DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Agency for Toxic Substances
and Disease Registry
Atlanta GA 30333

June 12, 2006

Mr. Marc E. Kolanz
Brush Wellman, Inc
17876 Saint Clare Avenue
Cleveland, Ohio 44110

Dear Mr. Kolanz:

The purpose of this letter to provide a summary of ATSDR's response to Brush Wellman's written comments to ATSDR's plan for Testing for Beryllium Sensitization. ATSDR has also provided responses to your specific comments in Attachment A.

The Basis for the Testing

In 2002 ATSDR stated that current releases from the plant by airborne release or worker drag home did not present a public health hazard. ATSDR did not have sufficient information to determine whether past releases from these pathways was (or was not) a public health hazard.

In your written public comments to ATSDR, you state that ATSDR has no evidence of community-acquired Chronic Beryllium Disease (CBD). However, you go on to describe a household contact of a Brush Wellman-Elmore worker who developed chronic beryllium disease. This household contact was originally incorrectly diagnosed as having sarcoidosis. This patient had more than one potential pathway. ATSDR cannot (and Brush Wellman should not) ignore the potential contribution of living with a beryllium worker, which is a well-documented pathway for exposure and disease.

During the public comment period, ATSDR was contacted by community members who stated they were household contacts of Brush Wellman workers. These individuals reported to us their diagnosis of sarcoidosis without being tested for beryllium sensitization and expressed interest in participating in testing. Dr. Jonathan Borak, Medical Consultant to the Ottawa County Commissioners, stated during the expert panel in Ottawa County on April 25, 2006, that such cases should be treated as "sentinel events." ATSDR believes that these individuals and others who have requested testing should be tested. Additionally, local physicians and other health care providers should be educated to encourage Be-sensitization testing of local residents who are diagnosed with sarcoidosis.

In your comments, you mentioned that the Ottawa County Health Department has reported lower rates of death due to pulmonary disease in Ottawa County compared to state-wide and national rates. ATSDR has not reviewed Ottawa County Health Department records, nor has the analysis conducted by the health department been shared with ATSDR. However, we can say that the analyses described would not be expected to identify an excess of beryllium-

associated morbidity or mortality. The category "all lung disease" would be far too insensitive to identify an excess of CBD, a rare disease. However, ATSDR will review this analysis if it is provided to us.

ATSDR has recently requested and received a listing of CBD deaths among Ohio residents from 1990 to 2003. A total of 20 Ohioans died with beryllium disease listed as the underlying cause of death on their death certificates. These data were made available to ATSDR from the Ohio Department of Health. The cumulative mortality rate due to CBD per 100,000 persons, in the counties of Ottawa (7.32), Sandusky (3.24) and Wood (2.48) were ranked 1, 2, and 3 among all 88 Ohio counties during this time period. A table is attached (Attachment B) that describes information about these deaths, including the occupational information listed on the death certificates. ATSDR has not determined if these individuals were Brush Wellman workers, household contacts of Brush Wellman workers, or had resided near the Brush Wellman plant. ATSDR requests that Brush Wellman provide this information to us should it be available to your company. In order to move forward with the goal of completing ATSDR's public health efforts in Ottawa County within a reasonable time period, we are requesting that Brush Wellman provide to ATSDR any additional information in its possession concerning the occurrence of sarcoidosis, CBD, or beryllium sensitization among non-Brush Wellman workers who are household contacts of Brush Wellman employees or live within 25 miles of the Brush Wellman facility.

Community Interest

ATSDR has been contacted by 25 individuals who wish to be tested, including household contacts of beryllium workers who were told they had sarcoidosis without being tested for beryllium sensitization. ATSDR believes that local residents with sarcoidosis, the household contacts of beryllium workers, and persons who machine beryllium alloys are the most likely to benefit from the testing. We have not urged other community members to be tested, but we have offered testing to those who remain concerned and live within 1.25 miles of the plant. Thus, there is clear community interest in being tested.

Some former Brush Wellman workers have expressed interested in the testing. These persons are not eligible for ATSDR testing. We are asking that Brush Wellman consider testing former workers who express interest in testing.

Informing Key Stakeholders

ATSDR has routinely met with key stakeholders during its involvement in Ottawa County. Regarding the most recent plan, ATSDR's Deputy Director met with key stakeholders on March 24, 2006. This meeting was followed-up by making a draft of the testing plan available for public comment on April 1, 2006. On April 25, 2006, we traveled to Ottawa County to participate in several interactive sessions with stakeholders and the public. During this visit we

held an open expert panel (with key stakeholders invited), met with the county commissioners in their chambers, and conducted a public and press availability session in the community during the evening. Brush Wellman and the county commissioners were invited and represented at all of these events.

ATSDR has worked closely with Mr. Arndt, the current president of the Ottawa County Commissioners, to reduce community concerns. ATSDR shared with Mr. Arndt a copy of the advertisement announcing our community meeting and specifically requested his advice on crafting the announcement in a way so as to not unduly concern the community. ATSDR made its plan for testing available to the public for 30 days. While your company and Dr. Borak raised concerns, other knowledgeable health professionals have expressed verbal support for the plan.

In contrast to some of your statements, ATSDR has engaged in all 3 elements of community participation that you identify. ATSDR has communicated with the Ohio Health Department regarding our plans. The Ohio Health Department has provided ATSDR mortality statistics for the state of Ohio. The Ottawa County Health Department did not wish to be included in our planning until recently, but we are now in close contact with them.

In follow-up to a written request from the county commissioners, Dr. Sinks and the county health commissioner shared with each other the concerns of community members who have contacted either ATSDR or the commissioners. On the basis of that information we agreed that informing and educating health care providers and community members is warranted. We have also agreed that individuals in the community are in favor of the ATSDR plan and wish to be tested.

Benefits of Testing

ATSDR is not conducting a health study. We cannot generalize the findings of testing beyond those participants whom are tested. We are providing testing to individuals who wish to be tested. You argue that there is no clinical benefit from testing for Beryllium sensitization. Yet, the physicians on the expert panel assembled April 25, 2006, stated clearly that sensitized individuals should be referred for clinical evaluation and long term follow-up. The practice of Brush Wellman's Corporate Medical Director, Dr. David Deubner, is to refer employees (with or without symptoms) for clinical evaluation after one abnormal test, even if it is not confirmed. In addition to medical care, persons sensitized to beryllium may wish to reduce or eliminate future exposure. For example, Brush Wellman's material safety data sheet for copper beryllium master alloy states, "...it is generally recommended that persons who are sensitized to beryllium or who have CBD terminate their occupational exposure to beryllium."

In summary, ATSDR has sufficient grounds to offer testing for beryllium sensitization to persons who are concerned about past exposure beryllium. ATSDR has evidence of

community interest in the testing. Also, there is clear benefit for testing persons concerned about past exposure to beryllium who meet the testing plan criteria.

ATSDR looks forward to completing this service in a timely manner. We will maintain close contact with the Ottawa County Commissioners and the Ottawa County Health Commissioner throughout the reminder of this effort. We welcome your suggestions on how to validate if individuals requesting testing are current or former Brush Wellman employees or are household contacts of current or former Brush Wellman workers. Thank you for your interest in ATSDR's planned activities planned for Ottawa County Ohio.

Sincerely

Thomas Sinks

Thomas Sinks, Ph.D.
Deputy Director, National Center for Environmental Health/Agency for Toxic Substances and Disease Registry

Attachments

Attachment A

Chronic Beryllium Disease Deaths*
Ottawa, Sandusky, and Wood Counties, Ohio (1990-2003)

County	ICD	age	gender	year	occupation	type of business
Ottawa County						
Galen D Lemke	J632	58	M	1999	plant manager	ceramics Mfg
Francis R Bostater	503	63	M	1998	maintenance	manufacturing
Margaret A. Wehner	J632	71	F	2003	secretary	beryllium production
Sandusky County						
Louis F De Angelis	503	63	M	1995	chemical analyst	beryllium plant
Donald C Ickles	J632	67	M	2002	machinist	beryllium production
Wood County						
Carolyn J Mason	J632	67	F	2002	manager	department store
Marilyn P Miller	503	68	F	1998	mail carrier	U.S postal service
Charles R Basel	503	69	M	1995	machinist	manufacturing

* Ohio Department of Vital Statistics - Death Certificates - underlying cause of death listed as ICD J632 or 503.

Attachment B

Responses to **Section Specific Comments** from Mark Kolanz, Vice President, Environmental Health and Safety, Brush Wellman Inc.

Comments from Mr. Kolanz are in ***italics;*** Agency responses are **normal text.**

Section Specific Comments
Section 1.1 Summary
Brush Wellman finds the following statement misleading.

"During the 1990's, this facility released up to 1100 pounds of beryllium per year to the ambient air. After beryllium metal extraction ended in 2000, the amount released annually declined significantly. While current releases to the ambient air are not considered hazardous, little is known about the fate of beryllium that was: released to the air and deposited since 1953; incidentally taken home by the facility's beryllium workers; or, incidentally taken home by workers at machine shops contracting with the facility to machine beryllium alloys."

This paragraph has been revised to read as follows:

"The processing facility in Elmore has produced commercial beryllium metal and beryllium alloys for decades. During the 1990's, this facility released up to 1100 pounds of beryllium per year to the ambient air.[1] After beryllium metal extraction ended in 2000, the amount of beryllium released annually to ambient air declined significantly. While current releases are not considered hazardous, past violations of the EPA air contaminant limits occurred on three separate occasions (1980, 1989, 1990). To prevent incidental off site migration of beryllium dust on workers' clothes, this facility has had long-standing requirements for workers to wear company-supplied work clothes and to shower at the end of each shift. Until recently, these requirements were self-monitored. While the industrial hygiene practices at Brush Wellman have been exemplary in recent years, similar practices have not been instituted at the local machine shops that have contracted to work with beryllium alloys produced at the Brush Wellman facility in Elmore."

The terminology of "current releases" has only been applied by ATSDR in its 2006 blood testing plan.

In ATSDR's terminology, a site's category as a public health hazard (or not) implies "current" unless we specify "past" or "future."

ATSDR should also clearly define the difference between clinical chronic beryllium disease and surveillance of sub-clinical chronic beryllium disease.

ATSDR will not diagnose beryllium disease, whether it be preclinical or clinical in nature. ATSDR's purpose is to test individuals who are concerned about past exposure to beryllium with the BeLPT. We will tell individuals their results, including whether they have been confirmed as sensitized to beryllium. We will encourage those tested to seek appropriate follow up.

The reviewer's comments are paraphrased as problems with the BeLPT, including variability over time, a postulated (unknown) background level, the risks associated with medical follow-up, and a lack of clear evidence that treatment affects progression or survival.

The test, like all tests, does have limitations. We note that the BeLPT is routinely used by Brush Wellman as documented by Dr. Deubner's statement to the Ottawa County Commissioners' meeting on April 25th (2006) that about 570 of Elmore's 600 employees (95%) had been tested with the BeLPT.

You mentioned the potential risk of unnecessary medical procedures. ATSDR will not be performing medical procedures, other than collecting and testing the blood samples. We will refer individuals with abnormal results for further evaluation by knowledgeable area physicians, who must determine what is in the patient's best interest.

The presence of a background prevalence in the general population has been raised by Dr. Deubner, noting less than 1% confirmed sensitization among Brush Wellman prehires without work-related exposure. While other researchers have not seen evidence of confirmed background sensitization [Stange et al. 2004], we have revised the plan to include comparison with an assumed 1% background rate among residents within 1.25 miles of the facility.

We note that a lack of evidence of the effectiveness of an intervention (medical treatment, or pathway interruption) is neither evidence of a lack of effect nor justification that individuals who are sensitized should be uniformed or not referred to treatment. We will use the results in a way similar to Brush Wellman -- that is, as a "lagging indicator" that can assist with identifying and eliminating exposure. During the expert panel meeting of April 25th, the panelists all agreed that individuals with abnormal results should be referred to specialists that were knowledgeable about beryllium disease. We will encourage the individuals who need a specialist evaluation to see qualified area specialists, many of whom are also used by Brush Wellman for follow-up evaluations.

...the American Conference of Governmental Industrial Hygienists' (ACGIH) Biological Exposure Indices (BEI) Committee, as well as the United States Army, Navy, and Air Force, have all determined that the BeLPT should not be used as a screening tool.

You cite these documents outside of the context in which they were written. ATSDR has reviewed all these documents. None of them address the use of the BeLPT as intended by

ATSDR. The Army and Air Force memos are directed at occupational physicians who are evaluating Be exposed workers for clinical illness. These documents simply verify that Army and Air Force physicians should use the BeLPT in conjunction with the presence of respiratory symptoms to establish clinical CBD. The memos do not address the use of the BeLPT to reassure concerned workers about possible risk or to conduct exposure-based surveillance. The ACGIH document focuses on the correlation between airborne sampling for beryllium and urine levels of beryllium. It also mentions the BeLPT in the same context. ATSDR would not recommend the use of the BeLPT as an indicator or surrogate for airborne sampling. The BeLPT is an indicator of post exposure to beryllium – not current exposure. This is precisely why the BeLPT should be used.

Brush does not use or recommend BeLPT as a screening test for CBD because there is no known individual health benefit to the worker.

ATSDR is testing for sensitization, not screening for CBD. The benefits to the individual can include referral, if sensitized, to a knowledgeable lung specialist or reassurance if the test is normal. We note that Brush Wellman attaches value to the BeLPT by providing medical evaluations after abnormal results and supporting the choice of sensitized workers who want to lower or eliminate their exposure to beryllium by changing jobs or leaving the company with a severance package. These commendable actions are referred to by many as "screening" and contain what OSHA calls "worker removal protection" (i.e., of wages and benefits). Brush Wellman has indicated that 95% of their Elmore employees have participated in their BeLPT testing program.

Lastly, ATSDR's proposal is inconsistent with its 2002 ATSDR conclusions that biological testing of health community members was not appropriate based on the limitations of the BeLPT test.

Since our health consultation was released in 2002, Stange et al. [2004] published their landmark article and clarified the overall test parameters and the single test strengths (specificity) and weaknesses (sensitivity).

Section 2.1 Background Science

...it is well known the treatment of CBD is based on the treatment model developed for sarcoidosis.

ATSDR will not be involved in making diagnoses or selecting medical treatments.

Section 2.2 Modern Diagnostic Tests

ATSDR's statement "Current medical practice also accepts one "abnormal" and one "borderline" as sufficient confirmation of sensitization." is contrary to the vast majority of criteria used...

Some physicians, including one panel member, believe that the BeLPT is so specific that it does not even need to be confirmed to determine sensitization. The article cited by Dr. Borak (Welsh et al. 2004) clearly states that one abnormal and one borderline are sufficient evidence of sensitization (as are two abnormals).

Even so, we have revised the testing plan to incorporate the most conservative definition of sensitization we have heard -- two abnormal BeLPT results. We will make clear that other findings (one abnormal and one borderline, or three borderlines) also merit referral for medical evaluation.

Stating a predictive value for a confirmed positive BeLPT as 50% is misleading because such a rate has not been determined in the general population and even in the beryllium worker populations calculated rates ...range from 11% to 100%....these predictive values are for detection of ...mostly subclinical CBD.

After our statement on predictive value in the plan, we have added the following text:

> The PPV depends on the prevalence of the outcome in a population.
> In less exposed groups, the PPV is likely to be lower.

The ATSDR should disclose up-front in all of its communications that all post beryllium sensitization determination costs associated with any follow-up medical tests will be the responsibility of the individual...

We have been clear in written and verbal materials that ATSDR does not have funds to pay for further medical evaluations, should they be recommended.

Section 2.3 Justification

No comments requiring response.

Section 2.3.1 Exposure

No comments requiring response.

Section 2.3.3 Identifying Beryllium Sensitization and Disease

The comments of Stange are not relevant to community exposures nor is surveillance the same as screening by definition.

While the data is from workers, Dr. Stange concludes that the test is relevant for testing *groups exposed to beryllium.* Dr. Stange's point was that the PPV of the BeLPT was high enough to be meaningful. Brush Wellman describes their testing program as "surveillance," we have noted that it also contains the elements commonly described as "screening."

Machining risks have only been defined for machining of beryllium metal and beryllium oxide ceramics.
Balkissoon and Newman [1999] reported two cases to illustrate that machining 2% beryllium copper alloy can cause chronic beryllium disease.

Section 2.3.4 Benefits of Participation

...CBD does occur in persons who consistently test negative on the BeLPT test, the BeLPT is highly variable and unreliable, and no study has defined a negative test result as implying safety from beryllium disease.

We are testing for beryllium sensitization, not for CBD. A confirmed abnormal is highly specific for sensitization. The benefit to those who test normal is the reassurance that they likely are not sensitized. We know that approximately 1/3 of those sensitized may not have an abnormal test result. For example, if the prevalence of sensitization was 3% and 100 people were tested, then 1 person would be falsely told they are not sensitized. The remainder of those with normal test results would be correctly identified as not sensitized. This is sufficiently accurate to provide reassurance to those with normal test results.

3.1.2 Collecting, Handling, and Shipping Specimens

"Brush Wellman also questions why the ATSDR has not engaged the services of the Cleveland Clinic which is much closer to the Elmore site or Specialty Labs who have had the most consistent performance...based on Brush Wellman's years of experience."

Thank you for your insights on Specialty Labs -- we plan to add Specialty Labs for split-sample testing during the confirmation phase.

Section 3.1.3 Interpreting Test Results

...you cannot use a test to verify the exact same test.

As there is no true "gold standard" for comparison, Stange relied on the premise that after a few rounds of testing, true abnormals will be repeated and false abnormals will not be. This same logic is the basis routinely used for *clinical confirmation testing* – i.e., the concept that one abnormal might be a false positive, but after two abnormals you can believe that the individual is truly sensitized. The estimates by Stange et al. are the most credible estimates of BeLPT parameters to date.

It should also be noted that Stange found a rate of BeLPT positivity of 2.5% on a single test in his "unexposed population.

Stange identified 291 new hires and 167 unexposed current employees. (total unexposed tested = 458). When they were initially tested, there were 7 abnormal results. It follows that the prevalence among his unexposed population was 7 abnormal tests / 458 tested = **1.5%** (not 2.5%). Given the number tested, this is not very different from what Stange would have predicted (~1%). More importantly, none of these 7 people were ever confirmed as sensitized to beryllium and the prevalence for a confirmed abnormal was zero

---

Section 5.0 Human Subjects

No comments that require a response.

Section 6.1 Training

No comments that require a response.

American Conference of Governmental and Industrial Hygienists (ACGIH). Feasibility Assessment: Beryllium and Inorganic Compounds. 2003.

Balkissoon RC, Newman LS. Beryllium Copper Alloy (2%) Causes Chronic Beryllium Disease. JOEM Vol 41(4); 1999:304-308.

Guide to Clinical Preventive Services: Report of the U.S. Preventive Services Task Force. Baltimore: Williams & Wilkins, 1996.

Stange AW, Furman FJ, Hilmas DE. The beryllium lymphocyte proliferation test: Relevant issues in beryllium health surveillance. Am J Ind Med 46: 453-462, 2004.

United States Air Force. Memo: Beryllium Surveillance and Medical Monitoring Policy by Murray GH. Aug 28, 2002.

United States Army. Memo: Beryllium Surveillance and Medical Monitoring Policy by Weightman GW. Aug 15, 2002.