



Comments to OSHA

**Comments of the National Institute for Occupational Safety
and Health on the
Occupational Safety and Health Administration
Proposed Rule on
Occupational Exposure to Beryllium
and Beryllium Compounds**

[Docket No. OSHA—H005C—2006—0870]

RIN 1218—AB76

**Department of Health and Human Services
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
Cincinnati, Ohio**

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The National Institute for Occupational Safety and Health (NIOSH) has reviewed the Occupational Safety and Health Administration (OSHA) *Occupational Exposure to Beryllium and Beryllium Compounds; Proposed Rule* published in the *Federal Register* (FR) on August 7, 2015 [80 FR 47565]. NIOSH supports the OSHA effort to propose a reduced eight-hour Permissible Exposure Limit (PEL) of 0.2 micrograms (μg) per cubic meter (m^3) and to require additional protections including personal protective equipment (PPE), medical exams, other medical surveillance, and training. NIOSH offers the following responses and comments to OSHA.

I. Responses to OSHA questions

Health effects

1. OSHA has described a variety of studies addressing the major adverse health effects that have been associated with exposure to beryllium. Using currently available epidemiologic and experimental studies, OSHA has made a preliminary determination that beryllium presents risks of lung cancer; sensitization; CBD at $0.1 \mu\text{g}/\text{m}^3$; and at higher exposures acute beryllium disease, and hepatic, renal, cardiovascular and ocular diseases. Is this determination correct? Are there additional studies or other data OSHA should consider in evaluating any of these health outcomes?

Response to first question: Yes, NIOSH agrees with these determinations. The International Agency for Research on Cancer (IARC) determined that beryllium is a Group 1 (known) human carcinogen, with sufficient evidence for carcinogenicity in the human lung [Straif et al. 2009]. The key epidemiologic studies that supported the evaluation were the NIOSH study of lung cancer risk in U.S. Beryllium Case Registry patients [Steenland and Ward 1991] and the series of NIOSH studies conducted among beryllium processing plant workers at facilities in Ohio and Pennsylvania [Ward et al. 1992, Sanderson et al. 2001, Schubauer-Berigan et al. 2007, Schubauer-Berigan et al. 2011a,b]. These studies found that occupationally relevant levels of beryllium exposure were associated with lung cancer mortality. In particular, Schubauer-Berigan et al. [2011b] found that, depending on the choice of dose-response model, the mean time-weighted average concentration associated with a 1/1,000 lifetime excess absolute risk of lung cancer was between 0.0035 and $0.07 \mu\text{g}/\text{m}^3$. These concentrations are below the proposed OSHA standard of $0.2 \mu\text{g}/\text{m}^3$ but similar to the alternative OSHA PEL of $0.1 \mu\text{g}/\text{m}^3$; however, they suggest that lifetime lung cancer risk may be greater than 1/1,000 at either the proposed or alternative OSHA PEL.

Chronic beryllium disease (CBD) mortality in the pooled cohort study was found to be highly and significantly elevated across nearly all maximum annual beryllium exposure concentration categories, from $<10 \mu\text{g}/\text{m}^3$ to $>70 \mu\text{g}/\text{m}^3$, with no clear dose-response pattern; CBD standardized mortality ratios ranged from 3.4 to 19, compared to the U.S. population [Table 6 of Schubauer-Berigan et al. 2011a].

Response to second question: please see section II, comment 4 for additional information to consider from the Schubauer-Berigan et al. studies.

2. Has OSHA adequately identified and documented all critical health impairments associated with occupational exposure to beryllium? If not, what other adverse health effects should be added? Are there additional studies or other data OSHA should consider in evaluating any of these health outcomes?

Response to first question: There is evidence that other health outcomes, in addition to lung cancer, beryllium sensitization, and CBD, are related to occupational beryllium exposure. Schubauer-Berigan et al. [2011a] found evidence for dose-response associations between beryllium and several additional outcomes. From page 352 of Schubauer-Berigan et al. 2011a: “Urinary tract cancer, COPD, and the category related to cor pulmonale were elevated compared to the US population among higher exposed workers and showed strong associations with cumulative (when short-term workers were excluded) exposure, maximum exposure or both.” Cor pulmonale has been a long-understood sequelae of CBD [Ward et al. 1990], but its elevation as an underlying cause in a mortality study of beryllium processing workers suggests that it may represent an additional mortality burden of beryllium exposure. Other studies have also found an association between beryllium and chronic obstructive pulmonary disease (COPD) [Andrews et al. 1969; Hazan and Kazemi 1974], including studies with direct adjustment for smoking [Cherry et al. 2015; Kriebel et al. 1988]. It is anticipated that, if beryllium exposure causes diseases other than lung cancer or CBD, a reduction in the OSHA PEL would be expected to reduce the occurrence of these other diseases, as well.

Risk Assessment and Significance of Risk

4. OSHA has developed an analysis of health risks associated with occupational beryllium exposure, including an analysis of sensitization and CBD based on a selection of recent studies in the epidemiological literature, a data set on a population of beryllium machinists provided by the National Jewish Medical Research Center (NJMRC), and an assessment of lung cancer risk using an analysis provided by NIOSH. Did OSHA rely on the best available evidence in its risk assessment? Are there additional studies or other data OSHA should consider in evaluating risk for these health outcomes? Please provide the studies, citations to studies, or data you suggest.

Response to first question: NIOSH agrees with OSHA’s careful review of the available literature on beryllium sensitization and chronic beryllium disease, OSHA’s recognition of dermal exposure as a potential pathway for sensitization, and OSHA’s careful approach to assessing risk for beryllium sensitization and chronic beryllium disease at various concentrations and durations of exposure.

NIOSH also agrees that the study of lung cancer risk among workers hired before 1970 at three beryllium processing plants [Schubauer-Berigan et al. 2011b] provides the best available dataset to support quantitative risk assessment for lung cancer. The study found that lung cancer risk was significantly elevated at mean time-weighted average exposure levels above 4 $\mu\text{g}/\text{m}^3$ within three beryllium processing facilities with quantitative exposure information. It also found significant evidence of a lung cancer dose-response pattern. The study adjusted for a variety of potential

confounders, including exposure to asbestos and other lung carcinogens, and likely (i.e., expected) smoking behavior. The inclusion of two plants (in Elmore, Ohio and Hazleton, Pennsylvania (PA)) with much lower average exposure levels than the previously studied Reading, PA plant (analyzed in Sanderson et al. 2001 and Schubauer-Berigan et al. 2007), greatly increased the ability to detect risks at the lower exposure levels most relevant to the proposed PEL of $0.2 \mu\text{g}/\text{m}^3$, because most of the studied workers at those plants had average exposures below $2 \mu\text{g}/\text{m}^3$. There was no evidence that the lung cancer risk per unit of exposure differed between the plants [Schubauer-Berigan et al. 2011b].

Although direct information on cigarette smoking was unavailable for the full cohort, a cross-sectional evaluation of smoking among workers employed in 1968 showed little difference in smoking rates between the cohort and the general U.S. population, or across exposure levels within the cohort [Schubauer-Berigan et al. 2011a]. This finding was consistent with literature on how smoking patterns have changed over time between groups with different socioeconomic status; at the time of cohort enrollment before 1960, little difference in smoking rates would have been expected by education level [Garfinkel 1997].

5. OSHA preliminarily concluded that there is significant risk of material health impairment (lung cancer or CBD) from a working lifetime of occupational exposure to beryllium at the current TWA PEL of $2 \mu\text{g}/\text{m}^3$, which would be substantially reduced by the proposed TWA PEL of $0.2 \mu\text{g}/\text{m}^3$ and the alternative TWA PEL of $0.1 \mu\text{g}/\text{m}^3$. OSHA's preliminary risk assessment also concludes that there is still significant risk of CBD and lung cancer at the proposed PEL and the alternative PELs, although substantially less than at the current PEL. Are these preliminary conclusions reasonable, based on the best available evidence? If not, please provide a detailed explanation of your position, including data to support your position and a detailed analysis of OSHA's risk assessment if appropriate.

Response: NIOSH agrees that the risk of lung cancer will substantially decrease at either the proposed or alternative PEL levels. The most appropriate published quantitative analysis of lung cancer risk following beryllium exposure [Schubauer-Berigan et al. 2011b; Appendix Table 7] shows that, when asbestos-exposed and professional workers were excluded from the analysis, the hazard ratio (HR) at mean time-weighted average exposures of $2 \mu\text{g}/\text{m}^3$ was 1.92 (95% confidence interval (CI) 0.701, 5.26); at $0.2 \mu\text{g}/\text{m}^3$ the HR was 1.10 (95% CI: 0.890, 1.35), and at $0.1 \mu\text{g}/\text{m}^3$ the HR was 1.05 (95% CI: 0.943, 1.16). These estimates indicate a substantial decrease in lung cancer risk should occur as exposure levels are reduced but lifetime risks of lung cancer at each of the proposed or alternative PELs is above 1/1,000.

6. Please provide comment on OSHA's analysis of risk for beryllium sensitization, CBD and lung cancer. Are there important gaps or uncertainties in the analysis, such that the Agency's preliminary conclusions regarding significance of risk at the current, proposed, and alternative PELs may be in error? If so, please provide a detailed explanation and suggestions for how OSHA's analysis should be corrected or improved.

Response: NIOSH recommends that the proposed rule include discussion of healthy worker survivor bias in the studies used for risk assessment, especially for the sensitization studies. The absence of clear exposure-response relationships for a causative agent is often a consequence of

unknown selection processes. For example, if workers leaving employment have higher risk factors than others for the outcome under study, then long-term workers with high exposures should be compared with long-term workers with low exposures, not with all workers. Alternatively, if development of early symptoms is causing some workers to leave employment or transfer to lower exposures (i.e., the disease is determining their cumulative exposure), then the general relationship in the study population between cumulative exposure and outcome can be obscured or reversed. For example, in published reports of pulmonary effects of diacetyl, the onset of pulmonary impairment actually decreased with employment duration [van Rooy et al. 2009; Lockey et al. 2009]. Because beryllium has irritant and sensitizing effects, one would expect to observe related selection effects in worker populations.

7. OSHA has made a preliminary determination that the available data are not sufficient or suitable for risk analysis of effects other than beryllium sensitization, CBD and lung cancer. Do you have, or are you aware of, studies or data that would be suitable for a risk assessment for these adverse health effects? Please provide the studies, citations to studies, or data you suggest.

Response: NIOSH agrees that identified data for outcomes other than beryllium sensitization, CBD, and lung cancer are unsuitable for formal risk assessment. However, as noted in response to Question 2 above, additional health outcomes have been found in a variety of studies to be related to beryllium exposure. It is anticipated that, if beryllium exposure causes diseases other than lung cancer or CBD, a reduction in the OSHA PEL would be expected to reduce the occurrence of these other diseases, as well.

Scope

8. Has OSHA defined the scope of the proposed standard appropriately? Does it currently include employers who should not be covered, or exclude employers who should be covered by a comprehensive beryllium standard? Are you aware of employees in construction or maritime, or in general industry who deal with beryllium only as a trace contaminant, who may be at significant risk from occupational beryllium exposure? Please provide the basis for your response and any applicable supporting information.

Response to all questions: NIOSH supports expanding the scope of the proposed standard to include all operations in general industry, construction, and shipbuilding where beryllium exists only as a trace contaminant; that is, where the materials used contain no more than 0.1% beryllium by weight. NIOSH is concerned that workers may be exposed above the proposed OSHA PEL in such settings, including construction and shipyards (e.g., abrasive blasting with coal slags). A recent study by the Center for Construction Research and Training (CPWR) found that abrasive blasting with coal slags (which may contain trace quantities of beryllium) led to task-based air concentrations of up to 9.5 $\mu\text{g}/\text{m}^3$. Although the time-weighted average concentrations associated with this exposure were not reported, this concentration was nearly 50 times higher than the proposed PEL [CPWR 2013]. A NIOSH exposure assessment study of a coal slag blaster found that personal breathing zone and area air concentrations exceeded the proposed OSHA PEL [NIOSH 2007]. Although the blasters themselves may use PPE that limits exposure, bystanders and others (e.g., supervisors) may be exposed. In addition, workers may be exposed to beryllium when demolishing buildings or building equipment [Tharr 1993]. NIOSH

recommends that the standard be based on exposures received in the actual workplace setting, rather than the concentration of beryllium in the bulk material. Another group of workers who might require coverage under the new proposed standard is workers employed in dental offices, if beryllium-containing dental alloys are fabricated or modified in dental offices (see Footnote 1 of OSHA's Hazard Identification Bulletin:

https://www.osha.gov/dts/hib/hib_data/hib20020419.html).

OSHA is aware of two industries in the general industry sector that would be exempted from the proposed standard under proposed paragraph (a)(3): coal-fired electric power generation and primary aluminum production. Regarding power generation, NIOSH is not aware of any medical screening of workers exposed to beryllium in the form of fly ash using the BeLPT; therefore, a hazard may or may not exist. OSHA is encouraged to include electrical utility generators under the scope of the standard until available data demonstrate no risk of sensitization.

Exposure Monitoring

12. Is it reasonable to allow discontinuation of monitoring based on one sample below the action level? Should more than one result below the action level be required to discontinue monitoring?

Response to both questions: Decisions based on one exposure measurement are not reliable given the well-established right-skewed exposure distributions associated with jobs [Rappaport 1984]. The fewer samples collected, the less likely an extreme value will be shown, and the higher likelihood of showing compliance [Rappaport 1984]. Decisions need to account for exposure distribution [Ogden and Lavoué 2012]. The 95th percentile is one metric that can be used to make such decisions [Ogden and Lavoué 2012].

Work Areas and Regulated Areas

13. Does your workplace currently have regulated areas? If so, how are regulated areas demarcated?

Response to both questions: More specification is needed about how to demarcate the regulated areas. Strategies to prevent migration of beryllium outside designated areas include enclosure and the use of air locks in the form of air showers [NIOSH 2008].

Personal Protective Clothing and Equipment

19. The proposal requires PPE wherever work clothing or skin may become visibly contaminated with beryllium; where employees' skin can reasonably be expected to be exposed to soluble beryllium compounds; or where employee exposure exceeds or can reasonably be expected to exceed the TWA PEL or STEL. The requirement to use PPE where work clothing or skin may become "visibly contaminated" with beryllium differs from prior standards which do not require contamination to be visible in order for PPE to be required. Is "visibly contaminated" an appropriate trigger for PPE? Is there reason to require PPE where employees' skin can be exposed to insoluble beryllium compounds? Please provide the basis for your response and any applicable supporting information.

Response to first question: “Visibly contaminated” is not an appropriate trigger for PPE because biologically relevant amounts of beryllium that cannot be seen may load on the skin during finishing tasks [Day et al. 2007] or when handling a copper-beryllium tool [Stefaniak et al. 2011]. “Visibly contaminated” is also a subjective determination. Most work surfaces in manufacturing facilities are contaminated, even when airborne exposures are very low [Armstrong et al. 2014]. Tools that have been in a manufacturing facility will likely be contaminated and should be treated as such. NIOSH supports a regulation that would require appropriate PPE when there is potential for skin contact with beryllium or beryllium-contaminated surfaces.

Response to second question: PPE should be required when working in areas where beryllium exposure is present or when handling tools that have been in areas where beryllium is processed or handled. PPE should also be required where employees’ skin can be exposed to insoluble beryllium compounds because some of the so-called insoluble forms can dissolve and produce soluble beryllium ions in sweat. Studies have used a comprehensive model of the skin film liquids to measure dissolution of beryllium from insoluble particles collected at beryllium facilities [Stefaniak et al. 2011; Duling et al. 2012; Stefaniak et al. 2014]. The facility operations included mining and milling, primary production, machining, and finishing. The particles or particulate matter included mineral forms, process intermediates, hydroxide, metal, oxide, copper-beryllium alloys, and particles dissolved from tools made of copper-beryllium alloy. The dissolution of beryllium was greatly influenced by the pH of artificial sweat which becomes more acidic upon exertion and increases the availability of beryllium on the skin surface [Stefaniak et al. 2011; Duling et al. 2012; Stefaniak et al. 2014]. Importantly, dissolution rates of insoluble forms of beryllium in artificial sweat were equal to or faster than rates previously determined for the same materials in lung fluid models and in vivo studies of pulmonary exposure. Further, even minor superficial disruptions to the outer stratum corneum layer of the skin can greatly reduce its barrier protection and permit penetration of particles and/or dissolved metals [Larese-Filon et al. 2009]. Minor skin abrasions are common in industrial environments and may occur more often among persons working in environments with mechanical and physical stressors. Further studies are needed to determine the effect of abrasive scrubbing, long-term use of occlusive gloves, and respirator-use dermatitis on the skin barrier.

Housekeeping

22. The proposed rule requires that materials designated for recycling that are visibly contaminated with beryllium particulate shall be cleaned to remove visible particulate, or placed in sealed, impermeable enclosures. However, small particles (<10 µg) may not be visible to the naked eye, and there are studies suggesting that small particles may penetrate the skin, beyond which beryllium sensitization can occur (Tinkle et al., 2003). OSHA requests feedback on this provision. Should OSHA require that all material to be recycled be decontaminated regardless of perceived surface cleanliness? Should OSHA require that all material disposed or discarded be in enclosures regardless of perceived surface cleanliness? Please provide explanation or data to support your comments.

Response to first question: Materials should be decontaminated regardless of whether they are visibly clean for reasons noted in the response to question 19.

Medical Surveillance

24. Please review paragraph (k) of the proposed rule, Medical Surveillance, and comment on the frequency and contents of medical surveillance in the proposed rule.

Response: OSHA is proposing to require that low-dose computed tomography (LDCT) screening “*must be offered to employees who have been exposed to beryllium at concentrations above 0.2 µg/m³ for more than 30 days in a 12-month period for 5 years or more. The five years of exposure do not need to be consecutive...the CT scan must be offered to employees who meet the criteria of paragraph (k)(1)(i)(D) for the first time beginning on the start-up date of this standard, or 15 years after the employee’s first exposure to beryllium above 0.2 µg/m³ for more than 30 days in a 12-month period, whichever is later.*”

To assure that the benefit of the LDCT screening for early detection of lung cancer exceeds harm such as causing radiation-induced lung cancer, it is important that the screened population be at sufficiently high risk for lung cancer. A recent report by the Finnish Institute of Occupational Health (FIOH) on LDCT screening for lung cancer in asbestos-exposed workers provides guidance on a risk threshold. The FIOH recommended LDCT screening of workers “...with any asbestos exposure and a smoking history equal to the entry criteria of the National Lung Screening Trial (NLST) study; and workers with asbestos exposure, with or without a smoking history, which alone or together would yield an estimated risk level of lung cancer equal to that in the entry criteria of the NLST study” [Wolff et al. 2015]. The reason for this recommendation was that LDCT screening of the NLST population, which had a high risk for lung cancer, was documented to result in a favorable balance of benefits and harms. Quantitatively, the absolute risk for lung cancer in the NLST study population and thus the threshold absolute risk for lung cancer proposed by FIOH as a trigger for LDCT screening for early detection of lung cancer is 1.34% over 6 years [Vehmas et al. 2014].

NIOSH suggests that OSHA perform a careful, detailed evaluation of available data to document that its final recommendation on LDCT screening for early detection of lung cancer achieves a favorable balance between benefits and harms. Rough calculations suggest that some beryllium workers could acquire enough beryllium exposure and associated lung cancer risk for screening to potentially be beneficial. The table below shows background lung cancer risk in men at various ages over the next 10-year interval, the hazard ratio (HR) needed to reach an absolute risk of 1.34% over the 10-year interval, and the mean “daily weighted average” (DWA) beryllium exposure needed to achieve the necessary HR (from Table 4 of Schubauer-Berigan 2011b; note that a unique characteristic of the cohort, having the heaviest exposures early in employment, complicates assessment of cumulative exposure as a metric for assessing risk). (Also note that OSHA would need to adjust the intervals to 6 years to match FIOH; background lung cancer rates in the general population used in the example below are from NCI 2014.)

<u>Age</u>	<u>10-year absolute risk of lung cancer</u>	<u>HR needed to achieve risk of 1.34% over 10 years</u>	<u>Mean DWA Be exposure associated with HR</u>
30	0.0002	67.7	N/A ^a
40	0.0015	9.03	12 µg/m ³
50	0.0071	1.91	2 µg/m ³
60	0.0205	Use smoking-adjusted estimate	-- ^b
70	0.0371	Use smoking-adjusted estimate	--

^aN/A: not applicable. No beryllium exposure level produced a hazard ratio (HR) this high.

^b--: Exposure level will depend on smoking level, since 10-year absolute risk estimate was greater than 1.34% across the total population.

Based on the table, beryllium exposure does not trigger a need for screening at age 30. Between the ages of 40 and 50, the mean DWA level needed to trigger screening might be between 2 and 12 µg/m³ (OSHA would need to better define this based on a more sophisticated analysis). Above the age of 50, screening might be beneficial for those with a mean DWA beryllium exposure of 2 µg/m³. To make an LDCT recommendation, OSHA would need to estimate the quantitative relationships between years of exposure at or around the proposed PEL of 0.2 µg/m³, mean DWA beryllium exposure levels as reported by Schubauer-Berigan et al., and lung cancer risk.

The mortality study by Schubauer-Berigan et al. [2011b] found that a lag of 10 years was best-fitting for the relationship between beryllium exposure and lung cancer mortality. Therefore, NIOSH suggests that the proposed requirements for LDCT screening consider this lag interval.

The effects of smoking should also be considered. Workers with combined exposures to tobacco smoking and beryllium are expected to be at greater risk for lung cancer than those with exposure to the same level of beryllium without tobacco smoking, as is the case with asbestos and smoking [Wolff et al. 2015]. Thus, OSHA may wish to consider identifying different threshold beryllium exposures that would trigger LDCT screening for lung cancer in nonsmokers and in those with combined exposures to beryllium and smoking.

28. (first question): *Appendix A to the proposed standard reviews procedures for conducting and interpreting the results of BeLPT testing for beryllium sensitization. Is there now, or should there be, a standard method for BeLPT laboratory procedure?*

Response: Yes. Standardization of the BeLPT is needed. As reviewed by OSHA, the current interpretation is based on a “stimulation index” that is dependent on the protocol used by the service provider. The stimulation index may or may not be re-calculated periodically at a given lab.

II. Comments on E. Beryllium Lung Cancer Section

1. The Ward et al. 1992 cohort study is discussed in two places: page 47608, third column and page 47609, middle column. The first mention seems out of place in the chronological evaluation of cancer studies among beryllium processing workers.
2. Page 47610 middle column states: “*Another analysis of the study data using a different statistical method did not find a significantly greater relative risk of lung cancer with increasing beryllium exposures (Levy et al., 2007).*” OSHA should note that this “different statistical method” introduced by Levy et al. 2007 was found by NIOSH and many other researchers to introduce a downward bias in risk estimates [Schubauer-Berigan et al. 2007; Hein et al. 2009, 2011; Langholz and Richardson 2009; Wacholder 2009].
3. The PR cites Schubauer-Berigan et al. 2010a and b in several places. NIOSH recommends citing the final, printed versions of these manuscripts, 2011a and 2011b.
4. Page 47611, first column, end of section 2: the cited NIOSH update of the Ward beryllium cohort study [Schubauer-Berigan et al. 2011a] was accompanied by a detailed investigation of the lung cancer findings in this updated cohort [Schubauer-Berigan et al. 2011b]. This manuscript included very important supplemental findings about lung cancer risk in the subcohort that included the three plants with job-exposure matrices (JEMs). The authors explored the fit of different exposure-response relations between beryllium and lung cancer, as well as evaluated (indirectly) the likelihood of confounding by smoking and exposure to other lung carcinogens. This study is very informative for lung cancer risk assessment, and it would be helpful to describe its features and limitations in this summary.
5. Page 47616, middle column, first line: the OSHA reference to Schubauer-Berigan et al. 2010 Table 4 appears to refer to Schubauer-Berigan et al. 2011a. This should be specified. Also, Table 4 in Schubauer-Berigan et al. 2011b supports this statement and could be added.
6. Page 47616, third column, first paragraph under “2. *Cardiovascular Effects*”: Schubauer-Berigan et al. 2011a found evidence for dose-response associations between beryllium and outcomes other than lung cancer. From page 352 of Schubauer-Berigan et al. 2011a: “Urinary tract cancer, COPD, and the category related to cor pulmonale were elevated compared to the US population among higher exposed workers and showed strong associations with cumulative (when short-term workers were excluded) exposure, maximum exposure or both.” Also, Schubauer-Berigan et al. 2011a found (for the first time) evidence for a beryllium-related dose-response for the category of death containing cor pulmonale, as noted in the response to question 2 above.
7. Page 47623, Table A-3: both Schubauer-Berigan et al. 2010a and 2010b used exposure data from Sanderson et al. 2001, Chen 2001, and Couch et al. 2010. Schubauer-Berigan et al. 2008 used exposure data from Sanderson et al. 2001 only.

III. Additional comments

1. Page 47592, “3. Genetic and Other Susceptibility factors”

Comments: This section would benefit from clarification and improved organization. The first modern genetic reference is to McCanlies et al. 2004; however, two paragraphs later *HLA-DPB1* is discussed. The McCanlies reference is specifically about *HLA-DPB1*, and belongs in that later section. In discussions of Richeldi et al. 1993 and other studies, this same gene is referred to as *HLA-DP 1*—confusing because an older nomenclature convention actually refers to the *HLA-DPB1*E69* allele as *HLA-DP2*.

This sentence at the bottom of the second column is unclear about which “common allele” is described; a reference is needed: “*The more common allele of the HLA-DP 1 variant is negatively charged at this site and could directly interact with the positively charged beryllium ion.*” Regarding the common glutamate-69 allele, the PR notes that the molecule is negatively charged; however, some glutamate-69-containing molecules are more negatively charged. This is important because the more negatively charged molecules (-9 versus -7) carry the highest risk of CBD [Snyder et al. 2008].

2. Page 47593, first complete paragraph: “*While a study by McCanlies et al. (2007) found no relationship between TNF- α polymorphism and BeS or CBD, the inconsistency may be due to misclassification, exposure differences or statistical power (NAS, 2008).*”

Comment: The sentence implies that the McCanlies study was deficient; however, the National Academies of Science (NAS) 2008 report gave no indication that the study was deficient and noted that the McCanlies study is “large.” NIOSH suggests that the sentence be revised to accurately reflect NAS 2008.

3. Pages 47685-47686 state: *The proposed standard requires that a helical tomography (CT scan) be offered to employees exposed to airborne beryllium above 0.2 $\mu\text{g}/\text{m}^3$ for more than 30 days in a 12-month period, for a period of 5 years or more. The five years do not need to be consecutive, and the exposure does not need to occur after the effective date of the standard. The CT scan shall be offered every 2 years starting on the 15th year after the first year the employee was exposed above 0.2 $\mu\text{g}/\text{m}^3$ for more than 30 days in a 12-month period, for the duration of their employment. The total yearly cost for biennial CT scans consists of medical costs totaling \$1,020, comprised of a \$770 fee for the scan and the cost of a specialist to review the results, which OSHA estimates would cost \$250. The Agency estimates an additional cost of \$110 for lost work time, for a total of \$1,131. The annualized yearly cost for biennial CT scans is \$574.*

Comment: The OSHA cost projection should also account for costs associated with follow-up of abnormal LDCT findings identified in screening. In the National Lung Screening Trial (NLST), 24.2% of the LDCT tests were classified as positive [NLST 2011]. Follow-up of such positive findings generally involves performing one or more follow-up LDCT examinations to document stability of radiographic abnormalities. These examinations are performed sooner than the biennial frequency proposed to be required for screening, and so will add to the true cost of the screening program.

IV. Editorial comments

- Questions 5,6,7 on page 47573: place the health effects in order (i.e., CBD, sensitization, lung cancer).
- Page 47593, third column; page 47595, first and second columns; page 47599, third column, and elsewhere in the PR: Kreiss et al. 1993: a or b?
- Page 47606 cites Haley et al. 1991; however, Haley is listed as the sole author in the Reference list.
- Page 47610, third column and page 47611, first column: Schubauer-Berigan et al. 2010 is cited— this reference is not listed in References.
- Page 47621: Haley et al. 1989b is not in the Reference list.
- Page 47645, third column: neither Kreiss et al. 1992 nor Schuler et al. 2000 are in the Reference list.
- Page 47646, third column cites Schubauer-Berigan et al. 2011 and 2011a; 2011a is not in the Reference list.
- Page 47661, second column: Sanderson 2001: a or b?
- Page 47661: Schubauer-Berigan et al. 2010b is not in the Reference list.
- Page 47712, third column: “*In a study by Kelleher 2001, Martyny 2000, Newman, JOEM 2001) in a plant that...*” The Newman study was published in JOEH, Kelleher was published in JOEM. Also, these reports had multiple authors—et al. would be more appropriate.
- Page 47780, third column: NIOSH 1977 is not in the Reference list.
- Page 47817 of the Reference list has a 4-22-2011 personal communication to Schubauer-Berigan; please check whether it was intended to be included.
- Page 47818, second column: Thomas et al. is cited twice. The Tinkle references are out of order; 1997 needs a and b.
- NIOSH is not defined where first listed (page 47573), and is defined on pages 47579, 47615, 47642, 47673, 47750, and 47778.
- The 2011 NIOSH Beryllium Alert document “Preventing Sensitization and Disease from Beryllium Exposure” does not appear to be referenced in the PR. OSHA is encouraged to consider the document’s recommendations: <http://www.cdc.gov/niosh/docs/2011-107/pdfs/2011-107.pdf>.

No in-text citation was found for these studies in the Reference list:

- Page 47810: Day et al. 2005
- Page 47811: Finch et al. 1986 and 1998c

Beryllium References – Citations marked with an (+) have already been cited within the Proposed Rule (August 7, 2015)

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