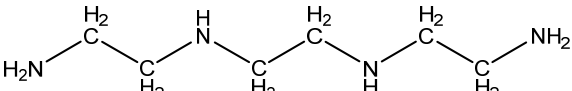


6	CAS No.: 112-24-3	Substance: Triethylenetetramine
Chemical Substances Control Law Reference No.: 2-163		
PRTR Law Cabinet Order No.: 1-278 (number after law revision*: 2-70)		
Molecular Formula: C ₆ H ₁₈ N ₄		
Molecular Weight: 146.23	Structural formula:	
		

1. General information

The aqueous solubility of this substance is 4.77×10^6 mg/L, the partition coefficient (1-octanol/water) ($\log K_{ow}$) is -2.7 (calculated value), and the vapor pressure is 0.0549 Pa (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0% and the bioaccumulation of the substance is thought to be limited. In addition, this substance does not hydrolyze.

This substance was classified as a Class 1 Designated Chemical Substance under the PRTR Law, but it was removed from the classification 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, which came into force on April 1, 2023.

The main use of this substance is as a raw material for other chemical products such as wet strength agents, lubricant additives, chelating agents, and surfactants. It is also used as a curing agent for epoxy resins. The production and import quantity in fiscal 2020 was less than 7,000 t. The production and import category under the PRTR Law was more than 100 t.

2. Exposure assessment

Total release to the environment in fiscal 2020 under the PRTR Law was approximately 4.2 t, of which approximately 3.1 t or 73% were notified releases. The majority of notified releases to the atmosphere and public water bodies were to public water bodies. In addition, approximately 19 t was transferred to waste and 0.0006 t to sewage. Major sources of notified releases were the electrical machinery manufacturing industry and the metal products manufacturing industry for releases to the atmosphere and the chemical industry for releases to public water bodies. Including unnotified releases, the majority of releases to the environment were to water bodies. 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 public water bodies in particular, the predicted proportion distributed to water bodies would be 97.3%, and where the largest quantities were estimated to have been released to public water bodies, the predicted proportion distributed to water bodies would be 97.0%.

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 2020 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 $0.081 \mu\text{g}/\text{m}^3$.

Data for potable water, groundwater, food, and soil to assess oral exposure could not be obtained. Thereupon, assuming ingestion solely from public freshwater bodies, a maximum predicted exposure of around less than $0.00048 \mu\text{g}/\text{kg}/\text{day}$ was obtained. However, when notified releases under the PRTR Law to public freshwater bodies in fiscal 2020 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 $0.11 \mu\text{g}/\text{L}$, and the oral exposure calculated thereof was $0.0044 \mu\text{g}/\text{kg}/\text{day}$.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around less than $0.012 \mu\text{g}/\text{L}$ for both public freshwater bodies and seawater. When reported releases to public freshwater bodies in fiscal

2020 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 0.11 µg/L.

3. Initial assessment of health risk

This substance is corrosive to the eyes, the skin and the respiratory tract. Inhalation will cause sore throat, cough, burning sensation, labored breathing, and shortness of breath and may cause lung edema. Ingestion will cause burns in the mouth and the throat, a burning sensation in the throat and the chest, abdominal pain, as well as shock or collapse. Contact with the skin will cause redness, pain, burns, and blisters. Contact with the eyes will cause redness, pain, loss of vision, and severe deep burns.

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 LOAEL of 15 mg/kg/day for oral exposure of triethylenetetramine dihydrochloride (based on copper excretion), determined from observed effects in humans, was converted to triethylenetetramine equivalent to obtain 10 mg/kg/day, and subsequently divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 1 mg/kg/day was deemed the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The 'non-toxic level' for inhalation exposure could not be identified.

Regarding oral exposure, the predicted maximum exposure level would be approximately less than 0.00048 µg/kg/day, assuming that the substance is absorbed via public freshwater bodies. The MOE (Margin of Exposure) would exceed 2,100,000 which is calculated from the 'non-toxic level' of 1 mg/kg/day and the predicted maximum exposure level. This would lead to the health risk judgment that no further work would be required at present. In addition, the MOE for reference would be 230,000 which is calculated from the maximum exposure level of 0.0044 µg/kg/day, estimated from the concentration in effluents from the high discharging plants based on the releases to public freshwater bodies reported in FY 2020 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, no further work would be required at present.

Regarding inhalation exposure, due to the lack of identified 'non-toxic level' and exposure concentrations, the health risk could not be assessed. However, the tentative 'non-toxic level' of 3.3 mg/m³ for inhalation exposure was derived from the conversion of the 'non-toxic level' for oral exposure, assuming that 100% of the inhaled substance is absorbed. The MOE for reference would be 41,000 which is calculated from the tentative 'non-toxic level' for inhalation exposure and the maximum concentration (annual mean) of 0.081 µg/m³ in ambient air near the operators that are releasing a large amount of the substance based on the releases to air reported in FY 2020 under the PRTR Law. 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		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 mg/kg/day	Humans	Excretion of copper	Drinking water	- µg/kg/day	MOE	-	○
				Freshwater	<0.00048 µg/kg/day	MOE	>2,100,000	
Inhalation	'Non-toxic level*' - mg/m ³	-	-	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 96-h EC₅₀ of 3,700 µg/L growth inhibition in the green alga *Raphidocelis subcapitata*, a 48-h EC₅₀ of 33,900 µg/L for swimming inhibition in the crustacean *Daphnia magna*, and a 96-h LC₅₀ exceeding 110,000 µg/L for the fish *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 37 µg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 468 µg/L for growth inhibition in the green alga *R. subcapitata* and a 21-h NOEC of 2,860 µg/L for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 4.6 µg/L was obtained.

The value of 4.6 µg/L obtained from the chronic toxicity to the green alga was used as the PNEC for this substance.

The PEC/PNEC ratio was less than 0.003 for both freshwater bodies and seawater. Further work to assess the ecological risk of this substance is considered unnecessary at this time. When reported releases to public freshwater bodies in fiscal 2020 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 0.11 µg/L. The ratio of this value to PNEC is 0.02. Further work to assess the ecological risk of this substance 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	4.6	Freshwater	<0.012	<0.003	○
					Seawater	<0.012		

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 implemented on April 1, 2023