4	CAS No.: 534-52-1	Substance: 4,6-Dinitro-*o*-cresol

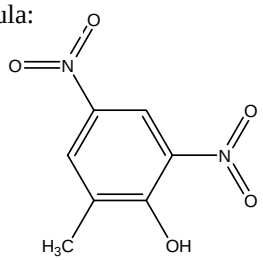
Chemical Substances Control Law Reference No.:3-2769

PRTR Law Cabinet Order No.:

Molecular Formula: $C_7H_6N_2O_5$

Molecular Weight: 198.13

Structural formula:



1. General information

The water solubility of this substance is 97–198 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 2.13, and the vapor pressure is 3.24×10^{-5}–3.8×10^{-4} mmHg (=4.3×10^{-2}–5×10^{-3} Pa) (20°C). This substance is judged not to be readily biodegradable (aerobic degradation), and not to be bioaccumulative or to be low bioaccumulative. Furthermore, the substance does not have any hydrolyzable groups.

The main uses were use as a pesticide against scale insects, spider mites and locusts on deciduous fruit trees and mandarin oranges, as a herbicide, and as a bactericide. The agricultural registration of this substance lapsed in Japan on February 22, 1975 (use classification: insecticide) and February 28, 1976 (use classification: herbicide). The production and import category under the PRTR Law is 0 t.

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2. Exposure assessment

Because this substance is not 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), 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 greater.

Data for setting the predicted maximum exposure to humans via inhalation could not be obtained, however an environmental study of a limited area reported a value of 0.014 μg/m^3 for a general environmental atmosphere. The predicted maximum oral exposure was estimated to be around 0.0027 μg/kg/day based on calculations from data for public freshwater bodies. 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.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around 0.068 μg/L for public freshwater bodies and 0.016 μg/L for seawater.

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3. Initial assessment of health risk

This substance is corrosive to eyes and irritating to skin. When inhaled, it may cause sweating, pyrexia, hyperthermia, nausea, shortness of breath, headache, convulsion and loss of consciousness. When orally taken, it may also cause an abdominal pain and vomiting. Contact of skin to the substance causes xanthosis. Its transdermal absorption may cause signs and symptoms similar to those observed for inhalation exposure. Contact of eyes to the substance makes them red and causes a pain. Its minimum lethal dose for humans has been reported to be 500 mg/kg for its transdermal exposure to children.

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

As for oral exposure to the substance, a NOAEL of 1.1 mg/kg/day (for reduced number of litters during the lactation period) obtained from reproductive/developmental toxicity tests on rats was deemed to be the lowest reliable dose

without any effect, and this was identified as its 'non-toxic level*'. As for inhalation exposure, its 'non-toxic level*' could not be identified.

As for its oral exposure, its mean exposure would be 0.0006 μg/kg/day and its predicted maximum exposure would be 0.0027 μg/kg/day, respectively, if its intakes through freshwater from public water bodies were assumed. The MOE would be 41,000 when calculated from the 'non-toxic level*' of 1.1 mg/kg/day and the predicted maximum exposure, and divided by 10 for conversion of the 'non-toxic level*' from animal experiments to an equivalent dose for humans. Since exposure to this substance in environmental media through intakes of food is considered to be limited, significant changes in the MOE is not likely, even when this exposure is combined. Therefore, further actions would not be required to assess health risk from oral exposure to this substance at present.

As for inhalation exposure to the substance, lack of available information on its 'non-toxic levels*' and exposure concentrations did not allow its health risk assessment. For reference, however, its 'non-toxic level*' for oral exposure, if 100% absorption were assumed, would be equivalent to its 'non-toxic level*' of 3.7 mg/m^3 for inhalation exposure. When combined with the predicted maximum concentration in the ambient air of 0.014 μg/m^3 reported for some location, the MOE derived would be 26,000. Therefore, collection of information would not be required to assess health risk from inhalation exposure to this substance in the ambient air.

Toxicity				Exposure assessment			Result of risk assessment			Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration					
Oral	Non-toxic level * ' 1.1 mg/kg/day	Rats	Decrease in number of litters during lactation period	Drinking water	—	μg/kg/day	MOE	—	×	○
				Freshwater	0.0027	μg/kg/day	MOE	41,000	○	
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 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 5,600 μg/L for growth inhibition in the green algae *Pseudokirchneriella subcapitata*; a 48-h EC_{50} of 145 μg/L for immobilization in the crustacean *Daphnia pulex*; and a 96-h $LC_{50\ of}$ 1,100 μg/L for the fish *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 1.5 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 310 μg/L for growth inhibition in the green algae *P. subcapitata*; a 21-d NOEC of 1,300 μg/L for reproductive inhibition in the crustacean *Daphnia magna*; and a 31-34-d NOEC of 183 μg/L for growth inhibition in the fish *Pimephales promelas* (fathead minnow). Also obtained was a 2-d NOEC of 1,000 μg/L for reproductive inhibition in the marine rotifer *Brachionus calyciflorus*. Accordingly, based on these chronic toxicity values and an assessment factor of 10, a predicted no effect concentration (PNEC) of 18 μg/L was obtained.

This 1.5 μg/L obtained from crustacean acute toxicity was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.05 for freshwater bodies and 0.01 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	Judgment based on PEC/PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)			
Crustacean *Daphnia magna*	Acute	EC_{50} immobilization	100	1.5	Freshwater	0.068	0.05	○	○
					Seawater	0.016	0.01		

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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 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.