7	CAS No.: 120-80-9	Substance: Pyrocatechol

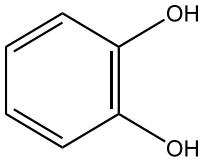
Chemical Substances Control Law Reference No.: 3-543 (Dihydroxybenzene)

PRTR Law Cabinet Order No.: 343

Molecular Formula: $C_6H_6O_2$

Molecular Weight: 110.11

Structural Formula:



1.General information

The aqueous solubility of this substance is 4.51×10^5 mg/1,000g (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 0.88 (pH unknown), and the vapor pressure is 3 Pa (25°C). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 83% and biodegradability is judged to be good. Further, this substance is believed to not contain any hydrolyzable groups.

From the perspective of human health effects, this substance is designated as a Priority Assessment Chemical under the Chemical Substances Control Law and is designated as a Class 1 Chemical Substance under the PRTR Law. The main uses of this substance are as a raw material for pharmaceuticals, polymerization inhibitor, in fragrances, and agricultural chemicals. It is also used as an oxygen absorber, plating treatment agent, and as a release agent to remove photoresist in the manufacture of semiconductors. This substance is a member of the polyphenol family and is found in plants and in cigarette smoke. The production and import quantity in fiscal 2021 was 3,611 t.

2.Exposure Assessment

Total release to the environment in fiscal 2021 under the PRTR Law was approximately 0.28 t, and all releases were notified. Most of the reported releases were to the atmosphere. In addition, 0.006 t was transferred to sewage and approximately 40 t was transferred to waste materials. The major source of notified releases to the atmosphere was the electrical equipment manufacturing industry, while the major sources of notified releases to public water bodies were the electrical equipment manufacturing industry and the chemical industry. A multi-media model used to predict the proportions distributed to individual media in the environment indicated that in regions where the largest quantities were estimated to have been released to the environment overall or to the atmosphere in particular, the predicted proportion distributed to soil would be 69.2%, and that to water bodies would be 30.1%. Where the largest quantities were estimated to have been released to public water bodies, the predicted proportion distributed to water bodies would be 90.9%.

The maximum expected concentration of exposure to humans via inhalation, based on ambient atmospheric data, was around 0.017 μg/m^3. Further, the mean annual value for atmospheric concentration in fiscal 2021 was calculated by use of a plume-puff model on the basis of releases to the atmosphere notified under the PRTR Law for fiscal 2021: this model predicts a maximum level of 0.068 μg/m^3.

Data for potable water, groundwater, public freshwater bodies, food, and soil to assess oral exposure could not be obtained. However, when releases to public freshwater bodies notified under the PRTR law in fiscal 2021 were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.012 μg/L, and a calculated average daily exposure of 0.00048 μg/kg/day. The exposure to this substance by intake from an environmental medium via food is considered slight, given the low bioaccumulation of the substance expected on the basis of its physicochemical properties.

Exposure to aquatic organisms based on water quality data could not be estimated. However, when releases to public freshwater bodies notified under the PRTR law in fiscal 2021 were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a

maximum value of 0.012 μg/L.

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3. Initial assessment of health risk

This substance irritates the skin and the respiratory tract and is corrosive to the eyes. Inhalation of this substance will cause a cough, sore throat, burning sensation behind the breastbone, labored breathing, and convulsions. Ingestion will cause abdominal pain, vomiting, diarrhea, convulsions, and respiratory arrest. Contact with the eyes will cause redness, pain, and severe burns. Contact with the skin will cause redness. The substance can be absorbed into the body through the skin and may cause convulsions.

Since not enough information was available on the carcinogenicity of the substance in humans, it could not be determined whether the substance is carcinogenic or not. However, considering the high incidences of pyloric gland adenomas observed in the glandular stomach in both sexes of rats and mice in the carcinogenesis study by oral administration, an assessment of the carcinogenic risk was deemed necessary as well. Therefore, the initial assessment was conducted for both non-carcinogenic and carcinogenic effects. Due to the lack of definite evidence on genotoxicity, it could not be determined whether this substance is a genotoxic carcinogen, precluding judgment of the existence of a carcinogenic threshold.

The non-carcinogenic LOAEL of 33 mg/kg/day for oral exposure (based on submucosal hyperplasia of the pyloric glands), determined from toxicity tests in male rats, was divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 3.3 mg/kg/day was deemed the lowest reliable dose and was identified as the 'non-toxic level' of the substance for oral exposure. Assuming that there exists a carcinogenic threshold despite the lack of reported threshold values in assessment documents, the carcinogenic NOAEL was set at the level of 33 mg/kg/day where no pyloric gland adenomas were observed. According to the comparison between the non-carcinogenic 'non-toxic level' and the carcinogenic NOAEL, non-carcinogenic effects would be caused at the lower level of this substance than carcinogenic effects. Considering the above, the 'non-toxic level' of 3.3 mg/kg/day calculated from the non-carcinogenic LOAEL was adopted as the lowest reliable dose regarding toxicity with thresholds. Assuming no thresholds, the cancer slope factor for oral exposure of 2.7×10^{-3} ～2.8×10^{-3} $(mg/kg/day)^{-1}$ (based on pyloric gland adenomas), determined from carcinogenicity tests in male rats, was adopted. Neither the 'non-toxic level' nor the unit risk could be identified for inhalation exposure.

Regarding oral exposure, due to the lack of identified exposure levels, the health risk could not be assessed. The maximum exposure level was estimated to be 0.00048 μg/kg/day according to the concentration in effluents from the high discharging plants based on the releases to public freshwater bodies reported in FY 2021 under the PRTR Law. The MOE (Margin of Exposure) for reference would be 140,000 which is calculated from the estimated maximum exposure level and the 'non-toxic level' of 3.3 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. The excess cancer incidence rate corresponding to the estimated maximum exposure level would be 1.3×10^{-9} which is calculated from the slope factor. Since exposure to the substance in environmental media via food is presumed to be limited, despite the lack of exposure level via food, including it in the calculation would not change either the MOE or the excess cancer incidence rate significantly. Therefore, as a comprehensive judgment, the collection of further information would not be required to assess the health risk of this substance via oral exposure.

Regarding inhalation exposure, due to the lack of identified 'non-toxic level' and unit risk, the health risk could not be assessed. However, the tentative 'non-toxic level' of 11 mg/m^3 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 MOE for reference would be 13,000 which is calculated from the tentative 'non-toxic level' for inhalation exposure and the predicted maximum exposure concentration in ambient air of 0.017 $\mu g/m^3$ 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. The tentative unit risk of 8.1×10^{-7} ～8.4×10^{-7} $(\mu g/m^3)^{-1}$ was derived from the conversion of the slope factor for oral exposure. The excess cancer incidence rate for reference corresponding to the predicted maximum exposure concentration in ambient air would be 1.4

$\times 10^{-8}$ which is calculated from the tentative unit risk. In addition, the MOE and the excess cancer incidence rate for reference would be 3,200 and 5.5×10^{-8}～5.7×10^{-8}, respectively, corresponding to the estimated maximum concentration (annual mean) of 0.068 μg/m^3 in ambient air near the operators that are releasing a large amount of the substance, based on the releases to air reported in FY 2021 under the PRTR Law. Therefore, as a comprehensive judgment, the collection of further information would not be required to assess the health risk of this substance via inhalation 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*'	3.3 mg/kg/day	Rats	Submucosal hyperplasia of the pyloric glands	Drinking water	- μg/kg/day	MOE	-	○
							Excess incidence rate	-	
	Slope factor	2.7×10^{-3} ~2.8×10^{-3} (mg/kg/day)$^{-1}$	Rats	Pyloric gland adenomas	Groundwater	- μg/kg/day	MOE	-	
							Excess incidence rate	-	
Inhalation	'Non-toxic level*'	- mg/m^3	-	-	Ambient air	0.017 μg/m^3	MOE	-	○
							Excess incidence rate	-	
	Unit risk	- (μg/m^3)$^{-1}$	-	-	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 96-h EC_{50} of 22,000 μg/L for growth inhibition in the Trebouxiophyceaen alga *Chlorella vulgaris*, a 48-h EC_{50} of 1,090 μg/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC_{50} of 3,500 μg/L for the fish *Pimephales promelas* (fathead minnow), and a 96-h LC_{50} of 31,300 μg/L for the immigrant triclad flatworm, *Girardia tigrina*. Accordingly, based on the acute toxicity value for the crustacean and an assessment factor of 100, a predicted no effect concentration (PNEC) of 10 μg/L was obtained.

Chronic toxicity data could not be obtained. As such, the value of 10 μg/L obtained from the acute toxicity to the crustacean was used as the PNEC for this substance.

Data for setting the predicted environmental concentration (PEC) could not be obtained for this substance. Accordingly, an assessment of ecological risk could not be made.

When releases to public freshwater bodies estimated from the reported transfer to sewage were divided by the ordinary water discharge of the national river channel structure database, estimating the concentration in rivers by taking into consideration only dilution gave a maximum value of 0.012 μg/L. The ratio of this value and PNEC was 0.001. Accordingly, based on a comprehensive review of the above findings, further work is considered unnecessary at this time.

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)		
Crustacean *Daphnia magna*	Acute	EC_{50} Swimming inhibition	100	10	Freshwater	—	—	○
					Seawater	—	—	

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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