5	CAS No.: 156-59-2	Substance: *cis*-1,2-Dichloroethylene

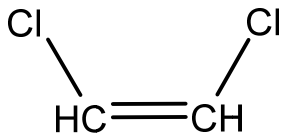
Chemical Substances Control Law Reference No.: 2-103 (Dichloroethylene)

Chemical Substances Control Law Reference No.: 632 (1,2-Dichloroethylene)

Molecular Formula: $C_2H_2Cl_2$

Molecular weight: 96.94

Structural Formula:



1.General information

The aqueous solubility of this substance is 6.4×10^3 mg/1,000 g (25℃), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.86 (pH unknown), and the vapor pressure is 2.68×10^4 Pa (25℃). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is thought to be nonexistent or low. Further, degradability screening tests indicated a residual ratio of 75% after 5 days (initial concentration: 2.5 μg/mL, pH: 7) for hydrolyzability.

This substance (as 1,2-dichloroethylene) is classified as a Class 1 Designated Chemical Substance under the PRTR Law. Further, water quality standards and environmental standards (soil, groundwater) are in place for this substance and trans-1,2-dichloroethylene.

This substance is produced as a byproduct during the production of 1,1-dichloroethylene and chloroethylene production, or formed in the environment as a decomposition product of other substances. In the past, it was used as a solvent for the manufacture of dyestuffs, fragrances, and thermoplastic resins, as well as a raw material for other chlorinated solvents. Currently, however, there are no known applications. The production and import volume of dichloroethylene in fiscal 2021 was 4,000 t.

2.Exposure assessment

Total release to the environment in fiscal 2021 under the PRTR Law was approximately 5.3 t, and all releases were notified. The major destination of notified releases was public water bodies. In addition, approximately 82 t was transferred to waste materials. The major source of notified releases to the atmosphere was the chemical industry, while the major source of notified releases to public water bodies was the sewage treatment sector. However, note that emissions from special requirement facilities (relevant facilities under the Mine Safety Law, domestic waste disposal facilities, industrial waste disposal facilities, sewage disposal facilities, etc.) may be overestimated because emissions may be calculated based on the lower limit of quantification. 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 57.9% and that to the atmosphere would be 41.7%. Where the largest quantities were estimated to have been released the atmosphere, the predicted proportion distributed to the atmosphere would be 94.2%.

A maximum expected concentration of exposure to humans via inhalation of around 0.011 μg/m^3 was reported as an annual average based on ambient atmospheric data, although it is less than the maximum detection limit for each month. Further, the mean annual value for atmospheric concentration in fiscal 2021 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 0.026 μg/m^3.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was 8.5 μg/L for public freshwater bodies and less than 4 μg/L for seawater. When releases to public freshwater bodies notified under the PRTR law in fiscal 2021 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 4.3 μg/L.

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3. Initial assessment of health risk

The Environmental Water-Quality Standards for public water and groundwater pollution have been established for this substance (*cis* isomer). The initial assessment of this substance scoped the health risk via inhalation exposure only, not covering the risk via oral exposure. Due to the lack of evidence on general toxicity of this substance (*cis* isomer) via inhalation exposure, the assessment was conducted based on evidence from toxicological studies on the mixture of *cis* and *trans* isomers and by extrapolation of evidence from oral exposure to inhalation exposure.

The mixture of this substance and the *trans* isomer irritates the eyes and the respiratory tract. The mixture at high concentration may cause effects on the central nervous system, resulting in lower level of consciousness. Inhalation of the mixture causes a cough, sore throat, dizziness, nausea, drowsiness, weakness, unconsciousness, and vomiting. Ingestion causes abdominal pain in addition to the same symptoms as inhalation. Contact with the skin will cause dry skin. 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 LOAEL of 500 ppm for inhalation exposure (based on the increased relative weights of the liver in females and of the kidney in males), determined from toxicity tests in rats exposed to the mixture of *cis* and *trans* isomers (*cis* isomer constitutes approximately 60% of the mixture) by inhalation, was adjusted according to exposure conditions to obtain 104 ppm and subsequently divided by a factor of 10 to account for uncertainty in using a LOAEL and by another factor of 10 to account for extrapolation to chronic exposure. The calculated value of 1.04 ppm (4.1 mg/m^3) was deemed the lowest reliable concentration and was identified as the 'non-toxic level' of the mixture for inhalation exposure. Toxicological evidence on *cis* isomer alone was obtained from an oral exposure study in rats which reported the LOAEL of 32 mg/kg/day (based on the increased relative weight of the kidney). This LOAEL was divided by a factor of 10 to account for uncertainty in using a LOAEL, and by another factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.32 mg/kg/day could be identified as the 'non-toxic level' of the *cis* isomer for oral exposure. The tentative 'non-toxic level' of 1.1 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. Both the 'non-toxic level' of the mixture and the tentative 'non-toxic level' of the substance for inhalation exposure were used for health risk judgment.

Regarding inhalation exposure, while the monthly monitored data indicated that the concentration in ambient air was less than the highest detection limit, the maximum annual mean concentration was reported to be approximately 0.011 $\mu g/m^3$. The MOE (Margin of Exposure) would be 37,000 which is calculated from the predicted maximum exposure concentration in ambient air of 0.011 $\mu g/m^3$ and the 'non-toxic level' of 4.1 mg/m^3 derived from the inhalation test of the mixture in rats 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 MOE for reference would be 10,000 which is calculated from the predicted maximum exposure concentration and the tentative 'non-toxic level' of 1.1 mg/m^3 derived from the conversion of the 'non-toxic level' for oral exposure of this substance and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. In addition, the maximum concentration (annual mean) in ambient air near the operators that are releasing a large amount of the substance was estimated to be 0.026 $\mu g/m^3$, based on the releases to air reported in FY 2021 under the PRTR Law. The MOE for reference would be 16,000 which is calculated from the estimated maximum concentration (annual mean) and the 'non-toxic level' of 4.1 mg/m^3 and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and would be 4,200 which is calculated from the tentative 'non-toxic level' of 1.1 mg/m^3 instead of the 'non-toxic level' of 4.1 mg/m^3. 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*'	(−) mg/kg/day	(−)	(−)	Drinking water	(−) μg/kg/day	MOE	(−)	(−)
					Groundwater	(−) μg/kg/day	MOE	(−)	
Inhalation	'Non-toxic level*'	4.1 mg/m^3	Rats	The increased relative weights of the liver in females and of the kidney in males	Ambient air	0.011 $\mu g/m^3$	MOE	37,000	○
					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 data were obtained: a 48-h EC_{50} of 59,690 μg/L for growth inhibition in the green alga *Raphidocelis subcapitata*, a 48-h EC_{50} of 40,200 μg/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC_{50} of 67,200 μg/L for the fish *Oryzias latipes* (medaka), and a 96-h LC_{50} exceeding 100,000 μg/L for the American wood frog (embryo) *Lithobates sylvaticus*, the green frog (embryo) *Lithobates clamitans,* and the American toad (embryo) *Anaxyrus americanus*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 400 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 73,600 μg/L for growth inhibition in the green alga *R. subcapitata*, and a 21-d NOEC of 4,510 μg/L for reproductive inhibition on the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 45 μg/L was obtained.

The value of 45 μg/L obtained from the chronic toxicity to the crustacean species was used as the PNEC for this substance.

The PEC/PNEC ratio is 0.2 for freshwater bodies and less than 0.09 for seawater. Accordingly, <u>further work to evaluate ecological risk is considered necessary.</u>

When releases to public freshwater bodies notified under the PRTR law in fiscal 2021 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 4.3 μg/L. The ratio of this value to PNEC is 0.096.

Further, a QSAR study of chronic toxicity in fish was conducted, resulting in an estimated chronic toxicity towards fish of 1,000 μg/L. Therefore, there is a possibility that the chronic toxicity is lower than the chronic toxicity towards crustaceans calculated from experiments of 4,510 μg/L, that forms the basis of PNEC. Based on full knowledge of the chronic toxicities towards the three groups of organisms, dividing by an assessment factor of 10 results in >100 μg/L, and the ratio of this value and PEC is less than 0.1. However, some concerns remain, such as the fact that the results of the QSAR estimates of chronic toxicity in fish are based on extrapolation.

<u>Based on a comprehensive review of the above findings, efforts to collect further data are considered necessary taking into consideration determination of ecological risk by the PEC/PNEC ratio.</u>

For this substance, <u>future trends in exposure data (measured environmental data and PRTR data) should be monitored, and collecting information on aquatic organism toxicity should be considered when necessary.</u>

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*	Chronic	NOEC Reproductive inhibition	100	45	Freshwater	8.5	0.2	▲
					Seawater	<4	<0.09	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	The substance was not subject to evaluation.	(－)
	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