MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

August 3, 1999

TO: File for Tridecanol (68526-86-3)

FROM: Dan O'Brien, Toxics Unit

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for tridecanol is 2 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; EPA's Integrated Risk Information System (IRIS) and Health Effects Assessment Summary Tables (HEAST); American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) Booklet; National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Chemical Hazards and Registry of Toxic Effects of Chemical Substances (RTECS); National Toxicology Program (NTP) World Wide Website (WWW), MDEQ Library; International Agency for Research on Cancer (IARC) WWW; Chemical Abstract Service (CAS) On-line and National Library of Medicine (NLM) Toxline (1967–April 14, 1999), Chemical Evaluation Search And Retrieval System (CESARS), Handbook of Environmental Data on Organic Chemicals, Patty's Industrial Hygiene and Toxicology, Merck Index and the Condensed Chemical Dictionary.

The CAS identity search on 68526-86-3 indicates that tridecanol (also called tridecyl alcohol) is a commercial mixture of straight chain, eleven to fourteen carbon, iso-alcohols, that is rich in the thirteen carbon alcohol. Physically, it is a low-melting white solid with a pleasant odor. It is employed in esters for synthetic lubricants, plasticizers, and in the synthesis of other tridecyl compounds; and in detergents, perfumes and antifoaming agents (Hawley, 1981).

It should be noted here that a previous review of the toxicological literature for tridecanol concluded that available data were insufficient for screening level development, noting specifically in a memo to the chemical file dated 5/11/94 that "there was no inhalation data available for tridecyl alcohol." However, this is not, in fact, the case. Scala and Burtis (1973) performed acute toxicity tests on a variety of branched-chain alcohols, including tridecanol. Structurally, the tridecanol test agent they used was composed "mainly" of tetramethyl-1-nonanols. Their inhalation studies involved a single six-hour exposure of groups of ten random bred Swiss mice, Wistar rats and English Short Hair guinea pigs under dynamic conditions followed by a 24-hour holding period. Animals were housed in groups by species and had *ad libitum* access to feed and water during

the post-exposure holding period. Observations were made for mortality, clinical signs, and changes in body weight. Necropsies were performed on all animals at the time of death or at termination of the study. Exposures were made "at atmospheres nearly saturated with vapors of the alcohol." Chamber concentrations were estimated nominally rather than being measured analytically. The exposures did not result in any mortality. The only clinical signs were reported to be slight irritation of the eyes and upper respiratory passages, which resolved spontaneously following termination of exposure. At necropsy, all tissues and organs were normal in appearance. Because no deaths occurred, no Lethal Concentration 50 (LC_{50}) could be calculated. However, the concentration to which the animals were exposed can nonetheless be used as a conservative bounding estimate of an LC_{50} for the purposes of screening level development.

These same authors also conducted oral and dermal Lethal Dose 50 (LD_{50}) and Draize eye irritation studies on the same series of alcohols. In the oral studies, groups of five male fasted Sprague-Dawley rats were gavaged with tridecanol in corn oil. Observations for clinical signs were made on the day of dosing and subsequently for 7 to 14 days. Gross necropsies were performed on animals as they died or at termination following the observation period. Clinical signs of toxicity were central nervous system depression and labored respiration, and when deaths occurred, they did so by four days post exposure. The authors do not list the actual dose levels employed, nor the occurrence and distribution of deaths across those dose levels, but rather an estimated LD_{50} of 4.75 g/kg, noting that estimation was employed because the mortality pattern was "not suitable for analysis." This reasoning was not explained further. The dermal LD_{50} in rabbits was listed as > 2.6g/kg, (the highest dose level tested). No clinical signs were observed. Tridecanol scored as a moderate eye irritant in the Draize assay, primarily due to a persistent corneal lesion in one of the animals tested. Median scores for the group as a whole decreased to 0 by 72 hours post exposure, suggesting that the agent may be somewhat less irritating than the Draize score implies.

The only other toxicological data identified for tridecanol appeared in a study (Rhodes *et al.*, 1984) designed to investigate the peroxisomal proliferating effects of a series of plasticizer alcohols at a single dose (1 mmol/kg-day).[1] No major pathological signs of hepatotoxicity were noted following daily gavage exposure of groups of ten male Wistar rats to doses of 184 mg/kg-day tridecanol for two weeks. Incidence of minor histologic changes (slight centrilobular hypertrophy, slight to moderate glycogen vacuolation, slight to moderate centrilobular "fat" vacuolation) in the liver induced by tridecanol exposure occurred in 20 to 40% of the exposed rats, but body weight gains, relative liver and testicular weights, peroxisomes, catalase, and blood chlolesterol and

[1]Dose level was chosen to approximate the dose of the plasticizer diethylhexyl phthalate (117-81-7) that was associated with hepatocellular neoplasms in a previous assay

triglyceride concentrations did not differ significantly from controls. Because the study was, by design, limited to a small number of physiological endpoints mostly specific to the liver and evaluated only one dose level, it does not adequately characterize the potential scope of systemic toxicity of tridecanol, and it is not suitable as the basis for derivation of a screening level.

Derivation of the ITSL: In developing a screening level for tridecanol, one is necessarily limited to acute exposure data due to the lack of longer term studies. Since an adequate acute inhalation toxicity trial (Scala and Burtis, 1973) exists, it takes precedence over the only other available study, an LD_{50}, for derivation of a screening level. While the highest concentration of tridecanol to which the animals were exposed by Scala and Burtis (12 ppm) failed to induce any mortality, it can still be used as a conservative surrogate exposure concentration for purposes of screening level derivation. For tridecanol, 1 ppm = 8.19 $\mu g/m^3$ (Lington and Bevan, 1994); $\therefore$ 12 ppm = 98.28 $\mu g/m^3$.

Per R 232(1)(f) of part 55, Act 451, as amended:

$$\mathbf{ITSL} = \frac{LC_{50}}{(500)(100)}$$

$$= \frac{98.28\ mg/m^3}{50{,}000}$$

$$= 0.002\ mg/m^3 \times \frac{1000\ \mu g}{1\ mg}$$

$$= \mathbf{2\ \mu g/m^3}$$

And per 232(2)(c), an **annual averaging** time applies.

References

Hawley GG (1981). The Condensed Chemical Dictionary. Tenth Ed. Van Nostrand Reinhold Company, New York, p. 1044.

Lington AW, Bevan C (1994). Patty's Industrial Hygiene and Toxicology, 4th Ed. (Clayton, G.D and Clayton F.E., Eds.), Volume II, Part D, Chapter Thirty: Alcohols. John Wiley and Sons, Inc., New York, pp. 2588-2589.

Rhodes C, Soames T, Stonard MD, Simpson MG, Vernall AJ, Elcombe CR (1984). The absence of testicular atrophy and *in vivo* and *in vitro* effects on hepatocyte morphology and peroxisomal enzyme activities in male rats following the administration of several alkanols. *Toxicol Lett* **21**:103-109.

Scala RA, Burtis EG (1973). Acute toxicity of a homologous series of branched-chain primary alcohols. *Am Indus Hyg Assoc J* **34**(11):493-499.

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