

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Octyl Acetate 15-S-3 (CAS # 108419-32-5)
FROM: Robert Sills, AQD Toxics Unit Supervisor
SUBJECT: Octyl Acetate ITSL change in the averaging time from 24 hrs to annual
DATE: January 25, 2017

The current ITSL for Octyl Acetate is 78 ug/m³, with annual averaging time (AT).

Previously, the ITSL was established on October 14, 1992 at 110 ug/m³ with 24 hr averaging time (see attached justification memo). The averaging time (AT) assigned to the ITSL previously was 24 hours, as per the default methodology at that time (Rule 232(2)(b)). The ITSL derivation applied a total uncertainty factor (UF) = 1000, which consisted of a UF = 10 for each interspecies extrapolation, intraspecies variability, and subchronic-to-chronic conversion (the study duration was 90 days). The current file review concludes that the AT for the ITSL may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b).

The current file review also noted that in the derivation of the previous ITSL of 110 ug/m³ the dose conversion from the point of departure (POD) (a NOAEL) of 100 mg/kg did not provide the details of the route-to-route dose conversion, and apparently did not account for the 5/7 day dosing regimen. Therefore, the ITSL is now recalculated as follows:

$$\text{POD} = \text{NOAEL}(\text{adj}) = 100 \text{ mg/kg} \times \frac{5 \text{ d}}{7 \text{ d}} = 71.4 \text{ mg/kg-d}$$

$$\text{ITSL} = 71.4 \text{ mg/kg-d} \times \frac{1000 \text{ ug}}{\text{mg} \times (\text{UF}_T = 1000)} \times \frac{\text{kg-d}}{0.916 \text{ m}^3} = 78 \text{ ug/m}^3 \text{ (annual AT)}$$

Where:

UF_T = total uncertainty factor = 1000, consisting of 10X for each interspecies extrapolation, intraspecies variability, and subchronic-to-chronic conversion for a 90-day study.

0.916 m³ per (kg-d) is the recommended default inhalation rate per body weight for adult SD rats with combined sexes or sexes not specified (EPA, 1988). (In this particular case, the sexes were combined).

Reference:

EPA. 1988. Recommendations for and documentation of biological values for use in risk assessment. PB 88-179874.

Michigan Department of Natural Resources

Interoffice Communication

October 14, 1992

To : Octyl Acetate file (CAS # 108419-32-5)

From : Gary Butterfield

Subject : ITSL for Octyl Acetate

There is no occupational exposure limits for this material upon which to base the ITSL. There is no toxicity data available via the inhalation route of exposure. There is a 90 day rat gavage study and a teratology also administered by gavage. In the 90 day gavage study (Daughtrey et al (1989a)), Sprague-Dawley rats were given 100, 500 or 1000 mg/kg on 5 days per week. Rats exhibited increased liver weights in males and females dosed at 500 mg/kg and 1000 mg/kg, however, there was no pathologic changes in the liver tissue. Kidney weights were increased in both sexes at the 1000 mg/m3 dose level. There also was a non-significant reduction in body weights in the high dose rats of both sexes. The authors went on to attempt to describe these changes as not providing evidence of a toxic effects. In the teratogenicity study, Daughtrey et al (1989b), gavaged pregnant Sprague-Dawley rats on gestation days 6 to 15 with 100, 500 or 1000 mg/kg. Maternal toxicity was observed at the 500 and 1000 mg/kg dose levels as evidenced by reduced body weights, reduced food consumption, and at the 1000 mg/kg dose increased incidence of clinical observations. Increased fetal malformations were also observed at the 1000 mg/kg dose level however the authors attributed the increase to the maternal toxicity. However, the maternal effects at 500 mg/kg and 1000 mg/kg can be used as evidence supporting the adverse effects observed in the 90 day study at 500 and 1000 mg/kg. Thus a NOAEL of 100 mg/kg can be identified from these two studies.

An oral rat NOAEL of 100 mg/kg converts to inhaled dose of 110 mg/m3/d. Following EPA's RfC guidelines, this NOAEL is also considered to be the NOAEL(adj) dose. Assuming there is no portal-of-entry effects, and 100 % absorption via inhalation the NOAEL(adj) = NOAEL(hec). The RfC can be derived from NOAEL(hec) by applying a 1000 fold uncertainty factor, based on 10 to adjust for the less than lifetime study, 10 for rat to human, and 10 for sensitive individuals. Thus the RfC=110 ug/m3/d and the ITSL is 110 ug/m3 with a 24 hr average.

References:

Daughtrey et al. 1989a. A subchronic study of octyl acetate in rats. Fund Appl Toxicol 12:313-320.

Daughtrey et al. 1989b. Evaluation of the teratogenic potential of octyl acetate in rats. Fund Appl Toxicol 13:303-309.