9	CAS No.: 87-62-7	Substance: 2,6-Dimethyl aniline

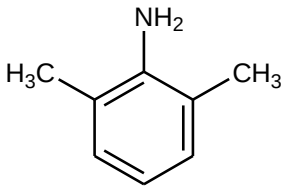
Chemical Substances Control Law Reference No.: 3-129 (dialkyl (C =1–5) aniline)

PRTR Law Cabinet Order No.: 1-163 (Cabinet Order No. after revision*: 1-215)

Structural Formula:

Molecular Formula: $C_8H_{11}N$

Molecular Weight: 121.18



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

1. General information

The aqueous solubility of this substance is 8.24×10^3 mg/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 1.78, and the vapor pressure is 0.13 mmHg (=17 Pa) (25°C). Biodegradability (aerobic degradation) is not considered to be favorable, and the substance is not considered to bioaccumulate to a high degree. The substance does not have any hydrolyzable groups.

This substance is designated as a Type II 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). It is primarily used as a raw material for dyestuffs, pigments, pesticides and pharmaceuticals. The production and import category under the PRTR Law is 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2006 under the PRTR Law was 0.002 t, and all releases were reported. All reported releases were to the atmosphere, while there was also transfer to waste of 0.037 t. Only 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, 59.9% would be distributed to soil and 32.5% would be distributed to water bodies.

Data for setting the predicted maximum exposure to humans via inhalation could not be obtained, but there is a report of less than 0.00054 μg/m^3 when data from a limited area (Kawasaki City) was used. 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 0.00055 μg/m^3.

The predicted maximum oral exposure was estimated to be less than around 0.00016 μg/kg/day based on calculations from data for groundwater. The value calculated from data for public freshwater bodies was around 0.00068 μg/kg/day. The value of around 0.00068 μg/kg/day was adopted as the estimated predicted maximum oral exposure for this substance. 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 around 0.017 μg/L for public freshwater bodies and less than around 0.004 μg/L for 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 reduced locomotor activity and hepatocyte 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 around 0.00068 μg/kg/day, when intakes of freshwater from public water supply were assumed. Its margin of exposure (MOE) would be 29,000 when calculated from its 'non-toxic level*' of 1 mg/kg/day and the predicted maximum exposure, then divided by 10 due to the fact that 'non-toxic level*' was obtained from animal experiments, and divided again by 5 when its carcinogenicity was considered. 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 inhalation exposure to this substance, its 'non-toxic level' could not be identified, and its exposure concentrations were yet to be obtained. Its health risk 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 0.00054 μg/m^3 in the ambient air estimated from the report for some location, MOE will be more than 120,000.

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 0.00055 μg/m^3 in the ambient air, and MOE will be 120,000.

Its half-life in the atmosphere is 0.4 to 4.0 hrs. When released to the atmosphere, most of it is expected to go to media other than the ambient air, and 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	Decrease in locomotor activity and hepatocyte hypertrophy	Drinking water	– μg/kg/day	MOE	–	×	○
				Freshwater	< 0.00068 μg/kg/day	MOE	29,000	○	
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 more than 100,000 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*; a 48-h EC_{50} of 20,000 μg/L for swimming inhibition in the crustacean *Daphnia magna*; and a 96-h median lethal concentration (LC_{50}) of more than 97,900 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 200 μg/L was obtained. With regard to chronic toxicity, the following reliable data were obtained: a 72-h no observed effect concentration (NOEC) of 32,000 μg/L for growth inhibition in the green algae *P. subcapitata*, and a 21-d NOEC of 2,230 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 22 μg/L was obtained. The value of 22 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.0008 for freshwater bodies and less than 0.0002 for seawater. Accordingly, further work is thought to be unnecessary at this time.

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	22	Freshwater	0.017	0.0008	○
					Seawater	<0.004	<0.0002	

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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	No need for further work.		○

［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.