9	CAS No.: 139-13-9	Substance: Nitrilotriacetic acid

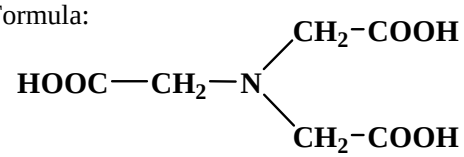
Chemical Substances Control Law Reference No.: 2-1276

PRTR Law Cabinet Order No.: 1-233

Molecular Formula: $C_6H_9NO_6$

Molecular Weight: 191.14

Structural Formula:



1. General information

The aqueous solubility of this substance is 5.91 x 10^4 mg/L (25°C) and the partition coefficient (1-octanol / water) (log Kow) is -3.81. The vapor pressure is 3.00 x 10^{-5} mmHg (= 4.00 x 10^{-3} Pa) (25°C). The substance is determinated to be persistent but not highly bioaccumulative. In addition, it does not have hydrolyzable groups.

This substance is a Type 2 Monitoring Chemical Substance under the Law Concerning the Examination and Regulation of Manufacture, etc. of Chemical Substances and a Class 1 Designated Chemical Substance under the Law concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management (PRTR Law). Its primary uses are as a cleaning agent builder, water softening agent, surfactant additive, depleting agent for radioactive contamination, synthesis and chelating agent, and eluting agent for the refining of rare earth elements. Production and import quantities under the PRTR Law came to 100 tons.

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2. Exposure assessment

Total release to the environment in FY2003 under the PRTR Law came to 0.14 tons, all of which was reported. All of the reported quantity was released to the public water bodies. Chemical Industry accounted for all of the reported release.

The distribution into each environmental medium as determined by means of a multimedia model was 99.2% for water bodies.

No predicted maximum exposure concentration for inhalation exposure to human beings could be established. The predicted maximum oral exposure was estimated to be 6.8 μg/kg/day. As this substance is released to water bodies and the probability of distribution in water bodies is high, a study of exposure from drinking water is thought to be needed.

The predicted environmental concentration (PEC) that indicates exposure to aquatic organisms was estimated to be 130 μg/L for freshwater public water bodies. However, a PEC based on measurement data for seawater public water bodies could not be established.

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3. Initial assessment of health risk

Even brief exposure to this substance may result in irritation of the eyes, skin and respiratory tract. If inhaled, it may cause coughing and sore throat. Contact with the eyes or skin may cause redness.

There are many studies that show evidence that this substance causes cancer in laboratory animals, and the substance probably causes cancer in humans as well. This is thought to be due to cytotoxicity at high concentrations; the possibility that it is caused by genetic damage is thought to be low. Accordingly, a threshold value was judged to exist for carcinogenicity of the substance. While it is difficult to show the threshold value for carcinogenicity, it probably is a higher value than the concentration at which the non-carcinogenic effects were evident. Accordingly, an initial assessment of the substance was conducted based on information of non-carcinogenic effects.

As the ‘Non-toxic level’ was observed, used to estimate the margin of exposure (MOE), a no observed adverse effect level (NOAEL) of 0.03% (concentration in feed; 10 – 20 mg/kg/day when converted into the substance; end point = nephrosis), obtained from rat medium- and long-term toxicity testings, was obtained for oral exposure. To provide a safety margin, a value of 10 mg/kg/day was established. It was not possible to establish a ‘Non-toxic level’ for

inhalation exposure.

With regard to oral exposure, when intake of food and freshwater from public water bodies was postulated, the maximum predicted exposure was 6.8 μg/kg/day. As the 'Non-toxic level' of 10 mg/kg/day and the maximum predicted exposure were established by means of animal testing, the value was divided by 10, and out of consideration for carcinogenicity, it was further divided by 5 to derive an MOE of 29. Accordingly, efforts to collect information with regard to the health risk from oral exposure to this substance are needed.

With regard to inhalation exposure, it was not possible to determine the health risk. However, as the substance is released to the environment in water bodies only, and subsequently it is predicted that almost all of the substance will be distributed in water bodies, there is thought to be little need to gather information, etc. on inhalation exposure in order to evaluate the health risk with regard to inhalation exposure to the substance in the ambient air.

Knowledge of toxicity				Exposure assessment		Result of risk assessment			Judgment
Exposure path	Guidelines for risk assessment	Animal	Impact assessment guideline (endpoint)	Exposure medium	Predicted maximum exposure quantity and concentration				
Oral	No observed adverse effect level 10 mg/kg/day	Rat	Nephrosis	Drinking water / food	– μg/kg/day	MOE	–	×	▲
				Freshwater / food	6.8 μg/kg/day	MOE	29	▲	
Inhalation	No observed adverse effect level –	–	–	Ambient air	– μg/m^3	MOE	–	×	×
				Indoor air	– μg/m^3	MOE	–	×	×

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4. Initial assessment of ecological risk

With regard to acute toxicity, reliable information of a 72-hour EC_{50} growth inhibition value of 30,000 μg/L was found for the algae *Pseudokirchneriella subcapitata*, a 48-hour EC_{50} immobilization value of 106,815 μg/L was found for the crustacea *Daphnia magna* (water flea), and a 96-hour LC_{50} value exceeding 100,000 μg/L was found for the fish *Oryzias latipes* (medaka). Accordingly, an assessment factor of 100 was used, and a predicted no effect concentration (PNEC) of 300 μg/L was obtained based on the acute toxicity values. With regard to chronic toxicity, reliable information of a 72-hour no observed effect concentration (NOEC) growth inhibition value of 300 μg/L was found for the algae *P. subcapitata*, and a 21-day NOEC reproduction value of 30,000 μg/L was found for the crustacea *D. magna*. Accordingly, an assessment factor of 100 was used, and a PNEC value of 3 μg/L was obtained based on the chronic toxicity values. As the PNEC for the substance, a value of 3 μg/L obtained from the chronic toxicity for the algae was used.

The PEC/PNEC ratio was 40 for freshwater bodies. This substance is thought to be a candidate for further work.

Hazard assessment (basis for PNEC)			Assessment factor	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/PNEC ratio	Result of assessment
Species	Acute / chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Algae	Chronic	NOEC growth inhibition	100	3	Freshwater	130	40	■
					Seawater	–	–	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Efforts to gather information are needed.	▲
	Inhalation exposure	Risk cannot be determined. However, there is thought to be comparatively little need to collect information, etc.	×
Ecological risk	This substance is thought to be a candidate for further work.		■

［Risk judgments］ ○: No need of further work ▲: Requiring information collection
■: Candidates for further work ×: Impossible of risk characterization