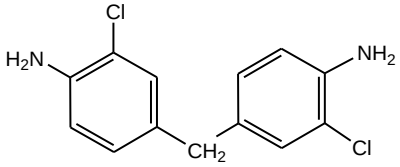
4	CAS No.: 101-14-4	Substance: 3,3'-Dichloro-4,4'-diaminodiphenylmethane

Chemical Substances Control Law Reference No.: 4-95 and 4-96 (as poly(di-tetra) chloro-4,4'-diaminodiphenylmethane) and 4-275 (as o-chloroaniline−formaldehyde condensation product)

PRTR Law Cabinet Order No.: 1-120 (Cabinet Order No. after revision*: 1-160)

Molecular Formula: $C_{13}H_{12}Cl_2N_2$ Structural Formula:

Molecular Weight: 267.15



*Note: No. according to revised order enacted on October 1, 2009.

1. General information

The aqueous solubility of this substance is 13.9 mg/L (24°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 3.91, and the vapor pressure is 3.9×10^{-6} mmHg (=5.2×10^{-4} Pa) (25°C, calculated value). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is thought to be nonexistent or low. Its half-life for hydrolysis is more than 800 years at 25°C (pH =7).

This substance is designated as a Type II and III Monitoring Chemical Substance under the Law Concerning the Examination and Regulation of Manufacture, etc. of Chemical Substances. It was also 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), and this continues to be the case after the revision of substances regulated by the PRTR Law (enacted on October 1, 2009). All of this substance is used as a curing agent for urethane resins utilized in waterproofing materials, flooring materials, and all-weather-type paving materials. The production and import quantity in fiscal 2007 was 2,696 t.

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2. Exposure assessment

Total release to the environment in fiscal 2006 under the PRTR Law was 0.014 t, and all releases were reported. All reported releases were to the atmosphere, while there was also transfer to waste of 32 t. The rubber products industry and the chemical industry reported releases.

A multi-media model to predict the distribution into each environmental medium indicated that in regions where the largest quantity was estimated to have been released to the atmosphere, the proportion distributed to soil would be 92.8%.

Data for setting the predicted maximum exposure to humans via inhalation could not be obtained. On the other hand, the mean annual value for atmospheric concentration in fiscal 2006 calculated using a plume-puff model based on reported releases to the atmosphere according to the PRTR Law was a maximum of 0.0023 μg/m^3. The predicted maximum oral exposure was estimated to be less than around 0.0018 μg/kg/day based on calculations from data for public freshwater bodies and food.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was less than around 0.03 μg/L for both public freshwater bodies and seawater.

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3. Initial assessment of health risk

This substance may cause effects on the blood, possibly generating methemoglobin. Inhalation exposure to this substance causes cyanosis in the lips, nail beds and skin, delirium, convulsion, dizziness, headache, nausea and loss of consciousness while oral inhalation causes abdominal pain in addition to these symptoms. In addition to burning sensation caused by contact with this substance, these health conditions can be caused by dermal absorption as well.

As for its non-carcinogenic effects, information on its general toxicity and reproductive toxicity has been obtained. As for its carcinogenicity, experiments on animals have provided its evidences, so the substance is likely to be carcinogenic to humans. Initial assessments have been conducted both on its non-carcinogenic and carcinogenic effects.

A no-observed-adverse-effect-level (NOAEL) of 2 mg/kg/day (for splenic hemosiderosis, relative increase of kidney weight to body weight) obtained for its non-carcinogenic effects through oral exposure from mid-term and long-term toxicity tests for rats was divided by 10 due to their short test periods to produce 0.2 mg/kg/day as its 'non-toxic level*'. As for its carcinogenicity, it was assumed that there was no threshold, and 1.5 $(mg/kg/day)^{-1}$ (for transitional papillary epithelia of bladder) from experiments on dogs was established as its slope factor.

As for its inhalation exposure, its 'non-toxic level*' could not be identified, and its unit risk could not be obtained when it was assumed that there was no threshold.

As for its oral exposure, its maximum exposure was estimated to be less than around 0.0018 μg/kg/day, when intakes of freshwater in public bodies and also food intakes were assumed. Its margin of exposure (MOE) would be more than 1,100, when calculated from its 'non-toxic level*' of 0.2 mg/kg/day and its estimated maximum exposure, then divided by 10 due to the fact that the 'non-toxic level*' was obtained from animal experiments, and divided again by 10 when its carcinogenicity was considered. On the other hand, the excess incidence rate of its carcinogenicity for the estimated maximum exposure would be less than 2.7×10^{-6} when calculated from the slope factor. Since its excess incidence rate could be more than 10^{-6}, health risk associated with oral exposure to this substance could not be determined.

Total discharge of this substance to the environment is 0.014 t. It will hardly distribute in water when its allocation into each medium is considered. It has not been detected in fresh and marine public water or in food. These suggest that the excess incident rate for its carcinogenicity would not be more than 10^{-6}. It would not be required to collect information on its oral exposure for the assessment of health risk associated with oral exposure to this substance.

As for inhalation exposure to this substance, its 'non-toxic level' or unit risk could not be identified, and its exposure concentrations were yet to be studied. Its health risk could not be assessed.

Total discharge of this substance to the environment is 0.014 t, and all of it is released to the atmosphere. Its vapor pressure is 3.9×10^{-6} mmHg at 25℃, and its half-life in the atmosphere is 0.83 to 8.3 hrs, and it would not distribute in the atmosphere when its allocation into various media is considered. The 'non-toxic level' for its oral exposure, if 100% absorption is assumed for it, turns to be the 'non-toxic level' of 0.67 mg/m^3 for its inhalation exposure. Unit risk for inhalation exposure will be 4.3×10^{-4} $(\mu g/m^3)^{-1}$ if its slope factor is converted for inhalation. Its emission reported under the Law Concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management would suggest its concentration of 0.0023 $\mu g/m^3$ in the ambient air, and MOE will be 2,900 and the excess incident rate for carcinogenicity will be 9.9×10^{-7}. Collection of information on its inhalation exposure to assess health risk associated with exposure to it in the ambient air would not be required.

Information of toxicity					Exposure assessment		Result of risk 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'	0.2 mg/kg/day	Rats	Splenic hemosiderosis, increase in relative kidney weight, etc.	Drinking water & food	– μg/kg/day	MOE	–	×	(○)
							Excess incidence rate	–	×	
	Slope factor	1.5 $(mg/kg/day)^{-1}$	Dogs	Transitional papillary epithelium of the bladder	Freshwater & food	< 0.0018 μg/kg/day	MOE	> 1,100	○	
							Excess incidence rate	$< 2.7\times10^{-6}$	×	
Inhalation	'Non-toxic level'	– mg/m^3	–	–	Ambient air	– $\mu g/m^3$	MOE	–	×	(○)
							Excess incidence rate	–	×	
	Unit risk	– $(\mu g/m^3)^{-1}$	–	–	Indoor air	– $\mu g/m^3$	MOE	–	×	×
							Excess incidence rate	–	×	

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 is available for the short-term exposure, 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 median effective concentration (EC_{50}) of more than 853 µg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*; a 48-h EC_{50} of 916 µg/L for swimming inhibition in the crustacean *Daphnia magna*; and a 96-h median lethal concentration (LC_{50}) of 606 µg/L for the fish species *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 6.1 µg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h no observed effect concentration (NOEC) of 545 µg/L for growth inhibition in the green algae *P. subcapitata;* and a 21-d NOEC of 9.5 µg/L was obtained for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.095 µg/L was obtained. The value of 0.095 µg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was less than 0.3 for both freshwater bodies and seawater body. Accordingly, judgment is not possible at this point in time.

This substance is primarily used as a curing agent for urethane resins. Total release to the environment is 0.014 t, and all releases are to the atmosphere. More than 90% of the substance that is released to the atmosphere is distributed to the soil, and the distribution to public water bodies is estimated to be less than 1%. Transfer to waste is 32 t, and although release to the environment from waste treatment facilities is unknown, the possibility of transfer to water is considered to be low from the viewpoint of its physicochemical properties. Accordingly, the need for collecting data for the purpose of initial assessment of the ecological risk of aquatic organisms being exposed to this substance to is considered low.

However, in instances such as a change in applications, new concentrations appearing in public water bodies, or releases to public water bodies presenting a potential ecological risk to aquatic organisms, then detailed collection of data would be considered necessary including chronic toxicity testing of fish species.

Hazard assessment (basis for PNEC)			Assessment factor	Predicted no effect concentration PNEC (µg/L)	Exposure assessment		PEC/ PNEC ratio	Result of assessment
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (µg/L)		
Crustacean (water flea)	Chronic	NOEC Reproductive inhibition	100	0.095	Freshwater	<0.03	<0.3	×（○）
					Seawater	<0.03	<0.3	

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

［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.