13	CAS No.: 106-91-2	Substance: 2,3-Epoxypropyl methacrylate

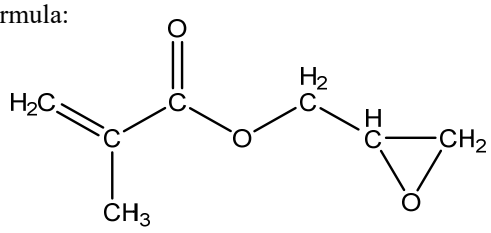
Chemical Substances Control Law Reference No.: 2-1041

PRTR Law Cabinet Order No.: 1-417

Molecular Formula: $C_7H_{10}O_3$

Molecular Weight: 142.15

Structural Formula:



1.General information

The aqueous solubility of this substance is approximately 5×10^4 mg/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.96 (25°C), and the vapor pressure is 3.2 mmHg (= 420 Pa) (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 94%, and degradability is judged to be good. Its half-life for hydrolysis is 2.83 d (pH = 4, 25°C), 3.66 d (pH = 7, 25 °C), and 2.22 d (pH = 9, 25°C).

This substance is classified as a Class 1 Designated Chemical Substance under the PRTR Law. This substance is used mainly as a raw material for automotive coating resins. It is also used as a raw material for various synthetic resins including resin modifiers and adhesive resins. The production and import quantity in fiscal 2016 was 7,000 t. The production and import category under the PRTR Law is more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2016 under the PRTR Law was approximately 2.2 t (reported releases) . In addition, approximately 58 t was transferred to waste materials and 0.0003 t to sewage. The chemical industry reported large releases to both the atmosphere and public water bodies. A multi-media model used to predict the proportions distributed to individual media in the environment indicates that in regions where the largest quantities were estimated to have been released to the environment overall or the atmosphere in particular, the predicted proportion distributed to water bodies was 96.6%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around less than 0.059 μg/m^3. The mean annual value for the atmospheric concentration in fiscal 2016 was calculated by use of a plume-puff model on the basis of releases to the atmosphere reported according to the PRTR Law; this model predicts a maximum level of 0.25 μg/m^3.

Data for potable water, ground water, public freshwater bodies, food and soil to assess oral exposure could not be obtained. When releases to public freshwater bodies in fiscal 2016 reported according to the PRTR Law 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 gives a maximum value of 0.0030 μg/L. Using this estimated concentration for rivers to calculate oral exposure gives 0.00012 μg/kg/day. The risk of 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.

Data capable of withstanding assessment for water quality could not be obtained and therefore, the predicted environmental concentration (PEC) could not be set. When releases to public freshwater bodies in fiscal 2016 reported according to the PRTR Law 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 gives a maximum value of 0.0030 μg/L.

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3. Initial assessment of health risk

This substance is severely irritating to the eyes, skin and respiratory tract. The substance causes cough, sore throat and labored breathing if inhaled, and causes sore throat, burning sensation in the throat and chest and abdominal pain if ingested. Contact with the skin or eyes causes redness, pain and burns.

As sufficient information on the carcinogenicity in humans was not available, it could not be determined whether the substance is carcinogenic to humans or not. However, significant and dose-dependent tumorigenesis in nasal cavity, peritoneum and mammary glands was observed in all dose-groups in the carcinogenesis study by inhalation in rats. Considering the above, assessment of the carcinogenic risk was deemed necessary as well, and initial assessment was conducted for both non-carcinogenic and carcinogenic effects.

The non-carcinogenic NOAEL of 10 mg/kg/day for oral exposure (based on squamous cell hyperplasia in forestomach), determined from toxicity tests in rats, was divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 1.0 mg/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level*' of the substance for oral exposure. No information enabling the determination of the cancer slope factor for oral exposure assuming no threshold could be obtained. The non-carcinogenic LOAEL of 0.6 ppm for inhalation exposure (based on respiratory metaplasia of olfactory epithelium and gland, and eosinophilic change in nasopharynx), determined from toxicity tests in mice, were adjusted according to exposure conditions to obtain 0.107 ppm (0.62 mg /m^3) and subsequently divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.062 mg/m^3 was deemed to be the lowest reliable dose and was identified as the 'non-toxic level*' of the substance for inhalation exposure. Since the unit risk for cancer assuming no threshold was not available, benchmark-dose modeling was applied to estimate the unit risk value. The unit risk for which the excess incidence rate of cancer was the highest identified by this original calculation ranged from 5.8×10^{-5} to 6.7×10^{-5} $(\mu g/m^3)^{-1}$. This range was determined on the basis of mesothelioma incidence in male rats.

With regard to oral exposure, owing to the lack of identified exposure levels, the health risk could not be assessed. The maximum exposure level, estimated according to the concentration in effluents from the high discharging plants reported in FY 2016 under the PRTR Law, would be 0.00012 μg/kg/day. The MOE would be 170,000, when calculated from this level and the 'non-toxic level*'of 1.0 mg/kg/day, 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 in animals. The slope factor converted from the unit risk for inhalation exposure to oral exposure would be 0.19-0.22$(mg/kg/day)^{-1}$. The excess cancer incidence rate would be less than 2.3×10^{-8} - 2.6×10^{-8}, when calculated from the slope factor above. Since exposure to the substance in environmental media via food is presumed to be limited, including it in the calculation would change neither the MOE nor the excess incidence rate significantly. Therefore, no further work would be required at present to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, the predicted maximum exposure concentration in ambient air was less than 0.059 μg/m^3, approximately. The MOE would exceed 21, when calculated from the predicted maximum exposure concentration and the 'non-toxic level*'of 0.062 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 in animals. The excess cancer incidence rate corresponding to the predicted maximum exposure concentration would be less than 3.4×10^{-6} - less than 4.0×10^{-6}, when calculated from the unit risk. On the other hand, the maximum concentration (annual mean) in ambient air near the operators releasing large amount of this substance was estimated to be 0.25 μg/m^3 based on the releases to air reported in FY 2016 under the PRTR Law. The MOE would be 5 and the excess incidence rate would be comprised between 1.5×10^{-5} and 1.7×10^{-5}, respectively falling below 100 and exceeding 10^{-6}, when calculated from this concentration. Therefore, collection of information would be required to assess the health risk of this substance via inhalation in ambient air, starting from data on concentrations in ambient air near the operators releasing large amount of

this substance.

Toxicity						Exposure assessment		Result of risk assessment		Judgment
Exposure Path	Criteria for risk assessment			Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration			
Oral	'Non-toxic level*'	1.0	mg/kg/day	Rats	Squamous cell hyperplasia in forestomach	Drinking water	- μg/kg/day	MOE	-	○
								Excess incidence rate	-	
	Slope factor	-	$(mg/kg/day)^{-1}$	-	-	Public freshwater bodies	- μg/kg/day	MOE	-	
								Excess incidence rate	-	
Inhalation	'Non-toxic level*'	0.062	mg/m^3	Mice	Respiratory metaplasia of olfactory epithelium and gland, and eosinophilic change in nasopharynx	Ambient air	<0.059 $\mu g/m^3$	MOE	>21	(▲)
								Excess incidence rate	$<4.0\times10^{-6}$	
	Unit risk	5.8×10^{-5} - 6.7×10^{-5}	$(\mu g/m^3)^{-1}$	Rats	Mesothelioma	Indoor air	- $\mu g/m^3$	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 72-h EC_{50} of 32,200 μg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 24,900 μg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 2,830 μg/L for the fish species *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 28 μg/L is obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 2,360 μg/L for growth inhibition in the green algae *P. subcapitata* and a 21-d NOEC of 1,020 μg/L for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 10 μg/L is obtained.

The value of 10 μg/L obtained from the chronic toxicity to the crustacean species 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. However, when releases to public freshwater bodies in fiscal 2016 reported according to the PRTR Law 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 gives a maximum value of 0.0030 μg/L and the ratio of this value to the PNEC is 0.0003; accordingly, there is little need to collect new data regarding this substance.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Crustacean *Daphnia magna*	Chronic	NOEC reproductive inhibition	100	10	Freshwater	—	—	○
					Seawater	—	—	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	Further efforts to collect data required based on comprehensive review of existing relevant data.	(▲)
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

（▲）: Further efforts to collect data required based on comprehensive review of existing relevant data

（■）: Candidate for further work based on comprehensive review of existing data