the development of CBD, characteristics of dust and fume exposure are the most important aspects of susceptibility to disease. Without exposure, individuals with genetic susceptibility factors do not develop disease. The genetic risk might be de-emphasized.

59- Before discussing genetic factors there should be a section on Exposure Factors: This paragraph should discuss process related risk, machining generating small particles, inhalation of submicron particles in the deep lung, particle size, surface area. There are NIOSH studies that have looked at all of these things. The paper by Martyny et al, regarding particle size from machining aerosols was funded by a NIOSH cooperative agreement. Again the emphasis should be on exposure, not genetics.

60- 1st sentence, REMOVE: or less The published literature on “protective” genes is limited. Thus far in the document, no mention has been made of a protective effect, and it is confusing to the audience.

61- REMOVE 3rd sentence “This research...” This sentence overreaches our ability in the near future.

62- The last sentence may be difficult to understand: Consider this: “This is because the genes linked to sensitization and disease are found in a large percentage of the population and beryllium sensitization and **chronic beryllium disease have developed in workers who do not have these genes.**”

63- It is stated that “genetic research can be used to develop exposure standards to protect all workers...” I’m not sure this is true. And, I believe this to be a controversial topic. I think this statement should be removed and it simply said that “This research can be used to study laboratory animals for ways to prevent sensitization and disease and to explore new treatments for sensitization and disease in affected workers.”

64- Second sentence, CHANGE TO: “It occurred after high exposure to airborne beryllium.”

65- Following last sentence INSERT: “At high levels of exposure, acute bronchitis, tracheitis, nasal perforation, and conjunctivitis can occur”

66- After sentence 1, add: “The U.S. Health and Human Services’ National Toxicology Program lists beryllium as a known human carcinogen.” Reference: 10th Report on Carcinogens, December 2002.

67- Add a last sentence stating 0.5 ug/m³ will not be adequate to protect all workers, but it will lead to some risk reduction. There should be some mention of ALARA in this section.

68- Change sentence 2 to read: Current research suggests, however, that there may not be a safe exposure level for beryllium. OR Current research suggests, however, that there may not be an exposure limit for beryllium that will protect all workers.

References:

NIOSH Comments to DOE, March 9, 1999 (attached) which state “...NIOSH concurs with the DOE conclusion that the current PEL of 2 ug/m³ has not eliminated chronic beryllium disease and sensitization to beryllium, and the disease has occurred in workers exposed to levels lower than the detection limit”. (emphasis added)

Kelleher PC, Martyny JW, Mroz MM et al. Beryllium particulate exposure and disease relations in a beryllium machining plant. J Occup Environ Med. 2001; 43:238-49.

Henneberger PK, Cumro D, Deubner DD, Kent MS, McCawley M, Kreiss K. Beryllium sensitization and disease among long-term and short-term workers in a beryllium ceramics plant. Int Arch Occup Environ Health. 2001; 74:167-176.

Infante PF, Newman LS. Beryllium exposure and chronic beryllium disease. *The Lancet*. 2004; 363(9407):415-416.

69- 1st paragraph, 2nd sentence: After “However” add “workers are known to get beryllium disease at these levels.”

70- Change first sentence to read: “Multiple published studies conducted by NIOSH and others have shown that this OSHA standard is not adequate to protect all workers.”

71- Add the STEL of 10 ug/m³ under the ACGIH Standard.

72- Change sentence two to read: DOE ~~recently~~ lowered its beryllium exposure action limit (8-hour TWA) in 1999 to one-tenth of its former level...

73- First sentence following “use of respiratory protection,” INSERT medical surveillance using the BeLPT.

74- Revise sentence 1 to read: OSHA has stated that its current beryllium exposure standard does not adequately protect beryllium-exposed workers from developing chronic beryllium disease.

References: Letter from Assistant Secretary Charles N. Jeffress to Peter Brush, Acting Assistant Secretary for Environment, Safety and Health, U.S. Department of Energy, August 27, 1998. (Attached).

OSHA [2002] Request for Information. *Federal Register*. 67:70707 (November 26, 2002). Letter from Lee Newman to Jacqueline Rogers, DOE (March 3, 1999). “The current permissible exposure limit for beryllium of 2ug/m³ over an 8-hour working day and a never-to-be-exceeded peak concentration of 25 ug/m³ does not protect exposed workers from developing chronic beryllium disease.

75- Page 5, 1st paragraph, INSERT after last sentence: “Industrial hygiene evaluation was conducted and allowed the identification of high risk areas” (Kreiss papers from Tucson and Elmore; Henneberger paper; Martyny JOEM 1999, Kelleher JOEM 2001).

76- 1st paragraph, last sentence: Is it correct to say all workers with BeS and CBD left employment? Don’t some still work there?

2nd paragraph: In the discussion of rates among short and long term workers, as length of follow-up increases, rates of disease will change. This should be acknowledged. This is discussed again later in the paragraph and the differential in follow-up should be addressed.

77- Re: “In the past, physicians had...” This sentence reads funny—sets the reader up as if the past said X, but the future says Y. 1999 isn’t so “past”

78- REMOVE sixth sentence “Sensitization testing...” This is confusing and is not fact but subjective interpretation.

79- INSERT following last sentence: “Other industries in which cases of BeS and CBD have been reported in the medical literature include recycling, precision machining, jewelry making, and aircraft manufacture.

80- 2nd sentence should be changed to read: More action is needed to (1) improve protective measures for workers exposed to beryllium (2) reduce/minimize both overall exposures, and also the numbers of workers handling beryllium (3) educate workers about the hazards of working with beryllium (4) determine how characteristics of exposures [i.e. particle size, shape, surface area, chemical form] are related to increased risk (5) identify industrial sectors and businesses that use beryllium. REMOVE current (2) and (3) they are too research oriented for the audience NIOSH wishes to target for this health alert.

81- Revise sentence 2 to read: More stringent worker exposure limits are needed to protect workers from beryllium-related respiratory disease. More research is needed to (1) develop...

82- The Appendix might include a few additional industries and jobs. I recommend considering the following: a) machining: manufacturing various machined products from beryllium and

beryllium alloys. b) Beryllium refining: extraction of beryllium from ores and production of beryllium metal and various alloys. c) Mining: ore recovery from beryllium containing minerals. d) Beryllium milling: production of rods, wire, tubes, rolls, and foundry castings from beryllium containing alloys.

83- Add;

Martyny JW, Hoover MD, Ellis K, Mroz MM, Bucher Bertelson B, Maier LA, Newman LS. *Characterization of beryllium aerosols generated during machining operations*. Journal of Occupational and Environmental Medicine 2000; 42:8-18.

Kelleher PC, Martyny JW, Mroz MM, Maier LA, Ruttenber JA, Young DA, Newman LS. *Beryllium particulate exposure and disease relations in a beryllium machining plant*. Journal of Occupational and Environmental Medicine 2001; 43(3):238-249.

Henneberger PH, Goe SK, Miller WE, Doney B, Groce DW, *Industries in the United States with Airborne Beryllium Exposure and Estimates of the Number of Current Workers Potentially Exposed*. Journal of Occupational and Environmental Hygiene, 2003 1:648-59.

Stange AW, Hilmas DE, Furman FJ, Gatcliffe TR, *Beryllium Sensitization and Chronic Beryllium Disease at a Former Nuclear Weapons Facility*. Applied Occupational and Environmental Hygiene Volume 16(3):405-417.