4	CAS No.: 76-05-1	Substance: Trifluoroacetic acid

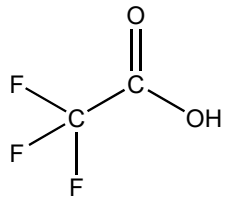
Chemical Substances Control Law Reference No.: 2-1185

PRTR Law Cabinet Order No.

Molecular Formula: $C_2HF_3O_2$

Molecular Weight: 114.02

Structural Formula:



1. General information

The aqueous solubility of this substance is 1.00×10^6 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.50 (calculated value), and the vapor pressure is 1.51×10^4 Pa (25°C). This substance has been reported to not biodegrade (aerobic degradation). Further, this substance is believed to not hydrolyze under ambient environmental conditions because it does not possess any hydrolyzable groups.

The main uses of this substance are as a raw material for catalysts, agricultural chemicals, and pharmaceuticals, and as a raw material for various intermediates. In addition, it is used as a blocking and deblocking promoter in the synthesis of peptides and antibiotics, as well as a reaction solvent for synthesizing proteins and an analytical solvent for NMR. In addition, the production and import quantity in fiscal 2019 was not disclosed because the number of reporting businesses was less than two.

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2. Exposure assessment

Because this substance is not classified as a Class 1 Designated Chemical Substance under the PRTR Law, release and transfer quantities could not be obtained. Predictions of proportions distributed to individual media by use of a Mackay-type level III fugacity model indicate that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to water bodies would be largest.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around 0.085 μg/m^3.

Data for potable water, groundwater, food, and soil to assess oral exposure could not be obtained. Further, assuming intake solely from public freshwater bodies, the maximum expected exposure was around 0.0084 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.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around 0.21 μg/L for public freshwater bodies and around 0.42 μg/L for seawater.

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3. Initial assessment of health risk

This substance is corrosive. Inhalation of this substance will cause a cough, sore throat, burning sensation, and labored breathing, and inhalation of the fumes may cause lung edema. Ingestion will cause a burning sensation in the throat and chest, abdominal pain, and shock or collapse. Contact to the skin will cause redness, pain, and serious skin burns. Contact to the eyes will cause redness, pain, and severe deep burns. It is considered that this substance does not undergo metabolic decomposition *in vivo*.

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 of 8.2 mg/kg/day for oral exposure (based on the increased weight of the liver, hepatocellular hypertrophy, and the increased levels of AST and ALT), determined from toxicity tests in rats, was divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.82 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. The 'non-toxic level' for inhalation exposure could not be identified.

Regarding oral exposure, assuming that the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.0084 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 9,800 which is calculated from the predicted maximum exposure level and the 'non-toxic level' of 0.82 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. 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 to assess the health risk of this substance via oral exposure.

Regarding inhalation exposure, due to the lack of identified 'non-toxic level', the health risk could not be assessed. However, the tentative 'non-toxic level' of 2.7 mg/m^3 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 3,200 which is calculated from the tentative 'non-toxic level' for inhalation exposure and the predicted maximum concentration in ambient air of 0.085 μg/m^3 approximately, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. 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' 0.82 mg/kg/day	Rats	The increased weight of the liver, hepatocellular hypertrophy, and increased levels of AST and ALT	Drinking water	- μg/kg/day	MOE	-	○
				Public Freshwater bodies	0.0084 μg/kg/day	MOE	9,800	
Inhalation	'Non-toxic level' - mg/m^3	-	-	Ambient air	0.085 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.

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4. Initial assessment of ecological risk

With regard to acute toxicity (for trifluoroacetic acid), the following reliable data were obtained: a 72-h EC_{50} of 11,400 μg/L for growth inhibition in the green alga species *Raphidocelis subcapitata*, a 48-h EC_{50} of 9,000,000 μg/L for swimming inhibition in the crustacean species *Daphnia magna*, a 96-h LC_{50} exceeding 8,000,000 μg/L for the fish species *Danio rerio* (zebra fish), and a 24-h LC_{50} of 70,000 μg/L for the planktonic rotifer *Brachionus calyciflorus*. Accordingly, based on these acute toxicity values and an assessment factor of 1,000, a PNEC of 110 μg/L was obtained.

With regard to chronic toxicity (for trifluoroacetic acid), the following reliable data were obtained: a 72-h NOEC of 100 μg/L for growth inhibition in the green alga species *R. subcapitata*, a 21-d NOEC of 25,000 μg/L for reproductive inhibition in the crustacean *D. magna*, and a 14-d NOEC of 30,000 μg/L for growth inhibition in the spiked water-milfoil *Myriophyllum spicatum*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 1 μg/L was obtained.

The value of 1 μg/L obtained from the chronic toxicity to the alga was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.2 for freshwater bodies and 0.4 for seawater; accordingly, efforts to collect data to judge ecological risk are considered necessary. A comprehensive review of the above findings draws the same conclusion. A delay in hatching of zebrafish embryos was observed in 6-day post-fertilization tests for this substance and efforts to collect data regarding chronic toxicity towards fish species are thus considered necessary. In addition, augmentation of environmental

concentration data is considered necessary after collecting data regarding emission sources.

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	1	Freshwater	0.21	0.2	▲
					Seawater	0.42	0.4	

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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	Requiring information collection		▲

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