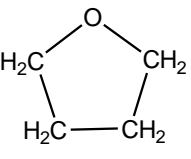


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|--|-------------------|----------------------------|
| 13 | CAS No.: 109-99-9 | Substance: Tetrahydrofuran |
| <p>Chemical Substances Control Law Reference No.: 5-53 PRTR Law Cabinet Order No.:</p> <p style="text-align: center;">Structural Formula:</p> <p>Molecular Formula: C₄H₈O Molecular Weight: 72.11</p> <div style="text-align: center;">  </div> | | |
| <p>1. General information</p> <p>This substance is freely miscible with water, the partition coefficient (1-octanol/water) (log K_{ow}) is 0.46, and the vapor pressure is 162 mmHg (=2.16×10⁴ Pa) (25°C). Biodegradability (aerobic degradation) is good. The substance does not have any hydrolyzable groups.</p> <p>The main applications of this substance are as a solvent for various resins, as a synthetic raw material, and as a reaction solvent for pharmaceuticals and pesticides. The production (shipments) and import quantity in fiscal 2004 was 10,000 to <100,000 t.</p> <p>-----</p> <p>2. Exposure assessment</p> <p>Because this substance is not a Class 1 Designated Chemical Substance under the Law Concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management (PRTR Law), release and transfer quantities could not be obtained. Predictions of distribution by medium using a Mackay-type level III fugacity model indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportions distributed to soil and water bodies would be higher.</p> <p>The predicted maximum exposure to humans via inhalation, based on general environmental atmospheric data, was approximately 0.18 µg/m³. In addition, the predicted maximum value for indoor air was 11 µg/m³. The predicted maximum oral exposure was estimated to be less than around 0.04 µg/kg/day based on calculations from data for bodies of public fresh water. The risk of exposure to this substance by intake from an environmental medium via food is considered slight.</p> <p>The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was estimated to be less than around 1 µg/L for public freshwater bodies and generally less than 1 µg/L for seawater.</p> <p>-----</p> <p>3. Initial assessment of health risk</p> <p>This substance is irritating to the eyes, skin and respiratory tract and may cause coma by causing effects on the central nervous system. Redness and painful irritation in the eyes is caused and dryness of the skin is caused by contact with this substance. Oral or inhalation exposure causes cough, dizziness, headache, nausea, sore throat and loss of consciousness. It has been reported that inhalation human T_{CLo} is 25,000 ppm (73,750 mg/m³, for general anesthesia).</p> <p>Sufficient information could not be obtained on its carcinogenicity, and its initial assessment was conducted on the basis of data on its non-carcinogenic effects.</p> <p>As for its oral exposure, its no-observed-adverse-effect-level (NOAEL) of 300 mg/kg/day for suppressed body weight increases obtained from its mid-term and long-term toxicity tests for rats was divided by 10, due to their short test periods, to produce 30 mg/kg/day as its 'non-toxic level*'. As for its inhalation exposure, its no-observed-adverse-effect-level (NOAEL) of 590 mg/m³ for relative increase of</p> | | |

liver weight to body weight was obtained for inhalation exposure from its mid-term and long-term toxicity tests for mice. It was then adjusted for exposure conditions to provide 105 mg/m³. This was divided by 10, due to their short test periods, to produce 11 mg/m³ as its ‘non-toxic level*’.

As for its oral exposure, the predicted maximum exposure was estimated to be less than around 0.04 µg/kg/day, when intakes of freshwater from public water supply were assumed. Its margin of exposure (MOE) would be more than 75,000 when calculated from its ‘non-toxic level*’ of 30 mg/kg/day and the predicted maximum exposure, and then divided by 10 due to the fact that ‘non-toxic level*’ was obtained from animal experiments. Since risk associated with exposure to this substance through food intakes from the environment is presumed to be minimal, this exposure will not increase MOE significantly, and no further action will be required at the moment to assess health risk from oral exposure to this substance.

As for its inhalation exposure, the predicted maximum exposure was estimated to be around 0.18 µg/m³, when its concentrations in the ambient air were considered. Its margin of exposure (MOE) would be 6,100, when calculated from its ‘non-toxic level*’ of 11 mg/m³ and the predicted maximum exposure, and then divided by 10 due to the fact that ‘non-toxic level*’ was obtained from animal experiments.

The predicted exposure in the indoor air is estimated to be around 11 µg/m³, and this will lead to MOE of 100. No further action would be required at the moment on the health risk of its inhalation exposure in the ambient and indoor air.

| Information of toxicity | | | | Exposure assessment | | Result of risk assessment | | | Judgment | | |
|-------------------------|------------------------------|----------------------|--------|-----------------------------------|-----------------|---|-------------------|-----|----------|---|---|
| Exposure Path | Criteria for risk assessment | | Animal | Criteria for diagnoses (endpoint) | Exposure medium | Predicted maximum exposure quantity and concentration | | | | | |
| Oral | ‘Non-toxic level’ | 30 mg/kg/day | Rats | Inhibited weight increase | Drinking water | — | µg/kg/day | MOE | — | × | ○ |
| | | | | | Freshwater | < 0.04 | µg/kg/day | MOE | > 75,000 | ○ | |
| Inhalation | ‘Non-toxic level’ | 11 mg/m ³ | Mice | Increase in relative liver weight | Ambient air | 0.18 | µg/m ³ | MOE | 6,100 | ○ | ○ |
| | | | | | Indoor air | 11 | µg/m ³ | MOE | 100 | ○ | ○ |

Non-toxic level *

- When a LOAEL is available, it is divided by 10 to obtain a level equivalent to NOAEL.
- When an adverse effect level is available for the short-term exposure, it is divided by 10 to obtain a level equivalent to an adverse effect level for the long-term exposure.

4. Initial assessment of ecological risk

With regard to acute toxicity, reliable data for a 24-h median lethal concentration (LC₅₀) exceeding 10,000,000 µg/L was obtained for the crustacean *Daphnia magna*. Accordingly, based on this acute toxicity value and an assessment factor of 1,000, a predicted no effect concentration (PNEC) exceeding 10,000 µg/L was obtained. With regard to chronic toxicity, reliable data of a 35- to 38-day no observed effect concentration (NOEC) of 216,000 µg/L was obtained for developmental inhibition in the fish species *Pimephales promelas* (fathead minnow). Accordingly, based on this chronic toxicity value and an assessment factor of 100, a predicted no effect concentration (PNEC) of 2,200 µg/L was obtained. The value of 2,200 µg/L obtained from the chronic toxicity to the fish was used as the PNEC for this substance.

The PEC/PNEC ratio was less than 0.0005 for both freshwater bodies and seawater. Accordingly, further work is thought to be unnecessary at this time.

| Hazard assessment (basis for PNEC) | | | Assessment factor | Predicted no effect concentration PNEC (µg/L) | Exposure assessment | | PEC/PNEC ratio | Result of assessment |
|------------------------------------|-----------------|-------------------------------|-------------------|---|---------------------|--|----------------|----------------------|
| Species | Acute / chronic | Endpoint | | | Water body | Predicted environmental concentration PEC (µg/L) | | |
| Fish (fathead minnow) | Chronic | NOEC Developmental inhibition | 100 | 2,200 | Freshwater | <1 | <0.0005 | ○ |
| | | | | | Seawater | <1 | <0.0005 | |

5. Conclusions

| | Conclusions | | Judgment |
|-----------------|---------------------------|---|----------|
| Health risk | Oral exposure | No need for further work. | ○ |
| | Inhalation exposure | Collection of information on health risk from exposure in ambient and indoor air not required at present. | ○ |
| Ecological risk | No need for further work. | | ○ |

[Risk judgments] ○: No need for further work ▲: Requiring information collection
■: Candidates for further work ×: Impossibility of risk characterization
(○) : Though a risk characterization cannot be determined, there would be little necessity of collecting information.
(▲) : Further information collection would be required for risk characterization.