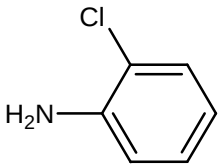
7	CAS No.: 95-51-2	Substance: *o*-Chloroaniline

Chemical Substances Control Law Reference No.: 3-194 (Chloroaniline)

PRTR Law Cabinet Order No.*: 1-89 (Chloroaniline)

Molecular Formula: C_6H_6ClN Structural formula:

Molecular Weight: 127.57



*Note: No. in Revised Cabinet Order enacted on October 1, 2009

1. General information

The aqueous solubility of this substance is 8.17 g/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.90, and the vapor pressure is 26.3 mmHg (=35 Pa) (25°C). Biodegradability (aerobic degradation) is limited, and bioaccumulation is judged to be non-existent or low.

This substance is designated as a Type II and Type III Monitoring Chemical Substance under the Law Concerning the Examination and Regulation of Manufacture, etc. of Chemical Substances. Chloroaniline 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). The main uses are as a raw material for 3,3′-dichloro-4,4′-diaminodiphenylmethane (used as a curing agent for urethane resins), pharmaceuticals and agricultural chemicals. The production quantity in 2009 was 500 t (estimated value), and the production and import quantity in fiscal 2009 was 724 t.

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2. Exposure assessment

Total release to the environment in fiscal 2008 under the PRTR Law was approximately 0.46 t and almost all releases were reported. The main destination of reported releases was public freshwater bodies. Besides this, 12 t was transfer to waste. The sole source of reported releases was the chemical industry. Including non-reported releases, releases to water bodies are estimated to have been the greatest. A multi-media model used to predict the distribution into each medium in the environment indicated that in regions where the largest quantities were estimated to have been released to the environment and public freshwater bodies as well as in regions where the largest quantities were estimated to have been released to the atmosphere, the proportion distributed to water bodies would be 99.0%.

Data for setting the predicted maximum exposure to humans via inhalation could not be obtained. Further, albeit past data, general environmental atmospheric data indicated a value of less than around 0.15 μg/m^3. Data exists based on general environmental measurements made more than 10 years ago, but taking into consideration trends in production and import quantities for this substance, the probability of marked increases in concentration is considered to be low. Meanwhile, the mean value of atmospheric concentration estimated from reported releases to the atmosphere under the PRTR Law was a maximum of 0.0040 μg/m^3.

A predicted maximum oral exposure of between around 0.0088 μg/kg/day and 0.2 μg/kg/day was adopted based on calculations from data for public freshwater bodies and food. The risk of exposure to this substance by intake from an environmental medium via food is considered slight based on estimates of oral exposure using estimated concentrations in fish species.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was about 0.22 μg/L for public freshwater bodies and less than around 0.06 μg/L for seawater.

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3. Initial assessment of health risk

The substance is irritable to the eyes. Signs and symptoms of poisoning via the oral, dermal or inhalation routes include the lips, finger nails and skin, dizziness, headache, shortness of breath, nausea, vomiting, weakness, confusion and unconsciousness.

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

With regard to oral exposure to the substance, a LOAEL of 10 mg/kg/day (for increased methemoglobin levels) obtained from mid-term and long-term toxicity tests in rats and mice was adjusted to 7.1 mg/kg/day taking account of exposure conditions. This value obtained was divided by 10 due to the short test periods and was further divided by 10 as is always the case for a LOAEL. 0.071mg/kg/day derived was deemed as a plausible value for the lowest dose of the substance and was identified as its 'non-toxic level*'. As for inhalation exposure, a LOAEL of 11 mg/m^3 (for increased methemoglobin levels) obtained from mid-term and long-term toxicity tests in rats was adjusted 2.0 mg/m^3 taking account of exposure conditions and was divided by 10 due to the short test periods and was further divided by 10 as is always the case with a LOAEL. 0.02 mg/m^3 derived was deemed as a plausible value for the lowest dose of the substance and was identified as its 'non-toxic level*'.

As for oral exposure, the estimated maximum exposures were approximately 0.0088 μg/kg/day and above and 0.2 μg/kg/day or below, when intakes through freshwater in public water bodies and through food were assumed. The MOE would be 36 to 810 when combined with the 'non-toxic level*' of 0.071 mg/kg/day and divided by 10 due to the need to convert the 'non-toxic level*' from the animal experiments to a human equivalent dose. The measurements of the concentrations of the substance in the environment did not allow for identification of health risk associated with its oral exposure. However, all of releases of the substance to public water bodies reported under Japanese PRTR in FY2008 were to the sea, and measurements of the concentrations in fish indicated that exposure to the substance from food intakes would not be likely. Collection of information on oral exposure would not be required for assessment of health risk from oral exposure to the substance.

With regard to inhalation exposure to the substance, the absence of information available on exposure concentrations did not allow for a health risk assessment. For reference, however, the maximum concentration in the ambient air was reported to be less than 0.15 μg/m^3 in 1990. When combined with the 'non-toxic level*' of 0.02 mg/m^3 and divided by 10 due to the 'need to convert the 'non-toxic level*' from the animal experiments to a human equivalent dose, the MOE would be greater than 13. The maximum annual average concentration of the substance in the ambient air around its major sources would be 0.0040 μg/m^3 on the basis of its emissions reported for FY2008 under Japanese PRTR, and the MOE calculated would be 500. Therefore, collection of information would not be required to assess health risk from inhalation exposure to this substance in the ambient air.

Information of toxicity					Exposure assessment			Result of risk Exposure assessment			Judgment
Exposure Path	Criteria for risk assessment		Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure quantity and concentration					
Oral	'Non-toxic level*'	0.071 mg/kg/day	Rats/Mice	Increased methemoglobin	Drinking water	—	μg/kg/day	MOE	—	×	(○)
					Fresh water	0.0088～0.2	μg/kg/day	MOE	36～810	×	
Inhalation	'Non-toxic level*'	0.02 mg/m^3	Rats	Increased methemoglobin	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 level equivalent to NOAEL.
- 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 72-h EC_{50} of 27,600 µg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 450 µg/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC_{50} of 5,130 µg/L for the fish species *Pimephales promelas* (fathead minnow), and a 48-h IGC_{50} of 140,000 µg/L for inhibition of growth in the ciliated protozoan *Tetrahymena pyriformis*. Accordingly, based on these acute toxicity values and an assessment coefficient of 100, a predicted no effect concentration (PNEC) of 4.5 µg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 3,200 µg/L for growth inhibition in the green algae *P. subcapitata*, a 21-d NOEC of 32 µg/L for reproductive inhibition in the crustacean *D. magna*, a 21-d NOEC of 32 µg/L for reproductive inhibition or mortality in the crustacean *D. magna*, and a 40-d NOEC of 1,900 µg/L for mortality in the fish species *Oryzias latipes* (medaka). Accordingly, based on these chronic toxicity values and an assessment coefficient of 10, a predicted no effect concentration (PNEC) of 3.2 µg/L was obtained. The value of 3.2 µg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.07 for freshwater bodies and less than 0.02 for seawater. Accordingly, further work is thought to be 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	End point			Water body	Predicted environmental concentration PEC (µg/L)			
Crustacean *Daphnia magna*	Chronic	NOEC reproductive inhibition	10	3.2	Freshwater	0.22	0.07	○	○
					Seawater	<0.06	<0.02		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Though a risk characterization cannot be determined, there would be little necessity of collecting information.	(○)
	Inhalation exposure	Though a risk characterization cannot be determined, there would be little necessity of collecting information.	(○)
Ecological risk	No need of further work at present.		○

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

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

（○）: Though a risk characterization cannot be determined, there would be little necessity of collecting information.

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