MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

August 29, 1996

TO: File for Diphenylmethylsilanol [DPMS] (CAS# 778-25-6)

FROM: Dan O'Brien, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level for diphenylmethylsilanol

The initial threshold screening level (ITSL) for diphenylmethylsilanol is 6 $\mu g/m^3$ based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: AQD chemical files, IRIS, HEAST, ACGIH TLV Booklet, NIOSH Pocket Guide to Chemical Hazards, RTECS, NTP Management Status Report, EPB Library, IARC Monographs, CAS On-line and NLM/Toxline (1967 -May 1, 1996), CESARS, Handbook of Environmental Data on Organic Chemicals, Patty's Industrial Hygiene and Toxicology, Merck Index and the Condensed Chemical Dictionary.

The toxicological data concerning DPMS are quite limited. Only two references were located, one of which was an unpublished Lethal Dose 50% (LD50) study provided to US by Dow Corning Corporation (DeVries and Siddiqui, 1984). This acute study was designed and carried out according to the toxicology methods recommended by the Organization for Economic Cooperation and Development OECD), and followed EPA'S Good Laboratory Practices (GLP) Regulations. Young Sprague-Dawley rats, weighing 225 ± 30 g, were assigned 5 per sex per dose group, to dose levels of 1260, 2520, 3780 or 5040 mg/kg body weight; dose levels were determined from oral range-finding tests. The animals were acclimated for a week, fasted for approximately 16 hours prior to dosing and then exposed to a single oral dose of DPMS (furnished as a 'clear, pale yellow liquid") by gavage. They were allowed Rodent Chow and water ad libitum during acclimation and after dosing. All animals were weighed at 24 hours, 7 days and 14 days after dosing, and were observed twice daily during the work week for the presence of clinical signs. A complete gross necropsy was performed on all rats at termination of the study. The LD50 (95% Confidence Interval [C.I.]) of 2104 (1585-2629) mg/kg was determined by the probit method of Finney. The LD50s, calculated for males and females separately, were slightly different (1972 and 21.75 mg/kg in females and males, respectively), but no significant differences in the dose response of males and females were observed in the study. Although death occurred as early as 24 hours post exposure in some animals, the majority died within 48 hours. Proportional mortality (females:males) for the various dose levels was as follows: 1260 mg/kg (0/5 : 1/5), 2520 mg/kg (4/5 : 2/5), 3780 mg/kg (5/5 : 5/5) and 5040 mg/kg (5/5 : 5/5). The primary signs of toxicity exhibited were lethargy, slight ataxia, diarrhea, urinary incontinence, tremors and coma culminating in death. Food consumption and body weight gains were depressed at the three highest dose levels, but the survivors in the 2520 mg/kg group recovered their original body weights by seven days post-exposure. There were no effects on food consumption or body weight gains in the lowest dose group. There were no gross lesions reported from any of the

animals at necropsy; the only abnormal finding was “heavy discharge from the mouth and urine covering much of the abdominal area of the body”. Based on these results, the authors concluded that the central nervous system is the most likely target organ of DPMS oral toxicity.

The only other report available for this chemical, located via the RTECS database (RTECS, 1996), investigated the structure-activity relationships of a number of organosiloxane compounds as they related to oral toxicity in the male reproductive system (Bennett et al., 1972), as well as some investigations into the pharmacokinetics of a few of the compounds. In that report, the only aspect of the larger study which evaluated DPMS utilized groups of ten male Sherman rats, 10-12 weeks old and weighing 250 g. Initial body weights were determined after overnight fasting. The agent was administered orally for seven days in a sesame oil vehicle at a constant dose of 2 ml/kg of body weight. After a week of daily exposures, the animals were again tasted overnight, and weighed on the morning of day eight prior to necropsy. The rats were anesthetized with methoxyflurane, decapitated and exsanguinated prior to dissecting and weighing other organs. Seminal fluid, seminal vesicle weight and prostate weight were all converted to a ratio with body weight and expressed as a percentage of control values. While statistical comparisons were made, the method was not specified. For DPMS, the results note that at a dose of 100 mg/kg, seminal fluid was 79% of control values and prostate weight was 85% of control values, both reported as statistically significant decreases at the 95% level. Seminal vesicle weight was slightly higher than controls, but not significantly so. At a dose of 10 mg/kg, there were no statistically significant differences between DPMS-dosed rats and controls, suggesting to the authors that DPMS was “an inactive compound at this dose”. These results provide some preliminary evidence that DPMS may be toxic to the male reproductive system, but the study was limited by it design to the study of a single endpoint. Consequently, it is not sufficiently comprehensive to serve as the basis for the quantitative derivation of a screening level.

No data concerning the carcinogenic or developmental effects of DPMS exposure were located in any of our searches.

Derivation of the ITSL: The almost total lack of toxicity data is the overwhelming consideration in setting a screening level for DPMS. However, the Dow correspondence (DeVries and Siddiqui, 1984) does provide an LD50 with a sufficient level of documentation for use in defining an ITSL. Although the authors of that study did not observe a significant difference between the dose-response relationships for males and those for females, the Dose Mortality Curve for the females was steeper, suggesting that females may be more sensitive to the effects of DPMS. Consequently, the LD50 reported for females (1972 mg/kg) is used here to calculate the ITSL. Per R232(l)(h) of part 55, Act 451:

ITSL = (LD50 mg/kg)/(500 x 40 x 100 x 0.167) x Wa/Ia

where:
Wa = Body weight of a female Sprague-Dawley rat (from MDEQ, 1996)
Ia = Daily inhalation rate of a female Sprague-Dawley rat (from MDEQ, 1996)

So,
ITSL = (1972 mg/kg)/(500 x 40 x 100 x 0.167) X (0.338 kg)/(0.972 m^3/kg)
ITSL = (0.00609 mg/m^3) x 1000 µg/mg
ITSL = 6.09 µg/m^3 ≈ 6 µg/m^3

Per 232(2) (e), an **annual averaging** time applies.

REFRENCES

Bennett, D.R., Gorzinski, S.J. and LeBeau, J.E. (1972). Structure-Activity relationships of oral organosiloxanes on the male reproductive system. Toxicol Appi Pharmacol 21:55-67.

DeVries, C.R. and Siddiqui, W.H. (1984). Acute oral toxicity study of diphenylmethylsilanol in rats, dated 10/22/84 . Toxicology Department, Dow Corning Corporation, Midland, MI, 11 pp.

Michigan Department of Environmental Quality (MDEQ), 1996. Default animal data for risk assessment (as based on U.S. EPA, 1988, Recommendations for and documentation of biological values for use in risk assessment, EPA Document 4 PB 88-179874).

RTECS (1996). Silanol, diphenylmethyl (778-25-6). In: Registry Toxic Effects Chemical Substances Database. National Institute for Occupational Safety and Health, Public Health Service, Centers for Disease Control, U.S. Department of Health and Human Services, and Canadian Centre for Occupational Safety and Health.

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