MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Isopropyl Acetate, CAS# 108-21-4

FROM: Margaret M. Sadoff, AQD Toxics Unit

SUBJECT: Update of Interim ITSL for Isopropyl Acetate

DATE: October 3, 2006

A search of the literature and the following databases was performed for information regarding isopropyl acetate: American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (2004), National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals (2005), Integrated Risk Information System (IRIS), Registry of Toxic Effects of Chemical Substances (RTECS), Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, CAS Registry Online, Hazardous Substance Data Bank (HSDB), National Library of Medicine/Toxline, Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Study Database, Entrez PubMed, and CalEPA's Toxicity Values Database.

Isopropyl acetate was last reviewed in 1992. An interim ITSL of 9,500 ug/m3 with an 8-hour averaging time was set at that time based on the OSHA PEL of 250 ppm (given as 950 mg/m3 but calculates to 1050 mg/m3 using standard conversion by molecular weight). No literature search was performed in 1992 to find data from which an RfC-based ITSL could be derived. Only an RfC-based ITSL would supersede an OEL-based ITSL according to AQD toxics rules hierarchy.

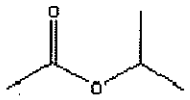
The current update was performed to determine the extent of the database for isopropyl acetate. The database is quite limited and no chronic studies were found that would meet the minimum criteria required to develop an RfC-based ITSL. However, the ACGIH TLV for this chemical was updated in 2003 and the TLV was lowered from 250 ppm to 100 ppm. This revised OEL was used to set a final ITSL for isopropyl acetate. (See Section on Occupational Exposure Limits and Potential for Human Toxicity.)

The final ITSL for isopropyl acetate is 4,200 ug/m3, 8-hour average.

Chemical Description, Uses & Exposure
(Sources: Toxline HSDB, RTECs)

Isopropyl acetate is a colorless liquid with a pleasant, fruity odor. Odor threshold ranges are 0.5 to 34 ppm (detection) and 0.91 to 42 ppm (recognition). It is used in the manufacture of plastics, artificial leather, dopes, films, and cements and as a solvent for a wide range of oils, fats, waxes, gums and resins. In addition it is also used as a synthetic fragrance and flavoring ingredient. Isopropyl acetate is naturally present in grape juice, nectarine, apple and milk volatiles. Since it is used as a flavoring agent, FDA classifies isopropyl acetate, like n-propyl acetate, as a Group 3 substance:

"Solvents in Class 3 may be regarded as less toxic and of lower risk to human health. Class 3 includes no solvent known as a human health hazard at levels normally accepted in pharmaceuticals. However, there are no long-term toxicity or carcinogenicity studies for many of the solvents in Class 3. Available data indicate that they are less toxic in acute or short-term studies and negative in genotoxicity studies. It is considered that amounts of these residual solvents of 50 mg/day or less would be acceptable without justification. This would equate to an inhalation value of 175 mg/m3."



MW = 102 1ppm = 4.17 mg/m3

If released to air, a vapor pressure of 60.4 mm Hg at 25 deg C indicates that isopropyl acetate will exist solely as a vapor in ambient air with an estimated atmospheric half-life of 4.6 days.

Occupational exposure may occur through inhalation and dermal contact. The general population may be exposed via inhalation of ambient air and food volatiles, ingestion of drinking water, and dermal contact with vapors, food and other products containing isopropyl acetate.

Animal Toxicity
(Sources: RTECs, Toxline HSDB, ACGIH)

Only acute animal toxicity is reported in the database. Rats survived exposure to air saturated with isopropyl acetate vapor for 30 minutes. Five out of six rats exposed to 32,000 ppm for 4 hours died within 14 days. One out of six rats died after exposure to 16,000 ppm. Mice exposed to 1,374 to 2,000 ppm isopropyl acetate vapor for a single 4-hour period showed concentration-related behavioral abnormalities in a test involving swimming patterns (note: this is not a scientifically accepted behavioral test but some researchers use it as an early indicator of CNS depression). One rat LC50 was reported at 50.6 mg/L (8-hour exposure). This same LC50 has been reported elsewhere as 17,100 ppm or 71,550 mg/m3 (4-hour exposure).

The mouse respiratory depression value for isopropyl acetate (RD50) was published as 4,259 ppm (17,760 mg/m3). Using this RD50 and the correlation values of 0.1 and 0.01 (for slight irritation and minimal or no effect, respectively), results in a range of possible TLVs from 43 to 440 ppm (180 to 1,835 mg/m3).

The rat oral LD50 is between 6,160 and 7,380 mg/kg. Based on observations in experimental animals exposed to similar acetates, isopropyl acetate may be a mild eye irritant and mild CNS depressant. At very high but sub-lethal concentrations, headache, nausea, dizziness, uncoordination and confusion may occur.

Occupational Exposure Limits and Potential for Human Toxicity
(ACGIH 2004, NIOSH 2005, RTECs)

There is no chronic human or animal toxicity information for carcinogenicity, developmental or reproductive toxicity. Isopropyl acetate failed to induce aneuploidy or other evidence of genotoxicity in yeast.

The lowest reported concentration for irritation in humans is 200 ppm (Silverman, et al, 1946). A 100 ppm value was identified as a sensory limit for 8-hour exposures based on these findings. Higher concentrations (not specified) resulted in nose and larynx irritation as well. Two incidences have been reported where liquid isopropyl acetate caused eye burns in workers. The eyes healed within 3 to 10 days and caused no permanent damage. There have also been reported occupational exposure symptoms such as eye irritation, tightness of the chest and coughing. Dermal contact with the liquid may lead to defatting and cracking of the skin.

In 2003, ACGIH updated the TLV for isopropyl acetate. From 1967 to 2002, the TLV was listed as 250 ppm (1040 mg/m3) with a STEL at 310 ppm (1290 mg/m3). In 2003, ACGIH lowered the TLV to 100 ppm (420 mg/m3) with a STEL of 200 ppm (840 mg/m3) to protect against eye and respiratory irritation, as well as the potential for narcotic effects. The updated TLV was based partly on new information from the mouse RD50 and partly on a reinterpretation of the human data from 1946.

OSHA recommended values are a PEL of 250 ppm (950 mg/m3) and an IDLH of 1,800 ppm (7,524 mg/m3). NIOSH did not agree with the OSHA PEL because the majority of human subjects exposed to 200 ppm in the 1946 irritation study did experience eye irritation. Therefore, NIOSH did not set an REL for isopropyl acetate but instead listed it in Appendix D. This appendix, entitled "Substances with No Established RELs" lists chemicals that have PELs but not RELs with the following qualification:

> "NIOSH questioned whether the PELs proposed (and listed below) for the following substances included in the Pocket Guide were adequate to protect workers from recognized health hazards."

This chemical is not believed to be a skin sensitizer. Employees with chronic respiratory, skin, liver, or kidney diseases have been identified as populations at increased risk from exposure to isopropyl acetate.

Update of ITSL

Only an RfC-based ITSL would supersede an OEL-based ITSL according to AQD toxics rules hierarchy. The occupational exposure limit set by ACGIH has been updated recently and is the most pertinent health protective value on which to base an ITSL pursuant to Rule 232(1)(c).

The final ITSL for isopropyl acetate is 4,200 ug/m3, 8-hour average.

MS:LH