

**MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY**

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**INTEROFFICE COMMUNICATION**

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**June 8, 2005**

**TO:** Memo to File for MCPA 2-EHE CAS #26544-20-7 (2-Methyl-4-Chlorophenoxyacetic Acid 2-Ethylhexyl Ester Isooctyl Ester of 2-Methyl-4-Chlorophenoxyacetic Acid)

**FROM:** Margaret M Sadoff

**RE:** Derivation of Initial Threshold Screening Level (ITSL)

**The Initial Threshold Screening Level (ITSL) for MCPA 2-EHE is 90 ug/m<sup>3</sup> with an annual averaging time.**

A search of the literature and the following databases was performed for information regarding MCPA 2-EHE: American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values, National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Integrated Risk Information System (IRIS), NIOSH's Registry of Toxic Effects of Chemical Substances (RTECS), Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, CAS Online (1967 to December 2003), Hazardous Substance Data Bank (HSDB), National Library of Medicine/Toxline, Health Effects Assessment Summary Tables (HEAST), and National Toxicology Program (NTP) Study Database.

There is very limited toxicity information available on MCPA 2-EHE. The database search retrieved one value - an LD50 in rats of 700 mg/kg found in RTECs. The literature search retrieved one article on acute toxicity to aquatic organisms and two occupational exposure studies to mixtures of phenoxy acid herbicides.

DOW AgroSciences provided a Material Safety Data Sheet (MSDS) for this chemical that listed an LC50 as > 4.5 mg/L. Other effects listed on the MSDS but for which no data were available are 1) eye and skin irritation, 2) effects on blood, kidney, liver and testes, and 3) birth defects in laboratory animals at doses toxic to the mother. DOW provided study summaries for reproductive and teratogenic studies conducted by Hazelton Labs and BASF. The Hazelton Lab studies report NOAELs for embryo/fetal toxicity that coincide with maternal toxicity values (25 to 30 mg/kg/day by oral gavage) and thus, fetal toxicity may be secondary to maternal toxicity. The BASF study was a summary/abstract translated from German which also reported a NOAEL for dams and fetuses of 60 mg/kg/day by oral gavage. No developmental ITSL was developed at the time of this review since 1) fetal toxicity was found to coincide with maternal toxicity in these studies, and 2) studies lacked sufficient detail to evaluate study quality, and 3) a conservative ITSL based on available LC50 data was deemed to be protective of maternal and fetal effects.

An LC50 value was reported from a DOW acute aerosol inhalation study in Fischer 344 rats conducted in 1987. The study was deemed to be of sufficient quality from which to derive an ITSL pursuant to Rule 232(f). The MSDS for MCPA 2-EHE states that vapors are minimal at room temperature (vapor pressure = 11.5mm @ 212C) but that mists or vapors from heated material may cause irritation or other effects. Therefore the acute inhalation test used an aerosol rather than a vapor exposure.

A group of six male and six female rats were exposed for a single 4-hour duration to a liquid aerosol of MCPA 2-EHE. The time-weighted average concentration was 4.4 mg/L which was the highest practically attainable concentration. The average mass median aerodynamic diameter of the liquid aerosol was 2.55 microns with a geometric standard deviation of 2.45.

There were no deaths reported at this exposure. Observations during and shortly after exposure included closed and/or squinted eyes, salivation, and porphyrin-like material around the eyes and nares. The ocular and nasal signs persisted for several days after exposure along with an additional observation of perineal wetness. All rats appeared clinically normal 5 days post exposure. The mean body weights of exposed rats were decreased by approximately 4% on the day after exposure but returned to pre-exposure body weights after 8 (male) and 11 (female) days. Subsequent gross pathologic examination of each animal did not reveal treatment-related lesions. The investigators concluded that this high exposure concentration produced signs of irritation without clinical signs of respiratory or systemic toxicity.

Using the LC50 of > 4.4 mg/L to derive the ITSL pursuant to Rule 232(f) for acute inhalation studies of 4 hours or more:

$$4.4 \text{ mg/L} \times 1,000 = 4,400 \text{ mg/m}^3$$

$$\text{ITSL} = \frac{4400 \text{ ug/m}^3}{500 \times 100} = 0.088 \text{ mg/m}^3 \approx \mathbf{90 \text{ ug/m}^3}$$

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