cancer standardized mortality ratio (SMR) for the German plants increased relative to the combined cohorts. SMR analysis by level of cumulative exposure (see Table 4 in the German paper) generated similar results to the combined cohort (also reflected in two additional tables in the client report) leading to our suggestion of a threshold.

We performed logistic regression analyses in the original study and, as described in our article, to investigate simultaneously the influences on the risk estimates of cumulative exposure, peak exposure, and smoking. We do not consider the results presented in Michaels et al's Table 1 to be reliable largely because of the substantial differences between the U.S. and German cohorts. Also, we note the instability of the models as reflected in the wide confidence intervals, the uncertain adequacy of the fit of the model, and the fact that the logistic regression did not take into account the time dependency of the cumulative exposure metric. The results of the logistic regression analysis for the German plants, described in our article and partially included in Michaels et al Table 2, were taken directly from Table 19 of the client report and were not, as suggested by Michaels et al, produced after the decision to report results separately by country. We have explained in both the publication and the client report that a "low" exposure category estimate was technically impossible, because there were no cases with all necessary data available in the "low" category in the German cohort.

Michaels et al's third point largely reiterates (by quoting OSHA) our own words: "Demonstrating a clear (and statistically significant) threshold response in epidemiological studies is difficult especially, as in this study, the number of available cases is relatively small, and the precise estimation of small risks requires large numbers."[1] We hope, however, that by presenting such results—even if only suggestive—we will stimulate additional useful epidemiologic research and expand scientific inquiry.

Finally, although offering no solution, Michaels et al do raise a legitimate regulatory/policy point: how can the regulatory community obtain all scientifically sound and relevant evidence for their deliberations? Policymakers and regulators readily rely on material published in the peer-reviewed scientific journals. It is understood—correctly or incorrectly—that the peer review process imparts some degree of consistency with current standards and therefore quality. Michaels et al previously asserted that "Parties involved in the rulemaking process should also be required to certify that they have submitted all relevant data to the public record, whether or not those data have undergone peer review."[6] They apparently include material that is not published and not subject to rigorous peer review to be among the "best available evidence" that OSHA is to use. We believe that this is not so straightforward and that fuller discussion is warranted.

We are disappointed that Michaels et al have chosen to speculate about (or at least not read carefully and represent accurately) our work for IHF and the publications derived from that work (especially because we did attempt to discuss these very points directly with Michaels during several phone conversations around May 2005). Nevertheless, we are grateful to the editor of *JOEM* for the opportunity (not offered by the journal in which Michaels et al first published their story[6]) to respond and to offer a clearer perspective on our research.

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The Beryllium Occupational Exposure Limit: Historical Origin and Current Inadequacy

To the Editor: We are writing in response to "The Beryllium Occupational Exposure Limit: Historical Origin and Current Inadequacy"[1] by Jonathon Borak. As Assistant Secretary of Energy for ESH, one of us (D.M.) was the federal official responsible for overseeing the Department of Energy's (DOE's) Chronic Beryllium Disease Prevention Program final regulation, which lowered the level triggering protection for beryllium-exposed

workers in the U.S. nuclear weapons complex from 2.0 $\mu g/m^3$ to 0.2 $\mu g/m^3$.

We share Dr Borak's conclusion that the current Occupational Safety and Health Administration (OSHA) occupational exposure standard (OEL) of 2.0 $\mu g/m^3$ is inadequate to protect workers from chronic beryllium disease (CBD). The scientific literature summarized by Dr Borak, particularly the cases among workers and community residents exposed to levels well below the current standard,[2,3] strongly suggests that there is no safe level of exposure to beryllium.

One clear policy implication of this literature is that the OSHA OEL needs to be dramatically strengthened and that beryllium exposure must be eliminated whenever possible to prevent CBD. Beryllium plays an important role in national security but given the metal's severe and well-established health effects, it is hard to justify using beryllium in golf clubs, bicycle frames, and other consumer products. Even if the workers manufacturing these products could be protected from all beryllium exposure, recent reports of CBD cases among metal recycling workers[4] underscore the need to remove beryllium from commerce.

The primary limitation of Dr Borak's editorial is his failure to recognize that OELs are shaped not only by science, but also by the actions of individuals and corporations, who wield political and economic power. In our view, one of the primary reasons the inadequate OEL for beryllium has remained unchanged is that Brush Wellman, the sole North American beryllium producer, has relentlessly opposed more protective standards for exposed workers.

In 1975, OSHA proposed a comprehensive standard to protect beryllium-exposed workers, including a plan to lower its workplace exposure limit to 1 $\mu g/m^3$, on the basis of beryllium's carcinogenicity.[5] OSHA's effort was foiled, however, by a collaboration of the DOE, the Department of Defense, and the beryllium industry.[6] (Secretary of Energy, Bill Richardson, acknowledged the industry–government intervention, explaining "Priority one was production of our nuclear weapons . . . [the] last priority was the safety and health of the workers that build these weapons."[7])

By the late 1980s, the existence of CBD cases among workers exposed to beryllium at levels below the existing standard led Dr Merril Eisenbud, the author of the Atomic Energy Commission's original (1949) standard, to end his support of the 2 $\mu g/m^3$ OEL.[8] This evidence also prompted the DOE to begin, in 1991, the administrative process of lowering the OEL applied in nuclear weapons facilities. Brush Wellman opposed the change, contending that DOE had no evidence "that the existing standard is unsafe or that the new proposed standard affords any greater degree or [sic] safety."[9]

Despite the compelling and growing evidence, Brush Wellman defended the 2 $\mu g/m^3$ OEL with a tautologic argument, essentially: "We will examine the work history of all workers with CBD; even if we do not find evidence they were exposed to levels above the standard, we will assume they have been, since CBD is only associated with excessive exposure levels." This can be seen in Brush's 1991 talking points, which advised its executives to defend the 2 $\mu g/m^3$ as follows: "(1) Experience over several decades has, in our view, demonstrated that levels of airborne beryllium within the OSHA threshold limit value afford a safe workplace. (2) In most cases involving our employees, we can point to circumstances of exposure (usually accidental), higher than the standard allows. In some cases, we have been unable (for lack of clear history) to identify such circumstances. However, in these cases we also cannot say that there was *not* excessive exposure"[10] (emphasis in original).

Around the same time, Brush Wellman also opposed the American Conference of Governmental Industrial Hygienists's (ACGIH's) efforts to lower the beryllium threshold limit value (TLV), writing "We feel the evidence for retaining the presently adopted TLV is compelling" [and] ". . . there is still no evidence of any diagnosed cases of CBD where the exposure level can be reasonable demonstrated to have been at or below the 2 μg level."[11]

Dr Borak states that in 1996 Brush Wellman (in a notice for customers) "expressed uncertainty that the OSHA PEL was adequately protective."[1] In its communications with regulatory officials, however, the manufacturer retained its traditional opposition. For example, in a meeting on the proposed DOE standard, an executive asserted that the company "is unaware of any scientific evidence that the standard is not protective. However, we do recognize that there have been sporadic reports of disease at less than 2 $\mu g/m^3$. Brush Wellman has studied each of these reports and found them to be scientifically unsound."[12]

By 1999, the ever increasing number of CBD cases rendered the claim that the old standard was safe less and less plausible. Yet, this did not compel Brush to endorse a more protective OEL. Rather, the manufacturer asked DOE to delay issuing a new standard, claiming that "important research is underway which may provide a scientific basis for a revision to the occupational standard for beryllium" and pointing to studies on particle size, particle number, and particle surface area.[13]

In retrospect, it is clear that Brush's interpretation of the evidence supporting the adequacy of the OEL was incorrect; independent experts recognized this inadequacy more than 15 years ago. The beryllium industry had a strong financial incentive to challenge the mounting evidence and to oppose regulatory action that would result in a lower exposure limit. It appears this incentive shaped the interpretation given to scientific evidence by scientists employed by the beryllium industry. A policy lesson here is that regulatory agencies should discount the interpretation of data by parties with financial conflict of interest.

Although the past cannot be changed, much can be done to better protect cur-

rent and future workers from beryllium exposure.

Now that Dr Borak, with the support of Brush Wellman, has acknowledged the current OSHA standard is inadequate, we sincerely hope that Brush Wellman will devote its resources and political muscle to urge OSHA to strengthen its OEL so that chronic beryllium disease becomes a disease of the past.

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Author's Response

To the Editor: I appreciate this opportunity to comment on the letter submitted by Dr Michaels and Ms Monforton, which was a response to my recent editorial on the occupational exposure limit for beryllium.[1] They do not disagree with my discussion of the science, but fault me for not discussing political and economic issues, particularly with respect to the actions and interests of Brush Wellman. The implication of their letter is that Brush Wellman obstructed lowering the beryllium occupational exposure limit and that their actions were inconsistent with the science.

I do not speak for Brush Wellman. My first contact with Brush Wellman was in 2002; I have no personal knowledge regarding the motivation or behavior of Brush Wellman and its executives during earlier times. When I proposed the literature review that was the basis for this editorial, it was accepted and supported without restrictions, limitations, or editorial control.

To the best of my knowledge, the unrestricted support that I received was not atypical for Brush Wellman. Based on publicly available records, similarly unrestricted support was provided over the past 15 years to researchers at National Jewish Medical and Research Center (National Jewish) and the National Institute of Occupational Safety and Health (NIOSH), which has led to extensive, detailed, and independent evaluations of numerous Brush Wellman facilities and many of its employees.* These do not seem to be the actions of a corporation bent on obstructing scientific progress or concealing its findings.

Perhaps the issues are just a matter of perspective. For example, consider the findings of a recent General Accounting Office (GAO) report on

*Service agreements between Brush Wellman and National Jewish and a Memorandum of Understanding (MOU) between Brush Wellman and NIOSH have been entered into evidence in civil litigation and are available from the author. With respect to its two major facilities in Tucson, Arizona, and Elmore, Ohio, the 1992 and 1994 agreements, respectively, funded National Jewish to develop and administer worker questionnaires, to review all personnel rosters, medical surveillance data, and industrial hygiene data, to estimate historical exposures, and to integrate that information with individual work and job histories. In addition, Brush Wellman paid for BeLPT and other clinical evaluations on a fee-for-service basis. The only restriction imposed by Brush Wellman was that individual confidentiality be protected: "National Jewish may . . . use Brush Wellman data in statistical compilations and researchers shall likewise be able to use the data and the statistical correlations . . . . Brush Wellman does not reserve in any way the right to control, direct or censor conclusions or report dissemination." In its MOU with NIOSH, which was reviewed by the NIOSH Board of Scientific Counselors and judged to be "a model for similar work with industry groups,"[7] Brush Wellman affirmed: "In the event of disagreement regarding interpretation or analyses, each party retains the right to disseminate their work."

†The GAO report provides an interesting perspective because in a letter officially appended to the report, Dr Michaels (then Assistant Secretary of the Department of Energy) wrote: "We found the report to be accurate."

the response of Federal agencies to "beryllium uses and risks."[2]† That report specifically addressed the proposed 1975 Occupational Safety and Health Administration (OSHA) standard described by Dr Michaels and Ms Monforton as having been "killed . . . by a collaboration of the DOE, the DOD and the beryllium industry." GAO noted that in 1977, OSHA received "about 150 written comments" and heard testimony from 46 individuals "representing business, government, labor, and academia"; in 1978, scientific panels were convened by NIOSH, the Centers for Disease Control and Prevention, and Health, Education, and Welfare to review the scientific evidence; also that year, the Secretaries of Defense and Energy expressed concerns about national security implications and the scientific basis of the proposal; in 1979, further meetings were held among the Department of Defense (DOD), Department of Energy (DOE), and OSHA; and finally, in the early 1980s, OSHA discontinued work on this standard "because of other regulatory priorities." Thus, whether it was actively "killed" or left to die of neglect may be a matter of perspective. OSHA did not officially revisit the beryllium issue until 1998 and a new permissible exposure limit (PEL) still has not been formally proposed.

As for DOE, it expanded its beryllium exposure monitoring and medical surveillance programs during the 1980s to 1990s and in 1999 reduced beryllium exposure among its workers by adoption of an action level lower than the OSHA PEL. On the other hand, DOE did not propose a lower PEL because it found the scientific evidence to be insufficient: "DOE reviewed the scientific evidence suggesting that the current OSHA 8-hour PEL does not sufficiently protect worker health . . . it is difficult to determine from this scientific evidence the exposure levels necessary to eliminate the risk of contracting CBD."[3] That statement, which still correctly describes the scientific evidence, does not differ significantly from conclusions of my editorial.

There are a number of likely reasons that the scientific evidence remains uncertain. Chronic beryllium disease (CBD) is a relatively rare disorder that develops with variable, but sometimes long latency, and is most often found in asymptomatic individuals. Also, historical exposure data (from DOE and others) have limited informational value because exposures were often above the OSHA PEL.[2] In addition, beryllium sensitization and CBD have only recently been studied prospectively in individuals without previous occupational exposures (eg, new hires) and there have been few longitudinal worker studies. Such factors combine to challenge studies of disease onset and frustrate efforts to identify exposure levels necessary to trigger CBD.

Another reason is the relatively inconsistent ways that beryllium sensitization and CBD have been studied. In a review of 19 published studies of beryllium workers, we found 10 different and often incompatible sets of diagnostic criteria for CBD.[4] Likewise, criteria for a positive BeLPT have varied among the five laboratories that perform the test and over time in most of those laboratories. Such inconsistencies make difficult the pooling of data (eg, meta-analysis) that might otherwise address the difficulties posed by the small numbers of reported cases.

In short, there are real deficits of scientific knowledge. Whether it is accordingly appropriate to strictly invoke the Precautionary Principle, as seemingly proposed by Dr Michaels and Ms Monforton, is a philosophical issue of much debate but little certainty.[5,6] Their view that there is "no safe level" of beryllium exposure seems tenuous at best and their assertion that my literature summary implied that conclusion is wrong. In that specific context, they are also wrong to suggest that I had read or relied on their references 2 and 3, both published and/or presented after my manuscript was submitted and accepted by the *Journal*.

Finally, with respect to the need to "discount the interpretation of data by parties with financial conflict of interest," I note in the interest of full disclosure that Dr Michaels has served as a paid plaintiffs' expert in litigation against Brush Wellman.

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Arsenic Exposure and Diabetes Mellitus Risk

To the Editor: Chiu et al[1] have presented the annual (and 3-year moving average) diabetes mellitus (DM) standardized mortality ratios (SMRs) for 1971 to 2000 for males and females from the Blackfoot disease (BFD) endemic area of southwest Taiwan. They have examined the temporal pattern of the data following the transfer by 1975 of the