MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

June 25, 1993

TO: File for Trimethylsilanol (CASI 1066-40-6)

FROM: Mary Lee Hultin, Toxics Unit

SUBJECT: Screening level for Trimethylsilanol (CAS# 1066-40-6)

The following sources were searched for toxicity data:

- RTECS
- EPA IRIS
- DNR EPB and NUTSHELL
- NIOSH
- ACGIH TLV
- NTP Management Status Report
- IARC Monographs
- HEAST
- CAS Online
- NLM Toxline database

The only useful data from these references included in vitro and in vivo genotoxicity assays. In the in vitro report, trimethylsilanol was negative in microbial assays and in the mouse lymphoma gene mutation assay. However, positive, dose-related responses were noted in the sister chromatid exchange assay in the absence of S-9 and in chromosome aberrations in the mouse lymphoma cells, with or without S-9 (Isquith, et al., 1988, y. 26, n.1). In the in vivo report, a transient, non-reproducible effect was seen in the rat bone marrow cytogenic assay. However, the authors stated that the effect was within the range of historical controls and concluded a lack of clastogenic activity in the rat bone marrow cytogenietic assay from trimethylsilanol (Isquith, et al., 1988, Food and Chemical Toxicology, v. 26, n.3).

Dow Corning provided a two-week maximum tolerated dose study in the rat, entitled “A TWO-WEEK MAXIMUM TOLERATED DOSE STUDY OF TRIMETHYLSILANOL IN THE RAT”. Groups of five male Sprague-Dawley rats were gavaged with either 0, 250, 500 or 750 mg/kg/day. Exposures continued for 5 days per week for two weeks. Clear CNS depression was noted, with ataxia, decreased locomotor activity, dyspnea, irregular respiration, weakening of the hind leg muscles and loss of consciousness seen in the two higher dose groups. One rat from the highest dose group died during the study. Significant reductions in total body weight gains were observed in animals at

the 500 and 750 mg/kg dose group as well. The author concluded that "no significant toxic or adverse effects in rats at the lowest dose level were demonstrated. However, it was noted that lethargy and mild ataxia were occasionally present in some of the animals treated with the 250 mg/kg dose. The severity of these effects was noted to decrease as the study progressed and no chemical related gross pathological alterations were observed. Because of the transient nature of the effects, 250 mg/kg will not be considered for a NOAEL.

Dow Corning also provided a report entitled "A Toxicological Evaluation of Trimethylsilanol (Me_3SiOH) and Dimethylsilanediol ($Me_2Si(OH)_2$) in the Rat". In this study, Sprague-Dawley rats (15 males and 5 females per group) were gavaged for 31 consecutive days. Dose levels were 3.33 ml/kg (33 mg/kg) or 10 ml/kg (100 mg/kg). Neither dose level was associated with deaths or alterations in tissue morphology and doses were not present beyond 48 hours in blood, liver, kidney or urine following cessation of dosing. (Sacrifices were conducted at 2 hr, 24 hr., and 48 hr. after the final dosing). Although histopathology on tissues from the 24 hr. post-dosing sacrifice was done at an independent laboratory (Industrial Bio-Test) and compared to historical rat data, no concurrent controls appear to have been used.

Due to the longer duration of the second study, the larger number of animals used and the use of both sexes of rats, this study will be used for screening level duration. 100 mg/kg appears to be a NOAEL. This would be in line when combined with the above-mentioned study which found slight effects at 250 mg/kg. A 15 fold safety factor will be used; 10 for duration of study plus 5 for quality (due to the lack of concurrent controls).

The screening level is derived as follows:

ITSL = 100mg/kg/(100 x 15) x 0.971 x 1 = 0.065 mg/m^3 = 65 µg/m^3

based on annual averaging

Inhalation rate/kg body weight = 0.971 m^3/kg/d

Absorption efficiency by route is unknown, thus default = 1