1	CAS No: 105-39-5	Substance: Ethyl chloroacetate

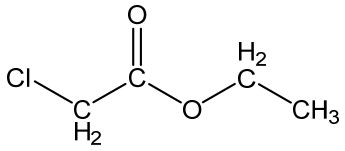
Chemical Substances Control Law Reference No.: 2-1149 (Monochloroacetic acid alkyl (C1-5) ester)

PRTR Law Cabinet Order No.: 1-99

Molecular Formula: $C_4H_7ClO_2$

Molecular Weight: 122.55

Structural Formula:



1. General information

The aqueous solubility of this substance is 1.23×10^4 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.94 (pH=5.0), the vapor pressure is 640 Pa (25°C), and its biodegradability (aerobic degradation) is 75% based on oxygen consumption. In addition, this substance hydrolyzes under acidic and basic conditions. Water soluble ethyl alcohol and chloroacetate are included among acid hydrolysis products while glycolic acid is formed by alkaline hydrolysis.

This substance is classified as a Class 1 Designated Chemical Substance under the PRTR Law, but it is to be 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, that will come into force on April 1, 2023.

The main uses of this substance are as a raw material for pharmaceuticals, fragrances, agricultural chemicals, adhesives and surfactants. The production and import quantity of monochloroacetic acid alkyl (C1–5) ester in fiscal 2019 was less than 1,000 t. The production and import category under the PRTR Law was over 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2019 under the PRTR Law was approximately 0.25 t; all of the releases were unnotified releases. In addition, 0.21 t was transferred to sewage. The largest unnotified 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 the atmosphere and public water bodies, the predicted proportion distributed to water bodies would be 97.2%.

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. In any case, atmospheric concentrations are believed to be low given that no releases to the atmosphere were reported under the PRTR Law.

Data for potable water, groundwater, public water bodies, seawater, food, and soil to assess oral exposure could not be obtained. However, albeit past data for a limited area, calculations for groundwater and public freshwater bodies gave a daily exposure of less than around 0.04 μg/kg/day. Further, when releases to public freshwater bodies estimated from reported transfer to sewage in fiscal 2019 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 3.0 μg/L, and the oral exposure calculated thereof was 0.12 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 for setting the predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be obtained. Further, past data indicated a maximum value of less than 1 μg/L for both public freshwater bodies and seawater.

Further, while there were no reported releases to public freshwater bodies under the PRTR Law in fiscal 2019, when the releases to public freshwater bodies estimated from reported transfer to sewage in fiscal 2019 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 3.0 μg/L.

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3. Initial assessment of health risk

This substance undergoes metabolic hydrolysis by the esterases *in vivo* to monochloroacetic acid and ethanol. This substance moderately irritates the respiratory tract and the skin and severely irritates the eyes, while the monochloroacetic acid produced by metabolic hydrolysis is corrosive to the eyes, the skin as well as the respiratory tract.

Not enough information was available on the carcinogenicity of the substance. As for non-carcinogenic effects, neither the 'non-toxic level' for oral exposure nor that for inhalation exposure could be identified due to the lack of evidence.

Regarding oral exposure, due to the lack of identified 'non-toxic level' and exposure levels, the health risk could not be assessed. In consideration of the fact that this substance is neither corrosive nor severely irritating, the systemic effect caused by monochloroacetic acid, a hydrolysis product of this substance, is likely the principal toxic effect of this substance. For reference, the LOAEL of 3.5 mg/kg/day for oral exposure of monochloroacetic acid (based on the increased weight of the spleen), determined from toxicity tests in rats, was divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.35 mg/kg/day was regarded as this substance's tentative 'non-toxic level' for oral exposure. The maximum exposure level was estimated to be less than 0.04 μg/kg/day, approximately, based on the past data on groundwater and public freshwater bodies reported in 2000. The MOE (Margin of Exposure) would exceed 880 which is calculated from the estimated maximum exposure level and the tentative 'non-toxic level', and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. In addition, the MOE would be 290 which is calculated from another estimation of the maximum exposure level of 0.12 μg/kg/day, calculated from the concentration in effluents according to the transfers to the sewage system, reported in FY 2019 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, the collection of further information would not be required to assess the health risk of this substance via oral exposure.

Regarding inhalation exposure, due to the lack of identified 'non-toxic level' and exposure concentrations, the health risk could not be assessed. Though the total release of the substance to the environment was reported to be 0.25 t in FY2019, the release of the substance into the air was reported to be 0 t, and predictions of the multimedia fugacity model indicated that the proportion distributed to air was very little. 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' - mg/kg/day	-	-	Drinking water	- μg/kg/day	MOE	-	○
				Groundwater	- μg/kg/day	MOE	-	
Inhalation	'Non-toxic level' - mg/m^3	-	-	Ambient air	- $\mu g/m^3$	MOE	-	○
				Indoor air	- $\mu g/m^3$	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 datum was obtained: a 48-h EC_{50} of 1,600 μg/L for swimming inhibition in the crustacean *Daphnia magna*. Accordingly, based on this acute toxicity value and an assessment factor of 1,000, a predicted no effect concentration (PNEC) of 1.6 μg/L was obtained.

Reliable chronic toxicity data could not be obtained. Therefore, the value of 1.6 μg /L obtained from the acute toxicity to the crustacean 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, albeit past data (more than ten years old), a maximum value of less than 1 μg/L was reported for public freshwater bodies and seawater. The ratio of this value and PNEC is less than 0.6.

Further, when releases to public freshwater bodies estimated from reported transfer to sewage in fiscal 2019 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 3.0 μg/L. The ratio of this value and PNEC is 1.9.

Accordingly, based on a comprehensive review of the above findings, efforts to collect data are considered necessary.

Efforts to elucidate releases to the environment, and production and import quantities of this substance are required. Further, data on environmental concentrations in the vicinity of major emission sources need to be augmented as well as augmenting toxicity information for aquatic organisms.

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)		
Crustacean *Daphnia magna*	Acute	EC_{50} Swimming inhibition	1,000	1.6	Freshwater	—	—	▲
					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	Requiring information collection		▲

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