2	CAS No: 100-41-4	Substance: Ethylbenzene

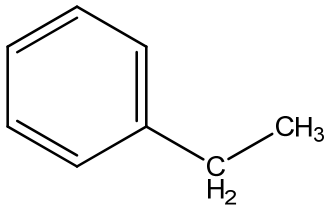
Chemical Substances Control Law Reference No.: 3-28, 3-60 (mono (or di) methyl (ethyl, bromoaryl, bromopropyl oxycarbonyl, or chloropropyl oxycarbonyl) benzene)

PRTR Law Cabinet Order No.: 1-53

Molecular Formula: C_8H_{10}

Molecular Weight: 106.2

Structural Formula:



1. General information

The aqueous solubility of this substance is 161 mg/1,000 g (25°C), the partition coefficient (1-octanol/water) (log K_{ow}) is 3.15, and the vapor pressure is 9.60 mmHg (= 1.28×10^3 Pa) (25°C). Biodegradability (aerobic degradation) is judged to be good.

This substance is designated as a Priority Assessment Chemical Substance and 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). The main uses of this substance are as a raw material for styrene and as a solvent for oil-based paints, adhesives, and inks. The production and import quantity in fiscal 2012 was 1,329,738 t. The production and import category under the PRTR Law is more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2012 under the PRTR Law was approximately 32,000 t, of which approximately 14,000 t or 44% of overall releases were reported. The major destination of reported releases was the atmosphere. In addition, approximately 3 t was transferred to sewage, and approximately 3,500 t was transferred to waste materials. Industry types with large reported releases were shipbuilding and repair, ship engine manufacturing, transportation equipment manufacturing, general machinery manufacturing, and metal products manufacturing for the atmosphere, and the food manufacturing and chemical industries for public water bodies. The largest release among releases to the environment including those unreported was to the atmosphere. 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 the atmosphere was 90.4%. In regions where the largest estimated releases were to public water bodies, the predicted proportions distributed to the atmosphere and soil were 69.9% and 29%, respectively. In regions where the largest estimated releases were to soil, the predicted proportions distributed to soil and the atmosphere were 71.1% and 28.6%, respectively.

The maximum expected concentration of exposure to humans via inhalation, based on ambient air, was around 10 μg/m^3. In addition, the maximum expected concentration of exposure for indoor air was 710 μg/m^3. The mean annual value for atmospheric concentration in fiscal 2012 was calculated by using a plume-puff model on the basis of releases to the atmosphere reported according to the PRTR Law; this model predicted a maximum level of 130 μg/m^3.

The maximum expected oral exposure was estimated to be generally less than 0.004 μg/kg/day on the basis of calculations from data for groundwater, and around 0.016 μg/kg/day on the basis of calculations from data for public freshwater bodies. A maximum expected oral exposure of around 0.016 μg/kg/day was adopted for this substance. However, calculations based on a level of 0.12 μg/kg/day for potable water in a study of a limited area gave a maximum expected oral exposure of 0.0048 μg/kg/day. In contrast, when releases to public freshwater bodies in fiscal 2012 reported according to the PRTR Law 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 14 μg/L. Using this estimated concentration for rivers to calculate oral exposure gave 0.56 μg/kg/day. The exposure level 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.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was around 0.4 μg/L for public freshwater bodies and around 0.05 μg/L for seawater. When releases to public freshwater bodies in fiscal 2012 reported according to the PRTR Law 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 14 μg/L.

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3. Initial assessment of health risk

This substance is irritating to the eyes, skin and respiratory tract. Chemical pneumonitis may occur if the substance is swallowed in its liquid form and reaches the lungs. The central nervous system may also be affected. When inhaled, coughing, sore throat, dizziness, lethargy and headache may occur, while burning sensation, in addition to these symptoms, may occur in the throat and in the chest. Contact of the substance with the eyes may cause redness and pain, while contact with the skin may cause redness.

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

With regard to the oral exposure to the substance, the NOAEL of 136 mg/kg/day (based on liver and kidney weights increase and cloudy swelling), resulting from mid-term and long-term toxicity tests on rats, was adjusted according to the test conditions, to obtain the exposure of 97 mg/kg/day, and was divided by a factor of 10 due to the short test periods. The outcome of 9.7 mg/kg/day was considered to be the reliable lowest dose of the substance and was identified as its 'non-toxic level*'. As for the inhalation exposure, the NOAEL of 75 ppm (based on hepatocellular syncytial degeneration and anterior pituitary hyperplasia), resulting from mid-term and long-term toxicity tests on mice, was adjusted according to the test conditions to obtain the exposure of 13.4 ppm (58 mg/m^3), and was identified to be the reliable lowest dose of the substance as its 'non-toxic level*'.

Concerning the oral exposure, the predicted maximum exposure level was approximately 0.016μg/kg/day, assuming the ingestion of water from public water bodies and freshwater. The MOE (Margin of Exposure) of 12,000 was derived from this level and the 'non-toxic level*' of 9.7 mg/kg/day, after the division by a factor of 10 to convert animal data to human data and further by 5 to take into account the carcinogenic properties of the substance. In addition, the MOE of 350 was derived from the maximum exposure level of 0.56 μg/kg/day; derived itself from the concentration in effluents from high discharging plants, predicted according to the reported data in FY 2012 under the PRTR Law. As exposure to the substance in the environment through diet is limited, the MOE would not change significantly even when this exposure is included. Therefore, no further action would be required at present to assess the health risk of this substance for the oral exposure.

Regarding the inhalation exposure to the substance, the predicted maximum exposure concentration in ambient air was approximately 10 μg/m^3. The MOE of 120 was derived from the substance's 'non-toxic level*' of 58 mg/m^3 and the predicted maximum exposure concentration, after the division by a factor of 10 to convert animal data to human data and further by 5 to take into account the carcinogenic effect of the substance. In addition, the MOE of 9 was derived from the maximum concentration in ambient air near the high discharging plants area of 130 μg/m^3 (annual mean), calculated according to the reported emissions in FY 2012 under the PRTR Law. Moreover, the predicted maximum exposure concentration in indoor air is approximately 710 μg/m^3, and the MOE derived from this level would be 2. Therefore, collection of further information would be required to assess the health risk for the inhalation exposure to this substance in ambient air and the substance is considered to be a candidate for further work concerning inhalation exposure in indoor 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*' 9.7 mg/kg/day	Rat	Liver and kidney weights increase, cloudy swelling	Drinking water	– μg/kg/day	MOE	–	×	○
				Groundwater	0.016 μg/kg/day	MOE	12,000	○	
Inhalation	'Non-toxic level*' 5.8 mg/m^3	Mouse	Hepatocellular syncytial degeneration and anterior pituitary hyperplasia	Ambient air	10 μg/m^3	MOE	120	○	(▲)
				Indoor air	710 μg/m^3	MOE	2	■	■

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.

4.Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 48-h EC_{50} of 1,340 μg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 1,810 μg/L for swimming inhibition in the crustacean *Daphnia magna*, a 96-h LC_{50} of 4,200 μg/L for the fish species *Oncorhynchus mykiss* (rainbow trout), and a 48-h LC_{50} of 37,800 μg/L in the nonbiting midge *Chironomus plumosus* (buzzer midge). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 13 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 96-h NOEC of 4,500 μg/L for growth inhibition in the diatom *Skeletonema costatum*, and a 7-d NOEC of 956 μg/L for reproductive inhibition in the crustacean *Ceriodaphnia dubia*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 9.5 μg/L was obtained.

The value of 9.5 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.04 for freshwater bodies and 0.005 for seawater. When releases to public freshwater bodies in fiscal 2012 reported according to the PRTR Law 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 14 μg/L, suggesting that locations with concentrations higher than the PNEC may exist. Accordingly, efforts to collect data on this substance are needed, as are measurements of environmental concentrations by taking PRTR data into consideration.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Judgment based on PEC/PNEC ratio	Assessment result
Species	Acute/ chronic	End point			Water body	Predicted environmental concentration PEC (μg/L)			
Crustacean *Ceriodaphnia dubia*	Chronic	NOEC reproductive inhibition	100	9.5	Freshwater	0.4	0.04	○	▲
					Seawater	0.05	0.005		

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work at present.	○
	Inhalation exposure (Ambient air)	Further information collection would be required for risk characterization.	(▲)

	Oral exposure (Indoor air)	The substance is considered to be a candidate for further work.	■
Ecological risk	Requiring information collection.		▲

［Risk judgments］ ○: No need for further work ▲: Requiring information collection

■: Candidates for further work ×: Impossibility of risk characterization

（○）: Although risk to human health could not be confirmed, collection of further information would not be required.

（▲）: Further information collection would be required for risk characterization.