

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Isophorone diisocyanate (CAS #4098-71-9)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: April 15, 2013

SUBJECT: Screening Level for Isophorone diisocyanate (CAS #4098-71-9)

The initial threshold screening level (ITSL) for isophorone diisocyanate (CAS #4098-71-9) is $0.45 \mu\text{g}/\text{m}^3$ with an 8-hour averaging time.

Isophorone diisocyanate (IPDI; also known as 3-isocyanatomethyl-3,5,5-trimethyl cyclohexylisocyanate or 5-isocyanato-1-(isocyanatomethyl)-1,3,3-trimethyl-cyclohexane) is an aliphatic diisocyanate with a cis and trans stereoisomers with similar reactivities. IPDI is a colorless or slightly yellow liquid with a pungent odor and a molecular weight of 222.3 g/mol. IPDI is used: in the synthesis of enamel coatings which are resistant to abrasion from automotive fluids, salts, acids, and degradation from ultraviolet light (examples include: exterior aircraft paint, water-proofing parking decks, roofs, balconies, and bridges); in textile coatings, foams, and varnish. IPDI is highly reactive with all substances containing an active hydrogen, such as water, acids, amines, phenols, mercaptans, amides, and urea. IPDI is also strongly irritating to the skin, eyes, and respiratory tract and can act as a skin, respiratory tract and lung sensitizer (Wikipedia, 2013; CDC, 2013).

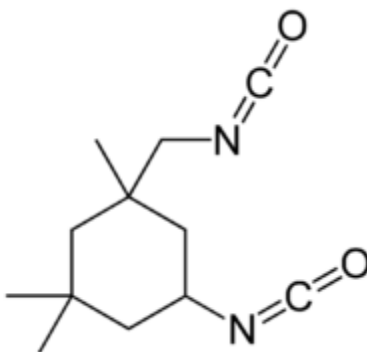


Figure 1. Structure of isophorone diisocyanate

A literature review was conducted to determine an initial threshold screening level (ITSL) for IPDI. The following references and databases were searched to derive the above screening levels: CCD, United States Environmental Protection Agency (US EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH),

American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values and Biological Exposure Indices (TLV/BEI) 2012 guide, National Toxicology Program (NTP) Study Database, International Agency for Research on Cancer (IARC), Acute Database, Chemical Abstract Service (CAS) Online (searched 2/25/13), National Library of Medicine (NLM)-online, EPA Aggregated Computational Toxicology Resource (ACToR) Database, US EPA TSCATS database, and Hazardous Substances Data Bank (HSDB).

The ACGIH set a threshold limit value-time weighted average (TLV-TWA) of 0.045 mg/m³, which is recommended for occupational exposure to IPDI based on a related compound toluene-2,4-diisocyanate for which quantitative exposure data is available.

An odor detection study where humans were exposed to IPDI for either 1 or 5 minutes showed that at 0.00025 mg/L the odor was just perceptible, but at 0.00064 mg/L IPDI caused slight irritation of the eyes and nose and at 0.00137 mg/L caused strong irritation of the mucous membranes of the eyes and the breathing passages, which could not be tolerated (IUCLID, 2000). If this study were used to determine an ITSL using the following equation

$$\text{proposed ITSL} = \frac{\text{NOAEL}}{10} \times \frac{1 \text{ min}}{60 \text{ min}}$$

Where the denominator, an uncertainty factor of 10, is for protection of sensitive subgroups. Using the 0.00025 mg/L dose as a (1 to 5 minute) NOAEL and converting mg/L to mg/m³ using the following equation

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

$$0.00025 \text{ mg/L} \times 1,000 = 0.25 \text{ mg/m}^3$$

Using this value as the NOAEL for the ITSL equation above:

$$\text{proposed ITSL} = \frac{0.25 \text{ mg/m}^3}{10} \times \frac{1 \text{ min}}{60 \text{ min}} = 0.00041667 \text{ mg/m}^3/\text{hr} = 0.42 \text{ } \mu\text{g/m}^3$$

Which would give an ITSL of 0.42 µg/m³ with a 1 hour averaging time.

In an LC₅₀ rat study performed by Bayer Corporation, 5 male and 5 female Wistar rats per group were given nose-only exposure to 0, 20.4, 53.3, 73.8, 104.6, or 410.3 mg/m³ isophorone diisocyanate for 4 hours followed by a 4-week observation. An LC₅₀ calculation was performed using a method developed by Pauluhn (1983). The LC₅₀ calculation was necessary since all rats survived at dose level 20.4 mg/m³, but 100% mortality occurred at 53.3 mg/m³. Rats exposure to 20.4 mg/m³ exhibited: reduced motility, piloerection, ungroomed coat, bradypnea, labored breathing, rales, sluggishness, nose and/or muzzle with red incrustations, and reddening of nose. The calculated LC₅₀ was determined to be 40 mg/m³. As a true LC₅₀ was not determined, if this study were to be used to determine an ITSL, a more conservative approach would be to

use the 20.4 mg/m³ dose level as the LC₅₀ as this level is showing obvious effects. If this study were used to determine an ITSL using the following equation

$$\text{proposed ITSL} = \frac{LC_{50}}{500 \times 100} = \frac{20.4 \text{ mg/m}^3}{500 \times 100} = 0.000408 \text{ mg/m}^3 = 0.41 \text{ }\mu\text{g/m}^3$$

Which would give an ITSL of 0.41 μg/m³ with an annual averaging time.

According to Rule 232(1)(c), the ITSL is determined by the occupational exposure level when one is available. ACGIH has a TLV-TWA of 0.045 mg/m³.

Based on the structural similarity of IPDI to toluene-2,4-diisocyanate, which has more detailed toxicity data. Using this value to calculate an ITSL using the rule above:

$$\text{ITSL} = \frac{OEL}{100} = \frac{0.045 \text{ mg/m}^3}{100} = 0.00045 \text{ mg/m}^3 = 0.45 \text{ }\mu\text{g/m}^3$$

This value is similar to the other calculated values for proposed ITSLs above. According to Rule 232(2)(a) the averaging time is 8 hours. The initial threshold screening level (ITSL) for IPDI (CAS # 4098-71-9) is 0.45 μg/m³ with an 8-hour averaging time.

References:

ACGIH. 2001. Isophorone Diisocyanate. TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. ACGIH Worldwide Signature Publications.

APCR. 2013. Air Pollution Control Rules, Promulgated pursuant to Part 55, Air Pollution Control, of the Natural Resources and Environmental Protection Act, Michigan Department of Environmental Quality. 1994, Act 451, as amended (NREPA).

CDC. 2013. International Chemical Safety Cards. Isophorone diisocyanate. Available online at: <http://www.cdc.gov/niosh/ipcsneng/neng0499.html>

IUCLID. 2000. IUCLID Dataset on 3-Isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate. CAS No. 4098-71-9. European Commission, European Chemicals Bureau. Available online at: http://esis.jrc.ec.europa.eu/doc/IUCLID/data_sheets/4098719.pdf

Pauluhn. 1983. Computer-Aided Estimation of the LD50/LC50 Bayer AG Report No. 11835, dated May 18, 1983.

Wikipedia. 2013. Isophorone diisocyanate. Available online at: http://en.wikipedia.org/wiki/Isophorone_diisocyanate

DL:lh