10	CAS No.: 5522-43-0	Substance: 1-Nitropyrene

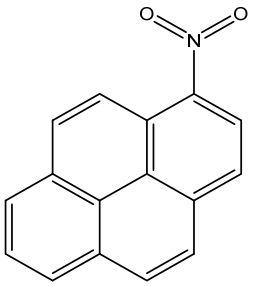
Chemical Substances Control Law Reference No.: 4-391

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{16}H_9NO_2$

Molecular Weight: 247.25

Structural Formula:



1. General information

The aqueous solubility of this substance is 0.0118–0.0214 mg/L (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 4.7, and the vapor pressure is 3.3×10^{-8} mmHg (= 4.4×10^{-6} Pa) (20°C). Some nitro-PAHs may gradually biodegrade (aerobic degradation) under certain conditions. Further, the substance does not possess any hydrolyzable groups; therefore, it does not hydrolyze under ambient environmental conditions.

There are no known applications for this substance, and it is believed to spontaneously form through combustion. The main sources are incineration plants and automobile exhaust. Production and import quantities are not reported under the PRTR Law.

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2. Exposure assessment

Because this substance is not classified as a Class 1 Designated Chemical Substance under the PRTR Law, release and transfer quantities could not be obtained. Predictions of proportions distributed to individual media by use of a Mackay-type level III fugacity model indicate that if equal quantities were released to the atmosphere, water bodies, and soil, the proportion distributed to soil would be largest.

The maximum expected concentration of exposure to humans via inhalation, based on general environmental atmospheric data, was less than around 0.00011 μg/m^3. Further, albeit for data covering a limited area, calculations for the ambient atmosphere gave a daily maximum exposure of roughly 0.0000058 μg/kg/day.

Data for potable water, ground water, public freshwater bodies, food, and soil to assess oral exposure could not be obtained. In lieu of such data, the maximum expected concentration of exposure was calculated to be around 0.0000072 μg/kg/day assuming intake solely from public freshwater bodies.

Further, data related to food could not be obtained. Therefore, maximum concentrations for fish species were used along with the average daily intake to calculate reference values for exposure by intake from an environmental medium via food. Past data for fish species indicate measured values below the detection limit (less than 0.068 μg/g). Therefore, recent water quality data (less than around 0.00018 μg/L) and a bioaccumulation factor (BCF, 1000) were used to estimate the concentration in fish; then the average daily intake of fish and shellfish (64.4 g/capita/day) was used to estimate exposure by intake from an environmental medium via food to be around less than 0.00022 μg/kg/day. Adding this to the oral exposure calculated from freshwater data gives around 0.00023 μg/kg/day.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around less than 0.00018 μg/L for both public water bodies and seawater.

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3. Initial assessment of health risk

No information was available on acute symptoms in humans. In a single-dose oral toxicity test in rats, administration of 5,000 mg/kg of this substance caused neither mortality, toxic symptoms, nor histological changes in tissues of various organs.

There is sufficient evidence in experimental animals for the carcinogenicity of this substance, which is considered to

have no threshold. The overall evaluation is that this substance is probably carcinogenic to humans. Considering the above, the initial assessment was conducted for both non-carcinogenic and carcinogenic effects.

The 'non-toxic level' for oral exposure could not be identified for non-carcinogenic effects. The non-carcinogenic LOAEL of 0.51 mg/m^3 for inhalation exposure (based on squamous metaplasia of the epiglottis), determined from toxicity tests in rats, was adjusted according to exposure conditions to obtain 0.091 mg/m^3, and subsequently divided by a factor of 10 to account for uncertainty in using a LOAEL and by another factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.00091 mg/m^3 was deemed to be the lowest reliable concentration and was identified as the 'non-toxic level' of the substance for inhalation exposure. Risk estimates for carcinogenicity based on evidence on this substance were not available. However, a slope factor of 1.2 (mg/kg/day)$^{-1}$ for oral exposure and a unit risk of 1.1×10^{-4} (μg/m^3)$^{-1}$ for inhalation exposure were adopted. These values were derived from the relative carcinogenic potency factors in comparison with benzo[a]pyrene.

With regard to oral exposure, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be less than 0.0000072 μg/kg/day, approximately. The MOE (Margin of Exposure) could not be assessed owing to the lack of identified 'non-toxic level'. The excess cancer incidence rate corresponding to the predicted maximum exposure level would be less than 8.6×10^{-9}, when calculated from the slope factor. This would lead to the health risk judgment that no further work would be required at present. In addition, the excess cancer incidence rate for reference corresponding to the exposure level of less than 0.00023 μg/kg/day would be less than 2.8×10^{-7}. This exposure level was estimated assuming that the substance is absorbed via fish and public freshwater bodies, in spite of unavailability of data on exposure via food. Therefore, as a comprehensive judgment, no further work would be required at present to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, the predicted maximum exposure concentration in ambient air was less than 0.00011 μg/m^3, approximately. The MOE would exceed 83, when calculated from the predicted maximum exposure concentration and the 'non-toxic level' of 0.00091 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 10 to take into consideration the carcinogenicity. The excess cancer incidence rate corresponding to the predicted maximum exposure concentration would be less than 1.2×10^{-8}, when calculated from the unit risk. The health risk judgment could not be determined because the MOE could be below or above judgment criteria. However, the MOE and the excess cancer incidence rate for reference would be 1,600 and 6.4×10^{-10}, respectively, when calculated from the maximum concentration of approximately 0.0000058 μg/m^3 reported in a restricted area. Therefore, as a comprehensive judgment, collection of further information would not be required to assess the health risk of this substance via inhalation in ambient air.

However, given that the multiple nitro-polycyclic aromatic hydrocarbons are present in ambient air, it is necessary to consider the health risk assessment of their combined exposure.

Toxicity				Exposure assessment		MOE & Excess incidence rate		Comprehensive judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration			
Oral	'Non-toxic level' - mg/kg/day	-	-	Drinking water	- μg/kg/day	MOE	-	○
						Excess incidence rate	-	
	Slope factor 1.2 (mg/kg/day)$^{-1}$	Mice	Gastric tumors	Public Freshwater bodies	<0.0000072 μg/kg/day	MOE	-	
						Excess incidence rate	<8.6×10^{-9}	
Inhalation	'Non-toxic level' 0.00091 mg/m^3	Rats	Squamous metaplasia of the epiglottis	Ambient air	<0.00011 μg/m^3	MOE	>83	○
						Excess incidence rate	<1.2×10^{-8}	
	Unit risk 1.1×10^{-4} (μg/m^3)$^{-1}$	Hamsters	Airway tumors	Indoor air	- μg/m^3	MOE	-	×
						Excess incidence rate	-	

Non-toxic level *

・When a LOAEL is available, it is divided by 10 to obtain a NOAEL-equivalent level.
・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 0.53 μg/L for growth inhibition in the diatom *Skeletonema costatum,* a 24-h EC_{50} of 1.32 μg/L for swimming inhibition in the copepod crustacean *Tigriopus japonicus*, and a 96-h LC_{50} exceeding 0.21 μg/L in the fish *Fundulus heteroclitus* (mummichog). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 0.0053 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 0.67 μg/L for growth inhibition in the green alga *Raphidocelis subcapitata* and a 21-d NOEC of 54 μg/L for reproductive inhibition in the crustacean *Daphnia magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 0.0067 μg/L was obtained.

The value of 0.0053 μg/L obtained from the acute toxicity to the diatom was used as the PNEC for this substance

The PEC/PNEC ratio is less than 0.03 for freshwater bodies and seawater; <u>further work is considered unnecessary at this time for determining ecological risk and the overall decision was the same.</u>

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Comprehensive judgment
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Diatom	Acute	EC_{50} Growth inhibition	100	0.0053	Freshwater	<0.00018	<0.03	○
					Seawater	<0.00018	<0.03	

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5. Conclusions

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