

**MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY**

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**INTEROFFICE COMMUNICATION**

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March 8, 2005

To: Isooctane file (CAS # 540-84-1)

From: Gary Butterfield

Subject: Screening level for isooctane

Isooctane is also commonly known as 2,2,4-trimethylpentane or just trimethylpentane or TMP. It is a colorless liquid with gasoline like odor. The melting point is -107C, and the boiling point is 99C. The vapor pressure for this liquid is quite high, being 41 mmHg at 20C. The molecular weight of TMP is 114.23 g/mol. TMP is one of the volatile components of gasoline, present as 10% of unleaded gasoline. There is a significant potential for exposure to TMP from fuels.

A draft screening level was developed for this chemical in 1996. However, it should be noted that the draft ITSL was based on animal study with exposure to Isopar-C and not isooctane. This work resulted in a permit's PAI for isooctane being approved without a screening level being established. During another evaluation in 2002, only toxicity data published between 1996 and 2002 was looked for. The toxicity data review conducted in 1996 was assumed to be complete, even though a screening level was not set at that time. The review for the establishment of the ITSL in 2004 again looked only for recently published articles on toxicity, of which no new data were found.

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 (1968 - Feb 2005), National Library of Medicine (NLM) - Toxline, and National Toxicology Program (NTP) Status Report.

The CAS and NLM on-line literature searches were conducted on Feb 28, 2005 to look for recently published toxicity studies. There has not been any recent inhalation toxicity studies on TMP published. There have been a few new oral toxicity studies in the past few years, where TMP is used as the positive control dose to cause male rat nephrotoxicity. TMP is known to cause male rat alpha-2u-globulin nephrotoxicity. It has been used as a positive control test substance in many toxicity studies which were looking at male rat nephrotoxicity from alpha-2u-globulin. There is no recent toxicity studies with TMP that could be used to calculate a screening level, as the use for purposes of positive control uses relatively high dose levels to cause the effects and the tests usually only looked for the nephrotoxicity endpoints. There are several

inhalation toxicity studies on a mixture that contained TMP that were published before 1996 (see the series of studies reported by Biodynamics). In the inhalation toxicity reports by Biodynamics, Isopar-C (CAS # 70024-92-9) was used as the test material. Isopar-C is a complex hydrocarbon mixture with carbon chain lengths of C7 and C8, of which TMP is only one component of the mixture. Biodynamics MSDS reports Isopar-C is a mixture of CAS numbers 64741-66-8 and 64742-88-7. Thus, those Isopar-C studies are of questionable use in setting a screening level for TMP, as the actual amount of TMP in the mixture is not known. Therefore those Isopar C studies are considered to be inadequate for setting a TMP screening level.

The ACGIH has set a TLV of 300 ppm (or 1400 mg/m<sup>3</sup>) for all isomers of octane. The TLV documentation cites prevention of narcosis as the basis for setting the TLV and STEL. There is also a 1977 NIOSH REL for C5-8 alkanes available, which the REL documentation says includes most forms of octane including isooctane. The REL is 350 mg/m<sup>3</sup> which converts to 75 ppm for octane. The ACGIH documentation faults the reasoning of NIOSH REL for using neurotoxic endpoints which are likely attributable to hexane. However, the NIOSH REL documentation points out that workers are only rarely exposed to only one pure alkane isomers, and usually are exposed to mixtures containing many different alkanes (most industrial grade solvents).

It is believed that the use of the NIOSH REL provides the best basis for setting an ITSL, under R232(1)(c). The ITSL is being established at 3500 ug/m<sup>3</sup> with 8 hour averaging. This is in light of there being no good quality toxicity studies conducted specifically with isooctane. This ITSL is also consistent with several other petroleum hydrocarbon ITSL's.

#### References:

ACGIH. 1991. Documentation of TLV and BEI - 6th edition.

Biodynamics. 1979b. A 12 week inhalation toxicity study of MRD-78-26 in the rat. IN: Eight Toxicity Reports on 2,2,4-Trimethyl Pentane (Isooctane). from EPA OTS0515208

Biodynamics. 1979a. A segment II teratology study in rats following inhalation exposure to MRD-78-25 and MRD-78-26. IN: Eight Toxicity Reports on 2,2,4-Trimethyl Pentane (Isooctane). from EPA OTS0515208

NIOSH. 1977. Criteria for a recommended standard ... occupational exposures to alkanes (C5-8). DHEW 77-151