MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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February 6, 2017

TO: File for Ethyl Acetate (CAS No. 141-78-6)

FROM: Mike Depa, Air Quality Division, Toxics Unit

SUBJECT: Derivation of Initial Threshold Screening Level

The initial threshold screening level (ITSL) for ethyl acetate is 3200 µg/m^3, with annual averaging time.

Previously, the averaging time (AT) assigned to the ethyl acetate ITSL was 24 hours, pursuant to Rule 232(2)(b) of the Air Pollution Control Rules promulgated at that time (July 1, 1992; see attached memo). The recently promulgated (December 22, 2016) Air Pollution Control Rule 232(2)(b) states that ITSLs based on Rule 232(1)(b) are assigned an annual averaging time. An updated literature review was not performed at this time.

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

Interoffice Communication

July 1, 1992

To : Ethyl Acetate (CAS # 141-78-6) File

From : Gary Butterfield

Subject : ITSL for Ethyl Acetate

A CAS-on-line search, through 4/92, did not find any chronic studies appropriate for calculation of an ITSL. An expert panel for cosmetic ingredients published a review of the toxicity data in 1989. They found ethyl acetate is considered to be relatively nontoxic. This conclusion is based on results from acute tests - oral, inhalation, dermal and I.P. routes of exposure. In a 24 week mouse lung tumor carcinogenicity assay, I.P. injections of ethyl acetate did not induce an increase in the number of lung tumors. Mutagenicity assays have found ethyl acetate to be negative in the Ames assay, Rec assay, and micronucleus assay. Positive results were indicated in yeast mitotic aneuploidy and in Chinese hamster fibroblast chromosomal aberrations. Ethyl acetate was found to be hydrolyzed to ethyl alcohol and acetic acid by the blood, in *in-vitro* studies. *In-vivo*, there is evidence of it also being rapidly metabolized by rats and humans (a half-life of 5 to 10 minutes was estimated). An article that was reviewed by the expert committee showed ethyl acetate has a respiratory retention of 60% and respiratory excretion rate of 3%. Following exposure to ethyl acetate, the exhaled breath had detectable levels for only a short period of time, a few breaths (supposedly due to its rapid metabolism).

ACGIH has established a TLV of 400 ppm (or 1400 mg/m^3) for ethyl acetate. According to ACGIH, this level of TLV should provide a large margin of safety for health effects, but may still be irritating to some workers. This makes use of the TLV for calculation of the ITSL questionable.

Limited amounts of acute toxicity data are found. Ethyl acetate is considered to have a relatively low acute toxicity. The oral LD5O was reported to be 11.3 g/kg (Smyth et al 1962). EPA has

established an RfD, of 0.9 mg/kg, for ethyl acetate based on an unpublished 90 day rat gavage study. This study was conducted for EPA's Office of Solid Waste (EPA 1986). In this study rats, 30 per sex per dose level, were gavaged with 0, 300, 900 or 3600 mg/kg/d. Male rats given 3600 mg/kg displayed signs of toxicity -depressed body weight, reduced food consumption and reduced organ weights. A NOAEL of 900 mg/kg was identified.

Due to the efficient absorption of ethyl acetate from air and the rapid metabolism (regardless of exposure route), it can be considered appropriate to convert the oral RfD to an ITSL.

ITSL = 0.9 mg/kg x (70kg/20m^3) = 3.2 mg/ m^3 with 24 hr average

References :

EPA. 1986. Rat oral subchronic study with ethyl acetate. EPA Office of Solid Waste, Washington DC. (as cited in IRIS)

Expert panel review. 1989. Final report on the safety assessment of ethyl acetate and butyl acetate. J Am Coil Toxicol 8:681-705.

IRIS. 1992. IRIS2 database.

Smyth et al. 1962. Am md Hyg Assoc J 23:95-107.