1	CAS No.: 84-65-1	Substance: Anthraquinone

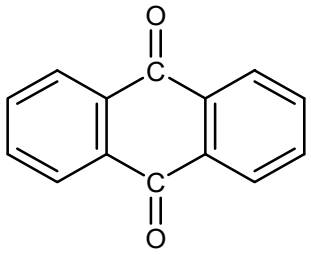
Chemical Substances Control Law Reference No.: 4-686

PRTR Law Cabinet Order No.:

Molecular Formula: $C_{14}H_8O_2$

Molecular Weight: 208.21

Structural Formula:



1. General information

The aqueous solubility of this substance is 1.4 mg/1000 g (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 3.39, and the vapor pressure is 1.16×10^{-7} mmHg (=1.55×10^{-5} Pa) (25 °C). Biodegradability (aerobic degradation) is judged to be good, and the substance does not possess any hydrolyzable groups.

The main use of this substance are as an intermediate for various dyestuffs including acid dyes, mordant dyes, vat dyes, and disperse dyes; also, it is an important starting material for anthraquinone-based dyes. The production and import quantity in fiscal 2017 was not disclosed because the number of reporting businesses was not more than two.

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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 could not be determined because ambient atmospheric and indoor air quality data could not be obtained. Further, albeit past data, the maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was roughly 0.0078 μg/m^3.

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, assuming intake solely from public freshwater bodies, a maximum expected exposure of around 0.018 μg/kg/day is obtained. Furthermore, maximum expected exposure values of around 0.26 μg/kg/day for public water bodies and around 0.048 μg/kg/day for soil are obtained based on past data, with the soil measurements being for a limited area. A reference value of around 0.31 μg/kg/day was obtained for maximum expected concentration of exposure by summing these values, whereas an exposure of 0.018 μg/kg/day was measured in fiscal 2017 at the same freshwater location where the exposure of 0.26 μg/kg/day was previously measured. The risk of exposure to this substance from an environmental medium is considered slight, given the low bioaccumulation of the substance expected on the basis of its physicochemical properties.

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3. Initial assessment of health risk

This substance may cause mechanical irritation. Inhalation of the substance causes cough. Contact with the eyes causes pain and redness.

As sufficient information on the carcinogenicity to humans was not available, it could not be determined whether the substance is carcinogenic or not. However, significant and dose-dependent tumorigenesis in kidneys of rats and livers of mice was observed in all dose-groups in the carcinogenesis study by oral administration. Considering the DNA damages caused by the substance in addition to the evidence above, assessment of the carcinogenic risk was deemed necessary as well, and initial assessment was conducted for both non-carcinogenic and carcinogenic effects.

The non-carcinogenic LOAEL of 1.36 mg/kg/day for oral exposure (based on increase in reticulocytes), determined from toxicity tests in rats, was divided by a factor of 10 to account for extrapolation to chronic exposure and by another factor

of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.014 mg/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. The cancer slope factor for oral exposure of 4×10^{-2} $(mg/kg/day)^{-1}$ (based on hepatic tumors), determined from carcinogenicity tests in male mice, was adopted assuming no threshold. Neither 'non-toxic level' nor unit risk could be identified for inhalation exposure.

With regard to oral exposure, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.018 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 16, when calculated from the predicted maximum exposure level and the 'non-toxic level' of 0.014 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 5 to take into consideration the carcinogenicity in animals. The excess cancer incidence rate corresponding to the predicted maximum exposure level would be 7.2×10^{-7}, when calculated from the slope factor. This would lead to the health risk judgment that collection of information would be required. In addition, the MOE and the excess cancer incidence rate for reference would be 1 and 1.2×10^{-5}, respectively, when calculated from the exposure level of approximately 0.31 μg/kg/day. This exposure level was derived from the maximum level in public freshwater bodies and soil based on past data. Since exposure to the substance in environmental media via food is presumed to be limited in spite of data unavailability, including it in the calculation would change neither the MOE nor the excess incidence rate significantly. Therefore, as a comprehensive judgment, collection of information would be required to assess the health risk of this substance via oral exposure, starting from data on exposure based on current releases.

With regard to inhalation exposure, owing to the lack of identified 'non-toxic level' and exposure concentrations, the health risk could not be assessed. However, the MOE for reference would be 120, when calculated from the tentative 'non-toxic level' for inhalation exposure of 0.047 mg/m^3 and the concentration in ambient air of approximately 0.0078 $\mu g/m^3$, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 5 to take into consideration the carcinogenicity in animals. The tentative 'non-toxic level' for inhalation exposure was derived from the conversion of the 'non-toxic level' for oral exposure, assuming that 100% of the inhaled substance is absorbed. The concentration in ambient air was derived from the maximum concentration in ambient air based on past data (reported in 2007). The excess cancer incidence rate for reference corresponding to the concentration of 0.0078 $\mu g/m^3$ would be 9.4×10^{-8}, when calculated from the tentative slope factor for inhalation exposure of $1.2\times10^{-5}(\mu g/m^3)^{-1}$. The tentative slope factor for inhalation exposure was derived from the conversion of the slope factor for oral exposure. 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.

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	MOE & Exces incidence rate		Judgment
Oral	'Non-toxic level'	0.014 mg/kg/day	Rats	Increase in reticulocytes	Drinking water	- μg/kg/day	MOE	-	▲
							Excess incidence rate	-	
	Slope factor	4×10^{-2} $(mg/kg/day)^{-1}$	Mice	Hepatic tumors	Public Freshwater bodies	0.018 μg/kg/day	MOE	16	
							Excess incidence rate	7.2×10^{-7}	
Inhalation	'Non-toxic level'	- mg/m^3	-	-	Ambient air	- $\mu g/m^3$ -	MOE	-	○
							Excess incidence rate	-	
	Unit risk	- $(\mu g/m^3)^{-1}$			Indoor air	- $\mu g/m^3$	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. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	Requiring information collection.	▲
	Inhalation exposure	No need for further work.	○

［Risk judgments］○: No need for further work ▲: Requiring information collection
■: Candidates for further work ×: Impossibility of risk characterization