5	CAS No: 95-76-1	Substance: 3,4-Dichloroaniline

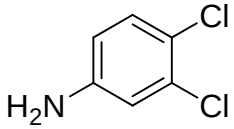
Chemical Substances Control Law Reference No.: 3-261 (dichloroaniline)

PRTR Law Cabinet Order: 1-156 (dichloroaniline)

Molecular Formula: $C_6H_5Cl_2N$

Molecular Weight: 162.02

Structural Formula:



1. General information

The aqueous solubility of this substance is 92.0 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 2.69, and the vapor pressure is 9.75×10^{-3} mmHg (= 1.30 Pa) (20°C). Biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is judged to be non-existent or low. Moreover, based on its chemical structure, the substance is not expected to undergo hydrolysis under environmental conditions.

This substance is designated as 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). Dichloroaniline is used as a raw material for other chemical substances, namely as a raw material for dyestuffs and pigments, and agricultural chemicals such as diuron and propanil. The production and import quantity of dichloroaniline in fiscal 2012 was less than 1,000 t. The production and import category of dichloroaniline under the PRTR Law is 1 to < 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2012 under the PRTR Law was approximately 0 t. In addition, approximately 0.015 t was transferred to sewage, and approximately 0.25 t was transferred to waste materials. Because emissions based on the PRTR Law could not be obtained, predictions of proportions distributed to individual media were made by using a Mackay-type level III fugacity model. This indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to soil would be largest.

The maximum expected concentration of exposure to humans via inhalation could not be obtained. The maximum expected oral exposure was estimated to be around less than 0.004 μg/kg/day on the basis of calculations from data for groundwater, and around 0.027 μg/kg/day on the basis of calculations from data for public freshwater bodies. A maximum expected oral exposure of around 0.027 μg/kg/day was adopted for this substance. The exposure level to this substance by intake from an environmental medium via food is considered slight, based on its low bioaccumulation.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, is around 0.68 μg/L for public freshwater bodies and around less than 0.1 μg/L for seawater.

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3. Initial assessment of health risk

This substance causes irritation to the eyes. It may affect blood, and methemoglobin may be produced. When inhaled, cyanosis, dizziness, headache, nausea, shortness of breath, confusion, convulsion and loss of consciousness may occur, while abdominal pain, in addition to these symptoms, may occur when ingested. Contact of the substance with the skin may induce absorption of the substance, and cause the exhibition of the symptoms as observed in poisoning through inhalation exposure. Contact with the eyes may cause redness, pain and blurred vision.

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

With regard to the oral exposure to the substance, the NOAEL of 5 mg/kg/day (based on inhibition of weight gain during gestation), obtained for reproductive and developmental toxicity tests on rats, was considered to be the reliable lowest dose of the substance and was identified as its ‘non-toxic level*’. As for the inhalation exposure, the LOAEL of

10 mg/m^3 (based on methemoglobinemia and reduction of the number of red cells), resulting from mid-term and long-term toxicity tests on rats, was adjusted according to the test conditions to obtain the exposure of 1.8 mg/m^3, after the division by a factor of 10 for the use as LOAEL and further by 10 for the short test periods. The outcome of 0.018 mg/m^3 was considered to be the reliable lowest dose of the substance and was identified as its 'non-toxic level*'.

Regarding the oral exposure to the substance, the predicted maximum exposure level was 0.027 μg/kg/day assuming the ingestion of water from public water bodies and freshwater. The MOE (Margin of Exposure) of 19,000 was derived from the substance's 'non-toxic level*' of 5 mg/kg/day and the predicted maximum exposure level and after the division by a factor of 10 to convert animal data to human data. As exposure to the substance in the environment through diet is limited, the MOE would not change significantly even when this exposure is included. Therefore, no further work would be required at present to assess the health risk to this substance for the oral exposure.

Concerning the inhalation exposure to the substance, the absence of information on exposure concentrations did not allow the health risk assessment. Although the total amount of emissions into the environment was 0 t according to the results on the predictions of the ratios distributed by each media, the substance would hardly be distributed in the atmosphere even when it is emitted. Therefore, collection of further information would not be required to assess the health risk of this substance for the inhalation exposure.

Toxicity				Exposure assessment		Risk characterization			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure level and concentration				
Oral	'Non-toxic level*' 5 mg/kg/day	Rat	Inhibition of body weight gain during gestation	Drinking water	– μg/kg/day	MOE	–	×	○
				Freshwater	0.027 μg/kg/day	MOE	19,000	○	
Inhalation	'Non-toxic level*' 0.018 mg/m^3	Rat	Methemoglobinemia and reduction of number of red cells	Ambient air	– 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.

4.Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 96-h EC_{50} of 450 μg/L for growth inhibition in the alga *Phaeodactylum tricornutum* (a diatom), a 48-h EC_{50} of 54 μg/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC_{50} of 1,940 μg/L for the fish species *Oncorhynchus mykiss* (rainbow trout), and a 96-h LC_{50} of 4.37 μg/L for the yellow-fever mosquito *Aedes aegypti*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.54 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 1250 μg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*; a 21-d NOEC of 2.5 μg/L for reproductive inhibition in the crustacean *D. magna*; a fifth-brood NOEC of 2.5 μg/L for reproductive inhibition in the crustacean *Ceriodaphnia* cf. *dubia*, which belongs to the same genus as *Ceriodaphnia* cf. *dubia*; a 182-d NOEC of less than 2 μg/L for reproductive inhibition or growth inhibition in the fish species *Poecilia reticulata* (guppy); and a 38-d NOEC of 3 μg/L for mortality/growth/reproduction in the polychaete worm *Ophryotrocha diadema*. Accordingly, based on these chronic toxicity values and an assessment factor of 10, a PNEC of less than 0.2 μg/L was obtained.

The value of 0.2 μg/L obtained from the chronic toxicity to the fish species was used as the PNEC for this substance.

The PEC/PNEC ratio exceeds 3.4 for freshwater bodies; accordingly, the substance is considered as a candidate for further work.

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)			
Fish species (guppy)	Chronic	NOEC reproductive inhibition/ growth inhibition	10	<0.2	Freshwater	0.68	＞3.4	■	■
					Seawater	<0.1	－		

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5. Conclusions

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

［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.