DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Centers for Disease Control and Prevention
National Institute for Occupational
Safety and Health
Robert A. Taft Laboratories
4676 Columbia Parkway
Cincinnati OH 45226-1998

February 22, 2011

Jacqueline D. Rogers
Office of Worker Safety and Health Policy
Office of Health, Safety and Security
U.S. Department of Energy
Docket No. HS-RM-10-CBDPP
1000 Independence Ave., SW
Washington, DC 20585

RIN 1992-AA39

Dear Ms. Rogers:

The National Institute for Occupational Safety and Health (NIOSH) has reviewed the Department of Energy request for information on *Chronic Beryllium Disease Prevention Program* published in the *Federal Register* on December 23, 2010 [75 FR 80734]. Our comments are enclosed. The references will be sent separately.

Please do not hesitate to contact me at 513/533-8302 if I can be of further assistance.

Sincerely yours,

Paul A. Schulte, Ph.D.
Director
Education and Information Division

Enclosure

National Institute for Occupational Safety and Health
NIOSH

Comments to DOE

Comments of the
National Institute for Occupational Safety and Health
On the
Department of Energy
Request for Information on
Chronic Beryllium Disease Prevention Program

Docket No. HS-RM-10-CBDPP
RIN 1992-AA39

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

2/22/11

The National Institute for Occupational Safety and Health (NIOSH) has reviewed the Department of Energy (DOE) request for information *Chronic Beryllium Disease Prevention Program* published in the *Federal Register* (FR) on December 23, 2010 [75 FR 80734]. NIOSH supports the DOE effort to gather data and other relevant information to develop a revised standard for its Chronic Beryllium Disease Prevention Program (CBDPP). The following comments are intended to assist DOE in determining the appropriate course of action regarding its CBDPP.

Background

On page 80734, DOE notes that *"Inhalation of beryllium particles may cause chronic beryllium disease (CBD) and beryllium sensitization."* The predominant locus of sensitization is not known since inhalation exposure is accompanied by skin exposure. The presence of sensitization in the blood lymphocytes, as determined by the beryllium lymphocyte proliferation test, prior to detection in the alveolar lymphocytes, as determined by the bronchoalveolar lavage LPT, provides evidence that systemic sensitization occurs before lung sensitization. Newman et al. [2005] followed 55 sensitized workers with periodic clinical evaluations; approximately 1/3 were diagnosed with CBD within a 4 ½ year period of follow-up.

1. DOE currently defers to the Occupational Safety and Health Administration (OSHA) for establishing the permissible exposure limits (PEL) and uses an action level as the administrative level to assure that controls are implemented to prevent exposures from exceeding the permissible exposure limits. Should the Department continue to use the OSHA PEL? Please explain your answer and provide evidence to support your answer.

NIOSH recommends that employers keep airborne concentrations of beryllium as low as possible because a safe exposure limit has not been determined [NIOSH 2011]. OSHA has stated that the current PEL may not adequately protect beryllium-exposed workers from developing chronic beryllium disease [OSHA 1998, 1999], and is currently developing a revised beryllium standard [75 FR 79806]. Two $\mu g/m^3$ does not protect workers from risk of developing beryllium sensitization or chronic beryllium disease. Epidemiological studies over the past 15 years demonstrate clear risk of sensitization and disease at exposures below the current PEL [Kreiss et al. 1997; Schuler et al. 2005; Mikulski et al. 2010; Henneberger 2001; Kelleher 2001]. As noted in previous comments to DOE [NIOSH 1999], NIOSH classifies beryllium as a potential occupational carcinogen. The International Agency for Research on Cancer (IARC) has classified beryllium as *known to be a human carcinogen* since 1981. Information addressing the adequacy of the OSHA PEL and the NIOSH recommended exposure limit (REL) for protection against the excess risk of cancer is provided in response to question 3.

2. Should the Department use the 2010 ACGIH threshold limit value (TLV) of 0.05 [mu]g/m\3\ (8-hour time-weighted average of 0.05 microgram of beryllium, in inhalable particulate matter, per cubic meter of air), for its allowable exposure limit? Please explain your answer and provide evidence to support your answer.

NIOSH assessment of the available evidence indicates that thoracic size particles that deposit in the conducting airways, and fine particles that deposit in the alveoli, contribute to the risk of beryllium sensitization and disease. Focusing only on the ISO/CEN/ACGIH inhalable sampling criteria for the ACGIH newly adopted threshold limit value (TLV®) does not sufficiently address exposure to thoracic and fine particles. Therefore, NIOSH recommends that beryllium exposures be kept as low as possible.

The recent ACGIH TLV for beryllium calls for inhalable sampling that is based, in part, on preventing sensitization [ACGIH 2009]. The ISO/CEN/ACGIH inhalable sampling criteria account for large particles capable of penetrating into the head-airways region (nasal passages, oral cavity, and/or nasopharynx). Large particles that deposit on the unciliated anterior nares of the nose are cleared by sneezing or nose blowing. All large particles that deposit in the ciliated nasal passages, oral cavity and/or pharynx are rapidly cleared by mechanical transport (mucociliary clearance) to the pharynx and swallowed (clearance half-time of 10 minutes) [ICRP, 1994]. The residence time of materials in the gastric compartment is short (few hours) and < 1% of soluble beryllium is absorbed in the gastrointestinal tract [WHO 2001]. Hence, given the fast clearance rate of particles from the head airways region and lack of absorption in the gastrointestinal tract, inhalable particles may not contribute to development of sensitization.

Because of their solubility, NIOSH considers thoracic and fine, respirable-size particles to be biologically relevant to beryllium sensitization and disease. Under the model developed by Stefaniak et al. [2003], the availability of dissolved beryllium to immune competent cells is the rate limiting step in risk. Thoracic size particles are chemically dissolved during mechanical clearance from the conducting airways, as demonstrated by Finch et al [1988] and Huang et al. [2011]. Finch et al. [1988] evaluated the dissolution of beryllium metal and oxide in artificial respiratory tract lining fluid. In that study, both materials released ions into artificial airway lung fluid, with metal dissolving faster than oxide. Huang et al. [2011] reported that beryllium silicates, hydroxide, and oxide dissolve in artificial respiratory tract fluid.

Fine particles that deposit in the alveoli are dissolved after being rapidly engulfed by macrophages. Once engulfed, these particles have slow mechanical clearance rates, with half-times on the order of hundreds to thousands of days. While sequestered in macrophage cells, particles undergo dissolution, thereby making soluble beryllium available for interaction with the immune system. Stefaniak et al. [2011] demonstrated that in a model of alveolar phagocytic cell liquids, fine beryllium particles collected from processes associated with elevated risk of disease dissolved at rates that were statistically significantly faster than particles from processes not associated with risk.

Approximately 20% of soluble beryllium is absorbed in the respiratory tract [WHO 2001]. The solubility of beryllium in lung fluids coupled with residence times of hours (conducting airways) to years (alveoli) supports the availability of beryllium ion for absorption and interaction with the immune competent cells in the lung. Based on these data and the biological plausibility of dissolution and absorption of beryllium ions in the conducting airways and alveoli, NIOSH recommends that DOE reduce exposures as low as possible.

3. Should an airborne action level that is different from the 2010 ACGIH TLV for beryllium (8-hour time-weighted average of 0.05 microgram of beryllium, in inhalable particulate matter, per cubic meter of air) be established? If so, what should be the level? Please explain each of your answers and provide evidence to support your answers.

With respect to sensitization and CBD, not enough data is currently available to perform the risk analyses necessary to support a specific airborne action level. The number of studies estimating individual beryllium exposure needed to quantify an exposure-response relationship is limited. NIOSH continues to investigate this issue. Given that the scientific evidence characterizing the relationship between exposure and response is evolving, NIOSH recommends that exposures should be kept as low as possible [NIOSH 2011]. However, NIOSH acknowledges that it may be necessary and appropriate for DOE to establish an airborne exposure limit and action level to carry out an effective industrial hygiene program for worker protection throughout the DOE complex.

The epidemiologic studies evaluating exposure-response for beryllium sensitization and CBD are few and exposure-response relations have been inconsistent. Some studies [Kreiss et al.1996; Henneberger et al. 2001; Kelleher et al. 2001; Rosenman at al. 2005] provide limited evidence for such a relationship, while others [Kreiss et al. 1997] show no relationship. Kelleher et al. [2001] found evidence of higher risk associated with smaller size particles. Studies with exposure estimates that were able to discriminate the lower end of the distribution identified many cases with low exposures: eight of twenty cases of sensitization and CBD at a beryllium metal machining facility had lifetime-weighted-average (LTW) exposures below 0.2 $\mu g/m^3$ [Kelleher et al. 2001], but no one with LTW average exposure under 0.02 $\mu g/m^3$ was sensitized or had CBD; Taiwo et al. [2008] found two workers with CBD whose average exposure was 0.16 and 0.04 $\mu g/m^3$ at an aluminum smelter; Henneberger et al. [2001] identified sensitization at average exposures below 0.20 $\mu g/m^3$, and cumulative exposures below 0.16 $\mu g\text{-}yr/m^3$.

NIOSH researchers recently evaluated the risk of lung cancer and other malignant and nonmalignant diseases in a pooled cohort study of workers at seven beryllium processing plants who were followed for mortality through 2005 [Schubauer-Berigan et al. 2010a]. This study found that rates of lung cancer, chronic obstructive pulmonary disease (COPD), and the category containing cor pulmonale were elevated by 17–23% compared to the U.S. population. The rate for the category containing chronic beryllium disease showed a 7.8-fold elevation. For three of these plants, quantitative estimates of beryllium exposure were available through the development of job-exposure matrices [Sanderson et al. 2001; Couch et al. 2010] based on a "daily weighted average" (DWA), which is similar to an 8-hour time-weighted average. Workers whose maximum beryllium DWA exposure was 10 $\mu g/m^3$ or greater had higher rates of lung cancer, urinary tract cancer, COPD, and the category containing cor pulmonale than workers with lower exposure [Schubauer-Berigan et al. 2010a]. Significant positive trends with cumulative DWA exposure were observed for nervous system cancers ($p=0.0006$) and, when short-term workers were excluded, lung cancer ($p=0.01$), urinary tract cancer ($p=0.003$), and COPD ($p<0.0001$). These findings were not likely to be influenced by smoking patterns, as very little difference in smoking rates was found for the cohort compared to the general population, nor was there much difference in smoking levels by beryllium DWA exposure within the cohort.

To evaluate the exposure-response patterns for lung cancer related to cumulative, maximum, and average (mean) DWA exposure, NIOSH researchers published a detailed assessment based on the three plants with quantitative exposure information [Schubauer-Berigan et al. 2010b]. This study found that (adjusting for confounding) lung cancer was strongly associated with mean ($p<0.0001$), maximum ($p<0.0001$), and cumulative ($p=0.0017$) beryllium DWA exposure. Specifically, this study found that working lifetime mean DWA exposures near the current OSHA PEL of 2 $\mu g/m^3$

were associated with a significantly elevated risk of lung cancer. This paper also explicitly evaluated the lifetime excess absolute risk (EAR) of lung cancer associated with the current NIOSH recommended exposure limit (REL) of 0.5 $\mu g/m^3$. Depending on the exposure-response model used, this EAR ranged from 0.61% to 4.9%. The mean DWA exposure associated with a one-in-one-thousand (0.1%) risk ranged from 0.0035 $\mu g/m^3$ to 0.082 $\mu g/m^3$, depending on the exposure-response model used. Thus, according to this study, time-weighted average exposures at the current OSHA PEL or NIOSH REL may confer an unacceptably high risk of lung cancer.

4. In the past DOE encouraged, but did not require, the use of wet wipes rather than dry wipes for surface monitoring. DOE's experience with wipe testing leads the Department to consider requiring the use of wet wipes, unless the employer demonstrates that using wet wipes may cause an undesirable alteration of the surface, in order to achieve greater comparability of results across the DOE complex and in response to studies demonstrating that wet wipes capture more of the surface contamination than do dry wipes. Should the Department require the use of wet wipes? Please explain your answer and provide evidence to support your answer.

NIOSH recommends the use of wet wipes unless surfaces are oily or fragile or can be damaged by contact with wetting agent(s). Choice of surface sampling method should include, for wet wipe sampling, ASTM D6966, *Standard Practice for Collection of Settled Dust Samples Using Wipe Sampling Methods for Subsequent Determination of Metals*. Equivalent wet wipe sampling methods have been published by NIOSH (e.g., methods 9102, 9110). If wet wiping causes alteration of the surface to be sampled, then dry wiping, tape stripping and vacuuming are alternative techniques [Ashley et al. 2009a]. In a limited study, wet wipe sampling was shown to be more effective than dry wipe sampling for beryllium [Dufay and Archuleta 2006].

The consensus guidance document Standard Guide for Strategies for Surface Sampling of Metals and Metalloids for Worker Protection, Method D7659 was recently published regarding strategies for surface sampling of metals and metalloids for worker protection [ASTM 2010]; however, a standardized wipe sampling method that can be applied to beryllium in all workplaces may not be appropriate and is not available. An ASTM standard specification for wipe sampling materials for beryllium in surface dust is currently being developed for publication in 2011.

In cases where wipe sampling is impractical and it is advisable to use vacuum sampling methods instead, ASTM D7144, *Standard Practice for Collection of Surface Dust by Micro-vacuum Sampling for Subsequent Metals Determination* and ASTM D5438, *Standard Practice for Collection of Floor Dust for Chemical Analysis* are validated and should be followed [Agrawal et al. 2006; Ashley et al. 2007a]. Creek et al. [2006] have published an overview of recent vacuum sampling methods for beryllium discussing methodologies and recommending harmonization of sampling methods. ASTM D7659, *Standard Guide for Strategies for Surface Sampling of Metals and Metalloids for Worker Protection* provides guidance for choosing appropriate surface sampling methods for beryllium. Ashley et al. [2009] provides an additional overview of surface sampling methods for metals including beryllium with the intent to assist the goal of providing standard surface sampling methods that will ensure comparability of data obtained from different locations and times.

5. Since the use of wipe sampling is not a common occupational safety and health requirement, how do current wipe sampling protocols aid exposure assessments and the

protection of beryllium workers? How reliable and accurate are current sampling and analytical methods for beryllium wipe samples? Please explain your answers and provide evidence to support your answers.

Wipe sampling results provide estimates of the levels of contamination on surfaces in work environments [Day et al. 2007, 2009; Vincent et al. 2009; Muller et al. 2010]. Beryllium-contaminated surfaces (i.e., tools, equipment, bench tops) represent sources from which dusts may be re-aerosolized or transferred to clothing and/or skin [Deubner et al. 2001; Day et al. 2007]. Evidence suggests that skin contact with beryllium materials is relevant to the development of beryllium sensitization [Day et al. 2006]. Evaluation of beryllium surface contamination enhances understanding of the potential for both inhalation and skin exposures and improves decision making regarding worker protection.

Several wipe sampling methods/protocols are available for elements including guidelines from OSHA [2007], ASTM [2003], and NIOSH [2003]; ASTM Method 7296 [2006] is specific for beryllium. The reliability and accuracy of these sampling methods are affected by many factors [Stefaniak, in press]. A high degree of variability results from the varying amount of pressure applied to surfaces while wiping within and between surveyors (i.e., light, medium, and firm pressure); not all surveyors may use templates for delineating surface area; many surfaces do not allow the use of a template (i.e., irregular shapes); and the composition of surfaces may have very different properties (i.e., smooth, rough, porous). Such factors create inherent variability in not only the masses of beryllium removed from surfaces but also the estimated surface area sampled. This variability affects the accuracy of estimates of contamination.

Wipe sampling and analytical methods for beryllium on surfaces have been evaluated and shown to meet desired performance criteria for analytical precision and bias (uncertainty). Papers and chapters on beryllium sampling and analysis have appeared in recent special issues of two peer-reviewed journals (*Journal of Environmental Monitoring*, Vol. 6, No. 6, 2006; *Journal of Occupational and Environmental Hygiene*, Vol. 6, No. 12, 2009), and in published monographs (Ashley K., Ed., *Beryllium – Sampling and Analysis* [ASTM STP 1473], ASTM International: West Conshohocken, PA, 2006; Brisson MJ and Ekechukwu AA, *Beryllium – Environmental Analysis and Monitoring*; Royal Society of Chemistry: Cambridge, UK, 2009). Many articles in these publications pertain to beryllium wipe sampling and analysis.

Wet wipe sampling methods (addressed above) enable collection of >75% of surface dust on smooth surfaces [Dufay and Archuleta 2006; Kerr 2004; EPA 1995].

NIOSH analytical methods 9102 and NIOSH 9110 for beryllium in wipe samples have been validated and standardized. Additionally, ASTM D7202, *Standard Test Method for Determination of Beryllium in the Workplace Using Field-Based Extraction and Fluorescence Detection*, been promulgated and validated [Agrawal et al. 2006; Ashley et al. 2007b; Ashley et al. 2005]. The use of (heated) dilute ammonium bifluoride for beryllium extraction has been shown to be effective, even for wipe samples containing refractory materials such as high-fired BeO. Ammonium bifluoride is also effective for quantitatively dissolving beryllium in silicate materials such as soils [Agrawal et al. 2008; Cronin et al. 2008]. This methodology is capable of distinguishing anthropogenic from natural sources of beryllium.

6. What is the best method for sampling and analyzing inhalable beryllium? Please explain your answers and provide evidence to support your answers.

The term "inhalable" refers to an exact model of the probability of particles being inhaled into the human airways as a function of their aerodynamic particle size; the specific equation to this model has been internationally accepted and published in 1983 as an ISO Technical Report (ISO TR 7708). Since the probability of inhalation is less than 100% for particles larger than 1 μm aerodynamic equivalent diameter (AED), not all airborne particles are included equally, and thus there is a concept of an "inhalable fraction" as the fraction of total airborne particles that are likely to be inhaled from an aerosol with a given particle size distribution. The concept of inhalable sampling has been applied to beryllium, although other size fractions may be more appropriate assessments for beryllium disease potential [Harper 2006]. Exposures to particulate substances carrying an "inhalable" designation should be accessed through sampling with a device (sampler) that collects the inhalable fraction of the aerosol.

The concept of "total fraction" has not been defined in terms of particle collection efficiency over the whole range of particle sizes that might be airborne in the ambient environment, and therefore the only definition that can be applied is operational, i.e., that portion of the aerosol that is collected by a specific sampling device [Harper 2009]. Sampling devices are not identical in performance and no personal sampling device is a completely efficient collector of the total aerosol. Sampling devices can collect a smaller fraction of the total aerosol than would be collected by a sampler that collected the inhalable fraction. Since the total fraction is defined by the performance of the sampling device, comparing the effect of sampling the inhalable fraction to the total fraction requires specification of the device being used to collect the total fraction. The difference in collected fractions is a function of the sampler performance and is also a function of the ambient particle size distribution. For certain size distributions there may be little or no difference in the collected fraction between samplers even if the samplers have different performance for other size distributions. The most common sampler used in the U.S. for the collection of the total fraction of aerosol is a filter of 37 mm diameter held in a cassette. The cassette can be used "open-face" where the entry inlet is most of the filter area, but it is more often used "closed-face" where a narrower 4 mm diameter entry inlet affords better protection to the fragile filter from accidental or deliberate trauma. This closed-face cassette (CFC) configuration is the basis of sampling Particulates Not Otherwise Specified in the NIOSH Manual of Analytical Methods (NMAM) Method 0500 and other NIOSH methods for specific particulates analyzed by chemical methods. Sampling with this cassette has been shown to be relatively efficient for particles up to an aerodynamic equivalent diameter of approximately 10 μm [Beaulieu et al. 1980], with the probability of particle capture falling off at larger sizes above 20 μm [Kenny et al. 1997], except when particles are projected into the atmosphere at high velocities. Total dust samples collected using 37-mm cassette samplers with analysis of the filter catch only should not be compared to the inhalable fraction obtained using samplers designed to collect the inhalable fraction. There is no universally accepted test method and accuracy criterion for determining which samplers meet the inhalable convention, although European Standards exist (EN 482:1994 (rev. 2006) *Workplace atmospheres. General requirements for the performance of procedures for the measurement of chemical agents*, and EN 13205:2001 *Workplace atmospheres - Assessment of performance of instruments for measurement of airborne particle concentrations*). EN13205 requires tests for all particles sizes over the range encompassed by the inhalable convention, whether such particles might be encountered in the workplace or not. In the laboratory, therefore, against the European Standard, not all samplers adequately meet the requirement for an inhalable sampler. However, many samplers have been shown to provide results comparable to a sampler operating in accordance with the inhalable convention against a reduced distribution of particle sizes, more similar to that which is most often encountered in the field. Thus, when selecting an inhalable sampler, it is necessary to take into account both laboratory and field studies.

At the time the concept of the inhalable fraction was being developed, a sampler was also being developed to meet the performance required to match this fraction. This sampler, known as the IOM sampler, has a 15 mm inlet and remains the only sampler developed *a priori* to meet the inhalable fraction [Vincent and Mark 1986]. Tests at the time and since have shown it to be reliable under certain circumstances, but also with substantial deviation in performance when used in conditions of directed air-flow [Roger et al. 1998] or when projected large particles are present. During the development of this sampler, it was noted that particles crossing the plane of entry would not always be collected on the filter but could be found instead on internal surfaces of the filter holder. These particles were considered significant in relation to the filter catch and an integral part of the total sample. Thus in later tests in comparison to the CFC sampler, these "wall deposits" (also known as wall losses) were included in the IOM sample. However, similar wall deposits in the CFC samples were generally not included, as it was not considered normal practice to do so at this time. Laboratory comparisons [Kenny et al. 1997] and field comparisons [Werner et al. 1996] of the IOM and CFC samplers revealed differences between them in most environments, with the magnitude of the difference increasing with increasing particle size. However, it has been noted that particles do collect on the internal surfaces of the CFC [Demange et al. 2002], and more recent studies have shown much of the observed differences in mass concentrations between the IOM and CFC samplers disappear when wall deposits of the CFC samples are incorporated in the same way as wall deposits of the IOM samples [Harper and Demange 2007], including environments containing wood dust particles, which are generally recognized to be amongst the largest airborne particles [Lee et al. 2010]. While a difference in the mass collection of IOM and CFC samplers can still be observed in the wood dust environment when wall deposits are incorporated for both samplers, the difference is not significant given the range of variation in paired samplers that is attributable to other environmental sources (as shown by matched sampler pairs). For a very wide range of metal-working environments, including primary ore crushing and beneficiation, primary and secondary smelting and casting operations, welding, grinding and final finishing of metals including aluminum, lead, iron and steel, solders, brasses and bronzes, where particle sizes tend to be smaller than in wood-working operations, multiple studies have demonstrated only minor differences between CFC and IOM samplers, provided wall losses are accounted for in both [Harper and Demange 2007; Harper 2009].

Recent laboratory studies [Lee et al. 2009] have shown minor differences in size distribution between particles on the filters and on the walls of both CFC and IOM samplers, up to 20 μm AED which is consistent with their likely accumulation by many different mechanisms, for example electrostatic attraction, diffusion, impaction and gravitational settling. Thus they should not be excluded considering the sample consists of all particles crossing the plane of entry of the sampler, which was the position taken by the developers of the IOM sampler, and also the position adopted by OSHA in the case of the CFC sampler. However, existing studies do not permit extrapolation of the observations from Lee et al. [2009] or any previous workplace study to particle sizes of approximately 20 μm to 100 μm aerodynamic diameter. Relevant OSHA sampling and analytical methods have been updated to clarify this position, although the standard OSHA gravimetric method (PV2121) has always included wall deposits due to its configuration, which includes an internal capsule weighed in its entirety. OSHA has also carried out tests to determine the most effective method of transferring wall deposits to the sample for digestion and analysis, and these tests concluded that mechanical wiping was superior to rinsing for quantitative removal [Stones et al. 2004]. OSHA recommends using a "smear tab" or a 1 x 2 inch portion of "Ghost wipe", wetted with deionized water [OSHA 2002].

Görner et al. [2010] has suggested a better match to the inhalable fraction for the largest particles of concern may be obtained through deployment of the CFC sampler with its entry inlet in the horizontal, rather than the vertical plane.

Thus, it has been shown that samplers meeting the requirements for inhalable sampling in the laboratory can exhibit non-ideal performance under specific environmental conditions that are not included in the laboratory test protocols, while it has also been shown that samplers that do not meet all the requirements for inhalable sampling in the laboratory according to European studies may be entirely adequate to inhalable sampling in real workplaces. There are also practical considerations of field deployment, such as worker acceptability of size and weight, calibration requirements, flow-rate specifications, disposability vs. re-use which may weigh against the selection of specific samplers. Given all these constraints, it is never possible to recommend a "best" sampler for all environments and circumstances. However, it may be possible to recommend a "best" sampler under the majority of environments encountered that also best meets the practical considerations noted above. The issues of inhalable sampling and criteria involved in selecting an inhalable sampler for beryllium are reviewed in Harper [2009].

To properly quantify the mass of beryllium in a sample using atomic spectroscopy or fluorescence analysis, the digestion or extraction procedure must be sufficient to completely solubilize the largest size particle of the least soluble form of beryllium in the sample. In the case of the inhalable fraction, samplers are designed to collect with 50% efficiency particles having 100 µm aerodynamic equivalent diameter. Given the wide variety of work tasks and differing physicochemical properties of beryllium materials, it is difficult to recommend a 'best' analytical method. However, variations of methods involving beryllium extraction using dilute ammonium bifluoride have been shown to be efficacious for high-fired beryllium oxide particles having a range of particle sizes that bracket the inhalable convention [Ashley and Oatts 2009; Goldcamp et al. 2009]. High-fired beryllium oxide is difficult to completely digest; use of this method is promising for other forms of beryllium such as metal which is known to be relatively more soluble. However, the ammonium bifluoride extraction protocol has not been evaluated using inhalable size particles of any other forms of beryllium than the oxide. A theoretical framework is available for evaluating the efficacy of analytical procedures used to analyze samples containing particulate beryllium compounds [Stefaniak et al. 2007]. This framework provides guidance on which factors to consider in developing analytical methods for particulate beryllium. The time required for complete digestion/extraction is dependent on the dispersity of particle sizes in a sample. In the workplace, beryllium aerosol may have monodisperse particle size, polysdiperse particle sizes, or have unknown particle sizes.

- In the case of monodisperse particles, a digestion procedure is sufficient when it completely dissolves all particles in the sample. An example of this situation is type UOX beryllium oxide powder, clusters of monodisperse primary particles with physical diameter

0.2 µm. As noted below, many analytical procedures exist which are efficacious for these sub-micrometer monodisperse oxides particle sizes and these methods can be evaluated for other sizes and forms of beryllium.

- For polydisperse particles, such as those encountered if using an inhalable sampler, a digestion procedure is sufficient for a sample that contains a range of aerosol particle sizes when the procedure is capable of completely dissolving the largest size particle in the distribution. An example of this situation is rough cutting beryllium oxide or metal billets.
    - Goldcamp et al. [2009] measured recoveries using four different temperatures and up to seven extraction times for a range of beryllium oxide particle sizes to identify conditions sufficient to provide quantitative results.
    - Rather than expensive iterative approaches, the framework advocates calculating digestion times necessary for quantitative recovery from an equation for polydisperse particle dissolution using a few measurements of beryllium recovery under defined conditions of temperature and time.
- For samples containing particles of unknown chemical form and sizes, calculations of digestion time using spike sample recovery data may depend upon the digestion of non-beryllium constituents in samples.
    - A prospective sequential digestion investigation, e.g., digestion of a representative sample or high masses of an appropriate reference material with filtration and analysis of the digestate, followed by digestion of residual particulate material on the filter and analysis of the digestate (repeating this protocol until beryllium is no longer detected in the filtered digestate), may be needed to adequately characterize the population of samples presented for analysis.
    - Note that once the digestion investigation is completed only limited routine sequential digestion may be required to assure recovery meets the pre-defined level of sufficiency.

NIOSH recommends that sample preparation and analysis of beryllium air filter samples be carried out in accordance with NIOSH 7704, NIOSH 7300 series, OSHA ICP methods, or one or more of the following consensus standard procedures:

- ASTM D7202, *Standard Test Method for Determination of Beryllium in the Workplace Using Field-Based Extraction and Fluorescence Detection*
- ASTM D7035, *Standard Test Method for Determination of Metals and Metalloids in Airborne Particulate Matter by Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES)*
- ASTM D7441, *Standard Practice for Separation of Beryllium from Other Metals in Digestion and Extraction Solutions from Workplace Dust Samples*

- ASTM D7439, *Standard Test Method for Determination of Elements in Airborne Particulate Matter by Inductively Coupled Plasma–Mass Spectrometry*

Methods ASTM D7202/NIOSH 7704 achieve detection limits for beryllium in air to 1 ng Be per sample or below, low enough to enable quantitative determination of this element, including short-term sampling in accordance with the newly revised ACGIH TLV; ICP-AES does not offer this capability.

Although the ICP-MS method was found to meet desired performance criteria (e.g., NIOSH accuracy criterion of ±25%) [Ashley et al. 2009b], the estimated uncertainty for ICP-MS was statistically significantly greater than for the molecular fluorescence method. For ICP-MS, laboratory performance at low [Be] was poor considering ICP-MS offers lower method detection limits than ICP-AES. Based on the interlaboratory data obtained, the ammonium bifluoride / molecular fluorescence method is better ruggedized than acid digestion /ICP-MS for occupational hygiene samples.

The use of (heated) dilute ammonium bifluoride for beryllium extraction has been shown to be effective, even for air filter samples containing refractory materials such as high-fired BeO [Ashley and Oatts 2009; Ashley 2011]. Unlike digestion or fusion procedures followed by atomic spectrometric methods, the methodology employing ammonium bifluoride and molecular fluorescence is field-portable. NIOSH recommends methods NIOSH 7704/ASTM D7202 based on laboratory performance [Ashley et al. 2007; Agrawal et al. 2006; Goldcamp et al. 2009]. However, other more traditional methods that entail sample digestion and atomic spectrometric analysis also satisfy the NIOSH criterion for accuracy [Kennedy et al. 1995].

DOE may wish to evaluate the option of moving to performance based analytical methods which can be validated using suitable reference materials. Such methods would minimize confusion regarding modifications to standard methods and allow procedures to be tailored to the unique needs of each site within DOE. Previously, NIOSH, DOE, the National Nuclear Security Agency, and the National Institute of Standards and Technology worked collaboratively to develop Standard Reference Material 1898: Beryllium oxide powder, an industrial material consisting of agglomerates of 0.2 μm diameter primary particles [Winchester et al. 2009]. This inter-agency approach should be revisited for development of larger particle size reference materials of relevant chemical forms of beryllium [Stefaniak et al. 2008].

7. How should total fraction exposure data be compared to inhalable fraction exposure measurements? Please explain your answer and provide evidence to support your answer.

A number of factors related to the sampler and the workplace influence exposure measurements. A single conversion factor for comparing total dust samples collected using 37-mm cassette samplers to the inhalable fraction obtained using inhalable samplers is not possible for all work situations. Studies have demonstrated that sampler design factors such as aspiration efficiency and inlet geometry result in differences in the efficiency by which inhalable particles are collected when sampling from the same aerosol distribution [Buchan et al. 1986; Kenny et al. 1997; Aizenberg et al. 2000]. Additionally, a number of workplace factors will influence sample collection, including wind speed during the task and sampler orientation [Buchan et al. 1986;

Kenny et al. 1997; Aizenberg et al. 2000; Witschger et al. 2004]. Where inhalable samplers have beencompared to the 37-mm cassette samplers (filter only) in the field, a single conversion factor has not been deemed appropriate, particularly for compliance samples that depend on a single determination [Harper 2009; Harper and Demange 2007].

8. Should surface area action levels be established, or should DOE consider controlling the health risk of surface levels by establishing a low airborne action level that precludes beryllium settling out on surfaces, and administrative controls that prevent the buildup of beryllium on surfaces? If surface area action levels are established, what should be the DOE surface area action levels? If a low airborne action level should be established in lieu of the surface area action level, what should that airborne action level be? What, if any, additional administrative controls to prevent the buildup on surfaces should be established? Please explain each of your answers and provide evidence to support your answers.

NIOSH recommends that DOE establish action levels for permissible concentrations of beryllium on surfaces and not consider controlling beryllium contamination on surfaces by lowering the airborne action level. Airborne levels will not preclude beryllium-containing particles from settling onto work surfaces given sufficient time. Analytical results of samples collected from work surfaces provide evidence of compliance with permissible levels of surface contamination [10 CFR Part 850]. The DOE "*removable contamination housekeeping level on surfaces*" must not exceed $3\mu g/100\ cm^2$ during non-operational periods. An action level of less than $3\mu g/100\ cm^2$ would require strict adherence to administrative controls including routine housekeeping, restricted access areas, minimizing the number of employees in the area, and specific protocols for entering and exiting the area. Damian [in press] recently recommended $0.07\ \mu g/100\ cm^2$ as a health risk-based surface contamination cleanup standard for occupational exposure to beryllium.

11. Currently, after the site occupational medicine director has determined that a beryllium worker should be medically removed from exposure to beryllium, the worker must consent to the removal. Should the Department continue to require the worker's consent for medical removal, or require mandatory medical removal? Please explain your answers.

NIOSH is not aware of data demonstrating the lung burden of beryllium sufficient to cause CBD. In addition, NIOSH is not aware of data demonstrating that medical removal of a sensitized individual decreases the likelihood of progressing to CBD, or CBD progressing in severity of disease. The National Academies report to the Air Force *Managing Health Effects of Beryllium Exposure* [NAS 2008] provides the following discussion and recommendation regarding medical removal:

> "No studies have measured the effects of removal from exposure to beryllium on sensitization or CBD. Other occupational diseases that result from immunologic sensitization to an occupational agent include hypersensitivity pneumonitis and occupational asthma. In both, the outcome is worse with continued exposure after disease develops. However, it is difficult to extrapolate those results to beryllium disease because both of those other conditions typically result in symptoms and pulmonary function changes within hours after exposure. In addition, CBD has different clinical characteristics from either of the other diseases. Older cases of CBD in people who had not been removed from exposure appear to have more severe disease compared to those who developed CBD

> more recently. However, it is not known whether that is due to the higher exposure concentrations of beryllium in former years, higher total pulmonary load of beryllium, or longer exposure after sensitization or onset of disease. It is unlikely that large cohorts of workers who are found to be sensitized to beryllium or have CBD will continue to work with beryllium exposure, and a research study to randomize workers to continue or avoid exposure would likely be considered unethical because of the potential severity of CBD. Therefore, the current clinical practice of a strong recommendation to remove CBD patients from exposure [Mapel and Coultas 2002; Kreiss 2005; Maier et al. 2006] is appropriate. Offering it to those with [beryllium sensitization] would also be prudent."

The National Academies suggests that the worker's consent be obtained, but that, should the worker elect to remain in a beryllium-exposed position, information be clearly communicated on the ongoing risk of exposure and that the worker be closely monitored.

References

Agrawal A, Cronin J, Tonazzi J, McCleskey TM, Ehler DS, Minogue EM, Whitney G, Brink C, Burrell AK, Warner B, Goldcamp MJ, Schlecht PC, Sonthalia P, Ashley K [2006]. Validation of standardized portable fluorescence method for determining trace beryllium in workplace air and wipe samples. J Environ Monit 8:619–624.

Agrawal A, Cronin JP, Agrawal A, Tonazzi JCL, Adams A, Ashley K, Brisson MJ, Duran B, Whitney G, Burrell AK, McCleskey TM, Robbins J, White KT [2008]. Extraction and optical fluorescence method for the measurement of trace beryllium in soils. Environ Sci Technol 42: 2066–2071.

Aizenberg V, Grinshpun SA, Willeke K, Smith J, Baron PA [2000]. Performance characteristics of the button personal inhalable aerosol sampler. AIHAJ 61:398–404.

Aizenberg V, Grinshpun SA, Willeke K, Smith J, Baron PA [2000]. Measurement of the sampling efficiency of personal inhalable aerosol samplers using a simplified protocol. J Aerosol Sci 31(2):169–179.

ACGIH [2009]. Beryllium and Compounds: TLV Chemical Substances. In: 7th Edition Documentation. Cincinnati, OH: American Conference of Governmental Industrial Hygienists. Pub #7DOC-059.

Ashley K [forthcoming]. Measurement of ultra-trace beryllium in occupational hygiene samples by extraction and fluorescence detection. J Chem Health Safety.

Ashley K, Agrawal A, Cronin J, Tonazzi J, McCleskey TM, Burrell AK, Ehler DS [2007b]. Ultra-trace determination of beryllium in occupational hygiene samples by ammonium bifluoride extraction and fluorescence detection using hydroxybenzoquinoline sulfonate. Analytica Chimica Acta 584:281–286.

Ashley K, Applegate GT, Wise TJ, Fernback JE, Goldcamp MJ [2007a]. Evaluation of a standardized micro-vacuum sampling method for collection of surface dust. J Occup Environ Hyg 4:215–223.

Ashley K, Braybrooke G, Jahn SD, Brisson MJ, White KT [2009a]. Standardized surface dust sampling methods for metals, with emphasis on beryllium. J Occup Environ Hyg 6:D97–D100.

Ashley K, Brisson MJ, Howe AM, Bartley DL [2009b]. Interlaboratory evaluation of a standardized inductively coupled plasma mass spectrometry method for the determination of trace beryllium in air filter samples. J Occup Environ Hyg 6:745–750.

Ashley K, McCleskey TM, Brisson MJ, Goodyear G, Cronin J, Agrawal A [2005]. Interlaboratory evaluation of a portable fluorescence method for the determination of trace beryllium in the workplace. J ASTM Int 2(9):1–8.

Ashley K, Oatts TJ [2009]. Sample dissolution reagents for beryllium – Applications in occupational and environmental hygiene. In: Brisson MJ, Ekechukwu A, eds. Beryllium –

Environmental Analysis and Monitoring; Cambridge, UK: Royal Society of Chemistry (RSC), pp. 89–101.

ASTM [2003]. Standard Practice for Collection of Settled Dust Samples Using Wipe Sampling Methods for Subsequent Determination of Metals, Method D6966.

ASTM [2006]. Standard Practice for Collection of Settled Dust Samples Using Dry Wipe Sampling Methods for Subsequent Determination of Beryllium and Compounds, Method D7296.

ASTM [2010]. Standard Guide for Strategies for Surface Sampling of Metals and Metalloids for Worker Protection, Method D7659.

Buchan R, Soderholm S, Tillery M [1986]. Aerosol sampling efficiency of 37-mm filter cassettes. Am Ind Hyg Assoc J 47:825–831.

Committee on Beryllium Alloy Exposures, Committee on Toxicology, National Research Council [2008]. Managing health effects of beryllium exposure. Washington, DC: The National Academies Press. [www.nap.edu/catalog/12464.html]

Couch JR, Petersen MR, Rice CR, Schubauer-Berigan MK [2010]. Development of retrospective job exposure matrices for exposures at a beryllium processing facility. Occ Environ Med published online October 25, 2010. doi: 10.1136/oem.2010.056630, 2010.

Creek KL, Whitney G, Ashley K [2006]. Vacuum sampling techniques for industrial hygienists, with emphasis on beryllium dust sampling. J Environ Monit 8:612–618.

Cronin JP, Agrawal A, Adams L, Tonazzi JCL, Brisson MJ, White KT, Marlow D, Ashley K [2008]. Interlaboratory evaluation of an extraction and fluorescence method for the determination of trace beryllium in soils. J Environ Monit 10:955–960.

Damian P [in press]. Development of a health risk-based surface contamination cleanup standard for occupational exposure to beryllium. Toxicol Mech Methods.

Day GA, Dufresne A, Stefaniak AB, Schuler CR, Stanton ML, Miller WE, Kent MS, Deubner DC, Kreiss K, Hoover MD [2007]. Exposure pathway assessment at a copper-beryllium alloy facility. Ann Occup Hyg 51(1):67–80.

Day GA, Stefaniak AB, Weston A, Tinkle SS [2006]. Beryllium exposure: dermal and immunological considerations. Int Arch Occup Environ Health 79(2):161–164.

Day GA, Virji MA, Stefaniak AB [2009]. Characterization of exposures among cemented tungsten carbide workers. Part II: Assessment of surface contamination and skin exposures to cobalt, nickel and chromium. J Expo Sci Environ Epidemiol 19:423–434.

Demange M, Gorner P, Elcabache J-M, Wrobel R [2002]. Field comparison of 37-mm closed-face cassettes and IOM samplers. Appl Occup Environ Hyg 17:200–208.

Deubner DC, Lowney YW, Paustenbach DJ, Warmerdam J [2001]. Contribution of incidental exposure pathways to total beryllium exposures. Appl Occup Environ Hyg 16(5):568–578.

Dufay SK, Achuleta M [2006]. Comparison of collection efficiencies of sampling methods for removable beryllium surface contamination. J Environ Monit 8:630–633.

EPA [1995]. Residential Sampling for Lead: Protocols for Dust and Soil Sampling–Final Report (EPA 747-R-95-001). Washington, DC: Environmental Protection Agency [http://www.epa.gov/lead/pubs/leadtpbf.htm].

Finch GL, Mewhinney JA, Eridson AF, Hoover MD, Rothernberg SJ [2008]. *In vitro* dissolution characteristics of beryllium oxide and beryllium metal aerosols. J Aerosol 19(3):333–342.

Goldcamp MJ, Goldcamp DM, Ashley K, Fernback JE, Agrawal A, Millson M, Marlow D, Harrison K [2009]. Extraction of beryllium from refractory beryllium oxide with dilute ammonium bifluoride and determination by fluorescence –A multi-parameter performance evaluation. J Occup Environ Hyg 6:735–744.

Görner P, Simon X, Wrobel R, Kauffer E, Witschger O [2010]. Laboratory study of selected personal inhalable samplers. Ann Occup Hyg 54:165–187.

Harper M [2006]. A review of workplace aerosol sampling procedures and their relevance to the assessment of beryllium exposures. J Environ Monit 8:598–604.

Harper M [2009]. Air Sampling. In: Brisson M, Ekechukwu AA eds. Beryllium: Environmental Analysis and Monitoring, Chap. 2, Cambridge, UK: Royal Society of Chemistry Publishing, pp. 17–67.

Harper M, Demange M [2007]. Analytical performance criteria concerning sampler wall deposits in the chemical analysis of airborne metals. J Occup Environ Hyg 4:D81–D86.

Henneberger PK, Cumro D, Deubner D, Kent M, McCawley M, Kreiss K [2001]. Beryllium sensitization and disease among long-term and short-term workers in a beryllium ceramics plant. Int Arch Occup Environ Health 74:167–76.

Huang W, Fernandez D, Rudd A, Johnson WP, Deubner D, Sabey P, Storrs J, Larsen R [2011]. Dissolution and nanoparticle generation behavior of Be-associated materials in synthetic lung fluid using inductively coupled plasma mass spectroscopy and flow field-flow fractionation. J Chromatogr A. [Epub ahead of print]PMID: 21167491.

ICRP [1994]. Human respiratory tract model for radiological protection. ICRP Publication 66. Ann ICRP 24(1-3).

International Organization for Standardization [1983]. Air quality–Particle size fraction definitions for health-related sampling. ISO, Geneva, Switzerland: ISO TR 7708-1983 [http://www.iso.org].

Kelleher PC, Martyny JW, Mroz MM, Maier LA, Ruttenber DA, Young DA, Newman LS [2001]. Beryllium particulate exposure and disease relations in beryllium machining plant. J Occup Environ Med 43:238–249.

Kennedy ER, Fischbach TJ, Song R, Eller PM Shulman SA [1995]. Guidelines for air sampling and analytical method development and evaluation. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 95–117 [http://www.cdc.gov/niosh/docs/95-117/].

Kenny LC, Aitken R, Chalmers C, Fabriès JF, Gonzalez-Fernandez E, Kromhout H, Lidén G, Riediger G, Prodi V [1997]. A collaborative European study of personal inhalable aerosol sampler performance. Ann Occup Hyg 41:135–153.

Kerr K [2004]. Sampling beryllium surface contamination using wet, dry and alcohol wipe methods [MS thesis]. Central Missouri State University.

Kreiss K [2005]. Beryllium and cobalt. In: Rosenstock L, Cullen MC, Brodkin CA, Redlich CA, eds. Textbook of Clinical Occupational and Environmental Medicine, 2nd ed, Philadelphia: Elsevier Saunders, pp. 950–954.

Kreiss K, Day GA, Schuler CR [2007]. Beryllium: a modern industrial hazard. Ann Rev Public Health 28:259–277.

Kreiss K, Mroz MM, Newman LS, Martyny J, Zhen B [1996]. Machining risk of beryllium disease and sensitization with median exposures below 2 micrograms/m3. Am J Ind Med 30:16–25.

Kreiss K, Mroz M, Zhen B, Wiedemann H, Barna B [1997]. Risks of beryllium disease related to work processes at a metal, alloy, and oxide production plant. Occup Environ Med 54(8):605–612.

Lee T, Chisholm WP, Slaven JE, Harper M [2009]. Size distributions of 0.5 to 20μm aerodynamic lead-containing particles from aerosol sampler walls and filters. Aerosol Sci Tech 43:1042–1050.

Lee T, Harper M, Slaven JE, Lee K, Rando RJ, Maples EH [2010]. Wood dust sampling: field evaluation of personal samplers when large particles are present. Ann Occup Hyg 55:180–191.

Mikulski MA, Leonard SA, Sanderson WT, Hartley PG, Sprince NL, Fuortes LJ [2010]. Risk of beryllium sensitization in a low-exposed former nuclear weapons cohort from the Cold War era. Am J Ind Med doi 10.1002/ajim.2091.

Muller C, Audusseau S, Salehi F, Truchon G, Chevalier G, Mazer B, Kennedy G, Zayed J [2010]. Beryllium contamination and exposure monitoring in an inhalation laboratory setting. Toxicol Indust Health 26(1):39–45.

NIOSH [1999]. NIOSH comments on the Department of Energy's proposed rule on Chronic Beryllium Disease Prevention Program, Docket No. EH-RM-98-BRYLM, March 9, 1999, NIOSH policy statements. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health.

NIOSH [2003]. NIOSH Manual of Analytical Methods 3rd Suppl: Elements on Wipes, Method 9102. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease

Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2003–154 [http://www.cdc.gov/niosh/docs/2003-154/pdfs/9102.pdf].

NIOSH [2003]. NIOSH Manual of Analytical Methods 3rd Suppl: Factors Affecting Aerosol Sampling, Chapter O. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2003–154 [http://www.cdc.gov/niosh/docs/2003-154/pdfs/chapter-o.pdf].

NIOSH [2011]. NIOSH alert: Preventing sensitization and disease from beryllium exposure. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2011–107 [http://www.cdc.gov/niosh/docs/2011-107/pdfs/2011-107.pdf].

Newman LS, Mroz MM, Balkissoon R, Maier LA [2005]. Beryllium sensitization progresses to chronic beryllium disease: a longitudinal study of disease risk. Am J Respir Crit Care Med 171(1):54–60.

OSHA [1998]. 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.

OSHA [1999]. Preventing adverse health effects from exposure to beryllium on the job. Washington, DC: U.S. Department of Labor, Occupational Safety and Health Administration, OSHA Hazard Information Bulletin 99–09–02 [www.osha.gov/dts/hib/hib_data/hib19990902.html].

OSHA [2002]. Method ID 125G: Metal and Metalloid Particulates in Workplace Atmospheres (ICP Analysis). Occupational Safety and Health Administration (OSHA), Division of Physical Measurements and Inorganic Analyses, OSHA Technical Center, Sandy City, Utah [http://www.osha.gov/dts/sltc/methods/inorganic/id125g/id125g.html].

OSHA [2007]. Evaluation Guidelines for Surface Sampling Methods. T-006-01-0104-M. OSHA Salt Lake Technical Center, Salt Lake City, UT.

Roger F, Lachappelle G, Fabriès JF, Gorner P, Renoux A [1998]. Behaviour of the IOM aerosol sampler as a function of external wind velocity and orientation. J Aerosol Sci 29 (suppl 1):S1133–S1134.

Rosenman K, Hertzberg V, Rice C, Reilly MJ, Aronchick J, Parker JE, Regovich J, Rossman M [2005]. Chronic beryllium disease and sensitization at a beryllium processing facility. Environ Health Perspect 113:1366–1372.

Sanderson WT, Petersen MR, Ward EM [2001]. Estimating historical exposures of workers in a beryllium manufacturing plant. Am J Ind Med 39:145–157.

Schubauer-Berigan MK, Couch JR, Petersen MR, Carreon-Valencia T, Jin Y, Deddens JA [2010a]. Cohort study of workers at seven beryllium processing plants: an update and quantitative exposure-response analyses. Occ Environ Med. Published online October 15, 2010. doi:10.1136/oem.2010.056481.

Schubauer-Berigan MK, Deddens JA, Couch JR, Petersen MR [2010b]. Risk of lung cancer associated with quantitative beryllium exposure metrics within an occupational cohort. Occup Environ Med published online November 16, 2010. doi: 10.1136/oem.2010.056515.

Schuler CR, Virji MA, Deubner DC, Stanton ML, Stefaniak AB, Day GA, Park JY, Kent MS, Sparks R, Kreiss K [forthcoming]. Exposure-response in short-term workers at a beryllium metal, oxide, and alloy production plant.

Stefaniak AB, Brink CA, Dickerson RM, Day GA, Brisson MJ, Hoover MD, Scripsick RC [2007]. A theoretical framework for evaluating analytical digestion methods for poorly soluble particulate beryllium. Anal Bioanal Chem 387:2411–2417.

Stefaniak AB, Day GA, Virji MA, Geer LA, Bello D [in press]. The Skin and the Work Environment. In: Anna DH, ed. The Occupational Environment: Its Evaluation, Control, and Management, 3rd ed. Fairfax, VA: AIHA Press.

Stefaniak AB, Hoover MD, Dickerson RM, Perterson EJ, Day, GA, Breysse PN, Kent MS, Scripsick RC [2003]. Surface area of respirable beryllium metal, oxide, and copper alloy aerosols and implications for assessment of exposure risk of chronic beryllium disease. AIHA J 64:297–305.

Stefaniak AB, Turk GC, Dickerson RM, Hoover MD [2008]. Size-selective poorly soluble particulate reference materials for evaluation of quantitative analytical methods. Anal Bioanal Chem 391:2071–2077.

Taiwo OA, Slade MD, Cantley LF, Fiellin MG, Wesdock JC, Bayer FJ, Cullen MR [2008]. Beryllium sensitization in aluminum smelter workers. J Occup Environ Med 50:157–162.

Vincent R, Catani J, Créau Y, Frocaut A-M, Good A, Goutet P, Hou A, Leray F, Andre-Lesage M-A, Soyez A [2009]. Occupational exposure to beryllium in French enterprises: A survey of airborne exposure and surface levels. Ann Occup Hyg 53(4):363–372.

Werner MA, Spear TM, Vincent JH [1996]. Investigation into the impact of introducing workplace aerosol standards based on the inhalable fraction. Analyst 121:1207–1214.

Winchester MR, Turk GC, Butler TA, Oatts TJ, Coleman CC, Nadratowski D, Sud R, Hoover MD, Stefaniak AB [2009]. Certification of beryllium mass fraction in SRM 1877 beryllium oxide powder using high-performance inductively-coupled plasma optical emission spectrometry with exact matching. Anal Chem 81:2208–2217.

Witschger O, Grinshpun SA, Fauvel S, Basso G [2004]. Performance of personal inhalable aerosol samplers in very slowly moving air when facing the aerosol source. Ann Occup Hyg 48:351–368.

WHO [2001]. Concise International Chemical Assessment Document 32: Beryllium and Beryllium compounds [http://www.who.int/ipcs/publications/cicad/en/cicad32.pdf].