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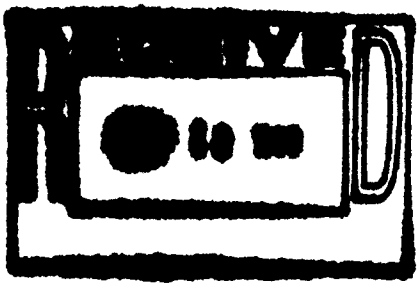

VIA FEDERAL EXPRESS

Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
79 Alexander Drive
Building 4401, Room 3127
MD:EC-14
Research Triangle Park, NC 27708

Re: Beryllium and Beryllium Compounds

Dear Dr. Jameson:

The National Toxicology Program (NTP) has announced its intent to review beryllium and beryllium compounds for possible updating of the current listing to a known human carcinogen. 64 Federal Register 15983 (April 2, 1999).

NTP has requested public comment on this nomination of beryllium and beryllium compounds as a known human carcinogen and "relevant information on the carcinogenic properties of the substances from completed or ongoing experimental animal or human epidemiology studies, as well as current production data, use patterns and human exposure information." Id. These comments are submitted on behalf of Brush Wellman Inc.

Comments that have previously been submitted by Brush Wellman Inc. and Dimitrios Trichopoulos, M.D., point out that excess incidence of lung cancer in workers in the Lorain plant can be attributed to exposure to sulfuric acid mist, a condition not considered by the authors of Ward, et al. and Steenland and Ward. These comments are supported by a recent review of the literature showing sulfuric acid mist to be a carcinogen by inhalation prepared by the US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry in its Toxicological Profile for Sulfur Trioxide and Sulfuric Acid 61-63 (December 1998).

Section 2.2.1.8 of that document, a copy of which is enclosed, states:

> In a study regarding the effect of air pollutants in nonsmokers, sulfates were not shown to be associated with cancer (Abbey et al. 1995). Increases in respiratory tract cancers were not observed among a cohort of 400 male workers at a sulfuric acid plant in Sweden

(Englander et al. 1988). The men were exposed to sulfuric acid aerosols at concentrations of <0.1-2.9 mg/m3 for at least 6 months. There was a significant (p=0.006) increase in bladder cancer in this population. The study authors suggested that bladder cancer in this population may not be a result of sulfuric acid aerosol exposure but may have been a result of chance or smoking or other facts such as diet.

A case of laryngeal cancer was reported in a man (life-long nonsmoker) exposed to sulfuric acid from poorly maintained batteries used to operate an electric forklift truck (Houghton and White 1994). The man operated a fork lift truck for 11 years. Exposure concentrations were not stated, but the man described the surface of the batteries as always being wet with sulfuric acid; he often suffered burns on his legs and clothing damage. Employment history did not reveal exposure to any other industrial carcinogens. Three cases of laryngeal cancer were reported among 78 workers at a factory that pickled stainless steel pipes (Ahlborg et al. 1981). Based on cancer registry data, 0.05 laryngeal cancer cases would have been expected in this population. All three persons with laryngeal cancer were moderate smokers. Exposures included sulfuric acid, nitric acid, oxalic acid, ammonium bifluoride, soap, sodium thiosulfate, sodium hydrosulfite, hydrogen fluoride, and low levels of chromium, nickel, and asbestos.

Occupational studies of isopropyl alcohol production workers (Alderson and Rattan 1980), soap production workers (Forastiere et al. 1987), and refinery and chemical plant workers (Soskolne et al. 1982, 1984, 1992) have reported small increases of upper respiratory tract cancers (nasal, laryngeal) and lung cancers in workers exposed to sulfuric acid aerosols. Exposure concentrations were not well characterized in these studies. In a study of workers from two battery manufacturers and two steel works in Britain, a small increase in upper respiratory tract cancers (e.g., lip, retromolar area, tongue, nasopharynx, tonsil, larynx, gum, and nasal sinus) was observed (Coggon et al. 1996). The study authors indicated that a small increase in risk occurred at 1 mg/m3, but not at lower concentrations. Although this study provides limited evidence that the risk of cancer in the upper respiratory and digestive system is increased, the risk estimate was based on a small number of cases, and the excess was not significant. The study does not provide any information on alcohol or tobacco use. There is also no information about exposure before 1970.

In a study of male steel workers exposed to acid mists during pickling operations at an average concentration of 0.2 mg/m3 for an average of 9.5 years, a statistically significant increase in laryngeal cancer was observed (Steenland et al. 1988). Nine of 879 workers were diagnosed with laryngeal cancer, while after adjusting for smoking 3.44 cases of laryngeal cancer were expected. All cases were either current or former smokers. Quantitative individual sulfuric acid exposure data were not provided. The study authors indicated that the pickling process did not generate appreciable levels of metal particulates. This population has also been studied for lung cancer (Beaumont et al. 1987; Steenland and Beaumont 1989). A total of 41 lung cancers in a cohort of 1,165

steelworkers were identified (Steenland and Beaumont 1989). The standardized mortality ratio (SMR) for lung cancer after adjusting for smoking for those with 20 years or more since first exposure was 1.5, with a 95% confidence interval of 1.05-2.27 (Steenland and Beaumont 1989). There was little evidence of a duration-response effect, and possible confounders such as exposure to nickel and silica were not considered in this study.

A case control study was conducted of 352 white males and laryngeal cancer and 1,050 white male controls admitted to a hospital between 1957 and 1965. Exposure to sulfuric acid was estimated through a review of occupational history. The risk of developing laryngeal cancer was significantly greater in heavy smokers with occupational exposures to sulfuric acid than in heavy smokers with no sulfuric acid exposure. Relative risks for laryngeal cancer were 2.43 and 2.05 in heavy smokers exposed to sulfuric acid for ≤20 years and heavy smokers exposed to sulfuric acid for <20 years, respectively) Cookfair et al. 1985). The study is limited because actual exposure concentrations were not known.

No studies were located regarding cancer in animals after inhalation exposure to sulfur trioxide or sulfuric acid.

I trust that this document will be of assistance in review of this subject by you and the panel at the December 16-17 external peer review meeting.

Very truly yours,

Ronald R. Janke/ows

Ronald R. Janke
Attorney for Brush Wellman Inc.

Enclosure
cc: Angie Wilson (w/enc)