

1	CAS No. 111-90-0	Substance: 2-(2-Ethoxyethoxy)ethanol
<p>Chemical Substances Control Law Reference No.: 2-422 (Diethylene glycol monoalkyl (C=1-4) ether), 7-97 (Polyoxyalkylene (C2-4,8) monoalkyl (or alkenyl) (C1-24) ether (n=1-150))</p> <p>PRTR Law Cabinet Order No.:</p> <p>Molecular Formula: C₆H₁₄O₃</p> <p>Molecular Weight: 134.17</p> <p style="text-align: center;">Structural formula:</p> <div style="text-align: center;"> </div>		

1. General information

The aqueous solubility of this substance is 1.00×10^6 mg/L (20°C), the partition coefficient (1-octanol/water) (log Kow) is -0.54 (pH unknown, 25°C, distilled water), and the vapor pressure is 17 Pa (25°C). The biodegradability (aerobic degradation) is judged to be good (based on a comparison with the biodegradability of similar chemical substances). Further, this substance does not possess hydrolyzable groups.

From the perspective of human health effects, this substance is designated as a Priority Assessment Chemical under the Chemical Substances Control Law. The main uses of this substance are as brake fluid, a solvent for various resins, and a raw material for plasticizers. It is also incorporated into cosmetics as a viscosity reducer, fragrance, and solvent. Additionally, existing information indicates that it is added as a film-forming aid in commercial and household water-based floor polishes. The production and import quantity in fiscal 2022 was 5437 t.

2. Exposure assessment

Because this substance is not classified as a Class 1 Designated Chemical Substance under the PRTR Law, release and transfer quantities could not be obtained. Estimated releases to the atmosphere in fiscal 2022 were 6 t based on the volatile organic compound (VOC) emissions inventory. Predictions of proportions distributed to individual media by use of a Mackay-type level III fugacity model indicate that if equal quantities were released to the atmosphere, water bodies, and soil, then the proportion distributed to soil would be largest.

The maximum expected concentration of exposure to humans via inhalation could not be defined because ambient atmospheric and indoor air quality data could not be obtained. Further, albeit based on a survey for a limited area, a maximum value for indoor air of around $7.1 \mu\text{g}/\text{m}^3$ was obtained.

Data for potable water, ground water, food, and soil to assess oral exposure could not be obtained. Thereupon, assuming ingestion solely from public freshwater bodies, an average daily exposure and maximum predicted daily exposure of around $0.019 \mu\text{g}/\text{kg}/\text{day}$ was obtained. The exposure to this substance by intake from an environmental medium via food is considered slight, given the low bioaccumulation of the substance expected on the basis of its physicochemical properties.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around $0.48 \mu\text{g}/\text{L}$ for public freshwater bodies and around $0.48 \mu\text{g}/\text{L}$ for seawater.

3. Initial assessment of health risk

This substance defats the skin, which may cause dryness or cracking, and mildly irritates the eyes.

Since not enough information was available on the carcinogenicity of the substance, the initial assessment was conducted based on information on its non-carcinogenic effects.

The NOAEL of $167 \text{ mg}/\text{kg}/\text{day}$ for oral exposure (based on hydropic degeneration of the liver and the proximal renal tubules), determined from toxicity tests in pigs, was divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of $17 \text{ mg}/\text{kg}/\text{day}$ was deemed the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The NOAEL of 16 ppm for inhalation exposure (based on necrosis in the ventral cartilage of the larynx), determined from toxicity tests in rats, was adjusted according to exposure conditions to obtain 2.9

ppm (16 mg/m³), and subsequently divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 1.6 mg/m³ was deemed the lowest reliable concentration and was identified as the ‘non-toxic level’ of the substance for inhalation exposure.

Regarding oral exposure, assuming that the substance is absorbed via public freshwater bodies, the predicted maximum exposure level was approximately 0.019 µg/kg/day. The MOE (Margin of Exposure) would be 89,000 which is calculated from the predicted maximum exposure level and the ‘non-toxic level’ of 17 mg/kg/day and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. This would lead to the health risk judgment that no further work would be required at present. Since exposure to the substance in environmental media via food is presumed to be limited despite the lack of exposure level via food, including it in the calculation would not change the MOE significantly. Therefore, as a comprehensive judgment, the collection of further information would not be required to assess the health risk of this substance via oral exposure.

Regarding inhalation exposure, due to the lack of identified exposure concentrations, the health risk could not be assessed. However, the predicted maximum exposure concentration was estimated to be 7.1 µg/m³ based on the measurement data on indoor air in a certain area in 2016. The MOE would be 23 which is calculated from the estimate of the predicted maximum exposure concentration and the ‘non-toxic level’ of 1.6 mg/m³ and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. The concentration in ambient air could not be estimated based on the releases into air, since no data on the release and the transfer of this substance are available without specification as a “Class I Designated Chemical” under the PRTR Law. Therefore, as a comprehensive judgment, the collection of information would be required to assess the health risk of this substance via inhalation in ambient air and in indoor air, starting from the data on the concentrations in ambient air near the operators that are releasing a large amount of the substance and in indoor air.

Toxicity				Exposure assessment		Result of risk assessment		Comprehensive judgment	
Exposure Path	Criteria for risk assessment		Animal	Criteria for diagnoses (endpoint)	Exposure medium				Predicted maximum exposure dose and concentration
Oral	‘Non-toxic level’	17 mg/kg/day	Pigs	Hydropic degeneration of the liver and the proximal renal tubules	Drinking water	– µg/kg/day	MOE	–	○
					Freshwater	0.019 µg/kg/day	MOE	89,000	
Inhalation	‘Non-toxic level’	1.6 mg/m ³	Rats	Necrosis in the ventral cartilage of the larynx	Ambient air	– µg/m ³	MOE	–	▲
					Indoor air	– µg/m ³	MOE	–	▲

Non-toxic level *

- When a LOAEL is available, it is divided by 10 to obtain a NOAEL-equivalent level.
- When an adverse effect level for the short-term exposure is available, 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, the following reliable data were obtained: a 72-h EC₅₀ of 14,900,000 µg/L for growth inhibition in the green alga *Raphidocelis subcapitata*, a 48-h LC₅₀ of 1,982,000 µg/L for the crustacean *Daphnia magna*, a 96-h LC₅₀ of 6,010,000 µg/L for the fish species *Ictalurus punctatus* (channel catfish), and a 48-h EC₅₀ of 7,611,000 µg/L for embryonic development abnormalities in the purple sea urchin species *Arbacia punctulata*. Accordingly, based on this acute toxicity value and an assessment factor of 100, a predicted no effect concentration (PNEC) of 19,000 µg/L was obtained.

Data could not be obtained for chronic toxicity. Accordingly, the value of 19,000 µg/L obtained from the acute toxicity to the crustacean species was used as the PNEC for this substance.

The PEC/PNEC ratio is less than 0.0003 for both freshwater bodies and seawater. According, further work to evaluate ecological risk is considered unnecessary at this time.

Ecotoxicity for this substance was estimated using QSAR because reliable data from the three organism groups for chronic toxicity could not be obtained. The estimates for chronic toxicity for algae and crustaceans showed that there was no effect

at around 100,000 µg/L, indicating no adverse effect. For this reason, even when taking into consideration the predictions for chronic toxicity, based on a comprehensive review of the above findings, further work is considered unnecessary at this time.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (µg/L)	Exposure assessment		PEC/PNEC ratio	Comprehensive judgment
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (µg/L)		
Crustacean <i>Daphnia magna</i>	Acute	LC ₅₀ Mortality	100	19,000	Freshwater	0.48	0.00003	○
					Seawater	0.48	0.00003	

5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work	○
	Inhalation exposure	Requiring information collection	▲
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