Miller, Diane M. (CDC/NIOSH/EID)

From: Marc_Kolanz@brushwellman.com
Sent: Monday, May 12, 2008 1:46 PM
To: NIOSH Docket Office (CDC)
Subject: 120 - NIOSH Alert: Beryllium

Follow Up Flag: Follow up
Flag Status: Yellow

Attachments: BWI Comments on NIOSH alert 5-12-2008.pdf; Attachment 1- Reword of worker & employer sections.pdf; Attachment 2 - Brush Wellman socio-economic experiences.pdf; Attachment 3 - Suggested rewording of Background section.pdf; Attachment 4 - reword of appendix re Be industries and products.pdf


BWI Comments on NIOSH alert 5...


Attachment 1- Reword of worker...


Attachment 2 - Brush Wellman s...


Attachment 3 - Suggested rewor...


Attachment 4 - reword of appen...

May 12, 2008

NIOSH Mailstop: C-34
Docket NIOSH 120
Robert A. Taft Lab
4676 Columbia Parkway
Cincinnati, OH 45226

Re: NIOSH Docket: NIOSH 120
NIOSH Alert: Preventing Chronic Beryllium Disease and Beryllium Sensitization

Attached below are the comments of Brush Wellman Inc., including four attachments, on the above referenced draft NIOSH Alert. Please respond indicating NIOSH's receipt of these comments.

Please contact me at 216-383-6848 if you have any questions.

Sincerely,

Marc E. Kolanz, CIH
Vice President,
Environmental Health & Safety
Brush Wellman Inc.
17876 St. Clair Ave
Cleveland, OH 44110

(See attached file: BWI Comments on NIOSH alert 5-12-2008.pdf)(See attached file: Attachment 1- Reword of worker & employer sections.pdf) (See attached file: Attachment 2 - Brush Wellman socio-economic experiences.pdf)(See attached file: Attachment 3 - Suggested rewording of Background section.pdf)(See attached file: Attachment 4 - reword of appendix re Be industries and products.pdf)

BRUSHWELLMAN
ENGINEERED MATERIALS

Brush Wellman Inc.
17876 St. Clair Avenue
Cleveland, OH 44110

May 12, 2008

NIOSH Mailstop: C-34
Docket NIOSH 120
Robert A. Taft Lab
4676 Columbia Parkway
Cincinnati, OH 45226

Re: NIOSH Docket: NIOSH 120
NIOSH Alert: Preventing Chronic Beryllium Disease and Beryllium Sensitization

(Submission is via e-mail)

Brush Wellman Inc. appreciates the opportunity to provide technical comments on the draft NIOSH Alert titled, Preventing Chronic Beryllium Disease and Beryllium Sensitization. Brush Wellman is the leading international supplier of high-performance engineered materials containing beryllium and is headquartered in Cleveland, Ohio. It is the only fully integrated supplier of beryllium, beryllium alloys and beryllia ceramic in the world. Since its founding in 1931, Brush Wellman has concentrated its operations and skills on advancing the unique performance capabilities and applications of beryllium-based materials. As a world leader in beryllium production and technology, Brush Wellman strives to remain a leader in medical knowledge of beryllium and in the environmental, health and safety aspects of the material.

Brush Wellman's current model to prevent chronic beryllium disease (CBD) is based on our knowledge, experience and understanding gained from our cooperative research efforts with NIOSH of the epidemiology related to the various chemical forms of beryllium, the etiology of beryllium disease, health risks posed by exposure intensity, and disease prevention methodologies tailored to specific processing methods. The 2007 NIOSH study by Cummings and other studies are demonstrating that the model is effective.

Brush Wellman believes that the issuance of a NIOSH Alert is an ineffective means to convey beryllium health and safety guidance to workers and employers in light of the substantial work that has been done to convert research findings into work practices that best protect workers. This research-to-practice information has been translated into an innovative computer based tool titled, The Interactive Guide to Working Safely with Beryllium and Beryllium-containing Materials, which has been distributed directly to over 8,000 customers and Brush Wellman workers. We believe that the significant resources of NIOSH would be better used if it would partner with Brush Wellman to assist in communicating this guide throughout the beryllium supply chain.

Brush Wellman's attached comments are split into two sections. The first section addresses the technical content and completeness of the draft NIOSH Alert. The second section addresses the issuance of this draft NIOSH Alert as it relates to the guidance established by the Office of Management and Budget Bulletin on Agency Good Guidance Practices issued as an Executive Order on January 18, 2007. The goal of these comments is to improve the accuracy of the information, ensure the most current scientific information is considered and to improve the effectiveness and relevance of the communication to workers and employers.

We believe NIOSH has an obligation to serve in a gate-keeping role to ensure that the scientific evidence forming the basis for its health and safety communications is complete, relevant and reliable and that opinions, hypotheses and limited studies do not divert NIOSH from its mission to *"develop information on safe levels of exposure to toxic materials and harmful physical agents and substances"*

Thank you for your consideration of our comments. Please contact me at 216-383-6848 if you have any questions.

Sincerely,

Marc E. Kolanz, CIH
Vice President,
Environmental Health & Safety

MEK/elm
Attachments

Comments of Brush Wellman Inc. to NIOSH on the:

Draft NIOSH Alert: Preventing Chronic Beryllium Disease and Beryllium Sensitization
Docket Number: NIOSH 120

May 12, 2008

Submitted by:
Marc E. Kolanz, CIH
Vice President
Environmental Health and Safety
Brush Wellman Inc.
17876 St. Clair Avenue
Cleveland, Ohio 44110

Summary of Key Comments

The draft NIOSH Alert statement to *"keep airborne concentrations of beryllium as low as possible, since no safe exposure limit for beryllium is known"* fails to accurately characterize and disclose to workers and employers the current state of knowledge regarding the identification of an appropriate occupational exposure limit. This is contrary to NIOSH's mission to *"develop information on safe levels of exposure to toxic materials and harmful physical agents and substances."*

In occupational health and safety, exposure limits are not conceptualized with the intent of achieving certainty of absolute protection for all persons. One reason for this is that it is impossible scientifically to define a safe exposure concentration for all workers for any material because this involves proving an absolute negative. This fact is recognized in every scientific venue that recommends or establishes occupational exposure limits (OELs). Since everyone is exposed to airborne beryllium-containing particulate (it occurs naturally in all soil), it is the collection and careful evaluation of good quality worker exposure data which is crucial to setting appropriate occupational exposure limits. Any NIOSH correspondence to workers and employers should clearly state that independent reviews by others have found sufficient evidence to adopt exposure limits or guidelines for occupational exposure to beryllium. For example, the State of California OSHA has adopted a permissible exposure limit for beryllium of 0.2 $\mu g/m^3$; the Department of Energy has adopted an exposure action level of 0.2 $\mu g/m^3$ and the primary producer of beryllium-containing materials, along with several other large companies, have adopted a recommended exposure guideline of 0.2 $\mu g/m^3$.

NIOSH's research study by Cummings is supportive of a recommended exposure limit of 0.2 $\mu g/m^3$ to prevent sensitization when used as part of a defined beryllium worker protection model. It is also notable that the findings of Cummings are supported by the NIOSH studies of Schuler and Stanton and the study by Madl, which is the only individual dose-response study performed to-date. We believe that the available scientific information is sufficient for NIOSH to fulfill its mission and duty to recommend an exposure limit for beryllium that protects against a material impairment of health. In fulfilling its duty, it is important for NIOSH to keep in mind that establishing occupational exposure limits for metals have historically been based on protection against material impairments and not laboratory detection of immune responsiveness when no health effect is evident.

NIOSH's Criteria for issuing an Alert are not met.

According to NIOSH, *"Alerts are brief publications, based on case reports, that are intended to reduce injuries and fatalities or diseases and to stimulate research on effective preventive measures. The primary audience consists of those people in a position to directly intervene in the work environment to quickly eliminate the problem and reduce the risk."* This Alert fails to meet the NIOSH criteria for an Alert because:

- This draft NIOSH Alert is not being prompted by case reports. The case reports first questioning the efficacy of the occupational standard occurred over 20 years ago.
- It is not likely that additional research will be stimulated by the Alert because a huge amount of beryllium research was prompted by those early case reports and has been underway for nearly 20 years and continues today.
- Clinical Chronic Beryllium Disease rarely occurs in the downstream user population.
- Other than partial inclusion of some of the elements of the Brush Wellman Inc. Beryllium Worker Protection Model, the Alert offers no new information beyond that which has already

been conveyed by either Brush Wellman via its periodic health and safety updates to its customer base or by OSHA in its 2002 OSHA Bulletin on beryllium; and this Alert was originally drafted four years ago and is not timely in its conveyance of information.

As an add-on to its existing 10-year research partnership with Brush Wellman Inc., NIOSH should consider working with Brush to further communicate Brush's computer based Interactive Guide to Working Safely with Beryllium and Beryllium-containing Materials (Interactive Guide) as a more effective communication alternative to issuing an Alert. In early 2008, the Interactive Guide was distributed to over 8,000 of Brush Wellman's customers and employees. NIOSH should focus its considerable resources on helping to convey this useful tool to a broader audience of workers and employers.

Any NIOSH communication of this type should be revised to enhance reader understanding by the target audience of workers and employers.

The current document is written more as a manuscript and, as such, is not very readable or useful to either an employee or an employer. Any NIOSH communication on beryllium should identify and disclose to employers and employees:

- Specific guidance on job tasks that generate particulate and have higher risks versus tasks that do not generate particulates and have lower risks.
- Guidance to the employer or the employee on likely harms and benefits of BeLPT testing based on the weight of scientific evidence versus opinion.
- The most current scientific findings based on an independent and thorough evidence-based review of the available scientific literature; and
- All of the components of the beryllium worker protection model jointly studied by NIOSH and Brush Wellman Inc.

NIOSH should advise workers and employers of the existence of the Interactive Guide available from Brush Wellman which describes the worker protection model that NIOSH and Brush Wellman have been studying. NIOSH does not have to endorse the Interactive Guide, but in the best interests of workers and employers, it should convey the fact that it exists.

The NIOSH recommendation to *"substitute less hazardous materials for those containing beryllium whenever feasible"* introduces the concept of feasibility without providing either a basis for the statement or a context in which to apply the recommendation.

Although it is an accepted industrial hygiene practice to substitute a less toxic material to reduce health risks, it is of little value to employers and employees who have a potential to be exposed to excessive levels of airborne particulates containing beryllium since the use of beryllium-containing materials is usually limited to applications where there are no substitutes. Beryllium-containing materials are usually the higher cost option and are used because they bring performance and reliability properties that are necessary for the proper function of the end-use product. Some readers will view this recommendation to substitute another material for beryllium as advice by our government to essentially stop all use of beryllium-containing materials. This is an inappropriate message for NIOSH to convey. In the context of this recommendation, NIOSH has a responsibility to take into account the overall public health benefits of beryllium in addition to the potential health risks to manufacturing workers and to convey that information to the audience.

If an Alert is issued, the title of the draft NIOSH Alert, "Preventing Chronic Beryllium Disease and Beryllium Sensitization," does not merit the inclusion of a preventive warning for beryllium sensitization nor should beryllium sensitization be used as part of the worker warning notices on pages iii and 1.

The prevention of beryllium sensitization does not merit a preventive warning in a NIOSH Alert to workers regarding beryllium. It is well established by the American National Standards Institute (ANSI) that for warnings to be effectively communicated, they must be easily understood and focused on the primary health effect of concern. In this instance, the primary health effect of concern is clinical chronic beryllium disease (CBD) which is a material impairment of health. The draft NIOSH Alert recognizes that the identification of beryllium sensitization does not include any health symptoms. We know of no ANSI, OSHA or other hazard communication warning criteria where sensitization, not involving symptoms, would merit a warning provision.

The draft NIOSH Alert recommends that all employers conduct medical surveillance for beryllium sensitization using the BeBLPT to allow employers to identify higher risk jobs and prioritize prevention efforts. This recommendation could only work under a carefully planned research protocol. In addition, NIOSH has not demonstrated an evidence-based foundation to support its recommendation. Without having first evaluated the serious socio-economic and legal implications to workers and employers, NIOSH should not be recommending an unreliable and inconsistent test that is not standardized in the hope that additional beneficial research will result

The draft NIOSH Alert states that *"Despite its limitations [BeBLPT], the BLPT is the best available tool to identify sensitization until a more precise test becomes available."* NIOSH's consideration of the BeBLPT as the "best available tool" does not provide a adequate justification for NIOSH to recommend its use. NIOSH makes its statement without disclosing the performance issues of the test or the labs that conduct the test and it omits the most recent study findings on this topic, namely the 2006 papers by Borak and Cher and the 2007 study by Donovan. The Cher paper identifies systematic performance problems with the labs performing the BeBLPT. The studies by Donovan and Cher demonstrate that the BeBLPT is not a reliable indicator of beryllium sensitization (BeS) due to the inconsistent performance of the test, the absence of a standardized method of testing, inconsistent test interpretation, the variability of test outcomes and the reversion of positive results to normal after retesting over time. Donovan also confirms the detection of BeBLPT identified beryllium sensitization in the general non-occupationally exposed population and demonstrates, longitudinally, the on/off detection of positive BeBLPT's in individual beryllium workers. The Borak paper is the only study to evaluate the value of BeBLPT using criteria established by the World Health Organization (WHO) focusing on five elements essential to judging effectiveness of preventive services: 1) burden of suffering, 2) accuracy and reliability of screening tests, 3) effectiveness of early detection, 4) harms of screening and 5) benefits outweighing harms. Borak concluded, *"There is currently insufficient scientific evidence to support the use of BeLPT for routine screening of asymptomatic individuals".*

NIOSH has also not evaluated the potential social, economic, psychological and legal consequences of its recommending that employers offer and workers take the BeBLPT. The use of this test has been known to result in job loss, change in employment status, life and health insurability issues or concerns, legal action between employee and employer, workers' compensation problems and family and personal mental health concerns. As a result, NIOSH needs to conduct a full evaluation and disclosure of these issues which are essential to workers and employers understanding the potential personal life-changing consequences that have been known to result from the offering of or taking of this test.

The draft NIOSH Alert does not disclose to employers the detailed procedures, protocols and high costs necessary to even consider what is necessary to implement a testing program to *"identify higher risk jobs and prioritize prevention efforts."* In almost every instance, such a recommendation cannot be scientifically justified based on population size constraints. A generalized recommendation for employers to screen workers using the BeBLPT serves no discernable value to employers or workers in small work populations because the results will be uninterpretable. Absent a government sponsored study, such screening would impose a huge financial burden on larger employers with no evidence that the analysis will be interpretable within the context of the individual workplace.

We believe that, based on the available scientific evidence demonstrating the performance problems with the BeBLPT and the absence of an analysis of the socio-economic consequences to workers and employers, NIOSH should not be recommending employers screen workers using the BeBLPT. NIOSH should recommend that beryllium workers be fully educated regarding the risks of CBD and the symptoms of cCBD, and be advised to tell their doctor of their history of beryllium work if they seek care for pulmonary symptoms, so that CBD may be considered in the differential diagnosis.

The draft NIOSH Alert recommends to all employers with workers who come into contact with beryllium-containing dusts, fumes, solutions and suspensions, to conduct medical surveillance for beryllium sensitization using the BeBLPT. This recommendation is untenable based simply on the fact that beryllium is a ubiquitous element and beryllium-containing dusts can be found in every single workplace in the world.

If all U.S. employers would heed the NIOSH recommendation to conduct the BeBLPT on all workers who come into contact with beryllium-containing dusts in any form and at any concentration, then all 100,000,000+ workers in the United States would undergo testing at a cost of over 30 billion dollars. Based on the Donovan study that detected beryllium sensitization in a worker population not known to be occupationally exposed to commercially produced beryllium, we would expect that 1,000,000 to 2,000,000 workers would be identified and medically labeled as beryllium sensitized simply due to the rate that BeBLPT-detected sensitization is identified in the general population.

The NIOSH Alert should inform workers and employers about the various forms of CBD.

The Draft NIOSH Alert does make the correct statement that the number of sensitized workers who will eventually develop CBD is unknown and that beryllium sensitization involves no health symptoms. However, the discussion that follows is not accurate because it does not clearly define to workers and employers what sensitization is nor does it differentiate the forms of CBD. It also uses confusing terminology such as "risk of sensitization" which uses the term "risk" in the context of frequency of occurrence rather than a health risk. NIOSH should clearly disclose to workers and employers the historical changes in the diagnostic criteria for Chronic Beryllium Disease that resulted in the identification of both clinical CBD (with health symptoms) and subclinical CBD (without health symptoms). This information is very important in aiding the understanding of these terms by workers and employers and should be fully disclosed.

How a CBD health risk is defined by NIOSH will have significant implications when weighing the benefits or harms to individuals associated with NIOSH's recommendations for medical surveillance and screening.

The discussion of the Newman 2005 paper suggests, but does not demonstrate, a progression rate from beryllium sensitization to CBD.

This inference should be removed from any NIOSH correspondence, including the Alert, because there is no longitudinal study that explores the natural history of BeS through cCBD.

The discussion of Skin Exposure in the Workforce Surveys section of the draft NIOSH Alert should disclose fully the available scientific evidence regarding skin exposures and not limit the information to a discussion of an unproven hypothesis.

The recent NIOSH studies exploring the hypothesis that sensitization to beryllium can occur via intact skin should not be used as a primary basis upon which to recommend employers and workers prevent skin contact with tiny beryllium particles or solutions containing beryllium. Brush Wellman continues to jointly research this hypothesis with NIOSH; however, the scientific evidence is certainly not sufficient to use these research findings as a primary basis for a recommendation to workers and employers. The keeping of fine beryllium-containing particulate off of the skin as an element of Brush Wellman's worker protection model is supported by the recent Cummings study. However, it is disingenuous to infer that keeping beryllium-containing particulate off the skin is a primary reason for the success of the worker protection model. At this point in time, it is unknown which elements of the worker protection model are apparently making the model successful. We only know that studies are demonstrating that implementing the entire model appears to be working. It is not appropriate for NIOSH to state or infer that keeping beryllium-containing dusts off the skin may be more important than other aspects of the model. To do so would be misleading to workers and employers as to what actions are necessary to work safely with beryllium-containing materials.

The draft NIOSH Alert appears to accept a conclusion that beryllium is carcinogenic in man without first having fully evaluated the studies that have been published since IARC and others last reviewed their cancer classifications for beryllium over ten years ago.

These more recent studies deal with sizeable cohorts exposed to very high levels of beryllium. Failure to find convincing evidence that beryllium workers have excess rates, combined with clear evidence that in beryllium workers, lung cancer is not related to degree of exposure, strongly supports a reclassification of beryllium as non-carcinogenic in humans.

The two case studies illustrated in the draft NIOSH Alert offer very little instructive benefit to workers and employers and should be removed.

Employers and workers will be much better served if the NIOSH Alert focuses on the actions that have been demonstrated to prevent chronic beryllium disease.

The NIOSH listing of Current Exposure Limits contains several inaccuracies which need to be corrected.

For instance, NIOSH cannot say that safe exposure limits have not been established for beryllium. In 2006, the State of California adopted an 8-hour time weighted average permissible exposure limit (PEL) for beryllium of 0.2 micrograms per cubic meter of air. This is a 10-fold reduction in the federal OSHA PEL.

Specific Comments

The draft NIOSH Alert statement to *"keep airborne concentrations of beryllium as low as possible, since no safe exposure limit for beryllium is known"* fails to accurately characterize and disclose to workers and employers the current state of knowledge regarding the identification of an appropriate occupational exposure limit.

In occupational health and safety, exposure limits are not conceptualized with the intent of achieving certainty of absolute protection for all persons. One reason for this is that it is impossible scientifically to define a safe exposure concentration for all workers for any material because this involves proving an absolute negative. This fact is recognized in every scientific venue that recommends or establishes occupational exposure limits (OELs). In addition, the setting of OEL's must include the selection of an appropriate health end-point on which to base the limit. It is important for NIOSH to keep in mind that establishing occupational exposure limits for metals have historically been based on protection against material impairments and not laboratory detection of immune responsiveness when no health effect is evident.[1]

While there has been uncertainty and debate surrounding the identification of a safe airborne exposure level for workers for several years, the draft NIOSH Alert statement that there is no safe exposure level is simply wrong. Every person is exposed to airborne beryllium via windblown dusts (all soil contains beryllium), emissions from the combustion of coal and tobacco smoke. Additionally, many household products, such as ceiling tiles, fertilizers, detergents, charcoal and kitty litter, contain beryllium. Since everyone is exposed to airborne beryllium-containing particulate, it is the collection and careful evaluation of good quality worker exposure data which is crucial to understanding CBD and in setting appropriate occupational exposure limits.

With regard to identifying an occupational exposure limit for beryllium, the draft NIOSH Alert mentions several studies without providing any reasoning or analysis to supports its recommendation of keeping exposures as low as possible. The NIOSH Alert must consider all of the studies relevant to this topic, including the NIOSH funded studies by Schuler[2] and Cummings, unless NIOSH has reason to believe that the results are not reproducible or scientifically sound.

A study that does provide the best evidence that there is a safe level is the study by Madl 2007[3]. Using over 3,000 personal air samples the Madl study is the first study to actually perform a complete dose reconstruction of persons defined as beryllium sensitized or diagnosed with CBD. In fact, the Madl study dose reconstruction also differentiates between those persons with sCBD (no symptoms) and cCBD.

In addition to the findings of Madl and assuming NIOSH believes that the studies by Shuler and Cummings are of scientific value, they should be used to support a NIOSH recommended exposure limit of 0.2 $\mu g/m^3$ since the Shuler study concluded, *"Sensitization and CBD were associated with an area in which beryllium air levels exceeded 0.2 mg/m^3, and not with areas where this level was rarely exceeded."* Additionally, the NIOSH study by Cummings demonstrated the effectiveness of a worker protection model that incorporates a recommended occupational exposure guideline of 0.2 $\mu g/m^3$.

The draft NIOSH Alert should also carefully consider the strength of the scientific evidence in the Department of Energy funded study by Johnson et al. 2001. We know of no air sampling data set for any substance that more thoroughly characterizes a worker population. The Johnson et al. study includes over 217,000 personal samples using an exposure assessment strategy that monitored

every worker on every day for 36 years. The Johnson study demonstrated that the Cardiff beryllium control model achieved compliance with the United Kingdom 2 $\mu g/m^3$ 8-hour Maximum Exposure Limit (MEL) over 98 percent of the time and prevented clinical chronic beryllium disease (cCBD). There is no other beryllium facility that has demonstrated the success of CBD prevention as that accomplished at the United Kingdom Atomic Weapons Establishment in Cardiff, Wales.

Contrary to the draft NIOSH Alert view of no safe level of exposure, the following brief summaries of the findings of Madl, Johnson, Schuler and Cummings provide sufficient evidence to define an appropriate OEL for beryllium when used in conjunction with the worker protection model.

Madl 2007

A major challenge for evaluating the exposure-response relationship for BeS and CBD is that most studies have used inconsistent sampling and exposure assessment methodologies and definitions for BeS and CBD[4]. These differences have often prevented direct comparisons between studies, as well as the identification of a clear exposure-response relationship for BeS and CBD. In the study by Madl et al. 2007, a large data set of 3,831 personal lapel and 616 general area samples provided an opportunity to use several methods to reconstruct each worker's exposure prior to the ascertainment of BeS or the diagnosis of subclinical or clinical CBD, followed by an exposure-response analysis to determine whether a threshold for BeS and CBD could be identified. Four different methods were used to reconstruct historical exposures of each worker as industrial hygiene data were pooled by year, job title, era of engineering controls and by complete work history (life-time weighted average) prior to diagnosis.

The Madl study concluded:

> *"Results showed that exposure metrics based on shorter averaging times (i.e., year versus complete work history) better identified the upper bound worker exposures which could have contributed to the development of BeS or CBD. It was observed that all beryllium sensitized and CBD workers were likely exposed to beryllium concentrations greater than 0.2 $\mu g/m^3$ (95^{th} percentile) and 90% were exposed to concentrations greater than 0.4 $\mu g/m^3$ (95^{th} percentile) within a given year of their work history. Based on this analysis, it would appear that BeS and CBD generally occurred as a result of exposures greater than 0.4 $\mu g/m^3$ and that maintaining exposures below 0.2 $\mu g/m^3$ 95% of the time may prevent BeS and CBD in the workplace."*

The authors noted that, in important respects, their study was the first of its kind stating that:

> *"An effective OEL is one that reduces or eliminates the risk of an adverse health effect or outcome in the majority of the working population. Unlike many other chemicals, identifying the exposure metric upon which to derive the OEL is particularly difficult for beryllium due to its immunologic pathogenesis. Historically, epidemiologic studies have studied BeS and CBD prevalence in relation to the mean or median beryllium concentration for the longest or most recent job title held. In general, these studies have found that certain job titles or operations may pose an increased or lesser risk of BeS and CBD, but none have shown an exposure-response pattern for these endpoints. The majority of these studies reconstructed worker exposures based on broad job classifications and have not evaluated the beryllium exposures which may have contributed to the identification of BeS or diagnosis of CBD in each worker. Our analysis is not only the first to reconstruct worker exposures to beryllium based on individual work history, but also is the first to evaluate a variety of exposure reconstruction methods and their influence on the exposure-response patterns for BeS and CBD. The results of our analyses show that the magnitude of the upper bound exposures, which may have led to the development of BeS and*

CBD, is typically not reflected in historical exposure estimates that are averaged over several years (e.g., LTW). Given the immunologic basis of BeS and CBD and that these endpoints have been documented, in some cases, as a result of relatively short-term exposures (e.g., < 1 year), it is important to not only understand central tendency estimates of exposure but also upper bound exposures.

In addition to understanding the plausible range of exposures which may contribute to the identification of BeS and diagnosis of CBD, for purposes of deriving an OEL, it is important to characterize the level of exposure below which the risk of disease is not substantially increased. The majority of studies conducted to date have involved cross-sectional studies which have not included adequate control comparison groups or an evaluation of worker-specific exposures. The analysis described in this study was the first to derive exposure estimates specific to each beryllium sensitized worker and CBD case. Because individual work exposures were derived based on specific job history and exposure data, this analysis provides a better understanding of the range of exposures to airborne beryllium that is associated with BeS or CBD. Based on this analysis of beryllium sensitized and CBD workers, it would appear that BeS and CBD generally occurred as a result of exposures greater than 0.4 µg/m^3 and that maintaining exposures below 0.2 µg/m^3 95% of the time may prevent BeS and CBD in the workplace."

Accordingly, the large exposure data set and dose reconstruction in Madl is unmatched by any other study.

Johnson 2001

The 2001 Department of Energy (DOE) study by Johnson reviewed and analyzed the results of the beryllium monitoring program at the Atomic Weapons Establishment beryllium facility in Cardiff Wales. The Cardiff study analyzes the single most extensive historical database of personal exposure monitoring data within the beryllium industry. A notable feature of the program was that it included personal exposure monitoring on every worker for every day worked over 36 years of operation. More than 200,000 personal samples were collected between 1981 and 1997 representing the last 16 years the facility was in operation. Based on these extensive sampling data, the Cardiff facility achieved compliance with the 2 µg/m^3 8-hour OEL 98 percent of the time. Since its inception, the Cardiff facility maintained a state-of-the-art exposure management program which included strict and consistent use of engineering controls, work practices, housekeeping, process containment, migration controls and the use of personal protective equipment. The Cardiff program resulted in one case of clinical CBD over 36 years of operation. Johnson concluded that the Cardiff experience *"...appears to have successfully prevented the incidence of clinical CBD with the exception of one unique case."*

Some scientists discount out-of-hand the Johnson study because it did not include a BeBLPT research component and only looked at identifying clinical CBD. Such criticisms are not warranted for a few highly significant reasons. First, based on the power of the huge numbers of samples taken on every worker on every day provides a high degree of scientific evidence that is unmatched by any other study. Second, all workers were enrolled in a medical surveillance program looking specifically for CBD which included monthly pulmonary function testing, annual physicals and annual chest x-rays. Third, it is notable that the Cardiff physicians did use the BeBLPT, but discontinued its use due to concerns over reliability. The findings of Johnson clearly demonstrated that Cardiff's exposure management program and a high level of compliance with the 2 µg/m^3 8-hour OEL prevented clinical CBD.

Schuler 2005

The Schuler 2005 study performed a cross-sectional survey to examine prevalence of beryllium sensitization (BeS) and CBD, and relationships between BeS and CBD and work areas/processes at a copper beryllium alloy strip and wire finishing facility. The study concluded:

> "*Sensitization and CBD were associated with an area in which beryllium air levels exceeded 0.2 mg/m^3, and not with areas where this level was rarely exceeded.*
>
> *Employees at this copper beryllium alloy facility had similar prevalences of sensitization and CBD as workers at facilities with higher beryllium air levels.*"

Cummings 2007

As discussed in the draft NIOSH Alert, the study by Cummings et al. provides an analysis of the effectiveness of Brush Wellman's beryllium exposure control model. This model includes the use of an 8-hour time-weighted average exposure action limit of 0.2 µg/m^3. This study demonstrates that this exposure control model, in use since 2000, has been effective in reducing the detection of beryllium sensitization from over 8% to 1%, which is same as the background rate found in the non-occupationally exposed population. This exposure control model is very similar to the exposure control model used at the Cardiff facility as described by Johnson.

Brush Wellman's Beryllium Worker Protection Model is a comprehensive and multifaceted approach for reducing occupational exposure to beryllium particles. The model focuses on keeping beryllium work areas clean and to keeping particles and solutions containing beryllium out of the lungs, off the skin, off of clothing, in the work process, in the work area and on the plant site. Worker and management education and motivation are important components. A combination of engineering, work practice and personal protection approaches are used as needed to attain the reduction in potential occupational exposure. The Beryllium Worker Protection Model is based on our knowledge, experience and understanding gained from the most recent joint studies with NIOSH and others, which include the potential exposure risks posed by the various chemical forms of beryllium and disease prevention methods tailored to specific material processing operations, engineering, work practice control, and personal protective measures that have been demonstrated to be effective in preventing sensitization and CBD at Brush Wellman facilities.

NIOSH should disclose to workers and employers that independent reviews by others have found sufficient evidence to adopt exposure limits or guidelines for occupational exposure to beryllium. For example, the State of California OSHA has adopted a permissible exposure limit for beryllium of 0.2 µg/m^3; the Department of Energy has adopted an exposure action level of 0.2 µg/m^3 and the primary producer of beryllium-containing materials, along with several other large companies, have adopted a recommended exposure guideline of 0.2 µg/m^3. We believe that in light of the available scientific information, there is no justifiable basis for NIOSH to suggest there is no safe limit for beryllium and that NIOSH should be able to recommend an occupational exposure limit for beryllium.

NIOSH's criteria for issuing an Alert are not met.

According to NIOSH, *"Alerts are brief publications, based on case reports, that are intended to reduce injuries and fatalities or diseases and to stimulate research on effective preventive measures. The primary audience consists of those people in a position to directly intervene in the work environment to quickly eliminate the problem and reduce the risk."* This Alert fails to meet the criteria for an Alert. It is not reasonable to expect that additional research will be stimulated by the

Alert, nor is it likely there will be quick intervention. For nearly the past twenty years, well over fifty research studies have been published investigating concerns related to the efficacy of the current occupational standard and the development of control measures to better protect employees. Today, there are at least another dozen research studies on beryllium health and safety currently underway. Brush Wellman has been conveying directly what interventions are and are not effective to its customers. We have also been conveying this information via publications, articles and presentations to scientific audiences, regulatory agencies and other interested stakeholders. The case studies cited do nothing more than add confusion and feebly support the NIOSH's perceived need to test for sensitization, which as a lagging metric, clearly cannot *"quickly eliminate or reduce the risk."* Furthermore, the cases cited only add more confusion as nothing is stated relative to the vintage of the cases, the nature of exposure or the outcome of the cases which would be of interest to employers and employees. Additionally, the purpose of a NIOSH Alert to quickly eliminate the problem is moot since Brush Wellman has been specifically informing its customers regarding what is known and unknown about the science exploring the efficacy of occupational exposure standards for beryllium for more than the past ten years. Therefore, other than partial inclusion of some of the elements of the Brush Wellman Inc. Beryllium Worker Protection Model, the Alert offers no new information beyond that which has already been conveyed by either Brush Wellman via its periodic health and safety updates to its customer base or by OSHA in its 2002 OSHA Bulletin on beryllium. In addition, the intent of an Alert to convey information promptly is moot since it has taken NIOSH four years to issue a second draft. Therefore, NIOSH should consider other NIOSH venues for communication of its message such as the Current Intelligence Bulletins (CIBs), Information Circulars, Workplace Solutions, Health and Safety Guides or Technical Reports. NIOSH should consider partnering with Brush to further communicate Brush's computer based Interactive Guide to Working Safely with Beryllium and Beryllium-containing Materials (Interactive Guide) as a more effective alternative to issuing an Alert. In early 2008, the Interactive Guide was sent out to over 8,000 of Brush Wellman's customers and employees. NIOSH should focus its considerable resources on helping to convey this useful tool to a broader audience of workers and employers.

Any NIOSH communication of this type should be revised to enhance reader understanding by the target audience of workers and employers.

The current document is written more as a manuscript and as such is not very readable or useful to an employee or an employer. For example, the Alert is filled with references to papers that would be of no or little value to employers and particularly employees. The Alert does not adequately address the effects of particle size, and there is no specific guidance on job tasks that generate particulate and have higher risks versus tasks that do not generate particulates and have lower risks. The Alert does not give adequate guidance to the employer or the employee on BeLPT testing; e.g., what the result means to the individual, the costs of medical testing or the relative reliability of the test. The Alert also interjects confusion as to the value of doing any individual screening or medical surveillance when it states there is no safe level of exposure. Confusion is further exacerbated, by the fact that NIOSH states the Recommended Exposure Limit is 0.5 $\mu g/m^3$ while also stating there is no safe level.

It is also evident that the content of the draft NIOSH Alert does not reflect the most current scientific evidence. Based on a review of the references, there were very few added since the 2004 Stakeholder draft of this same document. As a result, several important studies appear to have not been considered which results in an incomplete disclosure of information to workers and employers that is important to their understanding of how to work safely with beryllium-containing materials. The development of the NIOSH Alert should include a scientific evidence based assessment of all of the available literature.

The Alert also does not address all of the components of a beryllium worker protection model that, based on the best available evidence, has proven to be effective in preventing chronic beryllium disease. What is truly disheartening is that even though NIOSH assisted in the evaluation of the Interactive Guide, NIOSH failed to include all of the components or even refer to the Guide as a useful tool. Attachment 1 is a suggested revision of the text in the Alert specific to worker and employers in an attempt to better convey the elements of the Interactive Guide.

Review of the investigations of beryllium workplaces conducted by NIOSH and others in the past fifteen years have reinforced insights on how to protect workers. These insights have lead to the adoption of a beryllium worker production model by the primary industry.

A NIOSH communication is the perfect opportunity to guide workers in the elements of the beryllium worker protection model. This model has been demonstrated to be effective by both the Johnson[5] and Cummings[6] studies. There is at present, no better information available upon which NIOSH can structure recommendations to workers and employees via a NIOSH Alert. In beryllium operations with previous high rates of CBD that handle beryllium and beryllium-containing materials in ways which generate airborne particulate containing beryllium, introduction of programs to consistently utilize engineering and work practice controls to keep beryllium work areas clean and to keep particulate containing beryllium out of the lungs, off the skin, off of clothing, in the work process, in the work area and on the plant site have experienced significantly lower rates of sensitization and clinical CBD.

Achievement of the above safety principles requires that they be operationalized into understandable and manageable standard operating procedures (SOPs) with worker participation, taught to all workers, and maintained through regular workplace audits. These audits require the development of leading measures, derived from the SOPs, that are the criteria by which management and workers assure themselves that the safety of the beryllium work environment is being maintained over time at the desired level.

As presented in the Interactive Guide, the Brush Wellman worker protection model[7] is broken down into eight simple elements in an effort to enhance worker understanding, its implementation and acceptance.

1. Keep beryllium out of the lungs
2. Keep beryllium work areas clean
3. Keep beryllium off of the skin
4. Keep beryllium off of clothing
5. Keep beryllium at the source
6. Keep beryllium in the work area
7. Keep beryllium on the plant site
8. Keep beryllium workers prepared to work safely

The main goal of the Beryllium Worker Protection Model is to keep beryllium out of the lungs. Keeping beryllium-containing particles out of the lungs will ultimately prevent CBD. The model incorporated an 8-hour action level for beryllium of 0.2 ug/m^3 which was later adopted as a recommended exposure guideline (REG). This guideline must be achieved with a very high degree of statistical confidence, if not, mandatory full-time respiratory protection is worn.

One of the cornerstones of the Beryllium Worker Protection Model is keeping beryllium work areas clean. The goal is to have work areas visibly clean, well lit, orderly and free of clutter. When work areas are disorganized, cluttered and dirty, it is more difficult to control worker exposure to potentially hazardous materials. Having all surfaces painted and visually attractive will make it

easier to determine when surfaces are not visibly clean. In addition, the performance criterion of visibly clean was readily understood by both management and workers.

Keeping beryllium off of the skin is highlighted to avoid beryllium-containing particles entering the skin through cuts, abrasions and rashes. Beryllium-containing particles on the skin can also result in inhalation exposure due to hand and arm contact with the face. Keeping beryllium off of the clothing is emphasized because beryllium-containing particles and solutions on clothing can be a source of worker exposure through redispersion into the air and from hand to face contact. It is also a major pathway in which beryllium can be carried out of the work area.

Keeping beryllium at the source is the first line of defense in controlling worker exposure. The idea is that if beryllium-containing particles are not produced by the process or are captured and never leave the source, then the particles cannot become airborne to reach the lungs of workers. Keeping beryllium in the work area is the second line of defense in controlling worker exposure as well as exposure to others. The goal is to make sure beryllium-containing particles and solutions do not spread from beryllium work areas to work and support areas where beryllium work is not performed. Keeping beryllium on the plant site is the third line of defense in controlling worker exposure as well as exposure to others. When beryllium-containing particles leave the plant site on people and things such as personal items, clothing, laundry, tools, products or equipment, potential exposure to others can result.

Lastly, keeping beryllium workers prepared is how the other elements are accomplished. If managers have prepared themselves and their organizations to manage beryllium operations and tasks, and workers know and have the skills to work properly, maintain equipment, recognize breakdowns or upset conditions take preventive actions and are motivated to do so consistently, experience has shown that leading measures can be consistently achieved, beryllium exposure can be controlled to desired levels and CBD can be prevented.

In this draft NIOSH Alert, the statement to *"substitute less hazardous materials for those containing beryllium whenever feasible"* provides no context in which to apply the recommendation; therefore, it may be misapplied.

Although it is an accepted industrial hygiene practice to substitute a less toxic material to reduce health risks, it is of little value to employers and employees who have a potential to be exposed to excessive levels of airborne particulates containing beryllium since the use of beryllium-containing materials is usually limited to applications where there are no substitutes. Beryllium-containing materials are usually the higher cost option and are used because they bring performance and reliability properties that are necessary for the proper function of the end-use product. Some readers will view the NIOSH recommendation to substitute another material for beryllium as advice by our government to essentially stop all use of beryllium-containing materials.

Although it is difficult to place a value on future innovations, it is clear that restricting the use of beryllium-containing materials will have unintended negative consequences for the development of advanced communications, alternative energy sources, military superiority and preventive medicine. Beryllium must certainly be handled safely in the workplace to prevent disease; however, in the context of this recommendation, NIOSH has a responsibility to take into account the overall public health benefits of beryllium in addition to the potential health risks to manufacturing workers.

Beryllium metal, beryllium alloys and beryllium oxide are used in critical applications which are vital to technology, offering property combinations not available in other materials, and allowing

designers to achieve world-class levels of innovation, performance, energy efficiency and reliability. Beryllium-containing materials have historically been on the cutting edge in technology development. Materials developed have provided the medical industry with increased reliability and durability in many types of equipment used in surgery, imaging, cardiology and diagnostic sensors, X-ray, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). It is the use of beryllium as an X-ray window which allows for the high resolution images used in the diagnosis and treatment of breast cancer. Today, beryllium-containing materials are being viewed as a technology enabling material in the development of alternative energy sources, particularly in solar technologies, and in fusion reactors such as the International ITER Project.

NIOSH needs to recognize that in most instances, the use of beryllium-containing materials is self limiting due to it usually being the higher cost alternative to other materials. With few exceptions, beryllium-containing materials are only used where their unique combination of properties are necessary to ensure a higher level of performance than alternative materials. The properties of beryllium that make it of value frequently involve life safety applications to lower safety and health risks. Examples of such applications include its use in fire sprinkler systems, aircraft wheel bearings, x-ray windows and sophisticated medical devices. The properties given by beryllium, compared to a second-best material, provide for the saving of many lives each year. For example, a past attempt to substitute a cheaper alternative design for the nickel beryllium spring which holds back the water in a fire suppression sprinkler head resulted in the new design failing to release the water during a fire. As a result, a product recall was initiated to replace over 35 million sprinkler heads.

Another life safety application involved the substitution of a beryllium-containing alloy as a spring in a pressure regulator in a rescue worker's self contained breathing apparatus (SCBA). The pressure sensing system used in many devices ranging from airplane altimeters to firemen's breathing equipment (supplied air) depends upon retaining a consistent and predictable response to deflection under pressure. In the case of emergency breathing tanks, this often occurs years after the tanks are filled. The tragic deaths of many fire fighters in the 1999 Mont Blanc, France tunnel fire was determined to have arisen from using a non-beryllium alloy pressure sensor bellows. This resulted in a gauge measurement showing ample breathing air reserves left in their emergency tanks when in fact the reading was false due to stress relaxation of the alternative alloy and the firefighters ran out of breathing air.

Any NIOSH recommendation on substitution should explain that determining feasibility should not result in the compromise of safety innovation, or prevent improvements in reliability, raw material utilization and energy conservation. Misuse of this recommendation can have the serious downstream risks of having consumers being forced into accepting products that are of lower quality, a shorter useful life, lower performance and lower reliability, thereby reducing both safety and environmental benefits.

This NIOSH recommendation is also particularly concerning considering the fact the other branches of our government recognize the need for beryllium-containing materials and the need for a continuous supply of beryllium as a strategic material. It is recommended that NIOSH confer with the Departments of Defense, Energy and Homeland Security to better understand their interests in beryllium for our national security.

Beryllium has been identified and specifically quoted as a strategic material by noted statesmen:

"If there is ever a third world war, it will be over energy and raw materials", said former US Defense and Energy Secretary, James Schlesinger. Resource wars will be a key issue in the future, asserted

Henry Kissinger. And the Pentagon concluded: "The world is just as vulnerable when it comes to titanium, niobium, tin, beryllium, germanium or platinum as it is with regard to oil". Reserves of other substances such as antimony or indium are likewise limited."

Beryllium sensitization should not be listed as a health effect nor be used as part of the worker warning notices on pages iii and 1.

The prevention of beryllium sensitization does not merit a preventive warning in a NIOSH Alert to workers regarding beryllium. It is well established by the American National Standards Institute (ANSI) that for warnings to be effectively communicated, they must be easily understood and focus on the primary health effect of concern. In this instance, the primary health effect of concern is clinical chronic beryllium disease (cCBD) which is a material impairment of health. The draft NIOSH Alert recognizes that the identification of beryllium sensitization does not include any health symptoms. We know of no ANSI, OSHA or other hazard communication warning criteria where sensitization, not involving symptoms, would merit a warning provision.

In preparing our comments on the Alert, we also reviewed over 60 existing NIOSH Alerts. During our review, we could find no instance where sensitization was identified in the document title or where a test result identifying a non-symptomatic event was included in a title or warning. We did not find a single instance where a sensitization warning was made regarding a non-symptomatic event. In addition, we could find no instance where a sensitization test result was used as part of a title, warning or a preventive statement. Sensitization without symptomology does not meet any agency or consensus standard to merit a preventive warning. The title of this NIOSH Alert and the primary warning should only warn of the primary health concern which is CBD. To do otherwise is counter to established warnings criteria and lessens the impact of the primary warning which is a disservice to the worker.

The draft NIOSH Alert has appropriately recognized beryllium sensitization a potential immune response, not a disease, and that it does not have any symptoms. In 1951, it was suggested that CBD was an immune-mediated disease and, subsequently, the term "beryllium sensitization" was initially defined by the beryllium skin patch test (BePT).[8] The use of the BePT was curtailed because simultaneous experimental application of soluble beryllium salts during multiple tests sensitized members (positive patch test) of the study control populations and because it was suggested that the test might exacerbate existing cCBD.[9] Beryllium sensitization (BeS), as it is used today, refers to the recognition of beryllium by the immune system which may be detected only via an in-vivo patch test, an in-vitro blood test (two positive BeBLPT results), or in-vitro bronchial lavage testing using soluble salts of beryllium such as beryllium sulfate. Beryllium sensitization is only definable as a test result. There is no gold standard test for the identification of beryllium sensitization. Beryllium sensitization is not a condition, health effect, illness or disability. With beryllium sensitization, there are no clinical symptoms and there is no measurable or material impairment of health.

The draft NIOSH Alert places its discussion of sensitization in the health effects section of the Alert. Since beryllium sensitization is not a health effect, this positioning of information is misleading to employers and workers. As the draft NIOSH Alert states, beryllium sensitization has no associated health symptoms. As a result, the discussion of beryllium sensitization should not be included in the health effects section of the NIOSH Alert.

NIOSH should evaluate and carefully consider the potential serious consequences which can result from its recommendation that employers conduct medical surveillance for beryllium sensitization using the BeBLPT.

The Alert fails to disclose some very important facts to both workers and employers regarding the overall performance of the BeBLPT, especially concerning its reliability and performance issues with the laboratories conducting the test. In addition, the NIOSH Alert needs to evaluate and disclose the potential social, economic, psychological and legal consequences of its recommending that employers offer and workers take the BeBLPT. The use of this test has been known to result in job loss, change in employment status, life and health insurability issues or concerns, legal action between employee and employer, workers' compensation problems, and family and personal mental health concerns. As a result, NIOSH needs to conduct a full evaluation and disclosure of these issues which are essential to workers and employers understanding the potential personal life changing consequences that have been known to result from the offering or taking of this test.

In the 2007 National Academy of Science (NAS) draft report on beryllium, it stated that the diagnosis of subclinical CBD or BeS may be associated with psychosocial stress or loss of income and makes reference to a case presentation at the 2005 International Beryllium Disease Conference in Montreal describing a young man with subclinical disease that resulted in job loss, major reactive depression, and unemployment (S. Tarlo, University of Toronto, personal commun., April 23, 2007). This NAS review was requested by Dr. Louis of the Air Force. Dr. Louis' presentation to the NAS specifically asked for a detailed evaluation of the risk benefits for an individual taking the BeBLPT. Dr. Louis requested an evaluation of the value of screening using the BeBLPT for early detection of pre-clinical disease before signs or symptoms are present. He specifically identified the following questions regarding the value of the BeBLPT.

- Burden of suffering
- Accuracy and reliability
- Effectiveness at early detection
- Harms of screening
- Benefits outweigh harms

On a related note, the analysis by Dr. Borak[10] evaluating the value of the BeBLPT as a screening tool pertains specifically to this issue. We are also attaching a 2003 white paper by Brush Wellman Inc. which reviews its socio-economic experiences using the BeBLPT (Attachment 2).

The need to evaluate potential harms to persons taking the BeBLPT is discussed in another study not identified in the draft NIOSH Alert. Cher et al. 2006, who identified a systematic laboratory error by the laboratories conducting the BeBLPT, appropriately discussed the medical harms (i.e., unnecessary lung bronchoscopy) and potential adverse life decisions facing workers who may be affected by identified systematic laboratory error. The authors state:

> *"The potential for clinical consequence is low because asymptomatic or subclinical CBD is not medically treated and the long-term effect of removal from beryllium exposure is unknown. More concerning would be decreases in test specificity, which would result in increased false positives, a lower positive predictive value, and therefore a larger number of unnecessary and more invasive clinical procedures such as biopsy. In addition to the potential medical harm in false positive results are the anxiety and life decisions resulting from receipt of "abnormal" test results. Even in the absence of demonstrable lung disease, workers with abnormal results are often advised to cease exposure to beryllium and are*

warned that they are at higher risk of developing CBD in the future. Active beryllium workers may make decisions to change careers or employers as a result of falsely abnormal test results, with significant social and economic consequences, and may consider themselves affected and impaired for their entire lifetime."

In 2005, Rosenman[11] published a retrospective study identifying socio-economic concerns among former workers of a primary beryllium extraction facility with high airborne beryllium exposures. Rosenman makes the following statement concerning the findings from the worker questionnaire.

> *"Reasons members of the cohort gave for not participating included that the individual a) had only worked for a short time; b) felt he or she was too old and that testing would not matter; c) did not have any health problems; d) did not want to jeopardize his or her current health insurance, especially with no compensation available (at the time the individual was contacted); and e) felt there was no effective treatment for beryllium disease."*

It is significant to note that Rosenman identified 43% of his cases of CBD in persons with clinical symptoms, but without a positive BeBLPT result. A similar finding has been reported by Bobka 1997[12].

These studies clearly identify that technical issues concerning the BeBLPT are intertwined with the real-world psychosocial and socioeconomic factors and that they too should be carefully considered by NIOSH as it considers the appropriateness of its NIOSH Alert recommendations to workers and employers. There are several other important studies relevant to the above BeLPT performance issues which deserve careful consideration by NIOSH and do not appear to have been included in the development of the draft NIOSH Alert.

The recommendation that all employers conduct medical surveillance for beryllium sensitization using the BeBLPT is not supported by evidence demonstrating the consistency of the test and the reliability of the test to consistently detect beryllium sensitization.

In its draft Alert, NIOSH identifies concerns regarding the performance of the BeBLPT, noting that it is not a foolproof test and that false positive and false negative results may occur. NIOSH goes on to say, *"Despite its limitations [BeBLPT], the BLPT is the best available tool to identify sensitization until a more precise test becomes available."* NIOSH makes this statement without disclosing the performance issues of the test or the labs that conduct the test.

The BeBLPT's accuracy in detecting beryllium sensitivity is inconsistent. Multiple scientific studies and data sets have established beyond any question that the BeBLPT test is neither sensitive nor specific enough to be consistently reliable. Based on several studies, following are reasons the BeBLPT is not reliable and has questionable utility for medical screening or medical surveillance.

1. No test method has been adopted by a standard setting organization.
2. The four commercial labs performing the test in the United States do not use a uniform and standardized method of testing and, in fact, use significantly different test methodologies.
3. Methods used to interpret tests are not consistent between laboratories.
4. Laboratory performance has been demonstrated to not be stable over time.
5. The BeBLPT has variable test outcomes on the same sample both within and between laboratories.
6. BeBLPT testing reveals significant numbers of reversals from positive to negative.
7. It has been demonstrated that BeBLPT-detected beryllium sensitization has been confirmed in 1 to 2% of the general non-occupationally exposed population.

8. A negative BeBLPT does not mean one is not sensitized to beryllium and will not test positive in the future.
9. In individual beryllium workers, a longer term study has demonstrated that BeBLPT-detected beryllium sensitization can switch on and off over time.

Several important studies relevant to the above BeBLPT performance issues deserve careful consideration by NIOSH, but do not appear to have been included in the development of the draft NIOSH Alert.

There are four key studies of BeBLPT performance which should be considered. A 2001 study by Deubner et al. identified a significant absence of agreement in BeBLPT results in tests conducted within and between laboratories. The study by Cher et al. 2006 demonstrated that persons can be misclassified as BeS due solely to the variation in the testing performance of the laboratories that conduct the BeBLPT. The laboratory instability problem was also noted in a 2005 NIOSH study by Schuler. It has been hypothesized that the lab instability over time could be due to using differing sources of human serum when conducting the tests and differences in test methodologies. A 2007 paper by Donovan et al. confirms the detection of BeBLPT identified beryllium sensitization in the general non-occupationally exposed population and demonstrates longitudinally the on/off detection of positive BeBLPT's in individual beryllium workers. The studies by Deubner, Cher, Schuler and Donovan demonstrate that the Beryllium Blood Lymphocyte Proliferation Test (BeBLPT) is not a reliable indicator of beryllium sensitization (BeS) due to the inconsistent performance of the test, the absence of a standardized method of testing, inconsistent test interpretation, the variability of test outcomes and the reversion of positive results to normal after retesting over time. Following is a brief summary of these studies.

Deubner 2001

A study by Deubner[13] evaluated the performance of laboratories performing the BeBLPT. Deubner analyzed data related to the variability of BeBLPT results within and among various laboratories, and the positive predictive value of the BeBLPT for CBD. The data analyzed was from research studies where every worker blood sample was split and tested by two different laboratories using the BeBLPT method. Deubner reviewed the paired results of three laboratories that had analyzed over 5,000 blood samples collected since 1992. He found that the BeBLPT results varied significantly both within each laboratory and from one laboratory to another. Specifically, the data Deubner analyzed showed that those laboratories which detected a positive result on the first blood test found a negative result 30% of the time on a second blood test on the same person. When two different labs (Labs A and B) tested the same blood sample, Lab A did not confirm 30% of Lab B positive results and Lab B did not confirm 30% of Lab A positive results. The level of agreement within and between labs was also evaluated using a kappa statistic. The level of agreement within samples taken at one lab was found to vary from fair to moderate agreement while the level of agreement between labs was found to vary from poor to moderate.

In addition, Deubner observed a number of cases in which the BeBLPT results changed from confirmed positive to confirmed negative upon re-testing. These data were derived from a survey conducted at Brush Wellman's Elmore, Ohio facility. There, 10 of 18 persons (55%) who were confirmed BeBLPT positive (two positive tests) in the early 1990s and who continued to work in beryllium operations, tested negative in 1999 based on a blood sample tested by two different laboratories. In light of these results, Deubner concluded his study by noting that *"substantial inter- and intra-laboratory disagreement exists among the laboratories that conduct this test."*

Schuler 2005

During a cross-sectional study of a beryllium alloy processing facility, the BeBLPT was administered to 152 workers. Two laboratories were used during the study. A concern was raised when it was determined that Lab A was found to be twice as likely as Lab B to report an abnormal result and five times more likely to report an uninterpretable or borderline test result. Lab A identified nine persons with confirmed abnormal results while all nine persons tested normal at Lab B. None of these 9 persons were found to have CBD. The researchers concluded that these nine persons were unlikely to be truly sensitized. As a result, they removed the nine workers from their evaluation of risk.

Cher 2006

The study by Cher et al. 2006 demonstrated that persons can be misclassified as BeS due solely to the variation in the testing performance of the laboratories that conduct the BeBLPT. The study is based on the analysis of over 8,800 BeBLPT results using Statistical Process Control methods. Because the reliability of the BeBLPT was unknown, the study used data from a surveillance program that offered testing for beryllium sensitization with the BeBLPT to assess the performance of the four commercial laboratories that conduct this test. The study population consisted of workers exposed to beryllium at Brush Wellman Inc. facilities over a ten-year period (1992–2001). The analysis used a standard statistical technique, statistical process control (SPC), to evaluate test reliability. The study design involved a repeated measures analysis of BeBLPT results generated from the company-wide, longitudinal testing. Analytical methods included use of (1) statistical process control charts that examined temporal patterns of variation for the stimulation index, a measure of cell reactivity to beryllium; (2) correlation analysis that compared prior perceptions of BeBLPT instability to the statistical measures of test variation and (3) assessment of the variation in the proportion of missing test results and how time periods with more missing data influenced SPC findings. The study found that all laboratories displayed variations in test results that were beyond what would be expected due to chance alone and that patterns of test results suggested that variations were systematic. The study concludes that laboratories performing the BeBLPT or other similar biological assays of immunological response could benefit from a statistical approach such as SPC to improve quality management.

Donovan 2007

Donovan[14] evaluated the performance of the beryllium blood lymphocyte proliferation test from general workforce survey data and a five-year survey of new employee data. More than 10,000 results, from nearly 2,400 participants over a 12-year period, were analyzed using consistent criteria to describe the performance characteristics of the BeBLPT. Thirteen of the 538 participants (2.4%) had at least one positive BeBLPT result when they started work at Brush Wellman. Nine of these individuals (1.7%) were confirmed to be positive during subsequent testing (two positive tests). Three of these nine new employees were identified as having a known occupational exposure or possible take-home exposures. The background prevalence of confirmed BeBLPT-positive responses among new hires with no known occupational exposure or possible take-home exposures to beryllium was 1.1% (6/535).

Positive BeBLPT results were observed in some workers within weeks or months of initial exposure, and the median time to the first positive BeBLPT result in confirmed positive individuals was five months. The prevalence of positive BeBLPT results was greatest during the first year of employment with an apparent peak in months four to eight. At least one negative or borderline/negative result was observed in 100% of new workers who underwent follow-up testing after they had been confirmed BeBLPT positive (two positive results). There was no correlation

between time of employment and an increasing prevalence of confirmed BeBLPT positive results in individual surveys. The study concluded:

> *"The detection of confirmed BLPT results in non-occupationally exposed persons, the apparent reversions of confirmed BeBLPT results, the identification of a positive BeBLPT peak prevalence period and variation in intra- and inter-laboratory test methods and test interpretation should be considered with caution when interpreting results from studies utilising the BeBLPT, especially when considering policy interventions such as worker removal. Additional research to refine BeBLPT performance or develop a new test is needed to reliably identify the relationship of sensitised workers to subclinical or clinical indicators of chronic beryllium disease."*

The fact remains that among the four commercial labs that offer this test in the United States, there is not agreement on the test methodology, interpretive decision rules, laboratory quality management or retesting protocols that different investigators or institutions have used, and no clear rationale to decide whose test protocol is superior. These inconsistencies, reliability and performance issues with the BeBLPT underscore why there are efforts underway at nearly every beryllium research center in the United States to try to identify a better metric to detect beryllium sensitization than the BeBLPT. NIOSH is obligated to disclose these problems to workers and employers. If an Alert is to be issued, NIOSH should not recommend that employers offer workers the BeBLPT.

The recommendation that all employers conduct medical surveillance for beryllium sensitization using the BeBLPT to allow employers to identify higher risk jobs and prioritize prevention efforts fails to convey the protocols necessary to implement such a recommendation. For example, such a recommendation usually cannot be scientifically justified due to population size constraints.

In general, NIOSH's recommendation to employers to conduct medical surveillance is being provided without NIOSH disclosing any of the details an employer would need to understand before embarking on such an effort. Medical surveillance efforts should be carefully planned, with clear objectives and definition of the population, adequate numbers of workers and high quality data. All aspects of the effort have to have quality standards developed and quality must be monitored. Resources for data management, analysis and interpretation have to be identified.

While identification of high risk operations by testing workers may be an important step in medical surveillance research, the current methodologies for detecting beryllium sensitization or surveillance for chronic beryllium disease are insensitive, unreliable and very expensive. Also, the low prevalence of positive BeBLPT results means that this is ineffective in smaller beryllium worker groups. The background rate in the non-occupationally exposed population of 1 to 2% positive makes analysis useful only when prevalence of positive BeBLPTs is very high (> 5%) in relatively large work groups (> 100 persons). There is enough known about the characteristics of exposure as the result of already published research or work in progress identifying what jobs are higher risk, that risks are fairly predictable. Having employers medically test workers is a diversion of effort from primary prevention and frequently gives a false illusion of safety, especially when worker groups are small (<100 persons).

Therefore, the test has great potential to produce misleading results for workers and management alike who, based on the recommendation in this draft NIOSH Alert, are advised to interpret the results with reference to the efficacy of their site exposure control programs. Due to the low prevalence of positive results in small work populations, the test has a significant likelihood of being

misleading in both directions, having low power to detect conditions that may be capable of causing disease. Further complicating the use of the BeBLPT is the fact that researchers have identified a background rate of positive BeBLPTs in the non-occupationally exposed population at 1 to 2%[15]. In monitoring a small population, should one or two positive tests occur, the impression of hazard would be given when, in fact, this is just as likely a chance occurrence of positive BeBLPTs in the non-occupationally exposed population.

The first reason NIOSH recommends that employers offer the BeBLPT to workers exposed to beryllium particulate is to identify higher risk jobs and prioritize prevention efforts. The draft NIOSH Alert provides no basis upon which to support this recommendation to employers. Due to the low occurrence of positive results, to be meaningful and interpretable, this approach can only be applied within the context of a study involving at least 100 exposed persons. Therefore, the vast majority of employers will not have enough people to discern higher risk jobs within their workplace. For NIOSH's recommendation to work, NIOSH would need to provide direct research support to beryllium-using work sites that have a sufficiently sized worker population to conduct a meaningful study. Without NIOSH's direct help to conduct and evaluate the necessary tests, the cost of such tests will be prohibitive, rendering the NIOSH recommendation a valueless statement. Though it is not stated in the draft NIOSH Alert, it would almost appear that NIOSH is making its recommendation to employers in the hope that data might be generated which could then be analyzed later by NIOSH researchers. We would hope that this is not the case.

In summary, a generalized recommendation for employers to offer the BeBLPT serves no discernable value to employers or workers in small work populations and, absent a government sponsored study, would impose a huge financial burden on larger employers with no evidence that the analysis will be interpretable within the context of the individual workplace.

The recommendation to all employers to conduct medical surveillance for beryllium sensitization using the BeBLPT to identify higher risk jobs and prioritize prevention efforts failed to identify, characterize and consider the consequences of the direct costs employers will incur attempting to implement its recommendation.

NIOSH did not characterize the potential costs to employers of implementing their recommendation. Though not interpretable, such studies would easily cost small employers tens of thousands of dollars and studies of this type for larger employers commonly exceed $100,000. NIOSH should have an obligation to inform employers of the economic impacts of its recommendations. In larger facilities, a sufficient number of people working with beryllium may exist to conduct a study that could differentiate potential job risks. However, the cost to perform such a study will certainly exceed $100,000. Even Brush Wellman, the primary beryllium producer, could not afford to conduct multiple studies on its own and has partnered with NIOSH for the past ten years working to answer questions about job risks.

The recommendation to all employers with workers who come into contact with beryllium containing dusts, fumes, solutions and suspensions to conduct medical surveillance for beryllium sensitization using the BeBLPT is not supported by evidence demonstrating any benefit to individual workers.

The aforementioned first reason given by NIOSH to recommend employers conduct medical surveillance using the BeBLPT was for the purpose of trying to identify higher risk jobs and prioritize prevention efforts. When applicable and feasible, this is a medical surveillance activity as is normally defined.

Definition: "Surveillance is the ongoing systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know. The final link in the surveillance chain is application of these data to prevention and control."
- Carl W Tyler Jr. MD and John M Last MD

The reasoning by NIOSH for employers to conduct medical surveillance does not represent a medical surveillance purpose, but, in fact, describes a medical screening or medical monitoring purpose. The following discussions of medical screening and medical monitoring provide reasoning and analysis as to why NIOSH should not be recommending employers conduct the BeBLPT with their workers.

Medical Screening:

The use of medical tests in medical screening programs for beryllium-induced effects should not be recommended by NIOSH under any conditions.

"Screening is the application of diagnostic tests or procedures to apparently healthy people with the aim of sorting them into those who may have a condition that would benefit from early intervention and those who do not." - John M Last MD

For example, it has been established that detection of high blood pressure in apparently healthy people followed by treatment of high blood pressure prevents heart disease and stroke. Therefore, screening otherwise healthy persons for high blood pressure followed by a known beneficial treatment is a recommended procedure in medical practice.

Beryllium medical testing is a good example of why individuals should not be screened in that:

"Screening for evidence of inapparent disease implies and can lead to interventions that will change the lives of persons who previously thought themselves to be well. Such persons may react in several ways to the knowledge that they have a disease of a condition that requires treatment; they may assume a sick role - develop symptoms, lose time from work, and become unduly worried about themselves." - John M Last MD

NIOSH should not recommend that beryllium workers receive medical tests because there is no basis on which to conclude that they will receive a personal health benefit as a result of detection of BeS, sCBD or early cCBD. The reason is there is no evidence for medical benefit as a result of reduction in exposure or removal from exposure of persons who are considered to be BeS, sCBD or cCBD. Treatment of persons with BeS and sCBD is not recommended and there is no evidence for benefit from early treatment of persons with sCBD or cCBD. Therefore, the requirement for screening, detection of persons with a condition *"that would benefit from early intervention"* is not met. While there is testimonial evidence that treatment of persons with cCBD may ameliorate symptoms, there is no evidence that treatment changes the long-term outcome of cCBD.

Furthermore, information regarding BeS and sCBD may have significant impacts on individual workers and their families. These impacts may include potential social and financial disruption, a natural tendency towards illness behavior and subjectivity in decisions to treat with corticosteroids which is known to have resulted in major deleterious effects of high dose and/or long-term use of corticosteroids on many organ systems.

NIOSH should recommend that beryllium workers be fully educated regarding the risks of CBD and the symptoms of cCBD, and be advised to tell their doctor of their history of beryllium work if they seek care for pulmonary symptoms so that CBD may be considered in the differential diagnosis.

Absent knowing the natural history of chronic beryllium disease, medical screening for sensitization is not recommended nor has removal from exposure been demonstrated to be effective.

The World Health Organization guidelines for medical screening were published in 1968. Recommending the BeLPT as a screening test is in violation of a number of these principles including:

- The natural history of the disease should be adequately understood.
- There should be an agreed policy on who to treat.
- The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.

The model of removal from exposure of individuals derived from toxicological disease models such as lead and mercury, or from some allergic models such as occupational asthma or allergic skin disease, does not to apply to cCBD where clinical improvement on removal from exposure is not known to occur. To put it simply, the strategy of allowing workers to work with beryllium until detected as BeS or sCBD and then removing them from exposure, lacks any factual basis for effectiveness and should not be recommended by NIOSH.

NIOSH's recommendation does not appear to be based on a scientific finding or analysis demonstrating that employers' testing of workers in general industry provide a benefit to the individual worker. Unlike examples in toxicology where removal from exposure or treatment of a condition at an early stage is of benefit to workers, no such evidence exists for benefit for the individual from detection of a positive BeBLPT or of subclinical or mild CBD. Since there is ample evidence for harms of testing using the BeBLPT (psychological, financial, social and medical), there is no rationale for using the test in other than diagnosis of the symptomatic person, or for well-designed and carried out medical surveillance efforts from which there is expected a public health benefit. It does not follow at all that procedures that yield a research benefit should be applied in general practice without a complete and separate cost/benefit and ethical analysis. Such an analysis of the BeBLPT leads to the conclusion that it should not be used as a routine test on workers.

The draft NIOSH Alert provides no scientific basis to recommend the counseling of workers about measures that may prevent progression to clinical CBD because:

1. No beryllium disease treatment center medically treats people identified as beryllium sensitized or diagnosed with non-symptomatic CBD. Note: a few cases have occurred where positive BeBLPT individuals have been unnecessarily treated with steroids, thus causing significant side effects in otherwise healthy individuals.
2. Clinical chronic beryllium disease has been diagnosed in persons with consistently normal BeBLPTs.
3. The risk of progression from non-symptomatic CBD to symptomatic CBD is not known.
4. There is no evidence that removal from exposure changes the natural history of beryllium sensitization, sCBD or cCBD.

5. There is no evidence that treatment of clinical CBD changes the long-term outcome of the disease, either progression or survival.
6. There has been no formal analysis of the significant socio-economic impacts of advising beryllium workers as to a beneficial course of action using the BeBLPT when for screening, monitoring or surveillance.
7. The BeBLPT is a lagging measure and, as such, does nothing for an individual worker in the context of preventing the identification of beryllium sensitization or CBD or further protecting workers who are currently exposed to beryllium containing particulate.

Because the natural history of beryllium disease remains unknown, it is not uncommon for a person with a series of positive tests to be provided a medical recommendation for no further beryllium exposure which may force a job change. Such a finding often triggers a recommendation to undergo a bronchoscopy with lung biopsy, which is a procedure with significant hazards, for the purpose of diagnosing asymptomatic CBD. Both of these recommendations are commonly made with little to no consideration of the psychological, financial, social and medical well being of the individual. This is all the more significant since no medical treatment is known or recommended to prevent either sensitization or subclinical CBD.

This draft NIOSH Alert recommendation implies, without any analysis, that subsequent medical testing is a benefit to an individual who tests positive using the BeBLPT. It appears that NIOSH did not consider the 2006 study by Borak et al. which is the only study to have reviewed the reliability and appropriateness of using the BeBLPT as a screening tool. Borak concluded that the accuracy and reliability of the BeBLPT is insufficient for screening of asymptomatic individuals. Borak used criteria established by the World Health Organization (WHO), focusing on five elements essential to judging effectiveness of preventive services: 1) burden of suffering, 2) accuracy and reliability of screening tests, 3) effectiveness of early detection, 4) harms of screening and 5) benefits outweighing harms. He identified that the prevalence of beryllium sensitization and chronic beryllium disease in asymptomatic individuals is unknown and that there are important gaps and deficiencies in the available evidence. He found the accuracy and reliability of the BeLPT to be uncertain and that the clinical benefits of early intervention have not been confirmed or quantified in asymptomatic individuals. Borak concluded, *"There is currently insufficient scientific evidence to support the use of BeLPT for routine screening of asymptomatic individuals."* The Borak paper is highly relevant to determining the value of medical monitoring, medical surveillance and medical screening as those terms are used and applied in common practice.

Interpretation of the value of recommending no further exposure and/or prescribing an invasive diagnostic bronchoscopy is further complicated by the findings of the Donovan study which identified a background rate in the non-occupationally exposed population of 1 to 2% using the BeBLPT. NIOSH should evaluate ethically its recommendation in light of the use of the BeLPT resulting in persons undergoing bronchoscopy due to a natural background rate of BeBLPT identified sensitivity.

NIOSH's statement that *"despite its limitations [BeBLPT], the BLPT is the best available tool to identify sensitization until a more precise test becomes available,"* reads as an endorsement of the test as being good enough for NIOSH to recommend its use to employers. Just because this test is believed to have been valuable in the context of cross sectional research studies involving hundreds of workers, it does not mean that use of the test translates into a value for an individual. It is clear that the harms of BeLPT testing clearly outweigh the benefits and, as a result, NIOSH should remove its recommendation for employers to conduct BeBLPT testing.

The recommendation to all employers with workers who come into contact with beryllium containing dusts, fumes, solutions and suspensions to conduct medical surveillance for beryllium sensitization using the BeBLPT is untenable because beryllium is a ubiquitous element.

Beryllium-containing dusts can be found in every single workplace in the world. Every person is exposed to airborne beryllium via windblown dusts (all soil contains beryllium), emissions from the combustion of coal and tobacco smoke. Additionally, many household products, such as ceiling tiles, fertilizers, detergents, charcoal and kitty litter, contain beryllium naturally. In the workplace, natural beryllium is in the soil brought into workplaces on people's shoes, it is in the concrete block, concrete floors, metals and roofing materials that comprise the building's structure. It occurs naturally in common materials used in industry every day such as oil dry, oil, steel, copper, sandpaper and grinding wheels. It also is commonly found in foods due to uptake of elements in soil. If all U.S. employers would heed the NIOSH recommendation to conduct the BeBLPT on all workers who come into contact with beryllium-containing dusts in any form and at any concentration, then all 100,000,000+ workers in the United States would undergo testing at a cost of over 30 billion dollars. Based on the Donovan study that detected beryllium sensitization in a worker population not known to be occupationally exposed to commercially produced beryllium, we would expect that 1,000,000 to 2,000,000 workers would be identified and medically labeled as beryllium sensitized simply due to the rate that BeBLPT detected sensitization occurs in the general population.

NIOSH should inform workers and employers about the various forms of CBD.

The Draft NIOSH Alert correctly states that the number of sensitized workers who will eventually develop CBD is unknown. However, the discussion which follows that statement does not clearly define what sensitization is, nor does it differentiate the forms of CBD. In addition, the NIOSH Alert should also clearly disclose to workers and employers the historical changes in the diagnostic criteria for Chronic Beryllium Disease that resulted in the identification of both clinical CBD (with health symptoms) and subclinical CBD (without health symptoms). This information is very important in aiding the understanding of these medical terms by workers and employers and should be fully disclosed.

This Alert should clearly identify that the diagnostic criteria for chronic beryllium disease (CBD) have changed over the past 40 years due to advances in medical and diagnostic technology. These changes have proven to be important when comparing findings of older studies to newer studies. The older studies (pre-1989) refer solely to the identification of persons with clinically evident disease (clinical/symptomatic CBD), whereas the vast majority of cases identified in studies since 1989 describe predominantly surveillance detected cases of CBD where the people have no or little clinical evidence of a health effect or symptoms. How a CBD health risk is defined by NIOSH will have significant implications when weighing the benefits or harms to individuals associated with NIOSH's recommendations for medical surveillance and screening.

In recent years, various individuals and organizations have reported that the number of diagnosed cases of CBD has increased since the 1980s. The main factors for this increase are the change in diagnostic criteria for CBD, improvements in medical detection technology and an increase in the number of workers evaluated for subclinical CBD primarily as part of cross-sectional research studies.

Before the late 1980s, workers were diagnosed with CBD only when they exhibited clinical (observable) symptoms of CBD and changes in their chest x-ray or lung function test. Symptoms could include unexplained dry cough; shortness of breath, especially with activity and fatigue.

During the late 1980s and early 1990s, the criteria by which CBD was diagnosed changed, and workers began to be diagnosed with CBD without clinical symptoms or measurable impairment. This diagnosis became possible as a result of the application of new technology in medical testing and evaluation. Workers diagnosed with CBD in the absence of x-ray or lung function changes or symptoms of disease are referred to as having subclinical CBD, meaning that they have no clinical symptoms or measurable impairment. These workers are typically diagnosed based on sensitization and the presence, upon biopsy, of microscopic biological lung formations called granulomas. Workers with subclinical CBD may never develop clinical CBD or may develop clinical CBD over time. The vast majority of persons diagnosed since this change do not have outward symptoms of disease and have no material impairment of health.

Workers with surveillance CBD or subclinical CBD may never develop cCBD or may develop cCBD over time[16]. While the natural history of sCBD is not yet known, studies conducted by Brush Wellman, NIOSH and National Jewish Medical and Research Center have established that the rate of sCBD or surveillance CBD is many times the historical rate of cCBD. The cumulative rate of surveillance CBD in studies conducted by Brush Wellman, NIOSH and others (up to 12%) is much higher than the historical rate of cCBD[17] in the same worker populations (1-2%). It is, therefore, logical to conclude that in most persons, there is no significant progression of their subclinical disease. If most subclinical cases of CBD progressed to a clinical state, early studies obviously would have shown much higher rates of cCBD because most of the studies were done at facilities with active medical surveillance programs looking for clinical signs and symptoms of CBD.

NIOSH should also inform workers and employers that cross sectional studies of beryllium operations conducted from the early 1990s to the present have utilized inconsistent definitions of CBD. The most common definition for subclinical CBD today is detection of beryllium sensitization in blood or lung fluid plus granuloma detected upon lung biopsy with normal chest X-ray and lung function test[18]. However, Kreiss[19] and Henneberger[20] defined CBD using both the clinical and subclinical definitions, but also included those workers found to be lung sensitized with no granulomas. Another example can be found in Kelleher[21] where the study expands upon the common definition to include mononuclear cell infiltrates and lymphocytosis in place of granulomas. Additionally, at the 3rd International Beryllium Research Conference (2007), Dr. Dweik of the Cleveland Clinic stated that six biopsies are needed to accurately characterize the diagnosis of CBD. These definitional inconsistencies between studies can result in very significant differences as to the interpretation and meaning of these studies. These differences are all the more relevant to individual workers.

NIOSH should clearly describe how it used the information from these studies to arrive at its recommendations. Such a disclosure will better inform workers and employers so they may fully understand their potential health risks. In addition, NIOSH should note how these differing definitions of CBD can influence the interpretation of these beryllium studies as a result of most of these studies having small worker populations and a low incidence of CBD. NIOSH should exercise considerable caution when relaying guidance to workers and employers relevant to its recommendations based on its review and comparison of studies involving small populations and differing definitions of CBD.

Providing workers and employers with complete definitions and a clear description of the history of these medical terms will improve their understanding of the associated issues. The following offers definitions and information relevant to improving the understanding of these terms by workers and employers.

Acute Beryllium Disease (ABD)

ABD is an acute toxic chemical pneumonitis resulting from high exposure to soluble beryllium compounds (beryllium salts such as beryllium fluoride and beryllium chloride) or low-fired beryllium oxide. ABD has not been seen for decades and low-fired beryllium oxide has not been commercially available since 1950.[22] The onset of symptoms of ABD was usually immediate, but could be delayed from several hours up to three days. Symptoms included dypsnea, fatigue, fever, night sweats and cough. Pulmonary function tests revealed obstructive lung disease with impaired gas exchange. Most of the cases of ABD usually resolved completely. However, some were fatal or were followed by development of chronic beryllium disease.[23, 24] Cases of ABD have only been shown to occur when airborne concentrations of soluble beryllium salts or low fired beryllium oxide exceed 100 µg Be/m^3.[25] Airborne exposures to beryllium metal, beryllium oxide or beryllium alloy fumes or dust are not associated with acute or short-term respiratory reactions.

Clinical Chronic Beryllium Disease (cCBD)

Clinical chronic beryllium disease (cCBD) was the only form of CBD diagnosed before the late 1980's when clinical symptoms were observed, along with changes in chest x-rays or lung function tests. The clinical course of cCBD is considered highly variable since the symptomatic disease may not develop or it may develop slowly over time. The earliest manifestations of cCBD are the symptoms of shortness of breath, dry cough, or wheeze, and in some, night sweats or fatigue. In addition to cCBD, these symptoms may be found in persons with other lung diseases and in persons with no diagnosable disease.[26] Chest radiographs can be normal, but often range from small nodular opacities, with an upper level predominance, to formation of conglomerate masses.[27] Progression may lead to weight loss, cor pulmonale with heart failure, disability and death.

Subclinical Chronic Beryllium Disease (sCBD)

Subclinical CBD (sCBD) is a term that originated in the late 1980s when a change in the criterion for diagnosis of CBD was first suggested.[28] The diagnosis of sCBD, which is also referred to as surveillance CBD, is based on abnormal lymphocyte proliferation tests for beryllium sensitization in blood or lung fluid and the presence, upon lung biopsy, of non-caseating granulomas. Granuloma formation can exist with no symptomology or physical impairment of health. With sCBD, there are no clinical symptoms and there is no measurable impairment.

BeBLPT Identified Beryllium Sensitization

Tests for beryllium sensitization today are conducted not on the person, but on blood separate from the person. Sensitization to beryllium is a measurement of lymphocyte proliferation in a laboratory test tube when lymphocytes are challenged with a soluble beryllium salt. As stated earlier, beryllium sensitization is only definable as a test result. There is no gold standard test for the identification of beryllium sensitization. Beryllium sensitization is not a condition, health effect, illness or disability. With beryllium sensitization, there are no clinical symptoms and there is no measurable or material impairment of health. Since BeS is only defined today as an in-vitro test result (BeBLPT), BeS should not be used as a health end-point by NIOSH in making its recommendations to workers and employers.

In order for workers and employers to clearly understand what beryllium sensitization is, it is important that they understand what it is not. For clarity of message to workers and employers, NIOSH should clearly differentiate beryllium sensitization from the common occupational health term of "chemical sensitizer". Workers and employers need to understand that the sensitization which

may result from beryllium exposure and detected via the blood lymphocyte proliferation test is not the same as normally considered for a compound or substance referred to as a sensitizer.

The concept of a chemical sensitizer is well documented and widely understood by occupational health professionals. A sensitizer, as defined by OSHA is, *"a chemical that causes a substantial proportion of exposed people or animals to develop an allergic reaction in normal tissue after repeated exposure to the chemical."* [29] A chemical allergy is generally considered to be an adverse reaction to a chemical resulting from previous sensitization to that chemical or to one that is structurally similar. After an initial allergic reaction to a chemical, very small subsequent exposures can evoke a severe response. The range of chemical sensitization response is broad and generally manifests itself in forms such as a skin rash, eye irritation, allergic asthma or even anaphylactic shock. The American Conference of Governmental Industrial Hygienists description of sensitization includes the following statement, *"However, after a person is sensitized, subsequent exposure may cause intense responses, even at low exposure concentrations (well below the TLV®)."*

As defined above, chemical sensitization has not been demonstrated in persons exposed to insoluble forms of beryllium either in massive or particulate forms. The term "beryllium sensitization," as it is used today, is confined to the recognition of beryllium by the immune system which may be detected only via an in-vivo patch test, an in-vitro blood test, or in-vitro bronchial lavage testing using only soluble salts of beryllium such as beryllium sulfate as the chemical challenge. Beryllium sensitization is an immunological response and not a health effect, illness or disability.

No dermal sensitization reaction, such as skin rash, hives, irritation of the nose, throat, skin or eye, is associated with dermal exposures to insoluble forms of beryllium. There is no short-term immunological mediated respiratory reaction, such as allergy or asthma involving shortness of breath, chest tightness, wheeze, cough and irritation, associated with airborne exposures to insoluble forms of beryllium. Insoluble forms of beryllium include beryllium metal, beryllium aluminum composites (AlBeMet®), beryllium oxide and alloys containing beryllium, such as copper beryllium. These insoluble forms comprise nearly the entire commercial market for beryllium.

NIOSH should clearly identify for insoluble forms of beryllium, the differences between beryllium sensitization and the common occupational health term of sensitization. In addition, employers and workers should also be informed that skin reactions and lung reactions have occurred with exposures to beryllium salts, such as beryllium sulfate and beryllium fluoride. Though beryllium salts are rarely found in commerce, it would be appropriate for the NIOSH to designate soluble beryllium salts as a chemical sensitizer.

The discussion of the Newman 2005 paper which suggests a progression rate from beryllium sensitization to CBD should be removed.

The draft NIOSH Alert briefly reviews the statements made in the small longitudinal study by Newman in 2005. We respectfully request that NIOSH consider the following additional points regarding this study as a basis for removing any reference to the Newman study. Absent a detailed explanation, the NIOSH discussion of Newman 2005 does not provide full disclosure to workers and, thereby, promotes fear, distrust and anxiety because the natural history has yet to be clearly defined.

The Newman et al. study was a small (55 persons) group of persons who mostly had worked in the nuclear weapons industry during a period when compliance with a 2.0 $\mu g/m^3$ 8-hour TWA Occupational Exposure Limit (OEL) had not been demonstrated[30]. These persons were selected by

their willingness to undergo repeated bronchoscopy with lung biopsy. The study acknowledges the limitation that *"Individuals who may have had normal pathology on first evaluation and who then developed abnormal pathology on subsequent evaluation may have been missed on initial evaluation because of sampling error".* In this study, the outcome measured was sCBD. Subclinical CBD is not a material impairment of health. The study does not explore who may go on to develop cCBD, which is a material impairment of health. There is no longitudinal study that explores the natural history of BeS through cCBD.

Newman et al also found that 12 of 55 persons (22%) who were initially confirmed BeBLPT abnormal (two positive tests) reverted to normal in the follow-up period. This finding is consistent with a study by Donovan (2007) who found that workers BeBLPT results oscillated between positive and negative over time. From multiple BeBLPT surveys and ongoing BeBLPT surveillance of active beryllium workers, it is apparent that the natural history of CBD is very similar to that of pulmonary sarcoidosis. Like the oscillating detection of BeS using the BeBLPT, sCBD based on detecting granuloma in the lung may come and go as often occurs in cases of sarcoidosis. Newman et al does not report whether a periodic bronchoscopy was continued once granulomas were detected or whether such subsequent biopsies detected granulomata. Consequently, the study does not address the frequency with which sCBD, like BeBLPT positivity, reverses to normal.

Due to the small size of the study cohort and the study's stated and unstated limitations, we suggest NIOSH carefully evaluate the significance of this study in characterizing the persistence of sCBD or its relation to the natural history of cCBD. The progression of CBD is not well understood and NIOSH is premature in using this study to conjecture the clinical progression of CBD. As elucidated by Cullen 2005[31] regarding the Newman study, there is a need to demonstrate that some significant portion of cases detected by screening not only develop pathologic changes characteristic of CBD, but also manifest disease. He further states, *"Although the data are not presented in a form sufficiently transparent to address this entirely, it still appears from what is presented that among the 55 patients followed an average of 4.8 years, no more than a handful have developed significant clinical manifestations; only one is reported to be under treatment with steroids.. Although the prognosis was certainly poor for clinically recognized cases of CBD in the era of high exposure, before institution of control measures in the 1950s, it remains premature, based on available information, to apply this prediction uncritically to those less heavily exposed and recognized asymptomatically by screening. If anything, available data suggest a much more indolent course, at least for some. Given the potential for significant negative psychosocial and economic impact on those having a positive test, evidence that only a small fraction of those identified become sick would sharply alter the risk-benefit ratio for screening, possibly undermining its rationale."*

Workers with surveillance CBD or subclinical CBD may never develop cCBD or may develop cCBD over time[32]. While the natural history of sCBD is not yet known, studies conducted by Brush Wellman, NIOSH and National Jewish Medical and Research Center have established that the rate of sCBD or surveillance CBD is many times the historical rate of cCBD. The cumulative rate of surveillance CBD in studies conducted by Brush Wellman, NIOSH and others (up to 12%) is much higher than the historical rate of cCBD[33] in the same worker populations (1-2%). It is, therefore, logical to conclude that in most persons, there is no significant progression of their subclinical disease. If most subclinical cases of CBD progressed to a clinical state, early studies would have shown much higher rates of cCBD because most of the studies were done at facilities with active medical surveillance programs looking for clinical signs and symptoms of CBD.

There is one study that, upon careful examination of the data presented, does provide some additional insight into the potential for progression to CBD. One approach to assess the rate of progression is to study former beryllium workers many years after the end of occupational exposure.

A 2005 study by Rosenman[34] reported on testing of a cohort of 577 beryllium workers 25+ years after their last exposure in a Be processing plant that closed in 1978. Rosenman opined that high Be exposure levels caused these workers to have higher sensitization rates and CBD prevalence than groups in other studies. However, analyzing the Rosenman findings of CBD that match the definition of CBD which is used in recent cross-sectional studies indicates that the prevalence rates that Rosenman reported are easily within the typical range of values reported in these recent studies. The Rosenman study states a prevalence of 7.6% CBD and 14.6% BeS. A closer analysis of Rosenman's findings clearly shows that the definitions of CBD used by Rosenman to define prevalence are not comparable to all of the other recent studies. First, the 7.6% includes both definite and probable cases of CBD, whereas all of the other studies would only include the definite cases of CBD as defined by Rosenman. Removing the probable cases reduces the prevalence of CBD to 5.5%, including the nine pre-study CBD cases. The recent studies all used the BeBLPT to identify persons to undergo further work-up via bronchoscopy. Applying that same definition for case inclusion to the Rosenman study results in a CBD prevalence of 3.3%. This prevalence is actually lower than many beryllium cross-sectional studies, even though this facility was a high exposure primary beryllium production facility (including exposure to beryllium salts from extraction operations and beryllium oxide production). This facility would be very similar to the Kreiss 1997 Elmore primary beryllium production facility cross sectional study where the prevalence for CBD was 4.6%. In addition, the detection of BeS at 14.6% stated by Rosenman is also not comparable to all the recent studies.

Rosenman's method was to add his BeS double positives to the total number of CBD cases (definite and probable CBD) regardless of how the cases were first identified (i.e., chest radiograph versus BeBLPT). To make this study comparable to all the other recent studies, one must take note that of the 577 workers, 60 persons were referred for follow-up testing for having two positive BeBLPTs for a prevalence of 10.4%. If you include the nine cases of CBD identified pre-study and assume they all had two positive BeBLPT's the prevalence is at most 12%. This rate is very similar to the Elmore BeS prevalence of 9.4%. Thus, Rosenman's conclusion that this facility had a much greater prevalence over time as compared to recent cross-sectional studies does not hold up under careful examination. Thinking apples to apples, if one compares Elmore to the similar facility studied by Rosenman, CBD found as a result of BeBLPT surveillance was no different in a former worker cohort that had been last exposed over 25 years ago than in a current worker cohort. In fact, if one looks at other prevalence rates at secondary beryllium processing facilities, such as Kreiss 1996 (Tucson prevalence CBD=4.4, BeS=5.9, Henneberger 2001(Tucson prevalence CBD=5.3, BeS=9.9), Schuler 2005 (BWI Reading prevalence CBD=3.9, BeS=6.5), it appears that detected CBD is completely comparable or it could be viewed that the rates found by Rosenman are actually somewhat lower for CBD and the detection of BeS is somewhat higher. Therefore, it is reasonable to suggest that Rosenman demonstrates that the risk of CBD does not increase over time and that detection of BeS remains constant or may increase slightly over time. This analysis supports the experience of Brush Wellman and others that the rate of clinically evident disease resulting in a material impairment of health is no higher today than compared to the historical rates of cCBD.

The discussion of Skin Exposure in the Workforce Surveys section fails to disclose the available scientific evidence regarding skin exposures rather than a discussion of an unproven hypothesis.

The recent NIOSH studies exploring the hypothesis that sensitization to beryllium can occur via intact skin should not be used as a primary basis upon which to recommend employers and workers prevent skin contact with tiny beryllium particles or solutions containing beryllium. Brush Wellman continues to jointly research this hypothesis with NIOSH; however, the scientific evidence is certainly not sufficient to use these research findings as a primary basis for a recommendation to workers and

employers. Before exploring this issue further, Brush Wellman does wish to make it clear that Brush Wellman agrees that it is good industrial hygiene work practice to keep beryllium-containing dust or solutions off the person's skin and work clothing as part of an overall beryllium control program. This reasoning is primarily based on controlling all routes and pathways of exposure. The reasoning certainly considers the hypothesis that beryllium sensitization may result via skin penetration; however, it also considers reducing exposures via the important pathway of direct transfer of beryllium-containing particulate to the breathing zone or directly to mucous membranes of the nose and mouth via hand to face or clothing-to-face contact[35]. These are important pathways that the NIOSH Alert should emphasize because such potential for exposure are likely not adequately captured or represented by conventional breathing zone air sampling. The overall evidence for keeping fine beryllium-containing particulate off of the skin as an element of Brush Wellman's worker protection model is supported by the recent Cummings (2007) study. However, it is disingenuous to infer that keeping beryllium-containing particulate off the skin is a primary reason for the success of the worker protection model. At this point in time, it is unknown which elements of the worker protection model account for its success to date. While the entire model appears to be working, it is not appropriate for NIOSH to state or infer that skin protection may be more important than other aspects of the model. To do so would be misleading to workers and employers as to what actions are necessary to work safely with beryllium-containing materials.

There is evidence that skin exposure to soluble beryllium salts can result in a delayed sensitization to beryllium. This was demonstrated in human studies conduct by Curtis in the early 1950s. In addition, and as referenced in the draft NIOSH Alert, a hypothesis has been put forth by Tinkle 2003 and Day 2006 which suggests that being sensitized to beryllium, either through a skin wound or via penetration of small beryllium particles through intact skin, could result in sensitization to beryllium which, upon receiving a subsequent inhalation dose of airborne beryllium, could result in CBD.

Though unproven by any scientific study, the entry of particles containing beryllium through wounds or breaks in the skin resulting in sensitization is a generally accepted scientific theory. However, there is only limited anecdotal evidence to support this theory.[36] There is also general agreement in the scientific community that CBD requires a sufficient lung dose of beryllium particulate. The scientific literature is void of studies that prove sensitization via a subcutaneous skin dose of soluble or insoluble beryllium, and predisposes or increases the likelihood of a person to contract CBD when later exposed to a sufficient airborne concentration of beryllium. Though it would likely not be a popular theory, it is just as plausible that a subcutaneous skin dose may prompt a beneficial immune defense reaction prior to a sufficient lung dose of beryllium. This likens to the procedure used for years to desensitize persons from allergens (i.e., subcutaneous allergy shots). It is equally plausible that a lung dose sufficient to prompt CBD can initiate sensitization, followed by CBD (i.e., requiring no pre-sensitizing dose via the skin or any other pathway). This theory is supported by the fact that beryllium has been demonstrated to have a longer retention time in the lung as compared to other metals.[37] In addition, sensitization detectable when testing lung fluid may well be independent of sensitization detected when testing blood. There is evidence for this in that sensitization testing of lung fluid can yield a positive sensitization test in the presence of a negative blood test and vice-versa. Also, Curtis found examples of patients who had acute pneumonitis from exposure to airborne beryllium salts without detecting beryllium sensitization via the patch test. All of the above, including the Tinkle and Day hypotheses, are unproven theories with the exception that there is general agreement that to cause CBD a sufficient lung dose is required via an inhalation exposure to airborne beryllium.

There is very little evidence that skin penetration of insoluble forms of beryllium-containing materials is a significant contributor to overall exposure, and there are no studies that demonstrate skin absorption of insoluble beryllium results in a systemic effect. To the contrary, the study by Curtis,

the only human study looking for evidence of a beryllium sensitization reaction occurring through intact human skin, found no sensitization reaction using insoluble forms of beryllium.[38]

Following are brief reviews of the individual studies done by Curtis, Tinkle and Day.

Curtis 1951

The 1951 study by Curtis is not referenced in the draft NIOSH Alert. Curtis 1951 provides the only data where skin exposure testing was performed on humans. The Curtis study that found 8 of 16 controls (not occupationally exposed to beryllium), who had been skin patch tested, developed an allergic-eczematous dermatitis (sensitization) using soluble beryllium salts. Curtis ruled out anions, acidity and primary irritancy of beryllium salts as direct factors in causing allergic dermatitis. He also found examples of patients who had acute pneumonitis from exposure to airborne beryllium salts without skin sensitization. In patch testing using insoluble forms of beryllium, Curtis concluded that there was no sensitization as the result of applying beryllium oxide powder, beryllium metal powder and disks of metallic beryllium to the skin. Curtis did find two cases of skin sensitization handling metallic beryllium powder, but concluded that they were the result of residual beryllium fluoride in the powder. The problem of residual beryllium fluoride in metallic beryllium powder was resolved in the early 1950s when the additional purification step of vacuum casting was added to the processing methodology. Dr. Curtis' work demonstrates the absence of sensitization via the skin with insoluble forms of beryllium. Insoluble forms of beryllium comprise nearly the entire market for beryllium-containing materials. Dr. Curtis also did not identify a link between skin sensitized persons and subsequent CBD.

Tinkle 2003

Dr. Sally Tinkle's research[39] exploring a link between skin sensitization and CBD in humans is not demonstrative of such a link and its use to make recommendations to employers and workers is speculative. Dr. Tinkle's work describes the beryllium sensitization of mice and the potential for particulate (plastic beads) to penetrate intact cadaver skin. Both of these research efforts by Dr. Tinkle were well done; however, Dr Tinkle has stated her work cannot be applied to humans.[40] Dr. Tinkle's study regarding the penetration of particulate through intact human cadaver skin was performed with plastic beads, not beryllium. Since beryllium is ubiquitous in soil, averaging about 1000 micrograms of beryllium per kilogram of soil, Dr. Tinkle's theory could apply to any particulate material, including skin contact with soil. Therefore, anyone who has ever had their hands in dirt could be subject to beryllium sensitization via the skin. Dr. Tinkle did achieve beryllium sensitization of some mice using an insoluble beryllium oxide. As is appropriate for initial research of a new hypothesis, her mouse skin test method was optimized by enhancing skin penetration through a combination of steps including shaving, using Nair® and putting the beryllium oxide in a liquid suspension known to be a skin de-fatting solvent. In addition, it remains unknown if the mice stayed sensitized because they all had to be sacrificed and their blood pooled to have enough to conduct the test. It is well known from numerous animal experiments with beryllium inhalation exposure that, unlike humans, animals can be made sick with exposure to airborne beryllium, but the health effects disappear when the exposure stops.[41] Therefore, it should not be presumed that there is a direct relationship between skin contact and sensitization in humans based on Dr. Tinkle's studies. Nor does her study in any way confirm a link from skin sensitization to CBD.

Day 2006

The study by Day proposes a hypothesis that beryllium sensitization may occur via skin contact, but does not provide data to prove or disprove the hypothesis. The Day study does not explore a link from skin sensitization to CBD.

The section of the NIOSH Alert titled, BACKGROUND, contains descriptive information on properties and uses of beryllium which could be enhanced to improve understanding by workers and employers.

Brush Wellman suggests this section be reworded as shown in Attachment 3. Also, suggested revisions to the APPENDIX are provided as Attachment 4.

The health effects section of the draft NIOSH Alert should be expanded to include a discussion and scientific consideration of the most recent research findings on the potential carcinogenicity of beryllium. The most recent scientific evidence is clearly demonstrating that beryllium is not carcinogenic to humans.

The draft NIOSH Alert appears to accept a conclusion that beryllium is carcinogenic in man without first having fully evaluated the studies that have been published since IARC and others last reviewed their cancer classifications for beryllium over ten years ago.

Evaluating the available literature on the potential carcinogenicity of exposure to beryllium, along with the history behind some of that literature, can have bearing as to the value of the information in the literature and whether findings, statements and conclusions provided in the cancer references are pertinent and whether there is new knowledge that either supports, supersedes or invalidates earlier findings or interpretations. The most recent evidence clearly demonstrates that beryllium is not carcinogenic to humans and is provided below for consideration by NIOSH in its review of beryllium.

Recent studies by Levy (2002[42], 2007[43]), Brown (2004[44]) and Deubner (2007[45]) provide evidence that exposure to beryllium does not convey a significant risk of cancer to humans. Levy 2007 and Deubner 2007 identified a significant methodological error in Sanderson which negates the use of Sanderson as a dose/response cancer link for beryllium. Levy 2007 provides a reanalysis of the Sanderson study which demonstrates that when the artifact is corrected, the conclusion is that the lung cancer in this population was not associated at all with beryllium exposure, whether defined as time worked, or cumulative average or maximum exposure. Deubner 2007 confirms the methodological artifact identified by Levy using repeated data simulations.

Levy 2002

The Levy 2002 study clearly illustrates that simply replacing the smoking adjustments used in the Ward[46] study with other commonly accepted smoking adjustments[47] results in a data analysis which varies between statistical significance and non-significance. Ward studied seven beryllium plants, but found only one of seven plants had a statistically significant cancer risk after adjusting for smoking. Levy evaluated the same data for this single plant using two different smoking models. Levy found the U.S. Veterans model showed a lower, yet still significant, risk while the Wagoner model showed no significant risk. The use of common statistical smoking adjustments, which result in standard mortality ratios which vary between statistical significance and non-significance, does not provide reasonable evidence of known carcinogenic risk.

Levy also performed an analysis on the at-risk plant using a combined city-county cancer rate versus the county-wide cancer rate used by Ward. Levy included city rates because most of the workers lived in the city versus the surrounding rural countryside. Levy utilized a weighted average of combined city/county rates based on the percentage of workers living in the city plus the percentage of workers not living in the city. This is particularly important because the largest industry in the city in which the Lorain plant was located was steel making (ore through final product) during the time this plant existed in the 1940s. Ward's use of the cancer rate for the entire county dilutes the cancer risk by disproportionately including those persons living in rural areas away from pollutants in the city. Therefore, Levy's methodology is a better estimate of the referent rate.

Levy's comparison to a weighted city/rural referent rate resulted in a non-significant statistical cancer risk at this plant without even considering smoking risks. Levy's finding demonstrates that minor differences in the referent population used to estimate cancer risk can easily move the beryllium cancer risk estimate in and out of statistical significance. Again, this low statistical confidence does not provide reasonable evidence to support a known human carcinogen cancer classification for beryllium.

Notwithstanding the findings of Levy, Ward found no statistically significant cancer risk when considering all seven plants in total and adjusting for smoking. These risk values remain the lowest ever used to designate a known human carcinogen.[48] There are numerous substances that have higher risk values which have not been classified as a known human carcinogen.

Levy's analysis, using three smoking adjustment models, concurs with Ward's regardless of the smoking model employed. Levy's findings reveal that the analysis of potential beryllium carcinogenic risk can too easily shift from statistical significance to non-statistical significance due to small variations in estimating the smoking risk of the control groups and the background cancer risk demographics of the local population. Dr. Levy concluded:

"There is no statistical association between beryllium exposure in these workers and lung cancer when using the most appropriate population cancer rates."

Brown 2004

A 2004 study by Brown et al. identified a cohort of 16,303 production era workers employed at the Department of Energy Rocky Flats Plant for six months or more between 1952 and 1989.[49] This is a very important study because it is the first to use a study cohort different than that used for every other beryllium cancer study. For this cohort, a job exposure matrix was used to estimate exposures to various chemicals including beryllium. The fabrication of plutonium pits was the primary production activity at Rocky Flats and beryllium was used in the production of the pits. The Rocky Flats Beryllium Health Surveillance Program (BHSP) database, containing 23,196 records, was obtained. The BHSP was a Department of Energy effort to identify and contact all current and former employees of the DOE at Rocky Flats, its prime contractors and subcontractors to obtain information about exposure to beryllium and evaluate each for signs of beryllium disease. For beryllium, exposure estimates were made from a few hundred air samples collected during production era activities. Annual exposure estimates for each worker were generated by linking workers to a job exposure matrix developed from monthly job and building assignments from 1951 to1989. Historical records of chemical usage were reviewed and a list of job titles and organizational names was developed. In-person interviews were conducted with persons who held jobs having an exposure potential to document the tasks performed by each job title, the materials used and to identify jobs with similar exposures.

The study concluded: "*No associations were found between lung cancer mortality and cumulative external penetrating radiation dose or cumulative exposures to asbestos, beryllium, hexavalent chromium, or nickel.*"

Levy 2007 and Deubner 2007

These two studies are particularly relevant to an evaluation of whether cancer risk can be estimated for various exposure levels. These studies confirm that Sanderson 2001 contains a serious methodological artifact which invalidates the conclusions of Sanderson.

A methodological artifact in the Sanderson paper was immediately suspected by Deubner et al.[50], but it was only in 2007 that a paper describing and correcting this artifact was published by Levy. The study by Deubner, more completely elucidating the methodological artifact, was published in September 2007. The artifact occurs as a specific effect of the Cox proportional hazards model, notably the combination of imbalances created between cases and controls by the control selection procedure with the truncation of exposure estimates at the same age in both cases and controls. Controls are selected with older age at censor (age at death or at last follow-up) than their cases, which produces imbalances between cases and controls with respect to variables associated with age at censor, most importantly older age at hire. When exposure is truncated at the age of death of the case minus a latency period (lagged) in both cases and controls, the difference in age at hire results in a higher rate of lagging to zero of exposure in cases and controls. This effect was greatly exaggerated by log transformation of the exposure variables. Results exactly comparable to those of Sanderson can be derived from null hypothesis simulations, demonstrating that the findings in Sanderson are artifacts.

One approach to control of the artifact was performed by Levy 2007, who compared the lung cancer cases to the controls with the closest ages at censor. With the artifact thus controlled, there were no differences in lagged or unlagged exposure. This established with dose reconstruction what was suspected from Ward 1992 and earlier studies[51], that lung cancer in beryllium workers is not associated with the degree of exposure to beryllium.

Levy 2007 also reduced the case control difference in age at hire by using controls closely matched to cases, and did not log-transform the exposure data. This reanalysis found no elevated odds ratios for any of the exposure variables: time worked in a beryllium manufacturing facility, or cumulative, average or maximum beryllium exposure. Therefore, Levy found no causal relationship between beryllium exposure and lung cancer.

Following is a summary of the Deubner findings. The Sanderson cohort-nested case control study exploring the relationship between beryllium exposure and lung cancer found workers who developed lung cancer to have worked fewer days and to have no higher cumulative, average or maximum beryllium exposure than other workers. However, when exposure was truncated (lagged) with lung cancer latency assumptions of 10 and 20 years, workers who developed lung cancer had higher lagged values for all four exposure metrics. The higher lagged exposure in cases was interpreted by Sanderson as indicating that beryllium exposure caused lung cancer. Deubner suspected that the lagged findings of higher exposure in lung cancer cases might be an artifact of the study design. Deubner investigated the index study design using data supplied by NIOSH.

Deubner applied the index study design to a closely related cohort using randomly selected probands as cases. Values for average exposures were assigned to probands equal to, greater than and less than those assigned to controls (matches). He found that under certain lag scenarios, the nested study design produced a finding of higher average exposure in probands compared to

their matches even when this was clearly not the case. The empirical evaluation demonstrated that the study design produced a biased case-control lagged exposure difference under the null hypothesis in the direction of higher lagged exposure for cases compared to controls. Also, the study design could not distinguish qualitatively between null and alternate hypotheses. The reason for this bias was that the Sanderson study design selected controls with significantly higher *ages at hire* than cases. When exposure was lagged, the older *age at hire* of controls caused a higher proportion to "lag to zero", an effect magnified by the log transformation of the exposure variables.

Deubner's analysis determined that the Sanderson study finding was due to a methods artifact that is correctable by closer matching of controls to cases. With the artifact corrected, lung cancer cases had no higher exposure than controls whether exposure was unlagged or lagged, suggesting that lung cancer in these beryllium workers was not caused by their exposure to beryllium.

Published concurrently with Deubner 2007 is an editorial by Dr. Garabrant[52] commenting on the significance of Deubner's finding and cautioning that other studies may be subject to the same methodological flaw.

These above beryllium studies deal with sizeable cohorts exposed to very high levels of beryllium. Failure to find convincing evidence that beryllium workers have excess rates, combined with clear evidence that in beryllium workers, lung cancer is not related to degree of exposure, strongly supports a reclassification of beryllium as non-carcinogenic in humans.

Employers and workers will be much better served if the NIOSH discussed actions that have been demonstrated to prevent chronic beryllium disease rather than the two case studies which contain little educational value.

Case study 1 describes a series of events based on non-quantifiable exposure information. The secretary's exposure to airborne beryllium could have been very large since renovation activities and ,in particular, the opening of ventilation ductwork may produce exposures well in excess of the current occupational exposure limit. If the person's skin problems cannot be linked to the former use of soluble beryllium salts in the laboratory, then the secretary's skin problems are not likely due to beryllium. The use or handling of insoluble forms of beryllium-containing materials has not been demonstrated to cause such skin reactions. Building renovations often involve numerous materials that are well known to cause skin issues, the most obvious being fiberglass insulation and mineral fibers. NIOSH should not ignore the obvious and unless soluble beryllium salts were involved, the draft NIOSH Alert should not imply or suggest that the secretary's skin problems were linked to beryllium. To include such a statement would be misleading to workers and employers. Other than the lesson learned that a significant exposure to beryllium dust may occur during renovation work, Case 1 does not identify any direct benefit to this worker since she was identified with subclinical CBD which requires no treatment. A good hazard communication program describing the potential routes of exposure and the symptoms of clinical CBD would serve such individuals just as well.

Case 2 also describes a person with subclinical CBD. Again, a good hazard communication program can achieve the same result if the person were ever to develop symptoms. Case 2 does nothing to demonstrate the value of such medical surveillance. This person has no knowledge other than he may or may not ever progress to clinical CBD. NIOSH needs to evaluate the psychological, social and economic harms and benefits and then make its recommendations accordingly.

Workers and employees would be much better served if NIOSH would delete the case studies and instead provide a summary of the best available evidence along with a fairly detailed

recommendation on what workers and employers need to do to work safely with beryllium-containing materials.

The listing of Current Exposure Limits contains inaccuracies which should be corrected.

The 1977 NIOSH REL for beryllium is not a suggested limit, but an adopted limit by NIOSH. We are not aware that NIOSH has made a determination that the REL does not prevent beryllium sensitization or chronic beryllium disease. This statement should be removed or scientifically supported. NIOSH cannot say that safe exposure limits have not been established for beryllium. In fact, after considering the available science, in 2006, the State of California adopted an 8-hour time weighted average permissible exposure limit (PEL) for beryllium of 0.2 micrograms per cubic meter of air. This is a 10-fold reduction in the federal OSHA PEL. Please refer to our earlier comments on the NIOSH recommendation to keep airborne concentrations of beryllium as low as possible.

OSHA has not stated that the current PEL does not adequately protect beryllium-exposed workers from developing chronic beryllium disease. OSHA made the following statement:

> *"The OSHA has recently obtained information suggesting that OSHA's current 2 micrograms per cubic meter of air (micrograms/m3) eight-hour time-weighted average (TWA) permissible exposure limit (PEL) for beryllium in the workplace may not be adequate to prevent the occurrence of chronic beryllium disease (CBD)."*

The statement in the draft NIOSH Alert regarding the U.S. Department of Energy (DOE) exposure limit for beryllium is wrong. The U.S. DOE permissible exposure limit for beryllium is 2 micrograms per cubic meter of air 8-hour time-weighted average. The draft NIOSH Alert reference to DOE setting action limits is also not correct. The DOE has adopted action levels, not limits, to prompt various actions on the part of facilities that operate under DOE oversight. Since this section is a review of exposure limits, the references to action levels should be removed or at least clarified. The NIOSH Alert should clarify that the DOE beryllium rule requires medical surveillance be offered, including the blood BeLPT, but that participation is voluntary for workers.

The draft NIOSH Alert refers to two DOE surface contamination limits which are, in fact, listed by the DOE as an operational removable contamination level and a free release removable contamination level. The DOE was very careful not to call these two values limits because, as similarly noted in the draft NIOSH Alert, these two values are based on a review of cleaning performance determined by an opinion poll of the DOE labs. Since these values are not limits, are not based on any health assessment and do not represent a health exposure limit, they should be removed from this section.

In the listing of other limits, the ACGIH TLV is accurately stated. However, NIOSH should refrain from referencing proposed limits that are currently under consideration and open for public comment. For example, the ACGIH has proposed three different TLVs for beryllium in the past nine years. Workers and employers are likely confused enough without listing proposed limits. The reference to Canadian and United Kingdom limits are both outdated and not accurate.

The draft Alert states, *"NIOSH requests that the information in this Alert be brought to the attention of workers and employers by the following: trade associations, editors of trade journals, safety and health officials, labor organizations, members of the academic and public health communities, advocacy groups, workers' compensation insurance companies, distributors of materials that contain beryllium, and the mass media."*

It's interesting to note that "manufacturers of beryllium-containing materials" were not listed.

Summary of Brush Wellman Inc. Comments
re: OMB Final Bulletin on Agency Good Guidance Practices

The draft NIOSH Alert on Preventing Chronic Beryllium Disease and Beryllium Sensitization fails to conform to the requirements of the Final Bulletin for Agency Good Guidance Practices issued by the Office of Management and Budget on January 18, 2007 ("Bulletin"). The draft Alert departs from the Basic Agency Standards for Significant Guidance Documents established by the Bulletin. The draft Alert fails to include the term "guidance" or its functional equivalent.

The Draft Alert is Subject to the OMB Final Bulletin on Agency Good Guidance Practices.

NIOSH's consideration and preparation of its draft Alert on Preventing Chronic Beryllium Disease and Beryllium Sensitization are subject to Office of Management and Budget Bulletin No. 07-02, Final Bulletin for Agency Good Guidance Practices, issued on January 18, 2007 ("Bulletin"). The Bulletin sets requirements for the (1) preparation, (2) issuance and (3) use of significant guidance documents by Executive Branch departments and agencies, including NIOSH. The CDC has previously identified NIOSH Alerts as significant guidance documents. See, e.g., NIOSH Alert: Preventing Fire Fighter Fatalities Due to Heart Attacks and Other Sudden Cardiovascular Events, NIOSH Publication No. 2007-133. The draft Alert is also subject to the Bulletin as a "guidance document." The Bulletin defines this term as "an agency statement of general applicability and future effect, other than a regulatory action . . . that sets forth a policy on a statutory, regulatory or technical issue." By publishing a Federal Register notice inviting public comment on this draft Alert, NIOSH indicates that it is being correctly treated as an economically significant guidance document.

The Alert Does Not Comply with the Basic Agency Standards for Significant Guidance Documents Mandated by the OMB Final Bulletin.

The OMB Bulletin establishes a variety of Basic Agency Standards for Significant Guidance Documents which are both procedural and substantive. These standards include several procedural requirements that mandate significant guidance documents to be:

(1) prepared by agency employees trained in the Standards;

(2) prepared pursuant to written procedures for approval;

(3) issued only after approval by appropriate senior agency officials; and

(4) followed by agency employees unless there is appropriate justification and supervisory concurrence.

For economically significant guidance documents, such as the draft Alert, the Bulletin also requires publishing a Federal Register notice announcing the issuance of the draft for public comments and preparing and posting on the agency's website a "robust" response-to-comments document.

One of the Bulletin's substantive requirements is that a significant guidance document shall include the term "guidance" or its functional equivalent. The draft Alert does not identify itself as "guidance" or any functional equivalent of this term. This defect is significant because it includes a variety of information, including warnings, recommendations for workers and employees, discussions of risks and health effects, reviews of health effects, work force surveys and a listing of selected exposure limits (including non-regulatory limits) relative to beryllium. The only heading that might connote that this document is "guidance" is the word "Recommendations" which appears on page 9. This word is insufficient to meet this standard. It is not prominent, given its position on page 9 at the top of a list of actions which have already been presented on pages iii and iv in identical form.

These standards are designed to achieve the purposes of the Bulletin, one of which, as reflected in the definition of "significant guidance documents," is to avoid unnecessarily issuing a document "that may reasonably be anticipated to . . . [c]reate a serious inconsistency or otherwise interfere with an action taken or planned by another agency." This purpose is particularly relevant with respect to draft Alert because practices for working with beryllium are the subject of past and prospective rulemaking action by OSHA and the Department of Energy.

[1] Documentation of the Threshold Limit Values and Biological Exposure Indices, 7th Ed. ACGIH® Publication#0100, ISBN: 1-882417-43-7 Copyright © 2001

[2] Schuler C., Kent M., Deubner D., Berakis M., McCawley M., Henneberger P., Rossman M., Kreiss K. Process-Related Risk of Beryllium Sensitization and Disease in a Copper–Beryllium Alloy Facility. Am. J. Ind. Med. 47:195–205 (2005)

[3] Madl A.K., et al. Exposure-Response Analysis for Beryllium Sensitization and Chronic Beryllium Disease Among Workers in a Beryllium Metal Machining Plant. JOEH 4:6 448-466 (2007).

[4] Borak J., Woof S.H., Fields C.A. Use of Beryllium Lymphocyte Proliferation Testing for Screening of Asymptomatic Individuals: An Evidence-Based Assessment. J Occup Environ Med 48(9): 937-947 (2006).

[5] Johnson J., et al. Beryllium Exposure Control Program at the Cardiff Atomic Weapons Establishment in the United Kingdom. Appl Occup Environ Hyg 16(5): 619-630 (2001).

[6] Cummings K.J., et al. Enhanced preventive programme at a beryllium oxide ceramics facility reduces beryllium sensitization among new workers. Occup Environ Med 64:134-140 (2007).

[7] Deubner D., Kent M. Keeping Beryllium Workers Safe: An Enhanced Preventive Model. JOEH 4:D23-D30 (2007).

[8] Sterner J.H., Eisenbud M. Epidemiology of Beryllium Intoxication. Arch Indus Hyg Occup Med 4: 123–151 (1951).

[9] Waksman, B.H. Discussion of "The diagnosis of beryllium disease with special reference to the patch test" by GH Curtis. Arch Ind Health 19:154-156 (1959).

[10] Borak J., Woolf S.H., Fields C.A. Use of Beryllium Lymphocyte Proliferation Testing for Screening of Asymptomatic Individuals: An Evidence-Based Assessment. J Occup Environ Med 48(9): 937-947 (2006).

[11] Rosenman K., et al. Chronic Beryllium Disease and Sensitization at a Beryllium Processing Facility. Environ Health Perspect 113(10): 1366-1369 (2005).

[12] Bobka C., Stewart L., Engelken G., Golitz L., Newman L. Comparison of In Vivo and In Vitro Measures of Beryllium Sensitization. J Occup Environ Med 39(6): 540-547 (1997).

[13] Deubner D., Goodman M., Iannuzzi J., Variability, Predictive Value, and Uses of the Beryllium Blood Lymphocyte Proliferation Test (BLPT): Preliminary Analysis of Ongoing Workforce Survey. Appl Occup Envron Hyg 16(5): 521-526 (2001).

[14] Donovan E.P., et al. Performance of the beryllium blood lymphocyte proliferation test based on a long-term occupational surveillance program. Int Arch Occup Environ Health. 81: 165-178 (2007).

[15] Yoshida T., Shima S., Nagaoka K., et al. A Study on the Beryllium Lymphocyte Transformation Test and the Beryllium Levels in the Working Environment. Industrial Health 35: 374-379 (1997).

[16] Maier L.A. Beryllium Health Effects in the Era of the Beryllium Lymphocyte Proliferation Test. Appl Occup Environ Hyg 16(5): 514-520 (2001).

[17] Eisenbud M. The Standard for Control of Chronic Beryllium Disease. Appl Occup Environ Hyg 13(1): 25–31 (1998).

[18] Rossman M.D. Chronic Beryllium Disease: A Hypersensitivity Disorder. Appl Occup Environ Hyg 16(5): 615-618 (2001).

[19] Kreiss K., Mroz M.M., Newman L.S., et al. Machining Risk of Beryllium Disease and Sensitization with Median Exposures Below 2 $\mu g/m^3$. Am J Ind Med 30: 16–25 (1996).

[20] Henneberger, et al. Beryllium Sensitization and Disease Among Long-term and Short-term Workers in a Beryllium Ceramics Plant. Int Arch Occup Environ Health 74: 167-176 (2001).

[21] Kelleher P., Martyny J., Mroz M., Maier L., Ruttenber AJ., Young D., Newman L. Beryllium Particulate Exposure and Disease Relations in a Beryllium Machining Plant. JOEM 43(3): 238-249 (2001)

[22] Eisenbud M. Health Hazards from Beryllium, The Metal Beryllium. D. W. White, Jr., J.E. Burke, (eds.): The American Society for Metals 620-640 (1955).

[23] Van Ordstrand, H.S., Hughes R., De Nardi J.M., et al. Beryllium Poisoning. JAMA 129:1084 (1945).

[24] United States Department of Energy Lawrence Livermore National Laboratory. Document 14.4. Implementation of the Chronic Beryllium Disease Prevention Program Requirements. December 2, 2004.

[25] Eisenbud, M.: Origin of the Standards for Control of Beryllium Disease (1947–1949). Environ. Res. 27:79–88 (1982).

[26] Murray JF, Hudson LD, Petty TL, (eds.): Frontline Assessment of Common Pulmonary Presentations. Snowdrift Pulmonary Conference, Inc., Denver, CO

[27] Mueller-Quernhemim, J. Chronic Beryllium Disease. Orphanet (November 2005).

[28]Kreiss K., Newman L., Mroz M., Campbell P. Screening Blood Test Identifies Subclinical Beryllium Disease. J Occup Med 31(7): 603-608 (1989).
[29] United States Department of Labor Occupational Safety & Health Administration, Draft Guidance For Hazard Determination for Compliance with OSHA Hazard communication Standard. 6. Data Analysis Page 34/74.
[30] National Institute for Occupational Safety and Health. Health Hazard Evaluation Report: Rockwell International, Rocky Flats Plant, Golden, CO. Publication No. 84-510-1691. NIOSH, Cincinnati, OH (1986).
[31] Cullen M.R. Screening for Chronic Beryllium Disease: One Hurdle Down, Two to Go. Letter to the Editor. Am J Respir Crit Care Med 171: 3-4 (2005).
[32] Maier L.A. Beryllium Health Effects in the Era of the Beryllium Lymphocyte Proliferation Test. Appl Occup Environ Hyg 16(5): 514-520 (2001).
[33] Eisenbud M. The Standard for Control of Chronic Beryllium Disease. Appl Occup Environ Hyg 13(1): 25–31 (1998).
[34] Rosenman K., et al. Chronic Beryllium Disease and Sensitization at a Beryllium Processing Facility. Environ Health Perspect 113(10): 1366-1369 (2005).
[35] Deubner, D., et al. Contribution of Incidental Exposure Pathways to Total Beryllium Exposures. Appl Occup Environ Hyg 16(5): 568-578 (2001).
[36] Jones-Williams W., et al. Beryllium Skin Disease in Sarcoidosis and other granulomatous disorders. Elsevier Science Publishers pp 689-690 (1988).
[37] Rossman M.D. Chronic Beryllium Disease: Diagnosis and Management. Environ Health Perspect 104: 945–947 (1996).
[38] Curtis G.H. Cutaneous Hypersensitivity Due to Beryllium: A Study of 13 Cases. AMA Arch Dermatol Syph 64: 470–482 (1951).
[39] Tinkle S.S., et al. Skin as a Route of Exposure and Sensitization in Chronic Beryllium Disease. Environ Health Perspect 111: 1202-1208 (2003).
[40] Personal Communication between Marc Kolanz and Dr. Sally Tinkle
[41] Finch, G.L., Hoover, M.D., Hahn, F.F., Nikula, K.J., Belinsky, S.A., Haley, P.J. and Griffith, W.C. Animal models of beryllium-included lung disease. Environ Health Perspect 104 (suppl. S): 973-979 (1996).
[42] Levy P., Roth H., Hwang P., Powers T. Beryllium and Lung Cancer: A Reanalysis of a NIOSH Cohort Mortality Study. Inhalation Toxicology 14:1003-1015 (2002).
[43] Levy, P.S., Roth H.D., Deubner D.C. Exposure to Beryllium and Occurrence of Lung Cancer: A Reexamination of Findings from a Nested Case-Control Study. J Occup Environ Med 49: 96-101 (2007).
[44] Brown S.C., et al. Lung Cancer and Internal Lung Doses among Plutonium Workers at the Rocky Flats Plant: A Case-Control Study. Am J Epidemiol 160(2): 163-172 (2004).
[45] Deubner D.C., Roth H.D., Levy, P.S., Empirical evaluation of complex epidemiologic study designs: workplace exposure and cancer. J Occup Environ Med (2007).
[46] Ward, E., et al. A Mortality Study of Workers at Seven Beryllium Processing Plants. Am J Ind Med 22: 885-904 (1992).
[47] Mancuso T.F. Mortality study of beryllium industry workers' occupational lung cancer. Environ Res 21: 48-55 (1980).
[48] Trichopoulos, D., Comments of Dimitrios Trichopoulos, MD The Alleged Human Carcinogenicity of Beryllium Submitted to the National Toxicology Program – June, 1999.
[49] Report of Epidemiologic Analyses Performed for Rocky Flats Production Workers Employed Between 1952-1989. Department of Preventive Medicine and Biometrics, University of Colorado Health Sciences Center, Colorado Department of Public Health and Environment, March 3, 2003.
[50] Deubner D., Lockey J., Kotin P., Powers M., Miller F., Rogers A., Trichopoulos D. Lung Cancer Case-Control Study of Beryllium Workers – Editorial. Am J Ind Med. 40: 284-285 (2001).
[51] Doll R. Occupational Cancer: A Hazard for Epidemiologists. Intl J of Epidem 14(1): 22-31 (1985).
[52] Garabrant D., Case-Control Study Design: Spurious Associations Between Exposure and Outcome J Occup Environ Med (2007).

Attachment 1 – Suggested Reword "Workers" and "Employers" sections.

Workers

Workers exposed to particles, fumes, or solutions from beryllium-containing materials should take the following steps to protect themselves:

- Understand the health risks and follow all proper procedures for working with beryllium—including participation in safety training.
  - If you experience any signs or symptoms of chronic beryllium disease such as chronic cough or shortness of breath, seek prompt medical attention.
  - Learn to use the controls and follow the work procedures needed to work safely with beryllium-containing materials.
- Keep beryllium out of the lungs:
  - Make sure to follow standard operating procedures so that release of beryllium dusts, fumes, and beryllium-containing solutions and suspensions are controlled at the source.
  - Participate in respiratory protection programs when advised to do so.
  - Avoid the use of cleaning methods that may cause dust to become resuspended in air (dry sweeping, compressed air, and other dust-generating methods, for example).
- Keep beryllium work areas clean:
  - Keep work surfaces and work areas visibly clean, well lit, orderly and free of clutter.
- Keep beryllium-containing dusts and solutions off the skin:
  - Participate in skin protection programs. These programs may include wearing company-issued gloves, hats and clothing (with long sleeves and long pants) and at least daily washing of hands of face or showering (including hair washing) at the end of the workday.
- Keep beryllium-containing dusts and solutions off of clothing and shoes
  - Keep work clothing visibly clean
  - Wear protective over garments over personal or company provided work clothing whenever there is a potential for beryllium-containing dusts and solutions to contact clothing.
  - Do not blow-off clothing with compressed air or shake soiled clothing
- Keep beryllium-containing dusts and solutions at the source:
  - Utilize ventilation controls and follow work practice procedures to minimize the release of dust into the air or onto surfaces.
- Keep beryllium-containing dusts in the work area:
  - Utilize work practices such as shoe changing, tacky mats and vacuuming/cleaning to make sure beryllium-containing dusts and solutions are not spread to support areas and expose people where beryllium work is not being performed.

- Keep beryllium-containing dusts and solutions on the plant site:

  - Utilize procedures to keep beryllium-containing dusts and solutions from leaving the plant site on people and things such as personal items, clothing, laundry, tools, products or equipment.

Employers

Employers of workers exposed to particles, fumes, or solutions in excess of the recommended exposure guideline for beryllium should take the following steps to protect workers:

Develop leading and lagging measures to set goals and priorities to:

- control airborne beryllium-containing particle concentrations to levels reliably below the recommended exposure guideline;
- keep work areas visibly clean;
- prevent skin contact with beryllium-containing particles and solutions;
- keep clothing visibly clean;
- keep beryllium-containing particles and solutions in the work area;
- keep beryllium-containing particles on the plant site; and,
- ensure that engineering and work practice controls, and personal protective equipment programs, are, and remain effective.

Develop and implement procedures and work instructions to:

- reduce and maintain exposures reliably below the recommended exposure guideline;
- keep employee work clothing (including shoes) visibly clean;
- prevent exposure to airborne beryllium when handling or laundering the clothing;
- prevent the release of beryllium-containing particles and solutions from the source;
- prevent the release of beryllium-containing particles and solutions out of the work area; and,
- prevent the unintended release of beryllium-containing particles and solutions from the plant.

Develop and implement written procedures and work instructions designed to:

- prevent inhalation of airborne beryllium-containing particles;
- keep beryllium-containing particles and solutions at the source;
- prevent the release of beryllium-containing particles or solutions out of the work area;
- keep beryllium-containing particles from being carried off of the plant site on people and things such as personal items, clothing, laundry, tools, products or equipment; and
- protect workers and minimize the release of beryllium-containing particles during air cleaning system maintenance activities such as drum or filter changes

Keep Beryllium Out of the Lungs

- Obtain, read and understand the Material Safety Data Sheets before processing beryllium-containing materials at your facility.
- Make Material Safety Data Sheets readily available to workers and provide appropriate Hazard Communication training.
- Conduct an exposure assessment to evaluate and control potential airborne beryllium-containing particle exposures to reliably below the recommended exposure guideline. Include in your assessment an evaluation of the potential exposures resulting from adjacent

operations or support activities such as setup, cleanup and maintenance.

- Where engineering and work practice controls cannot reduce exposures to below the recommended exposure guideline, are not feasible, or while they are in their design and installation phase, implement an effective respiratory protection program that meets the requirement of OSHA 29 CFR 1910.134.
- Develop and implement a medical surveillance program for affected beryllium workers.

Keep Beryllium Work Areas Clean

- Develop and implement a housekeeping program that ensures that work areas are visibly clean, well lit, orderly, and free of clutter.
- Ensure floors, walls, furniture, fixtures and equipment surfaces are easy to clean to facilitate housekeeping. Paint, seal or condition as needed. Avoid the use of cloth furniture or fixtures in beryllium work areas.

Keep Beryllium Off of the Skin

- Provide reusable or disposable work clothing to employees, as appropriate:
  - shoes and socks, or shoe coverings/booties;
  - gloves;
  - hats or head coverings; and,
  - long sleeve shirts and long pants, or coveralls.
- Provide additional personal protective equipment such as impervious gloves, aprons and sleeve coverings wherever the potential exists for beryllium-containing particles and solutions to come into contact with skin or work clothing.
- Do not allow sleeves to be rolled-up on long sleeve shirts and coveralls.
- Ensure that adequate provisions for cleaning skin are in place and that cuts, rashes, abrasions, and breaks in the skin are treated and dressed in a manner that prevents contact with metal particles and process solutions.
- Train employees on the importance of skin cleanliness and the importance of maintaining cuts, abrasions, and skin breaks in a clean and covered condition.
- Instruct workers to practice good personal hygiene by washing hands, arms and face before eating, drinking, smoking, putting on protective equipment, or leaving the work area or the plant site.
- Provide and require workers to shower and wash hair if skin or hair contact with beryllium-containing particles and solutions can occur.

Keep Beryllium Off of the Clothing

- Provide reusable or disposable work clothing to employees, as appropriate:
  - shoes and socks, or shoe coverings/booties;
  - gloves;
  - hats or head coverings; and,
  - long sleeve shirts and long pants, or coveralls.
- Do not allow workers to remove reusable or disposable work clothing or personal protective equipment from the plant site.
- Provide additional personal protective equipment such as impervious gloves, aprons and sleeve coverings wherever the potential exists for beryllium-containing particles and solutions to come into contact with skin or clothing.

- Require employees to change work clothing that has become unexpectedly soiled.
- Require employees to report any incident where work clothing becomes soiled. Investigate and take corrective action as needed.
- Do not allow employees to shake, brush-off or use compressed air to remove dirt from their work clothing, over-garments protection or personal protective equipment because these activities can cause particles to become airborne. Provide High Efficiency Particulate Air (HEPA) vacuums for removing visible particles from clothing.
- When employees remove work clothing or over-garment protection that have been worn over personal clothing, require them to keep the potentially dirty side from coming into contact with their personal clothing.
- Provide separate lockers or a similar method to keep personal clothing separate from work clothing.
- If utilized, inform the commercial laundry in writing of the potential presence of beryllium-containing particles and solutions on the clothing, the exposure risks in handling and cleaning work clothing soiled with beryllium-containing particles and solutions, the Material Safety Data Sheets and the elements of the Beryllium Worker Protection Model.
- Store and transport work clothing, over-garment protection and personal protective equipment that are removed for laundering, cleaning, maintenance, or disposal in sealed, impermeable bags or other closed, impermeable containers.

Keep Beryllium at the Source

- Conduct an exposure assessment to evaluate and control potential airborne exposures to beryllium-containing particle exposures to reliably below the recommended exposure guideline. Include in your assessment an evaluation of the potential exposures resulting from adjacent operations or support activities such as setup, cleanup and maintenance.
- Conduct periodic inspections, preventative maintenance, and measurements to make sure that all engineering controls are operating properly. Immediately correct any deficiencies.

Keep Beryllium in the Work Area

- Establish beryllium work areas that are demarcated from the rest of the workplace in a manner that adequately establishes and alerts employees of the boundaries of the beryllium work area.
- Limit access to the beryllium work areas to persons authorized by the employer and required by work duties to be present in the beryllium work area.
- Require employees to report any incident of beryllium particles or chips being inadvertently carried out of the work area. Investigate and take corrective action as needed.

Keep Beryllium Workers Prepared

- Ensure that each employee has access to Material Safety Data Sheets.
- Prior to working with beryllium-containing materials, and as needed, provide the employee with training on and ensure that each employee understands:
  - The potential health effects of exposure to beryllium and the type of activities that can result in exposure to beryllium-containing particles above the recommended exposure guideline.
  - The elements of the beryllium worker protection program and the actions to take to control exposure.
  - The personal protective equipment requirements, and proper use and limitations of the

personal protective equipment provided.

- The written procedures and work instructions developed to process beryllium-containing materials and to prevent the inhalation of beryllium-containing particles.
- The engineering and work practice controls, and how to use these controls to minimize exposure.
- Where beryllium work areas are demarcated and that access is limited to persons authorized and required by work duties to be present in the beryllium work area.
- How to correct or report conditions or practices that are not normal and could result in uncontrolled exposure to beryllium-containing particles.
- The leading and lagging measures and audit procedures used to assure the safety procedures are in place and functioning as intended.
- The purpose and elements of the exposure assessment process and medical surveillance program.

Medical surveillance for beryllium health effects should include:

- A medical and work history with emphasis on past, present and anticipated future exposure to beryllium;
- Any history of respiratory system disorders such as asthma, shortness of breath, cough and wheezing;
- Any history of skin disorders, lesions or dermatitis;
- Smoking status and history;
- A physical examination with emphasis on the respiratory tract;
- Pulmonary function tests consisting of forced vital capacity (FVC), forced expiratory volume in one second (FEV(1)) and forced expiratory flow (FEF);
- A chest x-ray upon initial assignment and periodically thereafter as determined by the physician;
- A physical examination of the skin; and,
- Any additional tests deemed appropriate by the examining physician.

Provide the employee with a written medical opinion from the physician for each medical examination performed which contains:

- The physician's opinion as to whether the employee has any identified medical condition(s) that would place the employee at increased risk of material impairment to health from further exposure to beryllium;
- Any recommended limitations upon the employee's exposure to beryllium or upon the use of personal protective equipment such as respirators;
- Any medical conditions related to beryllium exposures that require further evaluation or treatment, and any special provisions for use of protective clothing or equipment; and,
- Any health risks associated with their exposures to beryllium and any options the employee should consider relative to their job or employment status.

Attachment 2

Summary of Brush Wellman Inc. Experiences and Observations Regarding the Socio-Economic Aspects/Effects of Conducting BeBLPT and CBD Surveillance Programs

Introduction

Brush Wellman Inc. is the leading international supplier of high performance engineered materials containing beryllium and is headquartered in Cleveland, Ohio. It is the only fully integrated supplier of beryllium, beryllium alloys and beryllia ceramic in the world. Since its founding in 1931, Brush Wellman has concentrated its operations and skills on advancing the unique performance capabilities and applications of beryllium-based materials. As a world leader in beryllium production and technology, Brush Wellman strives to remain a leader in medical knowledge of beryllium and in the environmental, health and safety aspects of the material as well. Brush Wellman has sponsored basic research concerning the environmental and health effects of beryllium.

The beryllium industry has long sought a practical and useful test that was capable of reliably predicting those individuals who may be susceptible to contracting CBD. No such test has yet been developed. A blood test, the beryllium blood lymphocyte proliferation test (BeBLPT), may be used to indicate whether a person is sensitized to beryllium. Sensitization to beryllium is not an illness or disability and as such is not considered a health effect. The BeBLPT is a laboratory test to measure if a response occurs when a water-soluble beryllium compound is added to immune cells isolated from a blood sample. The BeBLPT, in and of itself, does not detect sub-clinical or clinical CBD. Individuals who have a positive BeBLPT may be referred to a lung specialist for consultation to decide whether to undergo additional specific medical tests which are necessary to determine if sub-clinical or clinical CBD is present. Diagnosing sub-clinical CBD requires a biopsy to obtain samples of lung tissue using a medical out-patient procedure called bronchoscopy.

Over the period from 1992 through 2001, Brush Wellman has conducted thorough BeBLPT surveys at specific facilities with concomitant diagnosis, work history reconstruction and detailed statistical analysis, for the purposes of examining the relationship between sensitization, CBD and work place processes and exposures. These surveys have resulted in new concepts of the natural history of sensitization and CBD and of beryllium safety. Brush Wellman is now in the process of enhancing its beryllium safety program based on these new concepts. The BeBLPT is currently being used in ongoing testing at three higher CBD rate plants, with focus on the degree to which Brush is successful in preventing sensitization in new employees. Without an objective medical benefit, and with other risks inherent in the process, Brush Wellman uses the Be BLPT with two purposes in mind:

1. Assisting with the accuracy of diagnosis in symptomatic workers
2. As part of a well-defined medical surveillance plan, the design of which will yield information that is directly applicable to the improvement of safety programs which will decrease risk of beryllium sensitization or disease.

Testing with the BeBLPT is often done with the assumption of personal health benefit for the individuals involved. The first assumption is that persons working with beryllium, who

are found to be sensitized or have sub-clinical or clinical chronic beryllium disease (CBD), may benefit by removal from further beryllium exposure. The second assumption is that identification of sensitized workers for further monitoring, or "early" treatment of CBD at any stage, conveys a health benefit for the person.

While treatment of symptomatic individuals with CBD may relieve symptoms to a varying degree, scientists lack evidence that removal from exposure or treatment at any stage modifies the long-term outcome of the disease process. There is also no evidence to demonstrate that treatment of persons with sub-clinical CBD offers any long- or short-term benefit; indeed such persons generally do not receive any treatment. Therefore, the assumption of a personal health benefit is unfounded.

It is clear is that there are risks associated with the BeBLPT and the CBD identification and follow-up processes. These risks include pneumothorax during bronchoscopy, perceived decreased health with assumption of the sick role, damaging side effects of prednisone and other immune suppressant drugs, and reduction in work/employment options with potentially adverse social and economic consequences.

Brush Wellman Surveillance Programs and Worker Education

Brush Wellman has been conducting BeBLPT surveillance studies at select plants for over ten years. Brush Wellman has accumulated considerable experience in managing surveillance programs and the associated worker issues. The following are descriptions and examples from Brush Wellman's experience in conducting its surveillance programs as it relates to worker education, worker reactions to blood test results and worker reactions to a diagnosis of sub-clinical or clinical CBD.

Worker Education

Worker Education Summary– Beryllium Health & Safety

The extent of worker knowledge prior to conducting surveillance testing is an important factor to keep in mind when reviewing and understanding worker reactions to surveillance testing. Brush Wellman employees are provided beryllium health and safety orientation when first hired. Beryllium health and safety orientation is provided to both production and office workers, including sales and marketing personnel. The orientation process includes written beryllium health and safety information along with material safety data sheets and a document called a President's Letter. The President's Letter has been provided to new employees since 1949.

It is Brush Wellman's experience that some employee candidates or new employees will choose to not seek employment or will discontinue their employment with Brush Wellman in response to the provided beryllium health and safety information. Employees are periodically provided verbal and/or written updates on beryllium health and safety, particularly when new information becomes available. Appendix 1 provides a more detailed summary of Brush Wellman's general beryllium health and safety education process along with related examples from Brush Wellman's experience.

Pre- BeBLPT Testing Worker Education

Workers are educated regarding Brush Wellman's medical surveillance program. The use of annual health histories, pulmonary function testing and chest X-ray are established as standardized surveillance tools. Since the BeBLPT is invasive requiring a blood draw and because there is no standardized test method or standardized interpretation of the results, it is important to educate potential participants as to the benefits, disadvantages and unknowns of participating in a BeBLPT surveillance program.

Brush Wellman has found it important to communicate in advance key information regarding its surveillance program.

Why Brush Wellman conducts surveillance

Brush Wellman uses the BeBLPT with two purposes in mind:

1. Assisting with accuracy of diagnosis in symptomatic workers
2. As part of a well-defined medical surveillance plan, the design of which will yield information that is directly applicable to the improvement of safety programs which will decrease risk of beryllium sensitization or disease.

BeBLPT related medical risks and potential for repeat testing

1. Blood draw concerns including fear of needles, bruising, pain, muscle spasms and nerve damage. According to the American Red Cross, it is estimated that about 50% of the population fear needle sticks.
2. Test reliability or uninterpretable results can affect the number of times a worker gets a needle stick.
3. Test interpretation
   - Results can be uninterpretable requiring additional blood samples
   - Interpretation of test results can vary from lab to lab
   - Cannot quantify to the individual worker what a positive test result means as to their personal risk of disease.
4. Lost blood samples resulting in blood redraws. There are only five labs regularly conducting the BeBLPT in the United States. The labs request that they receive the blood within 24 hours to ensure viability of the blood cells. Samples have been lost due to lost shipments, delayed shipments and samples freezing or overheating during transit. Samples have also been lost or damaged at the laboratories.
5. Test reliability
   - The BeBLPT has high inter-laboratory variability (different results on split samples sent to two different labs). Studies have shown that laboratories which detected a positive result on a first blood test find a negative result 30% of the time on a second blood test on the same worker.
   - The BeBLPT has high test-to-test variability (different results on repeat tests on the same individual at the same lab). When two different labs (Labs A and B) tested the same blood sample, Lab A did not confirm 30% of Lab B positive results and Lab B did not confirm 30% of Lab A positive results.
   - Laboratory performance has not been stable over time

BeBLPT Results

1. A positive test result (confirmed sensitization) does not mean a person is sick.
2. A positive test result (confirmed sensitization) is not a diagnosis of CBD.
3. A positive test result (confirmed sensitization) cannot be used to forecast an individual's potential for a later diagnosis of CBD.

4. Sensitization is not an illness and is not treatable.
5. Positive results may reverse over time (it is not known why).
6. Negative results do not mean a person may not become positive over time.

Explain the Medical testing offered following confirmed positive BeBLPT

1. Describe bronchoscopy
   - Usually an outpatient procedure
   - Requires anesthesia
   - Involves passing a ¼ inch diameter flexible plastic tube through the nose, down the throat, and into the lung.
   - Through the tube the lung can be viewed, tiny samples of tissue will be taken, and a small amount of saline solution will be washed in and out of the lung to collect lung cells.
2. Risks of bronchoscopy
   - Pneumothorax (collapsed lung)
   - Bleeding
   - Infection
   - Death
3. Remind worker of the potential diagnostic outcomes of sub-clinical CBD and clinical CBD
4. Describe pros and cons of available treatments for early symptoms of clinical disease.

Explain Medical confidentiality

1. Employers are required to report occupational injuries and disease to State workers' compensation system and OSHA
   - BeBLPT positive (sensitization) is not reportable
   - Sub-clinical CBD and clinical CBD are reportable
2. Potential for inappropriate medical disclosure (i.e., insurance inquiries, etc.).

Explain Employment related issues

1. Most treating physicians recommend workers with sub-clinical or clinical CBD no longer work with beryllium.
2. Workers often want a change in job duties seeking what they perceive to be a job with a lower potential for beryllium exposure.
3. Can result in loss of job if the worker determines no "safe" job is available.
   - Note: There are few jobs within Brush Wellman's manufacturing facilities which do not involve some potential for beryllium exposure (absent the use of respiratory protection).
4. Workers' pay rate cannot always be ensured when accepting a different or lower skilled job.
5. Acceptance of a new job outside of normal production jobs can reduce both the eligibility and amount of overtime available to the worker. This can adversely affect the perceived quality of life by those workers who have grown used to, or financially dependant upon, overtime wages.
6. Knowledge of sensitization can be used to make career/job decisions/changes based on personal interpretation of risk.
7. Workers who accept Brush Wellman's CBD policy benefit option and seek new employment are mostly concerned with maintaining their current standard of living, obtaining comparable health insurance from a new employer and job security.

Worker Reaction to Test Results

Brush Wellman has observed the reactions and personal difficulties faced by workers who seek to understand the uncertainties surrounding their personal test results. The following is a summary, with descriptions and examples, from Brush Wellman's experience.

Reactions of Workers with BeBLPT Positive Test Results

Single BeBLPT positive result:
Workers typically want to undergo bronchoscopy even if further re-testing of their blood is negative, even though they won't be classified as "sensitized" and won't be eligible for Brush Wellman's CBD policy (unless they have CBD without a positive blood test).

Workers show a range of emotions at this point including:

- A matter-of-fact "Let's see what additional tests show"
- Anxiety, concern and/or fear of illness
- Concern or fear of further exposure to beryllium
- Uncertainty over what it means long term (concern that a single positive test means CBD now or later)
- Some even immediately leave the workplace

An initial "no big deal" reaction can be drastically changed by the opinions and influence of a spouse or family member reaction when the worker tells them of the result. Getting workers thinking about all the associated issues when they are given their test results (as soon as possible) tends to reduce the probability of a conversion to a non-constructive anger response. Sensationalism by the media has, at times, affected worker reaction by portraying positive sensitization results as a known predictor of a fatal disease outcome.

Double positive BeBLPT result:
Again a range of possible emotions and reactions including all of the above examples, but stronger regardless of level. Some become motivated to act in some way; i.e., get away from exposure (want to change job or leave employment) or move on with the diagnostic process. Some will move into anti-company anger at this point, most often in a non-constructive manner.

Some need family questions answered. Others delay informing their family, but have to if they schedule a bronchoscopy. The main issue here is that family members at times feel that they were not aware of the risks or of the degree of risk. While many of the employees had accepted the risks as communicated, these communications did not necessarily reach the spouse or family members. The spouse and family members tend to adopt a protective role, seeking to defend the employee from harm. This may take on an aggressive form or appear as suspicion or anger towards the company for doing this to their spouse. Receiving results sometimes acts as a trigger to surface or resurface unstable marital situations or other family conflicts.

The workers who share their test results with co-workers or are seeking an alteration in job duties can experience changes in the social behavior of co-workers ranging from empathetic reactions to very negative reactions. The negative reactions usually come from the co-workers' perception that the affected worker is getting special treatment (i.e.,

easier jobs, less exposure) and that the co-workers are having to do extra work and perform the higher potential exposure tasks.

Anxiety from BeBLPT positive test results can result from:

1. Blood sample loss/blood redraws (lost/damaged during shipping or in laboratory).
2. Uninterpretable results.
3. Inconsistent results (first round or later round testing). For example, a retesting of 18 workers who originally tested BeBLPT positive in 1993 found 55% to test BeBLPT negative at two labs in 1999.
4. Media exaggeration (usually emphasize persons on oxygen or a death).
5. Affects on home life due to loss of income
6. Job/career change anxiety (money and benefits concern).
7. Loss of overtime (money concerns).
8. Changes in social support structure, such as no longer working with the people with which you socialize.
9. Family planning concerns
10. Insurability (health and life insurance).

Reactions of Workers Diagnosed with CBD:

Reactions during CBD Notification Process:
Brush Wellman individuals are informed of BLPT positive and CBD generally by the Brush Medical Director or his designee. Some individuals have been informed of CBD by outside Brush contract doctors and some by their personal physicians. Some individuals were informed of CBD in person, by telephone or by letter. In short, notification of CBD to the affected individual has varied.

For example, one worker was informed of her CBD while at her office desk via a phone call from a Brush contract doctor. The worker collapsed to the floor and required medical attention. Her co-workers were unaware at that time as to what caused her to collapse.

In another case, an employee went home for lunch and while eating, decided to open the mail. The employee opened a letter from the medical facility who had performed her bronchoscopy and learned she had CBD. Brush had not received a copy of the letter yet, so Brush learned from the employee she had CBD. The employee was emotionally shaken and Brush was not yet prepared to arrange counseling.

During the bronchoscopy, doctors sometimes tell employees everything looks good so they probably do not have CBD. Some are then surprised when they are notified a month later by the doctor that they have, in fact, been diagnosed with CBD.

Some employees were told they had CBD by the diagnosing physician, but Brush Wellman's CBD policy administrator was not informed so there was no contact with the individual regarding Brush Wellman's CBD policy benefits, sometimes for up to several months. The worker tends to assume that Brush Wellman has been notified, so they interpret non-contact by Brush Wellman as not caring which typically leads to a very upset or even hostile employee.

One employee was told he had CBD and Brush filed a workers' compensation claim which was allowed for CBD. Months later, it was determined the individual did not have CBD. The individual was mistakenly diagnosed with CBD due to a report mix-up.

The coordination of informing a person of his/her diagnosis can be difficult due to the number of people or organizations involved in the process. The initial method of contact can substantially affect how that person views the information he/she has been provided and how he/she views the messenger. It is Brush's experience that the better the notification process is organized, the greater the opportunity to manage the reaction to a positive outcome. The same holds true for workers testing BLPT positive.

Ideally, a medical doctor should inform the individual of his/her CBD. The individual almost always has questions about CBD that are best answered by a doctor. When individuals are informed by someone other than a doctor, they tend to view the experience as trivializing the situation. The individual should also have an immediate opportunity to meet with a benefits administrator. The administrator should listen to the employee first, review the CBD policy, help the employee to inform their family and offer or make arrangements for personal counseling. Reviewing the options available prior to a worker receiving a CBD diagnosis tends to improve the communication process by managing the worker's expectations.

Diagnosis of Subclinical CBD (no symptoms) – Post Notification Reactions:
Includes all the aforementioned range of emotions and reactions listed for single or double positive BeBLPT results. A non-reaction is rare. The following should give some sense of the reactions Brush Wellman has encountered.

Immediate reactions to the diagnosis include:

- How long do I have to live?
- Tell me how the disease progresses and what can I expect?
- Can my family catch it from me?
- How do I tell my spouse? children? parents?
- Who will hire me with a disease like CBD?
- Should I continue to work at Brush?
- What is my potential future?
- How much exposure is harmful?
- Who will pay the medical bills for treatment related to CBD?
- How did this happen? I followed all the safety rules and still got sick.
- Some don't want anyone at work to know they have CBD.
- Some blame all of their physical ailments on CBD.

Individuals without symptoms (sub-clinical) tend to be concerned about:

- Getting sick
- Avoiding future exposure to beryllium
- Wanting to keep working for Brush, but at a job with little or no potential exposure to beryllium. They want their job adjusted to an area they perceive as cleaner.
- Reduction in pay due to loss of overtime.
- Brush changing or eliminating the CBD Policy benefits in the future resulting in the benefits not being there when needed.

Sometimes the diagnosis is non-conclusive, further frustrating the individual as to their health status. Under these circumstances, workers may take a negative approach focusing on minor data ambiguities or the inconvenience of the diagnostic process to maintain a heightened level of concern or allow their anger to build. If medical tests do not find CBD, the worker must still make a considered decision of whether to continue to work with beryllium.

Cultural differences can affect personal reactions to a CBD diagnosis. For example, Brush Wellman has observed that some Hispanic women tend to believe their husbands will leave them once they become aware of their diagnosis. As a result, some Hispanic women will tend to hide their diagnosis. Therefore, the first assistance with Hispanic women tends to be marital counseling.

Most workers with sub-clinical CBD will begin to re-code their health concept from well to chronically ill, and may initiate illness behavior. Many experience frustration because of the lack of medical information available to predict their future prognosis.
There is a sense by some workers that doctors in the community do not understand this disease. Workers tend to expect a special interest to be shown in the diagnosis, but busy practitioners may not have the time to become highly knowledgeable, and as a result, avoid questions, contact time, etc.

Future employment is often a concern. The individual can feel unable to leave Brush. This can be due to the fact that many started working with Brush at an early age and it is basically the only job they have known. Some have not searched for a job for a long time and fear the process of looking. Brush generally is a premium payer and finding other employment with comparable pay, benefits and job security is generally perceived as being very difficult. They want to continue to see their friends at work.

Some workers with CBD will become angry and separate emotionally from a prior positive relationship with the company. Family members may become very angry at this point. Family dynamics are very important in determining whether a person can remain focused and constructive relative to personal best interest. Family members feel they have to pick up the fight for the CBD-affected individual. The spouse may directly instruct the employee to not trust the company anymore.

With "someone to blame" for the illness, some perceive possible gains from a victim status. Others experience ongoing anger and a sense of being victimized which can grow or lessen over time. These emotions can lead to taking legal action against the company.

Most beryllium-affected individuals worry that Brush may not prosper as a company in the future enough to continue the CBD Policy or that Brush could simply just discontinue the policy for no reason. They tend to be very insecure about the future of the CBD Policy. Such concerns have also led to legal action against the company.

They are concerned that they can't buy life insurance, health insurance or mortgage insurance and some claim the only way they can purchase long-term care insurance is with an exclusion for disability due to CBD. Brush has made some special provisions for portability of the group life insurance benefit, but many employees do not buy adequate insurance until something bad happens to their health. That is when they begin to

realize their family obligations and needs and then blame Brush for their inadequate insurance situation.

Additional Observations

In one instance, surveillance at one Brush Wellman site resulted in 12 workers testing positive at one lab and negative at another lab. It appears that the 12 positives were all false-positives. This laboratory problem resulted in all 12 workers being offered and accepting a bronchoscopy along with the associated surgical risks. None of the 12 workers were found to have CBD.

The implications of laboratory performance not being stable over time are very serious, both for clinical use and for epidemiologic use. For the individual, it is not known how much of the test-to-test variability is due to laboratory variability over time and how much represents intrinsic variation in the expression of the sensitization in circulating immune cells. Epidemiologically, the implications are that it is problematical to compare the results of populations tested by different labs or at different points in time, certainly in terms of interpreting modest differences. This becomes even more problematical if one hopes, via medical surveillance, to identify risk or demonstrate improvement when prevalence or incidence are low or difficult to separate from background.

As a lagging (after the fact) measure, the BeBLPT prevents nothing by itself. Industrial hygiene air and surface measures are also lagging measures. Brush is trying to control the resources devoted to lagging measures, using the principle "if it is not going to change what is done, don't take the measurement" so that available resources can be allocated to activities which will determine the outcome (prevent sensitization and CBD) and also to leading (before the fact) measures. The latter is what creates confidence that preventive programs are progressing and being maintained over time.

Some workers with early clinical CBD, who begin taking prednisone, can experience a fall in pulmonary function values. Physicians will take credit for positive effects of treatment, but ascribe to the disease the negative effects of treatment, a process supported by the workers' compensation process.

Since the advent of the Department of Energy cold war compensation program where those diagnosed with CBD are eligible for a $150,000 lump sum tax-free payment, it is Brush Wellman's experience that the existence of this program is having the effect of many more workers seeking BeBLPT testing and bronchoscopy.

Following are issues to be considered by employers performing BeBLPT surveillance:

1. Medical removal practices
2. Job duty or job change in light of seniority issues
3. Presenting results individually and as a summary to the workforce
   - Absence of a predicable outcome
4. Orientation/education
5. Communication during the various stages in the process to individuals and the workforce
6. Production constraints
7. Loss of skilled workers/leaders
8. Worker/family counseling
9. Workers' compensation – State and Federal as applicable

10. Benefits policies/practices
11. Costs of BeBLPT and subsequent medical testing
12. Legal issues
13. Public relations
14. Media relations
15. Customer relations and communications
16. Increased employment costs for replacement workers
    - Employment searches and interviewing
    - Training costs
    - Manufacturing disruptions
17. Union campaigns/grievances

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Appendix 1

The following description is provided to enhance the reader's understanding of the level of beryllium-specific worker education which has taken place prior to the BeBLPT surveillance programs being initiated within Brush Wellman.

Worker Beryllium Health & Safety Education Description – Pre-employment through Hire

As required by the OSHA Hazard Communication Standard, all workers entering industries using beryllium must be informed of the potential health hazards associated with working with beryllium containing materials before they begin working with the material. Within Brush Wellman, that process begins with a new employee's first day on the job and applies to both production and management workers, including sales personnel. The environmental health and safety orientation process includes specific training on the potential adverse health effects of working with beryllium and how to safely work with beryllium-containing materials. Each new employee is also advised in writing via an informative document called a "President's Letter," which specifically reviews potential adverse health effects and employer/worker responsibilities. President's letters have been in use within Brush Wellman since 1949. Each new employee is also provided copies of pertinent material safety data sheets for beryllium-containing materials. The beryllium health and safety orientation process is applied to Brush Wellman workers, temporary and part-time workers and on-site contractors. The formal classroom part of the beryllium orientation program usually takes from 2-4 hours. Additional health, safety and environmental classroom training typically takes up most of a new employee's first week of employment depending on their job. Additional beryllium specific health and safety training also occurs during on-the-job training. Refresher classroom training on beryllium health and safety typically is done annually.

Today, it is a common practice within Brush Wellman for beryllium health and safety to be raised as part of the interview process. It is Brush Wellman's experience that some employment candidates disqualify themselves during the interview process due to their personal health and safety concerns about working with beryllium. During the time from initial contact through making an offer of employment, Brush Wellman estimates that 15-40% of salaried professional candidates and 15-25% of hourly worker candidates disqualify themselves due to their beryllium health and safety concerns. The sources of information upon which these candidates make their decision tend to include the health and safety information provided in Brush Wellman's pre-employment information package and the information on Brush Wellman's web site. Candidates most often cite either their own concern for their personal health or their spouse's concern for their health, typically after their review of Brush Wellman's health and safety package.

Brush Wellman has also observed that media reports can influence the availability of job candidates. For example, after the release of both the Toledo Blade and 20/20 stories, available professional salaried candidates noticeably declined. A similar decline was not obvious among hourly job candidates. The state of the job market and the competitiveness of the salary offered is a key factor to a candidate accepting a job offer. Professional salaried candidates tend to be more selective than do hourly worker candidates. Salaried professionals tend to view themselves as having a greater range of marketability than hourly workers. Hourly workers often view Brush Wellman as a high hourly pay opportunity versus other locally available jobs.

After accepting employment, some candidates choose to leave Brush Wellman during their orientation period (first week or two) on the job. During the orientation period, Brush Wellman estimates that 1-2% of salaried professionals and 3-5% of hourly workers choose to leave due to their beryllium health and safety concerns. The primary factor tends to be the beryllium orientation training they receive during their first few days. Again, they most often cite either their own concern for their personal health or their spouse's concern for their health as their reason for leaving.

In general, Brush Wellman also experiences a small number of workers, choosing to leave within their first few years, who cite beryllium health and safety concerns as their reason for leaving. This does not include workers who choose to leave based on a BeBLPT test result or a diagnosis of CBD. Workers who test BeBLPT positive are offered a five-year window of opportunity to leave Brush Wellman under Brush Wellman's current CBD policy. The policy allows for workers who are confirmed BeBLPT to accept a payment of 6 to 12 months of their base salary (based on years of service), medical benefits and career counseling. Workers diagnosed with sub-clinical or clinical CBD are offered a five-year window of opportunity to leave Brush Wellman under Brush Wellman's current CBD policy. The policy allows for workers who are diagnosed with sub-clinical or clinical CBD to accept a payment of 12 months of their base salary, medical benefits and career counseling. All employees have available to them an Employee Assistance Program (EAP) offering professional mental health counseling. Brush Wellman's EAP providers have been educated on beryllium health & safety issues. The CBD Policy also provides an additional counseling benefit for the affected individual and/or their family.

The CBD policy contains a safety net clause allowing any worker who leaves Brush Wellman, then becomes unable to work because of CBD related physical health effects, to return to the employ of Brush Wellman. The worker will receive an updated salary and benefits for the type of job they held when they left Brush and will either work for Brush within their physical limitations or stay home, with pay and benefits as a supplement to workers' compensation, until normal retirement age.

Brush Wellman has observed that salaried professionals tend to exercise their options under the CBD policy more often than hourly workers. The likely reason for this difference is the availability to salaried professionals of comparable pay in other industries and a greater willingness to relocate. On the other hand, hourly workers tend to not want to relocate and tend to be less confident of finding comparable pay.

Attachment 3 - Suggested rewording of Background section

Pulmonary risks may be associated with all beryllium-containing materials (including alloys of beryllium, beryllium metal and beryllium oxide materials) when these materials are heated or worked in ways that create fine dusts, fumes or mists.

- Beryllium may be encountered in the workplace in any of the following forms:
- Beryllium chemical compounds as solids or in solution such as beryllium hydroxide, beryllium fluoride, beryllium sulfate when extracted from beryllium-containing ores like beryl and bertrandite minerals
- A gray colored refined pure metal with unique physical properties including high strength, lightness (low density), stiffness, dimensional stability, fidelity of vibration transmission, high thermal conductivity, neutron-moderating properties, and X-ray transparency
- A gray colored metal matrix composite of beryllium metal blended with either aluminum or beryllium oxide (29 – 72% beryllium by weight).
- A white ceramic with electrical resistivity, a high melting point, and excellent thermal conductivity
- An alloy or mixture of metals usually containing less than 2% beryllium by weight and having special properties including antigalling behavior, castability, corrosion resistance, high electrical conductivity, durability, flexibility, nonsparking behavior, springiness (elasticity), and wear resistance* These materials can look like aluminum, nickel, copper, brass or gold depending on the formulation. Copper-beryllium alloys are the most widely used form of beryllium.
- An oxidized byproduct of metals melting, casting and recycling. Color can vary.

See Appendix for examples of industries and applications that use beryllium-containing materials.

Attachment 4

Appendix - Industries and Applications with Beryllium, Beryllium-Containing Alloys and Beryllium Oxide Ceramic

Aerospace:
- Beryllium metal and composites
  Engines, gyroscopes, mirrors (e.g., space telescopes), precision tools, rockets, satellites, structural components, and missile guidance systems
- Beryllium-containing Alloys
  Altimeters, braking systems, bushings and bearings for landing gear, electronic and electrical connectors

Automotive:
- Beryllium metal and composites
  Valve seats for drag racer engines
- Beryllium-containing Alloys
  Air-bag triggers, antilock brake system terminals, electronic and electrical connectors, steering wheel connecting springs

Biomedical:
- Beryllium metal and composites
  Scanning electron microscope components, X-ray windows
- Beryllium-containing Alloys
  Dental bridges, partials, and other prostheses
- Beryllium oxide ceramics
  Medical laser

Decommissioning and decontamination of worksites:
- Various beryllium-containing materials.

Defense:
- Beryllium metal and composites
  Heat shields, mast-mounted sights, missile guidance systems, nuclear weapon components, tank mirrors.
- Beryllium-containing Alloys
  Submarine hatch springs

Energy and electrical:
- Beryllium metal and composites
  Heat exchanger tubes, nuclear reactor components
- Beryllium-containing Alloys
  Microelectronics, microwave devices, oil field drilling and exploring devices, relays and switches.
- Beryllium oxide ceramics
  Heat exchanger tubes, microelectronics, microwave devices, relays and switches.

Fire prevention:
- Beryllium-containing Alloys
  Nonsparking tools, sprinkler system springs.

Instruments, equipment, and objects:

- Beryllium metal and composites
  Camera shutters, commercial speaker domes, computer disk drives, commercial phonograph styluses.
- Beryllium-containing Alloys
  Bellows, clock and watch gears and springs, computer disk drives, musical instrument valve springs, pen clips

Manufacturing:

- Beryllium-containing Alloys
  Injection molds for plastics, bearings.

Sporting goods and jewelry items:

- Beryllium metal and composites
  Beryl and chrysoberyl gemstones (including aquamarine, emerald, and alexandrite), and manmade emerald and other gemstones with distinctive colors.
- Beryllium-containing Alloys
  Golf clubs

Scrap recovery and recycling:

- Various beryllium-containing products.

Telecommunications:

- Beryllium-containing Alloys
  Cellular telephone components, electromagnetic shields, electronic and electrical connectors, personal computer components, rotary telephone springs and connectors, and undersea repeater housings.
- Beryllium oxide ceramics
  Transistor Mountings (Integrated Circuit Substrates)