MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

January 27, 1997

TO: File for germanium dioxide (CAS # 1310-53-8)

FROM: Marco Bianchi, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The Initial Threshold Screening Level (ITSL) for germanium dioxide is 7 ug/m^3 based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL/IRSL: IRIS, HEAST, NTP Management Status Report, RTECS, EPB-CCD, EPB library, CAS-online, NLM online, IARC, NIOSH Pocket Guide, and ACGIH Guide.

A complete reference check was conducted for germanium dioxide, but information was limited to a Dutch subacute rat inhalation study. This study, also made references to Japanese studies which reported human exposures from people who had orally taken germanium compound preparations.

In one of the Japanese references listed in the Dutch study, one human subject's oral intake of germanium (carboxyethylgermanium sesquioxide and/or $Ge0_2$ preparations; total intake approximately 30-40 g Ge) resulted in increases in serum creatinine and blood urea nitrogen 5-18 months after the start of intake, causing progressive decreased renal function. Discontinuation of the germanium intake stopped the progressive deterioration of renal function, but renal dysfunction persisted, without urinary disorders. After biopsy, renal histology revealed mild degenerative changes of distal tubular epithelium with dense granules and minor glomerular abnormalities. Deaths after chronic intake has been reported by Higuchi (1989), Matsusaka (1988), and Nagata (1985).

In the Dutch study by Arts et al., 1994, groups of Wistar rats were exposed to two acute (4 hr) and one subacute (4 wk) inhalation toxicity studies on germanium dioxide. In the acute studies, two groups of five rats of each sex were exposed to maximum attainable concentrations of either 3.1g (amorphous) or 1.4g (hexagonal) germanium dioxide for 4 hr. These concentrations were not lethal. Clinical and pathological observations included restlessness at the start of exposure (hexagonal grade) or during the entire exposure period (amorphous grade). Swallowing was observed soon after the start of exposure (amorphous). Piloerection started about 30-40 min after the start of exposure and lasted during the entire exposure period until shortly thereafter. Labored breathing was seen in a few rats half-way through the exposure period (hexagonal). After exposure, rats were found to be covered with a layer of dust. No abnormalities were

seen during the 14-day observation period. Body weights were reduced 7 days after exposure to amorphous Ge02; body weights were generally unaffected by exposure to the hexagonal grade. Gross examination of all rats exposed to hexagonal Ge02 showed grayish and spotted lungs. At microscopic examination, multifocal accumulation of alveolar macrophages was seen in almost all rats, whereas multifocal increased septal cellularity was observed in 30-50% of the rats. One male rat exposed to amorphous Ge02 showed multifocal alveolar bronchiolization; focal pneumonitis was observed in two male rats exposed to hexagonal Ge02. It was concluded that the 4 hr LC50 value of amorphous germanium dioxide was greater than 3.1 g/m³ and that of the hexagonal form greater than 1.4 g/m³.

In the subacute study, four groups of five rats of each sex were exposed to 0, 16, 72, and 309 mg hexaonal germanium dioxide/rn for 6 hr/day, 5 dayslwk for 4 wks. Two additional groups of 5 rats per sex, exposed either to 0 or to 309 mg/m3, were kept for a 33-day post-exposure period. At the end of the treatment period, changes were observed only in the high concentration group: these changes were decreased body weight gain (both sexes), decreases in hematocrit (females) and thrombocyte count (both sexes), and increases in neutrophil count (both sexes) and ‘hite blood cell count (females). On clinical chemistry evaluation, decreased fasting blood glucose (females), decreased total protein concentration (both sexes), increased plasma alanine aminotransferasc and aspartate aminotransferase activities (females) were observed. In addition, plasma urea nitrogen (males) and increased plasma bilirubin level (females) were observed. The primary target organ appeared to be the kidney. Urinary volume was elevated, and urine density and pi-I were lowered in both sexes. Relative weights of kidneys, spleen, heart and lungs were higher than in controls. Microscopic examination revealed effects on renal tubular epitheliurn consisting of degenerative, proliferative changes. Renal dysfunction was still present at the end of the recovery period, since none of the affected parameters had returned to normal and vacuolation of distal tubules was additionally seen. Effects on growth, kidneys, and liver were still present at the end of the 33-day recovery period. The no-adverse-effect- level in the 4 wk study using hexagonal germanium dioxide was 72 mg/m³.

The ITSL was determined asfbllows: NOAEL = 72 mg/m³

35 = safety factor for a 7-day study; can be adjusted if study is longer than 7-days.

ITSL = NOAEL/(35 x 100) x hours exposed per day/24 hours per day

ITSL = (72 mg/m³)/(25 x 100) x 6hrs/24hrs = 0.0072 mg/m³

ITSL = 0.007 mg/m^3 x 1000 ug/mg = 7 µg/m³

The ITSL for germanium dioxide = 7 µg/m³ based on annual averaging.

References: Arts J.H. et al., 1994. Acute and subacute inhalation toxicity of germanium dioxide in rats. Food Chemical Toxicology. Vol. 32; No. 11; ¡03 7-1046. MB:slb