7	CAS No.: 95-50-1	Substance: *o*-Dichlorobenzene

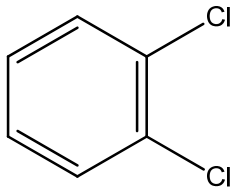
Chemical Substances Control Law Reference No.: 3-41 (Dichlorobenzene)

PRTR Law Cabinet Order No.: 1-181 (Dichlorobenzene)

Molecular Formula: $C_6H_4Cl_2$

Molecular Weight: 147.00

Structural Formula:



1. General information

The aqueous solubility of this substance is 150 mg/1,000 g (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 3.43, and the vapor pressure is 1.35 mmHg (=180Pa) (25°C). Biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is judged to be non-existent or low. The substance does not undergo biodegradation (anaerobic degradation). Also, the substance does not undergo hydrolysis in the ambient environment.

This substance is designated as a Priority Assessment Chemical Substance under the Chemical Substances Control Law from the perspective of effects on human health. Further, dichlorobenzene is a Class 1 Designated Chemical Substance under the PRTR Law.

The main uses of this substance are as an agricultural chemical raw material and as a solvent in the production process for tolylene diisocyanate. The production and import quantity in fiscal 2014 was 10,896 t. The production and import category under the PRTR Law is more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2014 under the PRTR Law as dichlorobenzene was approximately 8,800 t, of which of which approximately 90 t or 1% of overall releases were reported. The major destination of reported releases was the atmosphere. In addition, approximately 6.8 t was transferred to sewage and 680 t was transferred to waste materials. The chemical industry reported large releases to the atmosphere and public water bodies. The largest releases to the environment, including those unreported, were to the atmosphere.

A multi-media model used to predict the proportions distributed to individual media in the environment indicates that in regions where the largest quantities were estimated to have been released to the environment overall or the atmosphere in particular, the predicted proportion distributed to the atmosphere was 96.9%. In regions where the largest quantities were estimated to have been released to public water bodies, the predicted proportion distributed to the atmosphere was 93.6%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around 0.12 μg/m^3. In addition, the predicted maximum exposure for indoor air was around less than 0.2 μg/m^3 based on past data from a survey of a limited area. The mean annual value for the atmospheric concentration in fiscal 2014 was calculated by using a plume-puff model based on releases to the atmosphere (as dichlorobenzene) reported according to the PRTR Law: this model predicts a maximum level of 3.8 μg/m^3.

The maximum expected oral exposure was estimated to be less than 0.0013 μg/kg/day based on calculations from data for public freshwater bodies. Furthermore, the predicted maximum exposure calculated from data for public freshwater bodies and past data for food was more than around 0.0013 μg/kg/day and less than around 0.04 μg/kg/day. In contrast, when releases to public freshwater bodies in fiscal 2014 reported (as dichlorobenzene) according to the PRTR Law 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 6.0 μg/L. Using this estimated concentration for rivers to calculate oral exposure gave 0.24 μg/kg/day.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, is around 0.032 μg/L for public freshwater bodies, and around 0.10 μg/L for seawater. When releases to public freshwater bodies in fiscal 2014 reported (as dichlorobenzene) according to the PRTR Law 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 6.0 μg/L.

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3. Initial assessment of health risk

This substance is irritating to the respiratory tract. It causes coughs, drowsiness, sore throat and unconsciousness if inhaled, and causes burning sensation, diarrhea, nausea and vomiting if ingested. Contact with the eyes causes redness and pain, and contact with the skin causes redness, pain and dry skin.

As sufficient information on the carcinogenicity of the substance was not available, the initial assessment was conducted on the basis of information on its non-carcinogenic effects.

The NOAEL for oral exposure of 60 mg/kg/day (based on kidney tubular regeneration), determined from long-term toxicity tests in mice, was adjusted according to exposure conditions. The calculated value of 43 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 LOAEL for inhalation exposure of 50 ppm (based on relative liver weight increase and hypertrophy of the hepatocytes), determined from medium-term toxicity tests in rats, was adjusted according to exposure conditions to obtain 12.5 ppm (75 mg/m^3), and subsequently divided by a factor of 10 to account for extrapolation from sub-chronic to chronic exposure, and by another factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.75 mg/m^3 was deemed to be the lowest reliable concentration and was identified as the 'non-toxic level*' of the substance for inhalation exposure.

With regard to oral exposure, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.0013 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 3,300,000, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 43 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans.

Based on the concentrations in food as reported in 1999, and those in public freshwater bodies, the predicted maximum exposure level would range from 0.0013 μg/kg/day to less than 0.04 μg/kg/day approximately. The MOE derived from this exposure range would be more than 110,000 and up to 3,300,000. In addition, the maximum exposure level was calculated to be 0.24 μg /kg/day. This value derives from the estimated concentration in the effluents from the high discharging plants, according to the releases of total dichlorobenzenes reported in FY 2014 under the PRTR Law. The MOE would be 18,000 when calculated from this level. Therefore, no further work would be required at present to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, the predicted maximum exposure concentration in ambient air was 0.12 μg/m^3, approximately. The MOE would be 630, when calculated from the predicted maximum exposure concentration and the 'non-toxic level*' of 0.75 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. For comparison, the maximum concentration (annual mean) in ambient air near the operators releasing large amount of the substance was estimated to be 3.8 μg/ m^3, based on the releases of total dichlorobenzenes, as reported in FY 2014 under the PRTR Law. The MOE would be 20,

when calculated from this concentration. It means that the MOEs based on the releases of this substance could be below 100 at some locations. As for indoor air, the maximum concentration of this substance in indoor air in a restricted area, as reported in 1998 was less than 0.2 μg/m^3, approximately. The MOE would be over 380, when calculated from this concentration. Therefore, collection of information would be required to assess the health risk of this substance via inhalation in ambient air, while collection of further information on inhalation exposure to indoor air would not be required.

Toxicity				Exposure assessment		Result of risk assessment			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration				
Oral	'Non-toxic level*' 43 mg/kg/day	Mice	Kidney tubular regeneration	Drinking water	— μg/kg/day	MOE	—	×	○
				Public Freshwater bodies	0.0013 μg/kg/day	MOE	3,300,000	○	
Inhalation	'Non-toxic level*' 0.75 mg/m^3	Rats	Relative liver weight increase and hypertrophy of the hepatocytes	Ambient air	0.12 μg/m^3	MOE	630	○	(▲)
				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, the following reliable data were obtained: a 96-h EC_{50} of 2,200 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 662 μg/L immobilization in the crustacean *Ceriodaphnia* cf. *dubia*, a 96-h LC_{50} of 1,580 μg/L for the fish species *Onchorynchus mykiss* (rainbow trout), and a 48-h LC_{50} of 12,000 μg/L for the midge *Paratanytarsus dissimilis*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 6.6 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 2,580 μg/L for growth inhibition in the green algae *P. subcapitata*, and a 21-d NOEC of less than 100 μg/L for reproductive inhibition in the crustacean *Daphnia magna.* Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of less than 1 μg/L was obtained.

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

The PEC/PNEC ratio exceeds 0.03 for freshwater bodies and 0.1 for seawater. When releases to public freshwater bodies in fiscal 2014 reported (as dichlorobenzene) according to the PRTR Law 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 6.0 μg/L, suggesting that concentrations may exceed PNEC at certain locations. Accordingly, efforts to collect data on this substance are needed, as are measurements of environmental concentrations by taking emission sources into consideration, and augmentation of toxicity data.

Hazard Assessment（Basis for PNEC）			Assessment Coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure Assessment		PEC/PNEC ratio	Judgment based on PEC/PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)			
Crustacean *Daphnia magna*	Chronic	NOEC reproductive inhibition	100	<1	Freshwater	0.032	>0.03	▲	▲
					Seawater	0.10	>0.1		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work at present.	○
	Inhalation exposure (atmosphere)	Collection of further information would be required.	(▲)
	Inhalation exposure (room air)	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
Ecological risk	Requiring information collection.		▲

［Risk judgments］ ○: No need for further work ▲: Requiring information collection

■: Candidates for further work ×: Impossibility of risk characterization

（○）: Although risk to human health could not be confirmed, collection of further information would not be required.

（▲）: Further information collection would be required for risk characterization.