MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

August 29, 1996

TO: File for Cyclic Methyltrifluoropropylsiloxane (CAS No. 2374-14-3)

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

SUBJECT: Initial Threshold Screening Level for Cyclicmethyltrifluoropropylsiloxane

The initial threshold screening level (ITSL) for cyclic methyltrifluoropropylsiloxane (CMTFPS) is 0.6 µg/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 CMTFPS are quite limited. Of the few studies located, three involved dermal exposures to rabbits (EPA, 1992a,b; RTECS, 1996). The study cited in RTECS[1] reports a repeated dose of 4200 mg/kg for a period of 21 days. Toxic effects associated with this dose are reported as changes in liver weight, changes in serum total protein (TP), bilirubin and cholesterol, and changes in phosphatase enzymes.

Regarding toxicity via the oral route, three citations resulted from our searches. The first (Batulin et al., 1977), a study in Russian for which only the abstract was available to us, noted "changes were observed in blood indexes, indicative of toxicity". Further, these authors report that CMTFPS was "mutagenic in various processes of spermatogenesis following chronic administration". A second report is referred to only in a letter and a brief accompanying pathology report (EPA, 1992c). The study is described as "exploratory in nature" and involved repeated dosing of CMTFPS in 5% corn oil, apparently by gavage, "at doses near the reported LD5 value for a single dose of 0.252 g/kg". Under this repeated dosing schedule, the experimental animals received a multiple of the published Lethal Dose 50 (LD50) during the first week. The letter notes that the animals "were able to tolerate significantly higher doses than the published LD50 value"; effects reported included lethargy, difficulty walking ("in relation to the use of the hind legs"), slight nasal discharge and dehydration, and perineal wetness. On necropsy, a number of rats exhibited congested lungs, slight fatty infiltration of the liver,

[1] Drug Chem Toxicol 5:415.

splenic hemosiderosis, and the presence of proteinaceous casts (noted as “a common finding in older rats”). The author concluded that under the conditions of this study, a primary target organ could not be identified, but emphasized the appearance of central nervous system effects, characterized by lethargy and impaired walking. He stressed, however, the “exceedingly high doses” used, and the fact that the study’s design did not allow the results to be interpreted with any statistical validity; it seems clear that the work was only intended to serve as a general guide for further toxicological examinations. Neither of these studies is sufficiently documented to serve as the basis for derivation of a screening level.

The third oral study is an unpublished report obtained from the Dow Corning Corporation (Dow chemical, 1957). Little commentary and documentation are provided in the report, but this is not inconsistent with other studies performed during that time period. The context of the report suggests that the investigators were most concerned with the possible toxicity to workers due to inadvertent oral exposure. The basis for these conclusions were acute range finding tests in rats. No details of the methodology of these investigations are provided, but a summary table records an LD50 = 0.18 g/kg (180 mg/kg), with a 95% Confidence Interval [CI] of 0.11-0.29. This dose was characterized by the authors as “high acute oral toxicity”. Five dose levels (0.063, 0.126, 0.252, 0.5 and 1.0 g/kg) were used, with four rats in each dose group. Sex and strain of the animals were not specified. The agent was delivered as a 10% suspension in corn oil for the highest dose group, arid as a 5% suspension in the other four. At the highest dose level, all four rats died overnight; in the 0.252 and 0.5 g/kg groups, three of four animals were also dead by morning of the day following dosing. One of four animals in the 0.126 g/kg group died, and “marked liver and kidney pathology” were noted as responses for this group. At the lowest dose level, none of the four rats is recorded as dying, although a footnote states that “another rat intended for autopsy died during the night”. The only response noted for animals at 0.063 g/kg was “very slight initial weight loss”.

This same report (Dow Chemical, 1957) suggests that inhalation exposure to CMTFPS did not appear to be a concern to the authors; the report notes that “the vapors from this material heated 34°C and 160°C should cause no problem from single inhalation exposure”. Toxic effects due to vapor inhalation were categorized as follows: “Exposures do not cause any effects other than some very slight irritation or pain to the eyes or respiratory passages at the most”. An experiment in which two groups of three rats each were exposed to saturated atmospheres of CMTFPS for seven hours (with vapors generated by baths at 34°C and 160°C) recorded no deaths or toxic responses in either group.

No data concerning the carcinogenic, reproductive, or developmental effects of CMTFPS exposure were located in any of our searches. Derivation of the ITSL: The lack of toxicity data is the overwhelming consideration in setting a screening level for CMTFPS. Although the correspondence from Dow Chemical suggests that those investigators considered the chemical to be considerably more toxic via ingestion than by inhalation exposure, the inhalation data available are insufficiently detailed (primarily, with respect to the actual concentrations to which the animals were exposed, and how these concentrations were determined) to allow their use in quantitative development of a screening level. However, the Dow correspondence does provide an LD with a

sufficient level of documentation for use in defining an ITSL. So, per R232(1)(h) of part 55, Act 451:

ITSL= 1/(500 x 40 x 100) x LD50 mg/kg/(0.167) xWa/Ia
where:

Wa = Body weight of a sex- and strain-unspecified rat (default value from MDEQ, 1996)

Ia = Daily inhalation rate of a sex- and strain-unspecified rat (default value from MDEQ, 1996)

So,
ITSL = 1/(500 x 40 x 100) x (180 mg/kg x 0.395 kg)/(0.167 x 0.945 m^3/kg x 0.395 kg)
ITSL = (0.0000005) x 180 mg/kg/(0.158 m^3/kg)
ITSL = (0.0000005) x (1140.58 mg/m^3)
ITSL = (0.00057 mg/m3) x 1000µg/mg
ITSL = 0.57 µg/m^3, rounding to 1 significant figure = 0.6 µg/m^3

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

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OB:slb