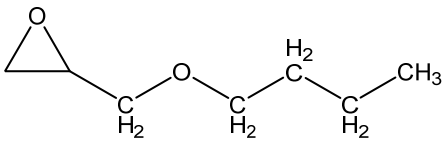
8	CAS No.: 2426-08-6	Substance: *n*-Butyl-2,3-epoxypropylether

Chemical Substances Control Law Reference No.: 2-392
PRTR Law Cabinet Order No.: 1-359 （number after law revision*: 2-97）

Molecular Formula: $C_7H_{14}O_2$
Molecular Weight: 130.18

Structural Formula:



1. General information

The aqueous solubility of this substance is 2×10^4 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.63, and the vapor pressure is 430 Pa (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 40% (mean value), and biodegradability is judged to be good. In addition, this substance hydrolyzes, with a residue ratio after 28 days of 42% (water + test substance). 3-butoxy-1,2-propanediol is formed as the product (46% formation ratio).

This substance is classified as a Class 1 Designated Chemical Substance under the PRTR Law, but it will be reclassified as a Class 2 Designated Chemical Substance by the Cabinet Order partially revising the Enforcement Order for the Act on the Assessment of Releases of Specified Chemical Substances in the Environment and the Promotion of Management Improvement promulgated on October 20, 2021, that will come into force on April 1, 2023.

The main uses of this substances are as an epoxy resin reactive diluent, a chlorinated organic chemical stabilizer, and a cotton modifier. The production and import quantity in fiscal 2019 was less than 1,000 t, and the production and import category under the PRTR Law was more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2019 under the PRTR Law was 0.23 t, and all releases were reported. In addition, approximately 2.6 t was transferred to waste and 0.001 t was transferred to sewage. The chemical industry and electrical machinery manufacturing industry were the main reporters of releases. A multi-media model used to predict the proportions distributed to individual media in the environment indicated that in regions where the largest quantities were estimated to have been released to the environment overall or to the atmosphere, the predicted proportion distributed to the atmosphere would be 81.1%.

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, the mean annual value for atmospheric concentration in fiscal 2019 was calculated by use of a plume-puff model on the basis of releases to the atmosphere reported under the PRTR Law: this model predicts a maximum level of 0.021 μg/m^3.

Data for potable water, groundwater, public freshwater bodies, seawater, food, and soil to assess oral exposure could not be obtained. Further, albeit past data, calculations for public freshwater bodies gave a daily exposure of less than 0.028 μg/kg/day.

Further, while releases to public water bodies in fiscal 2019 were not reported under the PRTR Law, transfer to sewage was reported. When releases to public freshwater bodies estimated from reported transfer to sewage in fiscal 2019 were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.021 μg/L.; the oral exposure calculated thereof is 0.00084 μg/kg/day. 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 less than 0.7 μg/L for both public freshwater bodies and seawater. Further, while releases to public freshwater bodies and seawater in fiscal 2019 were not reported under the PRTR Law, transfer to sewage was reported. When releases to public freshwater bodies estimated from reported transfer to sewage in fiscal 2019 were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.021 μg/L.

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3. Initial assessment of health risk

This substance irritates the eyes, the skin, as well as the respiratory tract. Inhalation will cause a cough and sore throat. Contact to the skin and the eyes will cause redness and pain.

Though the information was not available on the carcinogenicity of the substance to humans, tumorigenesis in nasal cavities was observed in rats and mice of both sexes in the carcinogenesis study by inhalation. Particularly, male mice developed tumors even in the groups exposed to relatively lower concentrations. Considering the necessity to include the carcinogenic risk in the risk assessment, the initial assessment was conducted for both non-carcinogenic and carcinogenic effects.

Neither the 'non-toxic level' nor slope factor could be identified for oral exposure. The non-carcinogenic LOAEL of 0.89 ppm for inhalation exposure (based on cuboidal changes of the respiratory epithelium and respiratory metaplasia of the olfactory epithelium), determined from toxicity tests in mice, was divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.089 ppm (0.47 mg/m^3) was deemed to be the lowest reliable concentration and was identified as the 'non-toxic level' of the substance for inhalation exposure. The unit risk for cancer of 2.2×10^{-5}～2.7×10^{-5}(μg/m^3) $^{-1}$ (based on hemangiomas of the nasal cavity), determined from carcinogenicity tests in male mice, was adopted assuming no threshold.

Regarding oral exposure, due to the lack of identified 'non-toxic level' and exposure levels, the health risk could not be assessed. However, the tentative 'non-toxic level' of 0.14 mg/kg/day for oral exposure was derived from the conversion of the 'non-toxic level' for inhalation exposure, assuming that 100% of the ingested substance is absorbed. The MOE for reference would exceed 100 which is calculated from the tentative 'non-toxic level' for oral exposure and the maximum exposure level of less than 0.028 μg/kg/day derived from the past data on public freshwater bodies in 1984, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans, and by another factor of 5 to take into consideration the carcinogenicity. The excess cancer incidence rate would be less than 2.5×10^{-6} which is calculated from the tentative slope factor of 7.3×10^{-2}～9.0×10^{-2}(mg/kg/day)$^{-1}$ for oral exposure derived from the conversion of the unit risk for inhalation exposure. This could be below or above the judgment criteria. On the other hand, the MOE and the excess cancer incidence rate would be 3,300 and 6.1×10^{-8}～7.6×10^{-8}, respectively, which are calculated from another estimation of the maximum exposure level of 0.00084 μg/kg/day, calculated from the concentration in effluents according to the transfers to the sewage system, reported in FY 2019 under the PRTR Law. 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 maximum concentration (annual mean) in ambient air, near the operators that are releasing a large amount of the substance, was estimated to be 0.021 μg/m^3, based on the releases to air reported in FY 2019 under the PRTR Law. The MOE for reference would be 450 which is calculated from the estimated concentration in ambient air and the 'non-toxic level' of 0.47 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 5 to take into consideration the carcinogenicity. The excess cancer incidence rate would be 4.6×10^{-7}～5.7×10^{-7} which is calculated from the unit risk of 2.2×10^{-5}～2.7×10^{-5}(μg/m^3)$^{-1}$. Therefore, as a comprehensive judgment, the collection of further information would not be required to assess the health risk of this substance via inhalation in ambient air.

Toxicity				Exposure assessment		MOE & Excess incidence rate		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' - mg/kg/day	-	-	Drinking water	- μg/kg/day	MOE	-	○
						Excess incidence rate	-	
	Slope factor - (mg/kg/day)$^{-1}$	-	-	Groundwater	- μg/kg/day	MOE	-	
						Excess incidence rate	-	

Inhalation	'Non-toxic level'	0.47	mg/m^3	Mice	Cuboidal changes of the respiratory epithelium and respiratory metaplasia of the olfactory epithelium	Ambient air	-	µg/m^3	MOE	-	○
									Excess incidence rate	-	
	Unit risk	2.2×10^{-5} ～ 2.7×10^{-5}	(µg/m3)$^{-1}$	Mice	Hemangiomas of the nasal cavity	Indoor air	-	µg/m^3	MOE	-	×
									Excess incidence rate	-	

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.

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4. Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 96-h EC_{50} of 35,000 µg/L for growth inhibition in the green alga species *Raphidocelis subcapitata*, a 48-h EC_{50} of 3,900 µg/L for swimming inhibition in the crustacean species *Daphnia magna*, and a 96-h LC_{50} of 65,000 µg/L for the fish species *Oncorhynchus mykiss* (rainbow trout). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 39 µg/L was obtained.

Reliable chronic toxicity data could not be obtained. Therefore, the value of 39 µg/L obtained from the acute toxicity to the crustacean was used as the PNEC for this substance. Data for setting the predicted environmental concentration (PEC) could not be obtained for this substance. Accordingly, an assessment of ecological risk could not be made.

Further, albeit past data (more than ten years old), a maximum value of less than 0.7 µg/L was reported for public freshwater bodies and seawater. The ratio of this value to PNEC is less than 0.02. In addition, when releases to public freshwater bodies estimated from reported transfer to sewage in fiscal 2019 were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.021 µg/L. The ratio of this value to PNEC is 0.0005.

Accordingly, 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 *Daphnia magna*	Acute	EC_{50} Swimming inhibition	100	39	Freshwater	—	—	○
					Seawater	—	—	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work	○
	Inhalation exposure	No need for further work	○
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

*Note: Number after revision of law to be implemented on April 1, 2023