MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

September 10, 2002

TO: 2-Methoxy-1-propanol acetate file (CAS # 70657-70-4)

FROM: Gary Butterfield

SUBJECT: Screening level for 2-Methoxy-1-propanol acetate

The initial threshold screening level (ITSL) for 2-methoxy-1-propanol acetate is being set at 500 ug/m3 with 24 hour averaging.

2-Methoxy-1-propanol acetate is also known as the beta isomer of propylene glycol monomethyl ether acetate or beta-PGMEA. Commercial PGMEA is made up of a mixture containing mainly alpha-PGMEA (CAS # 108-65-6) and only a small percentage of beta-PGMEA. The beta-PGMEA is considered to be a contaminant. 2-Methoxy-1-propanol acetate is a water soluble, liquid material with a molecular weight of 132.1 g/mol.

The following references or databases were searched to identify data to determine the screening level: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH) Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), Michigan Department of Environmental Quality (DEQ) library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1967- July 2000), National Library of Medicine (NLM) - Toxline, and National Toxicology Program (NTP) Status Report.

Standard secondary toxicity references (NTP, EPA IRIS, ACGIH, IARC, NIOSH, etc.) were searched for information on this chemical that could be used to set an ITSL. A July 17, 2000 CAS and NLM on-line literature search was conducted to look for any toxicity data.

NIOSH (1991) provides a good overview of the toxic effects of 2-methyl-1-propanol acetate. There is not much toxicity data available for this chemical, as it is a contaminant of commercial 1-methyl-2-propanol acetate. 2-Methyl-1-propanol acetate is not produced as a pure material for commercial use.

The only repeated dose toxicity study available using this actual chemical was reported by Merkle et al (1987). Groups of pregnant Wistar rats and Himalayan rabbits were exposed to determine if effects were caused to the fetuses or the reproductive process. Rats were exposed by inhalation to 0, 110, 550 or 2700 ppm for 6 hr/day on gestation days 6 to 15. There was evidence of embryotoxicity and teratogenicty in the higher dose groups in rats and rabbits from this study. Rabbits were found to be the more sensitive species with adverse effects occurring at lower dose levels. At the highest dose level (550 ppm) for rabbits, all fetuses (100%) had severe anomalies including heart defects and anomalies in the digits of the paw and the sternum. Male and female fetal body weights were also significantly reduced at this dose level .

In the intermediate dose level (145 ppm), no teratogenic effects occurred; however, female pup weight was significantly decreased. This study found no effects being observed at the lowest dose level tested in rabbits, 36 ppm or 200 mg/m3. Merkle et al (1987) also mention another study from internal BASF report that was not available for review. In this four-week inhalation study in Wistar rats there was no bone marrow or testicular effects at the highest dose of 2800 ppm.

The screening level can be calculated from the study by Merkle et al (1987), using EPA's RfC methodology and Guidelines for Developmental Toxicity Risk Assessment (57FR63798) as follows. The beta-PGMEA vapors can be considered to be a category 3 type gas as the toxic effects observed are extra-respiratory. Due to a lack of information on blood:gas partitioning, the default value of one is used for the animal to human ratio. This results in the NOAEL(hec) being equivalent to the NOAEL(adj).

NOAEL(adj) = (200 mg/m3) x 6/24 = 50 mg/m3
NOAEL(hec) = 50 mg/m3
RfC = (50 mg/m3)/(10 x 10) = 500 ug/m3

Where uncertainty factors of 10 were used for animal-to-human, and sensitive individuals. According to EPA's guidelines for Developmental Toxicity Risk Assessment, generally an uncertainty factor is not applied to account for the duration of exposure.

ITSL = 500 ug/m3 with 24-hour averaging

It should be noted that this ITSL is designed to ensure protection against developmental effects from exposure to beta-PGMEA. It is assumed that it should also be protective for other adverse effects since maternal toxicity was seen at higher dose levels than developmental toxicity, although no pathological or histopathological evaluation was done on the adult animals beyond examination of reproductive organs. The ITSL should be re-evaluated if additional data become available.

The compound beta-PGMEA generally expected to undergo hydrolysis to beta-PGME (CAS # 1589-47-5) and acetic acid as the first metabolic step. Thus, these two compounds (beta-PGMEA and beta-PGME) are expected to have similar toxicity and act in additive manner. If there is beta-PGME present in addition to the beta-PGMEA, both materials need to be evaluated together to determine the hazard index, using the ITSL for beta-PGME and the ITSL for beta-PGMEA. A hazard index of less than one indicates adverse effects would not be expected to occur due to the combined impacts of the two compounds.

References:

Merkle et al. 1987. Prenatal toxicity of 2-methoxypropylacetate-1 in rats and rabbits. Fund Appl Toxicol 8:71-79.

NIOSH. 1991. NEG and NIOSH basis for an occupational health standard: propylene gylcol ethers and their acetates. US Dept of Health and Human Services.