

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for n-butanol (CAS # 71-36-3)

FROM: Robert Sills, AQD Toxics Unit Supervisor

SUBJECT: n-Butanol ITSL change in the averaging time from 24 hrs to annual

DATE: December 5, 2016

The current ITSL for n-butanol (350 ug/m<sup>3</sup>) was established on July 22, 1992 (see attached). The averaging time (AT) assigned to the ITSL at that time was 24 hours, as per the default methodology at that time (Rule 232(2)(b)). The basis was the EPA (1990; IRIS) Reference Dose (RfD); an RfC was not provided by EPA (1990). In deriving the RfD, EPA applied a total UF = 1000, consisting of 10X for each interspecies extrapolation, intraspecies variability, and for extrapolating the subchronic (13 week) rat study to chronic duration. 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). Therefore, the AT is being changed from 24 hours to annual at this time.

Reference:

EPA. 1990. Integrated Risk Information System (IRIS database). Chemical file for n-butanol. Last revised 9/1/1990. Still current as of 12/5/16.

Michigan Department of Natural Resources

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Interoffice Communication  
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July 22, 1992

To : n-Butanol File (CAS # 71-36-3)

From : Gary Butterfield

Subject : ITSL for n-Butanol

The ACGIH TLV of 50 ppm (or 150 mg/m<sup>3</sup>) is based on butanol's ability to cause hearing loss and vestibular dysfunction in workers with long term occupational exposure, up to 3 to 11 years, at concentrations of 80 ppm. The toxicity basis for this particular TLV is significantly more substantial than many of the other TLV's.

However, the 1992 Toxics Rules gives greater priority to use of an EPA RfD, if it is appropriate to use oral data, over use of a TLV when developing an ITSL. EPA has established an RfD for n-butanol of 0.1 mg/kg/d. The RfD is based on a NOAEL of 125 mg/kg as identified in an unpublished 13 week gavage study conducted for EPA's Office of Solid Waste in 1986. In this study the next higher dose, of 500 mg/kg, caused reductions of hematological parameters, ataxia and hypoactivity. The appropriateness of using oral data when developing the ITSL needs to be evaluated. WHO (1987) provides information that implies it is appropriate to use oral data to base an inhalation ITSL. Among the information for appropriateness of using oral data that was presented by WHO is : butanol is readily absorbed through the lungs, skin, and gastrointestinal tract; butanol is metabolized via a non-exposure route specific method of alcohol dehydrogenase; and, absorbed butanol is rapidly eliminated from the blood. Additionally, observed toxic systemic effects, i.e., observed blood changes following gavage, would be expected to occur regardless of exposure route. This concept also tends to support the use of oral data when developing an ITSL. Another concept that supports the acceptability of using oral data when developing the ITSL is butanol's ability to be absorbed through the skin as well as oral and inhalation routes. Thus, demonstrating butanol's ability to be readily absorbed via many different routes.

Besides EPA (1986), other toxicity studies are available. For example, Nelson et al (1989) reported effects observed in rats during an inhalation teratology study. Rats were exposed to 3500, 6000 or 8000 ppm. A NOAEL of 3500 ppm was identified by reduced fetal weights at 6000 and 8000 ppm and increased skeletal malformations at 8000 ppm.

However, once it has been determined that it is acceptable to use oral data for calculation of the ITSL, there is a greater level of

confidence in the ITSL based on the extensively reviewed RfD, rather than an ITSL based on other available data. The ITSL based on the RfD can be calculated as follows:

$$\text{ITSL} = (0.1 \text{ mg/kg}) \times (70\text{kg}/20\text{m}^3) = 350 \text{ ug/m}^3 \quad 24 \text{ hr average.}$$

References:

ACGIH. 1986. Documentation of the TLV's and BEI's.

EPA. 1986. Butanol: rat oral subchronic study. EPA, Office of Solid Waste, Washington DC. TRI #032-006.

EPA. 1992. IRIS database.

Nelson et al. 1989. Lack of selective developmental toxicity of three butanol isomers administered by inhalation to rats. Fund Appl Toxicol 12:469-479.

WHO. 1987. Environmental Health Criteria # 65 - butanols.