18	CAS No.: 99-99-0	Substance: *p*-Nitrotoluene

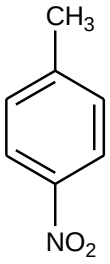
Chemical Substances Control Law Reference No.: 3-437 (Nitrotoluene)

PRTR Law Cabinet Order No.:

Structural Formula:

Molecular Formula: $C_7H_7NO_2$

Molecular Weight: 137.14



1. General information

The aqueous solubility of this substance is 345 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 2.42, and the vapor pressure is 0.164 mmHg (=21.9 Pa) (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0.8%, and bioaccumulation is thought to be nonexistent or low. The substance does not have any hydrolyzable groups.

The main application of this substance is an intermediate for *p*-toluidine, 2,4-dinitrotoluene, 2,4,6-trinitrotoluene, and *p*-nitrotoluene-*o*-sulfonate. The production quantity of this substance as reported by the OECD is 1,000 to <10,000 t/y.

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2. Exposure assessment

Because this substance is not 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), release and transfer quantities could not be obtained. 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 would be higher.

The predicted maximum exposure to humans via inhalation, based on general environmental atmospheric data, was approximately 0.0029 μg/m^3. The predicted maximum oral exposure was estimated to be between 0.0000045 μg/kg/day and 0.0004 μg/kg/day based on calculations from data for groundwater and soil, and around 0.024 μg/kg/day day based on calculations from data for public freshwater bodies and soil. A predicted maximum oral exposure of around 0.024 μg/kg/day was adopted 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 about 0.6 μg/L for public freshwater bodies and less than around 0.01 μg/L for seawater.

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3. Initial assessment of health risk

This substance is irritating to the eyes and may cause effects on the blood, possibly generating methemoglobin. Redness of the eyes is caused by contact with this substance. Inhalation exposure causes headache, cyanosis, dizziness and breathlessness while oral exposure may cause abdominal pain in addition to the symptoms as caused by inhalation exposure. Dermal exposure may also cause these symptoms.

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.

Lowest-observed-adverse-effect-levels (LOAELs) of 42 to 44 mg/kg/day for degeneration of renal tissue in females

and increased splenic extramedullary hematopoiesis in both females and males was obtained for oral exposure to this substance from the 13-week toxicity test for rats, and another LOAEL of 60 mg/kg/day for suppressed increase of body weight and tubule degeneration in females was obtained from the 2-year toxicity test for rats. These seemed to provide reliable information on its effects at low doses for identification of its 'non-toxic level'. Although they differed significantly in the test period, both of them provided similar LOAELs, and there was no noticeable difference in seriousness of the endpoints. It was suggested that duration of exposure did not need to be considered. The LOAELs obtained from the 13-week test was averaged to produce 43 mg/kg/day, and this was divided by 10 as is always the case with LOAEL to provide 4.3 mg/kg/day as the 'non-toxic level' of this substance. 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 0.024 μg/kg/day, when intakes of freshwater in public water bodies and soil were assumed. Its margin of exposure (MOE) would be more than 18,000 when calculated from its 'non-toxic level*' of 4.3 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. No further action, therefore, 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 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 14 mg/m^3 for its inhalation exposure. When combined with the predicted maximum concentration in the ambient air, MOE will be 480,000. Collection of information on its inhalation exposure to assess health risk associated with its inhalation exposure 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*' 4.3 mg/kg/day	Rats	Degeneration of the renal tissues in females, increase in the splenic extramedullary hematopoiesis of both males and females, etc.	Drinking water & soil	– μg/kg/day	MOE	–	×	○
				Freshwater & soil	0.024 μg/kg/day	MOE	18,000	○	
Inhalation	'Non-toxic level*' – mg/m^3	–	–	Ambient air	0.0029 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 10,000 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata;* a 48-h EC_{50} of 4,270 μg/L for swimming inhibition in the crustacean *Daphnia magna*; a 96-hour median lethal concentration (LC_{50}) of 36,500 μg/L for the fish species *Oryzias latipes* (medaka); and a 60-h median inhibition of growth concentration (IGC_{50}) of 79,500 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 43 μg/L was obtained. With regard to chronic toxicity, the following reliable data were obtained: a 72-h no observed effect concentration (NOEC) of 1,920 μg/L for growth inhibition in the green algae *P. subcapitata*; a 14-d

NOEC of 700 μg/L for reproductive inhibition in the crustacean *D. magna*; and a 21-d NOEC of 10,000 μg/L for growth inhibition in the hydra *Hydra oligactis*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) 7 μg/L was obtained. The value of 7 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.09 for freshwater bodies and less than 0.001 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	7	Freshwater	0.6	0.09	○
					Seawater	<0.01	<0.001	

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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.