MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

January 22, 2004

TO: File for tetrahydrofuryl methanol (97-99-4)

FROM: Marco Bianchi

SUBJECT: Initial Threshold Screening Level (ITSL)

The Initial Threshold Screening Level (ITSL) for tetrahydrofuryl methanol (THM) is 52 ug/m^3 based on an annual averaging time. A complete chemical search was conducted on this chemical in October, 2002, but the permit was withdrawn before an ITSL was established. At that time the following references or databases were searched to identify data to determine the ITSL/IRSL: IRIS-online, HEAST, NTP Management Status Report-online, RTECS, EPBCCD, EPB library, CAS-online, NLM-online, IARC-online, NIOSH Pocket Guide, ACGIH Guide, and TSCA 8(e) submittals. A complete review of these data sources resulted in no useful toxicological information except for the TSCA 8(e) submittals, but before a screening level could be derived, the permit applicant withdrew the chemical from the permit. Recently, a request was made to re-evaluate this compound to determine an ITSL.

Toxicity information that was used to set a screening level for THM comes from unpublished toxicity studies submitted to TSCA. However, these toxicity studies are only abstracts of the full studies. They include; a range-finding developmental rat study, a 90-day inhalation rat study, two 90-day oral rat studies, and two 90-day dog oral studies. Although the detailed information provided in these abstracts is not sufficient to derive an RfC, critical information is available on the toxicity of THM to derive an ITSL using the 7-day NOAEL formula as per Rule 232(1)(d).

In the range-finding developmental toxicity study, groups of 8 female rats were administered a single oral dose of 0, 10, 50, 100, 500, or 1000 mg/kg on gestation days 6-15. Results included 100% early resorptions observed at 500 and 1000 mg/kg. The 500 and 1000 mg/kg groups had depressed maternal body weights and reduced food consumption. Clinical observations included impaired mobility, and decreased muscle tone of hind limbs. Fetal body weights were reduced and filamentous tail was observed at 100 mg/kg.

For the subchronic inhalation study, groups of 14 male and 10 female rats were exposed to 0, 50, 150, or 500 ppm of THM 6 hrs/day, 5 days/wk, for 90-days. Four males of each group were sacrificed after the 34th exposure day to evaluate spermatogenic endpoints. Body weights of males were reduced at 150 and 500 ppm, which equaled 9.2 and 13.3%, respectively. Food consumption was also reduced in males, only. Other adverse effects included decreased platelet and hemoglobin, decreased MCH values in the high exposure group male and females. There were also decreased epididymal sperm counts and sperm motility, and increased abnormal morphological sperm in high dose males. Prostate were also reduced at mid- and high-exposures.

In one of two 13-week oral rat studies, groups of 20 male and 20 female rats fed diets of 0, 500, 1000, 5000, or 10,000 ppm. Males given 1000, 5000, or 10,000 ppm, and females given 10,000 ppm had reduced body weights. Some organ weights were reduced in males given 500

ppm and greater. In the other 13-week oral rat study, groups of 15 male and 15 female rats were fed diets containing 0, 1000, 3000, or 10,000 ppm. Statistically significant changes in depressed body weights were observed in mid- and high-dose rats. The low dose group of animals had non-statistically significant reduced body weights. For males, 10,000 ppm caused a decrease in testes weight, with testicular degeneration. No testes abnormalities were observed at 1000 and 3000 ppm.

In the first subchronic oral dog study, groups of 4 male and 4 female dogs were fed diets of THM at 0, 1000, 3000, or 6000 ppm for 90 days. The only adverse effect observed was body weight gain was reduced at 6000 ppm. In the other 90-day oral dog study, groups of 4 males were fed diets with 0, 200, 400 or 800 ppm THM. There were no differences in body weights, and no dose related effects on the testes.

In the 90-day rat inhalation study mentioned above, key toxicological data are available to derive an ITSL. A low- mid- and high-exposure group was used along with the appropriate control group. There were an appropriate number of animals per exposure group, and exposures were 6 hrs/day, 5 days/wk. Adverse effects were listed including changes in body weight and food consumption. Four males from each exposure group were also sacrificed during the study to evaluate spermatogenesis. The only parameter that wasn't listed in the study was a no-observable-adverse-effect-level (NOAEL). Even though the study investigators didn't establish a NOAEL, the data presented in the abstract suggests with some degree of confidence where this exposure value would be. According to the abstract, all of the listed adverse effects e.g., decreased body weights, platelet, hemoglobin, and MCH values etc, occurred in the mid- and high-dose groups. This suggests that an exposure of 50 ppm would be appropriate to use as a NOAEL. Since this study abstract isn't complete enough to derive a reference concentration (RfC), the ITSL will be derived as per Rule 232(1)(d) using a NOAEL of 50 ppm or 209 mg/m^3.

The ITSL was derived as follows:

NOAEL = 209 mg/m^3
10 = uncertainty factor; to account for using a NOAEL for a 90-day exposure period to estimate a NOAEL for a lifetime study.
100 = uncertainty factor; to account for specie differences and human population sensitivities.

$$\text{ITSL} = \frac{\text{NOAEL}}{10 \times 100} \times \frac{\text{hours exposed/day}}{24 \text{ hrs/day}}$$

$$\text{ITSL} = \frac{209 mg/m^3}{10 \times 100} \times \frac{6 hrs/day}{24 hrs/day} = 0.0523 mg/m^3$$

Conversion of mg/m^3 to ug/m^3

$$\text{ITSL} = 0.0523 mg/m^3 \times \frac{1000 ug}{1 mg} = 52.3 ug/m^3$$

The ITSL for tetrahydrofuryl methanol = 52 $\mu g/m^3$ based an annual averaging.

Reference:

1. TSCA 8(e). 1991. Initial submission: Letter submitting results from two subacute oral toxicity studies and one testicular maturation study on tetrahydrofurfuryl alcohol. Great Lakes Chemical Corp. Fiche #: OTS0535211.

2. TSCA 8(e). 1992. Supplement: Follow up letter from Great Lakes Chemical Corp concerning a 13-week dietary toxicity study with tetrahydrofurfuryl alcohol in rats. Great Lakes Chemical Corp. Fiche #: OTS0535211-1.

3. TSCA 8(e). 1992. Initial submission: Letter from Great Lakes Chemical Corp to USEPA regarding a developmental toxicity study in rats with tetrahydrofurfuryl alcohol dated 10/14/92. Fiche #: OTS0538320.

4. TSCA 8(e). 1995. Initial submission: Letter from Great Lakes Chemical Corp to USEPA submitting results in 90-day inhalation toxicity studies in rats with tetrahydrofurfuryl alcohol dated 8/31/95. Fiche #: OTS0557931.