MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

May 14, 1996

TO: File for 2-Methylpentane (107-83-5)

FROM: Marco Bianchi

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for 2-methylpentane is 17,600 $\mu g/m^3$ based on an 8 hr. averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, HEAST, NTP Management Status Report, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC, NIOSH Pocket Guide, and ACGIH Guide.

A complete reference check was conducted for 2-methylpentane (a hexane isomer), but information was limited to the ACGIH documentation. Little information is available for animal studies on individual isomers of hexane. Some human studies have shown that exposure to high concentrations of hexane isomers to cause mucous membrane irritation. Hexane isomers are predicted to have a low acute oral toxicity and can be absorbed through the skin.

The ACGIH has established a TLV of 500 ppm (1760 mg/m^3) for 2-methylpentane, while NIOSH has established a REL at 100 ppm (350 mg/m^3). In its justification of the TLV, the ACGIH believes it is the metabolites of n-hexane (primarily 5-hydroxy-2-hexanone and 2,5-hexanedione) that are responsible for its neurotoxicity, and not due to metabolites of hexane isomers. Based on known patterns of hepatic microsomal oxidation and marked variations in structures of the hexane isomers, it is considered unlikely that all hexane isomers would follow the same metabolic route in the body. Conversely, NIOSH in its criteria document concluded that all of the C_5-C_8 alkanes are potential neuropathic agents and should have the same PELs as those established at that time for n-hexane. ACGIH and OSHA believe it is inconsistent to base exposure limits for the isomers of hexane on their unproven neurotoxicity. These agencies consider it unlikely that all hexanes would follow the same metabolic route in the body, in view of the known patterns of xenobiotic biotransformation in animals and humans identified with the marked variations in structure of the various hexane molecules.

After examining support documents for n-hexane and hexane isomers, AQD concurs with the ACGIH that n-hexane solely causes peripheral neuropathies. In a study by Egan et al., (1980), 24 male Sprague Dawley rats exposed 22 hrs/day for up to 6 months at a concentration of 500 ppm of a n-hexane-"free" hexane mixture gave no evidence of neurotoxic effects. A second group of rats exposed to 100 ppm of methyl n-butyl ketone (positive control) developed histological evidence of peripheral neuropathy after four months of continuous exposure. Finally, rats exposed to 500 ppm of methyl ethyl ketone (negative control) did not develop any indication of polyneuropathy.

The components of the n-hexane-"free" hexane mixture contained:

2,3 -dimethyl butane	3.4%
2-methyl pentane	35.3%
3-methyl pentane	30.0%

methyl cyclopentane	24.6%
n-hexane	0.3%
cyclohexane	6.2%

From the results of this study, it appears that 2-methyl pentane behaves like the other hexane isomers in not causing polyneuropathy, especially being one of the major components of the mixture.

The authors state that animal experiments have shown that exposure to six-carbon aliphatic hydrocarbon molecules oxidized at the five and/or two position, i.e. a dione, or a keto-hydroxy derivative, results in the production of nerve tissue damage. Changing the positions of the oxygen moieties results in a total loss of activity. If this peculiar geometric configuration is essential to induce neurological damage, then none of the hexane isomers tested can be considered as potential neurotoxins; because of side-chain positions, relative hydrocarbon length and other structural limitations, these isomers could not be converted to the specific neurotoxic metabolites described above.

The Scientific Advisory Panel concurred with the ACGIH's opinion that it would be inappropriate to consider all C_5 to C_8 alkanes as neurotoxic producing compounds when they evaluated pentane (109-66-0) in June 1994. Based on data from two rat studies (Frontali et al., 1981 and Takeuchi et al., 1981), it was concluded that the only compound producing neurotoxicity out of the C_5 to C_8 range of alkanes was hexane.

Therefore, the ACGIH TLV for 2-methylpentane of 500 ppm or (1760 mg/m^3) will be used to derive an ITSL for this compound.

The ITSL was derived as follows:

ACGIH TLV = 1760 mg/m^3

1760 mg/m^3 ÷ 100 = 17.60 mg/m^3

$$17.60\ \text{mg/m}^3 \times \frac{1000}{1\ \text{mg/m}^3} = 17{,}600\ \text{ug/m}^3$$

The ITSL for 2-methyl pentane = 17,600 µg/m^3 based on 8 hr. averaging.

References:

ACGIH. 1994. Documentation of the TLVs and BEIs.

Egan G. et al., 1980. n-Hexane-"free" hexane mixture fails to produce nervous system damage. Neurotoxicology. 1:515-524.

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