6	CAS No. 2451-62-9	Substance: 1,3,5-Tris(2,3-epoxypropyl)-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione

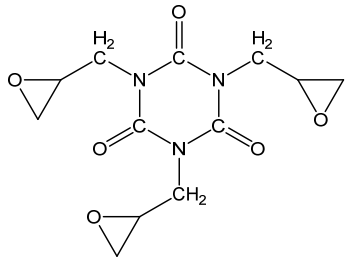
Chemical Substances Control Law Reference No.: 5-1052

PRTR Law Cabinet Order No.: 291

Molecular Formula: $C_{12}H_{15}N_3O_6$

Molecular Weight: 297.26

Structural formula:



1.General information

The aqueous solubility of this substance is 1.300×10^4 mg/L (0°C), the partition coefficient (1-octanol/water) (log Kow) is -1.07 (24.1°C, pH = 6.3, distilled water), and the vapor pressure is less than 7.2×10^{-4} Pa (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and the substance is not judged to be highly bioaccumulative. In addition, the half-life for hydrolysis was 5 d (pH = 7, 22°C), whereby hydrolysis products formed.

This substance is designated as a Class 2 Chemical Substance under the PRTR Law.

This substance is used as a curing agent for polyester powder coatings, a modifier for high-heat-generating electrical component molding materials, a modifier for solder resist ink (the ink coating printed circuit board surfaces), and as a raw material for optical semiconductor encapsulation resins. The production and import quantity in fiscal 2022 was 4000 t.

2.Exposure assessment

This substance was classified as a Class 1 Designated Chemical Substance prior to revision of substances regulated by the PRTR Law. Total release to the environment in fiscal 2022 under the PRTR Law was 0.018 t, and all releases were notified. A high proportion of notified releases was to public water bodies. Further, 0.0002 t was transferred to sewage, and approximately 26 t was transferred to waste. The major source of notified releases to both the atmosphere and public water bodies was the electrical equipment manufacturing industry. 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 and public water bodies in particular, the predicted proportion distributed to water bodies would be 99%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around 0.000040 μg/m^3. Further, the mean annual value for atmospheric concentration in fiscal 2022 was calculated by use of a plume-puff model on the basis of releases to the atmosphere notified under the PRTR Law for fiscal 2022: this model predicts a maximum level of 0.000079 μg/m^3.

Data for potable water, groundwater, 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 0.0011 μg/kg/day was obtained. Further, when releases reported under the PRTR Law in fiscal 2022 to public freshwater bodies estimated from the reported transfer to public freshwater bodies 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 0.016 μg/L. Calculating oral exposure based on this river concentration estimates gave a value of 0.00064 μg/kg/day. Transfers from sewage to rivers under the PRTR Law varies from year to year. For this reason, an assessment was carried out on the side of safety using data from fiscal 2017, representing a recent year for which transfers were at a high level. This gave a maximum predicted river concentration of 0.028 μg/L. Calculating oral exposure based on this river concentration estimates gave a value of 0.0011 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.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around 0.027 μg/L for public freshwater bodies. Data to set the predicted environmental concentration (PEC) for seawater could not be obtained. Further, when releases reported under the PRTR Law in fiscal 2022 to public freshwater bodies estimated from the reported transfer to public freshwater bodies 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 0.016 μg/L. Transfers to sewage under the PRTR Law vary from year to year. For this reason, an assessment was carried out erring on the side of caution using data from fiscal 2017, representing a recent year when transfers were at a high level. This gave a maximum predicted river concentration of 0.028 μg/L.

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3. Initial assessment of health risk

This substance severely irritates the eyes. Contact with the eyes will cause redness and pain.

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 for general toxicity of 30 ppm (1.3 mg/kg/day) for oral exposure (based on the suppression of body weight gain), determined from chronic toxicity tests in rats, was deemed the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The NOAEL of 1.79 mg/m^3 for inhalation exposure (based on toxic effects on spermatogonia and reduced fertility in males), determined from toxicity tests in mice, was adjusted according to exposure conditions to obtain 0.45 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.045 mg/m^3 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 alone, the predicted maximum exposure level was approximately 0.0011 μg/kg/day. The MOE (Margin of Exposure) would be 120,000 which is calculated from the predicted maximum exposure level and the 'non-toxic level' of 1.3 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. The oral exposure level was estimated to be 0.00064 μg/kg/day on the assumption that the concentration in river water could be calculated as a quotient of the release into public freshwater bodies reported in FY 2022 under the PRTR Law by the water flow based on the ordinary discharge obtained from the national river-networking structure database by considering dilution alone. The MOE for reference would be 200,000 which is calculated from the estimated exposure level and the 'non-toxic level' of 1.3 mg/kg/day and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. When the concentration in river water was estimated in the same way as the above using the data in FY 2017 when the discharge into rivers from sewage systems was highest in recent years in order to make a conservative assessment considering the yearly fluctuation in the transfers to sewage systems under the PRTR Law, the oral exposure level would be 0.0011μg/kg/day, giving an MOE of 120,000. Since exposure to the substance in environmental media via food is presumed to be limited according to the inference that the substance is not highly bioconcentrative, including it in the calculation would not change the MOE significantly. Therefore, as a comprehensive judgment, no further work would be required at present.

Regarding inhalation exposure, the predicted maximum exposure concentration in ambient air was approximately 0.000040 μg/m^3 based on measurement data. The MOE would be 110,000 which is calculated from the predicted maximum exposure concentration and the 'non-toxic level' of 0.045 mg/m^3 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. The maximum concentration (annual mean) in ambient air near the operators that are releasing a large amount of the substance was estimated to be 0.000079 μg/m^3 based on the releases into air reported in FY 2022 under the PRTR Law. The MOE for reference would be 57,000 which is calculated from the estimated maximum concentration (annual mean) in ambient air and the 'non-toxic level' of 0.045 mg/m^3 and subsequently divided by a factor of 10 to account for extrapolation

from animals to humans. Therefore, as a comprehensive judgment, no further work would be required at present.

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'	1.3 mg/kg/day	Rats	Suppression of body weight gain	Drinking water	– μg/kg/day	MOE	–	○
					Freshwater	0.0011 μg/kg/day	MOE	120,000	
Inhalation	'Non-toxic level'	0.045 mg/m^3	Mice	Toxic effects on spermatogonia and reduced fertility in males	Ambient air	0.000040 μg/m^3	MOE	110,000	○
					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.

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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 29,000 μg/L for growth inhibition in the green alga *Desmodesmus subspicatus*, a 24-h EC_{50} exceeding 100,000 μg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h LC_{50} exceeding 77,000 μg/L for the fish *Danio rerio* (zebra fish). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 290 μg/L was obtained.

With regard to chronic toxicity, the following reliable data was obtained: a 72-h NOEC of 6300 μg/L for growth inhibition in the green alga *D. subspicatus*. Accordingly, based on this chronic toxicity value and an assessment factor of 100, a predicted no effect concentration (PNEC) of 63 μg/L was obtained

The value of 63 μg/L obtained from the chronic toxicity to the green alga was used as the PNEC for this substance.

Data for setting the predicted environmental concentration (PEC) for seawater could not be obtained for this substance. The freshwater PEC/PNEC ratio was 0.0004. Accordingly, further work to evaluate ecological risk is considered unnecessary at this time.

When releases reported under the PRTR Law in fiscal 2022 to public freshwater bodies in fiscal 2022 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 0.016 μg/L, and the ratio of this value to PNEC is 0.0003. In addition, estimating river concentration based on data from fiscal 2017 when releases to rivers from sewage were at a recent high gives a maximum of 0.028 μg/L and the ratio of this value to PNEC is 0.0004.

In chronic toxicity studies on crustaceans, the toxicity value of this substance was, from the perspective of its partial structure, inferred to be lower than the minimum toxicity value (32,000 μg/L) observed for a group of similar substances possessing an isocyanuric acid structure. However, whether the value would fall below the toxicity values for algae and other organisms (6300 μg/L), which form the basis for the PNEC, or not could not be inferred, and no additional information was obtained that would allow the derivation of a PNEC reference value.

Based on the above, further work to evaluate ecological risk 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)		
Green algae	Chronic	NOEC Growth inhibition	100	63	Freshwater	0.027	0.0004	○
					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