3	CAS No.: 554-00-7	Substance: 2,4-Dichloroaniline

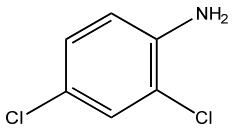
Chemical Substances Control Law Reference No.: 3-261 (Dichloroaniline)

PRTR Law Cabinet Order No.: 1-156 (Dichloroaniline) (number after law revision*: 1-180 (Dichloroaniline))

Molecular Formula: $C_6H_5Cl_2N$

Molecular Weight: 162.02

Structural Formula:



1. General information

The aqueous solubility of this substance is 450 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 2.91, and the vapor pressure is 1.5 Pa (20°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0% (average value), and bioaccumulation is thought to be nonexistent or low. Further, this substance is believed to not hydrolyze under ambient environmental conditions because it does not possess any hydrolyzable groups.

Dichloroaniline is classified as a Class 1 Designated Chemical Substance under the PRTR Law.

The main use of this substance is as an intermediate for dyestuffs and pigments. The production and import quantity in fiscal 2019 was less than 1,000 t. In addition, the production and import category under the PRTR Law was more than 1 t and less than 100 t.

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2. Exposure assessment

Total release of dichloroaniline to the environment in fiscal 2019 under the PRTR Law was 0 t, while 0.011 t was transferred to sewage. 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 soil would be largest.

The maximum expected concentration of exposure to humans via inhalation could not be defined because data for ambient atmospheric and indoor air quality could not be obtained.

Data for potable water, groundwater, public freshwater bodies, seawater, food, and soil to assess oral exposure could not be obtained.

Assuming intake solely from public freshwater bodies, the maximum expected concentration of exposure is around 0.00011 μg/kg/day. Further, albeit past data for a limited area, calculations for potable water gave a daily exposure of less than around 0.004 μg/kg/day.

While no releases to public water bodies were reported for dichloroaniline in fiscal 2019, transfers to sewage were reported. While the transfer ratio of dichloroaniline from sewage to public water bodies could not be obtained, releases to public water bodies were calculated assuming it was 100%, and furthermore all of the dichloroaniline transferred was assumed to be this isomer. Dividing this value by the ordinary water discharge of the national river channel structure database, and estimating the concentration in rivers by taking into consideration only dilution gives a maximum value of 0.0051 μg/L, and the oral exposure calculated thereof is 0.00020 μg/kg/day.

The risk of exposure to this substance by intake from an environmental medium via food is considered slight given that its bioaccumulation is considered to be low or nonexistent.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around 0.0028 μg/L for public freshwater bodies, and around 0.0024 μg/L for seawater. While no releases to public water bodies were reported for dichloroaniline in fiscal 2019, transfers to sewage were reported. Although the transfer ratio of dichloroaniline from sewage to public water bodies could not be obtained, releases to public water bodies were calculated assuming it was 100%, and furthermore all of the dichloroaniline transferred was assumed to be this isomer. Dividing this value 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 0.0051 μg/L.

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3. Initial assessment of health risk

This substance mildly irritates the skin. This substance may cause effects on the blood, resulting in the formation of methemoglobin. Inhalation will cause cyanosis to the skin, lips, and fingernails, as well as dizziness, headache, nausea, shortness of breath, confusion, convulsions, and unconsciousness. Ingestion will cause abdominal pain in addition to the same symptoms as inhalation. Contact to the skin will cause redness. The substance can be absorbed into the body via the skin and may cause the same symptoms as inhalation. Contact to the eyes will cause redness and pain. 3,4-dichloroaniline irritates the eyes and will cause the same symptoms as this substance described above.

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 evidence on the acute, sub-chronic, and chronic toxicity, it is not likely that the toxicity of this substance is markedly different from that of 3,4-dichloroaniline. The 'non-toxic level' for oral exposure determined from the reproductive and developmental toxicity test of 3,4-dichloroaniline was 5 mg/kg/day, and the predicted maximum exposure level of 3,4-dichloroaniline was approximately 0.00011 μg/kg/day. The MOE (Margin of Exposure) for reference would be 4,500,000 which is calculated from these values, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. In addition, the MOE would exceed 130,000 which is calculated from the estimated maximum exposure level of less than 0.004 μg/kg/day, approximately, according to the data in a certain area of drinking water. In addition, the MOE would be 2,500,000 which is calculated from another estimation of the maximum exposure level of 0.00020 μg/kg/day, calculated from the concentration in effluents according to the transfers of dichloroaniline 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. The total release of dichloroaniline to the environment was reported to be 0 t in FY 2019, 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	-	○
				Public Freshwater bodies	0.00011 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 data were obtained: a 48-h EC_{50} of 3,380 μg/L for growth inhibition in the green alga species *Raphidocelis subcapitata*, a 48-h LC_{50} of 500 μg/L for the crustacean species *Daphnia magna*, a 96-h LC_{50} of 5,670 μg/L for the fish species *Danio rerio* (zebra fish), and a 48-h IGC_{50} of 44,900 μg/L for reproductive inhibition in the ciliate *Tetrahymena pyriformis*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 5 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 2,040 μg/L for growth inhibition in the green alga species *R. subcapitata*, a 21-d NOEC of 5 μg/L for reproductive inhibition in the crustacean species *D. magna*, and a 35-d NOEC of approximately 320 μg/L for growth inhibition in the fish species *Gasterosteus aculeatus* (three-spined stickleback). Accordingly, based on these chronic toxicity values and an assessment factor of 10, a predicted no effect concentration (PNEC) of 0.5 μg/L was obtained.

The value of 0.5 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.006 for freshwater bodies and 0.005 for seawater. Further work to assess the ecological risk this substance is considered unnecessary at this time.

Albeit past data (more than ten years old), a maximum value of less than around 0.05 μg/L was reported for public freshwater bodies and seawater. The ratio of this value and PNEC is less than 0.1.

While no releases to public water bodies were reported for dichloroaniline in fiscal 2019, transfers to sewage were reported. While the transfer ratio of dichloroaniline from sewage to public water bodies could not be obtained, releases to public water bodies were calculated assuming it was 100%, and furthermore all of the dichloroaniline transferred was assumed to be this isomer. Dividing this value 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 0.0051 μg/L, and the ratio of this value to PNEC is 0.01. Accordingly, based on a comprehensive review of the above findings, there is little need to collect new data regarding this substance.

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	10	0.5	Freshwater	0.0028	0.006	○
					Seawater	0.0024	0.005	

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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	No need for further work		○

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

*Note: Number after revision of law to be implemented on April 1, 2023