4	CAS No: 88-73-3	Substance: 2-Chloronitrobenzene

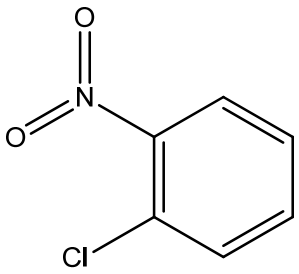
Chemical Substances Control Law Reference No.: 3-442 (Monochloro nitrobenzene)

PRTR Law Cabinet Order No.: 1-112

Molecular Formula: $C_6H_4ClNO_2$

Molecular Weight: 157.55

Structural Formula:



1. General information

The aqueous solubility of this substance is 441 mg/1,000 g (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 2.24, and the vapor pressure is 0.044 mmHg (=5.8 Pa) (20°C). Biodegradability (aerobic degradation) is judged to not be good, and bioaccumulation is judged to be non-existent or low. The substance does not have any hydrolyzable groups under ambient environmental conditions.

This substance is a Class 1 Designated Chemical Substance under the PRTR Law.

The main use of this substance is as a raw material for azo dyes. The production and import quantities in fiscal 2014 were not disclosed because the number of reporting businesses was less than two. The production and import category under the PRTR Law is more than 100 t.

---

2. Exposure assessment

Total release to the environment in fiscal 2014 under the PRTR Law was 0 t. Predictions of proportions distributed to individual media by using 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, based on ambient atmospheric data, was around less than 0.0012 μg/m^3. The predicted maximum oral exposure was estimated to be around 0.000092 μg/kg/day when calculated from data for public freshwater bodies. 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, was reported to be generally less than 0.0023 μg/L for both public freshwater bodies and seawater.

---

3. Initial assessment of health risk

This substance is irritating to the eyes. The substance affects blood and may cause the formation of methemoglobin. Inhalation or ingestion of the substance causes cyanosis of the lips, nail beds and skin, dizziness, headache, nausea, shortness of breath, confusion, convulsions and unconsciousness. The substance on the skin may be absorbed to cause the same symptoms as inhalation or ingestion. Contact with the eyes causes redness and pain.

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. However, the carcinogenicity was taken into consideration for this risk assessment, because there is sufficient evidence in experimental animals for the carcinogenicity of this substance.

The LOAEL for oral exposure of 4 mg/kg/day (based on the increase of relative weight of liver and exacerbation of chronic nephropathy), determined from long-term toxicity tests in rats, was divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.40 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 1.1 ppm (based on increased level of methemoglobin and respiratory epithelial hyperplasia), determined from medium-term toxicity tests in rats, was adjusted according to exposure conditions to obtain 0.20 ppm (1.3 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 0.013 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 less than 0.000092 μg/kg/day, approximately. The MOE (Margin of Exposure) would be over 87,000, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 0.40mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans, and by another factor of 5 to take into consideration the carcinogenicity in animals. Since exposure to the substance in environmental media via food is presumed to be limited, including this concentration in the calculation would not change the MOE significantly. 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 less than 0.0012 μg/m^3, approximately. The MOE would be over 220, when calculated from the predicted maximum exposure concentration in ambient air and the 'non-toxic level*' of 0.013 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 5 to take into consideration the carcinogenicity in animals. Therefore, no further work would be required to assess the health risk of this substance via inhalation in ambient air.

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*' 0.40 mg/kg/day	Rats	Increase of relative weight of liver and exacerbation of chronic nephropathy	Drinking water	— μg/kg/day	MOE	—	×	○
				Public Freshwater bodies	<0.000092 μg/kg/day	MOE	>87,000	○	
Inhalation	'Non-toxic level*' 0.013 mg/m^3	Rats	Increased level of methemoglobin and respiratory epithelial hyperplasia	Ambient air	<0.0012 μg/m^3	MOE	>220	○	○
				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 6,900 μg/L for growth

inhibition in the green algae *Chlorella pyrenoidosa* (Trebouxiophyceae), a 48-h EC_{50} of 3,200 μg/L for immobilization in the crustacean *Daphnia magna*, a 96-h LC_{50} of 25,500 μg/L for the fish species *Cyprinus carpio* (carp), and a 48-h IGC_{50} of 88,600 μg/L for population growth in the ciliate *Tetrahymena thermophila*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 32 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 21-d NOEC of 3,000 μg/L for reproductive inhibition in the crustacean *D. magna*, and a 33-d NOEC of 534 μg/L for growth inhibition in the fish species *Pimephales promelas* (fathead minnow). Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 5.3 μg/L was obtained.

The value of 5.3 μg/L obtained from the chronic toxicity to the fish species was used as the PNEC for this substance.

The PEC/PNEC ratio is less than 0.004 for both freshwater bodies and seawater; accordingly, further work is considered unnecessary at this time.

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 (fathead minnow)	Chronic	NOEC growth inhibition	100	5.3	Freshwater	<0.0023	<0.004	○	○
					Seawater	<0.0023	<0.004		

---

5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work at present.	○
	Inhalation exposure	No need for further work at present.	○
Ecological risk	No need for further work at present.		○

［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.