Harry Rowlings

File: NIOSH Report

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July 9, 1993

Dr. Ronald Ratney
Chair, Committee on Dusts
and Inorganic Substances
ACGIH
6500 Glenway Avenue
Building D-7
Cincinnati, Ohio 45211

Dear Dr. Ratney:

Brush Wellman, Incorporated (Brush) and NGK Metals Corporation (NGK) appreciate the opportunity to provide the Committee on Dusts and Inorganic Substances with information relevant to the possible review of the ACGIH guidelines for occupational beryllium exposure.

Brush and NGK are proud of their long histories of and reputations for safeguarding the health of their employees. As a part of that tradition, we attempt to carefully monitor and appropriately address health information on beryllium as it becomes available. This submission will address such information which has become available since the last ACGIH review of the beryllium guidelines.

In summary, after reviewing the relevant literature, it is our firm belief that there is no health-related reason to change the currently recommended exposure limit of 2 ug/m3. There is no evidence that beryllium disease, the only known effect of exposure to airborne beryllium, can occur when exposures are in compliance with the current guideline. While two recent studies have reported slight increases in lung cancer among beryllium-exposed persons, these results appear to be due to factors other than beryllium exposure. Specific comments now follow.

Studies of Chronic Beryllium Disease: The major recent study in the United States of Chronic Beryllium Disease (CBD) was by Cullen et al. (1987). The study reviewed medical records of workers in a precious metal refinery. In addition to beryllium, the workers were occupationally exposed to arsenic, cadmium, lead, and nickel, although the levels and possible effects of these exposures were not discussed.

Five workers were found to have granulomatous lung disease, and four of these were found hypersensitive to beryllium by an in vitro proliferative response test. The investigators thus considered these five workers as having CBD, and it is claimed that four of the five cases were exposed to beryllium levels below the current guideline levels.

The air quality monitoring data upon which this conclusion is based, however, occurred years after the workers had developed symptoms. These four workers had already developed symptoms by 1977 -- exposure data were from 1983. While the fifth worker to develop symptoms was diagnosed in 1985, the limited monitoring data indicated that his exposures were well in exceedance of the 2 ug/m3 exposure guidelines.

Another serious deficiency is that the hygiene data represent only two weeks of exposure monitoring. The authors imply that exposures had remained constant over the years, citing the results of an interview with workers as indicating this. Specifically, the workers knew of no structural or procedural changes which would have resulted in a long-term alteration of exposures. This would seem to provide little support for the use of two weeks of data as representing exposure levels over the course of several years. There was no further discussion of the representativeness of these data, an especially important issue if the plant was forewarned of the air quality monitoring.

In summary, the exposure data in this study are inadequate to support the authors' claim of an effect of exposure below the guideline level. The data covered only two one-week periods, and were collected many years after four cases of CBD were reported. The fifth case was observed in a worker exposed to levels well in exceedance of the 2 ug/m3 guideline.

Another recent study of CBD by Cotes (1983) in Great Britain, suffered similar deficiencies in industrial hygiene data. These studies are inconclusive at best.

Studies of Lung Cancer: A recent study by Ward et al. (1992) examined lung cancer death rates among workers at seven beryllium production facilities. This study was a follow-up to several prior studies of the beryllium worker cohort, and was intended to address the well-documented deficiencies of these earlier studies. In many respects this intention was met, and the study contains the longest follow-up and examines the largest cohort of any of the beryllium cohort studies. The main problem is with the interpretation of the study results.

The investigators report that lung cancer rates in two of the facilities, and in the cohort as a whole, were significantly elevated when compared to the rates in the general population. After the investigators' adjustment for smoking among the workers, only one of

the plants showed statistically significant rates. The rates in the overall cohort were no longer significant. Citing the unadjusted results, however, the investigators claim that the most likely cause of the significant findings is occupational exposure to beryllium.

A recent paper by Levy et al. (1993, submitted for publication) indicates that the Ward et al. interpretation of results is not well supported. The findings are shown to be more likely due to the investigators' failure to properly account for the confounding factors of smoking or locations of worker residence.

The smoking data upon which the Ward et al. adjustment was based were from a 1968 survey covering 16% of the cohort. Levy et al. point out that these data do not represent "vital portions of the cohort", such as workers at the only plant which showed significant lung cancer rates after the Ward et al. smoking adjustment. They further state that "Viewed another way, also not well represented in the survey were workers hired prior to 1960, among which group 93% of all lung cancer cases occurred." The Levy et al. paper reports other sources of uncertainty in the Ward et al. consideration of smoking, such as errors in the combining of the survey data with smoking risk data.

Another factor shown to explain the elevated crude lung cancer rates at the two plants is the high background rates in the cities in which most of the workers lived. Levy et al. collected mortality and population data for these cities, and it was found that lung cancer rates among the workers were not significantly higher than in their respective cities of residence.

In summary, the Ward et al. study results are most likely due to factors other than beryllium exposure. The investigators acknowledge some of the shortcomings and uncertainties in their consideration of confounding factors. Unfortunately, they treat these shortcomings as grounds for ignoring these factors, and claim that the significant crude results are most likely due to beryllium. The study is shown in a recent paper to suffer interpretation deficiencies similar to those of prior beryllium cohort studies.

Finally, another study conducted by Steenland and Ward (1991) examined lung cancer rates among persons entered in the Beryllium Case Registry. It was reported that rates among these individuals were higher than those of the general U.S. population. This study suffers many serious flaws, including some of those mentioned for the Ward et al. study (e.g. limited and questionable smoking data).

The most serious flaw, however, is the lack of assessment of beryllium exposure among the registry members. Criteria for inclusion in the registry studied "included either documented past exposure to beryllium or the presence of beryllium in lung tissue as

well as clinical evidence of beryllium disease." There is no indication as to what proportion of registry members actually had documented past exposures. It is further unclear how the investigators conducted their analyses by length of exposure and time since first exposure.

Summary and Conclusions: There have been a few studies reporting evidence of Chronic Beryllium Disease occurring in circumstances in which the current occupational exposure guideline is being met. These studies, however, have failed to confirm that the relevant exposures were in compliance with the guideline.

A recent study examined lung cancer rates among beryllium production workers at seven plants. While many of these workers were exposed to beryllium at levels far higher than the current guideline, only a slight increase in lung cancer rates was observed in the cohort. An independent analysis of these data indicated that this increase was likely due to either smoking or the high background lung cancer rates in the areas of worker residence.

A study of Beryllium Case Registry members contained numerous flaws, most notably failure to document beryllium exposure among its subjects. Such a study can provide little evidence on the possible effects of exposure.

In conclusion, we note that the ACGIH booklet containing the 1991-1992 listing of TLVs states that "Threshold Limit Values (TLVs) refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse health effects." Based on the available evidence, Brush and NGK believe that the current TLV for beryllium meets the outlined conditions, and that there is currently no reason to reconsider this guideline.

We would appreciate the opportunity to make a presentation at a future meeting of the committee in order to discuss the above comments in greater detail. Again, we are pleased to be able to participate in these proceedings.

Sincerely,

Yasuhito Niwa

Yasuhito Niwa
Vice President

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