10	CAS No.: 95-64-7	Substance: 3,4-Dimethyl aniline

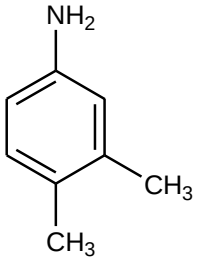
Chemical Substances Control Law Reference No.: 3-129 (dialkyl (C=1–5) aniline)

PRTR Law Cabinet Order No.: 1-164

Structural Formula:

Molecular Formula: $C_8H_{11}N$

Molecular Weight: 121.18



1. General information

The aqueous solubility of this substance is 3.8×10^3 mg/L (22°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.84, and the vapor pressure is 0.0279 mmHg (=3.72 Pa) (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 7.1%, and bioaccumulation is thought to be nonexistent or low. The substance does not have any hydrolyzable groups.

This substance is designated as a Type III Monitoring Chemical Substance under the Law Concerning the Examination and Regulation of Manufacture, etc. of Chemical Substances. This substance was classified 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). However, it was removed from the Class 1 Designated Chemical Substance list as a result of the revision of substances regulated by the PRTR Law (enacted on October 1, 2009). The main application is vitamin B2, with other applications also existing, but it has been reported that demand for this substance is declining due to changes in the manufacturing process for vitamin B2. The production and import category under the PRTR Law is 100 t. The latest production and import quantities are unknown.

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2. Exposure assessment

Total release to the environment in fiscal 2006 under the PRTR Law was 0 t. Predictions of distribution by medium using a Mackay-type level III fugacity model indicated that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to soil and would be higher.

Data for setting the predicted maximum exposure to humans via inhalation could not be obtained, but there is a report of less than 0.0051 μg/m^3 when data from a limited area (Kawasaki City) was used. The predicted maximum oral exposure was estimated to be less than around 0.001 μg/kg/day based on calculations from data for groundwater. The risk of exposure to this substance by intake from an environmental medium via food is considered slight.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was less than around 0.025 μg/L for both public freshwater bodies and seawater.

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3. Initial assessment of health risk

Diminished consciousness is caused as a result of exposure to high levels of this substance and MetHb may possibly be generated. Inhalation exposure causes dizziness, lethargy, headache and nausea while oral exposure causes cyanosis on the lips, nail beds and skin, dizziness, lethargy, headache, nausea and loss of consciousness.

Sufficient information could not be obtained on its carcinogenicity, and its initial assessment was conducted on the basis of data on its non-carcinogenic effects.

As for its oral exposure, its no-observed-adverse-effect-level (NOAEL) of 10 mg/kg/day for hepatic hypertrophy obtained from its mid-term and long-term toxicity tests for rats was divided by 10, due to their short test periods, to produce 1 mg/kg/day as its 'non-toxic level*'. As for inhalation exposure, its 'non-toxic level*' could not be identified.

As for its oral exposure, the predicted maximum exposure was estimated to be less than around 0.001 μg/kg/day, when intakes of groundwater were assumed. Its margin of exposure (MOE) would be more than 100,000 when calculated from its 'non-toxic level*' of 1 mg/kg/day and the predicted maximum exposure, and then divided by 10 due to the fact that 'non-toxic level*' was obtained from animal experiments. Since risk associated with exposure to this substance through food intakes from the environment is presumed to be minimal, this exposure will not increase MOE significantly, and no further action will be required at the moment to assess health risk from oral exposure to this substance.

As for its inhalation exposure, its 'non-toxic level *' could not be identified, and data at national-level were not available. Its health risk, therefore, could not be assessed. The 'non-toxic level' for its oral exposure, if 100% absorption is assumed for it, turns to be the 'non-toxic level' of 3.3 mg/m^3 for its inhalation exposure. When combined with the predicted maximum concentration of less than 0.0051 μg/m^3 in the ambient air estimated from data reported for some location, MOE will be calculated to be more than 65,000.

Its half-life in the atmosphere is 0.32 to 3.2 hrs. When released to the atmosphere, most of it is expected to go to media other than the ambient air. Its total release to the environment is zero ton. Collection of information on its inhalation exposure to assess health risk associated with its inhalation exposure 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*' 1 mg/kg/day	Rats	Hepatic hypertrophy	Drinking water	–	μg/kg/day	MOE	–	×	○
				Groundwater	< 0.001	μg/kg/day	MOE	> 100,000	○	
Inhalation	'Non-toxic level*' – mg/m^3	–	–	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 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 8,590 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata;* a 48-h EC_{50} of 1,090 μg/L for swimming inhibition in the crustacean *Daphnia magna*; a 96-h median lethal concentration (LC_{50}) of more than 97,900 μg/L for the fish species *Oryzias latipes* (medaka); and a 60-h median inhibition of growth concentration (IGC_{50}) of 235,000 μg/L for growth inhibition in the ciliated freshwater protozoan *Tetrahymena pyriformis*. Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 11 μg/L was obtained. With regard to chronic toxicity, the following reliable data were obtained: a 72-h no observed effect concentration (NOEC) of 2,940 μg/L for growth inhibition in the green algae *P. subcapitata* and a 21-d NOEC of 9.5 μg/L 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. Accordingly, a judgment cannot be made at this point in time regarding ecological risk. The latest production and import quantities are unknown for this substance and it has not been detected by monitoring surveys for the past 10 years. Moreover, no release estimates based on PRTR data exist, and for this reason, it was no longer a regulated substance after the review of substances covered by the PRTR Law. In the public water body survey of fiscal 2005, the substance was undetected at the lower detection limit of 0.0072 μg/L in freshwater bodies and seawater, albeit at only two locations, and the ratio of this limit and PNEC is less than 0.1. Accordingly, the need for collecting data for the purpose of initial assessment of the ecological risk of this substance to aquatic organisms is considered low. However, if production and imports increase, resulting in a potential ecological risk towards aquatic organisms, then detailed collection of data would be considered necessary.

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	<0.025	<0.3	×（○）
					Seawater	<0.025	<0.3	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	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.