8	CAS No.: －	Substance: Organic tin compounds (Monobutyltin compounds)

Chemical Substances Control Law Reference No.:
PRTR Law Cabinet Order No.:1-239 (Organic tin compounds)

1. General information

Monobutyl tin compounds is a generic term for compounds in which one butyl group is covalently bonded to a tin atom. They include monobutyltin trichloride (MBTC).

The vapor pressure of MBTC is 0.045 mmHg (=6 Pa). MBTC hydrolyzes immediately in water to form monobutyltin hydroxide.

Organic tin compounds are classified as Class 1 Designated Chemical Substances under the PRTR Law. The main uses of MBTC are as a glass surface treatment agent, polyvinylchloride resin stabilizer, and catalyst.

The production and import quantity of monobutyltin halides (Cl, Br, I) in fiscal 2015 was less than 1,000 t. The production and import category under the PRTR Law for organic tin compounds is more than 100 t. The production quantity as organic tin stabilizers in fiscal 2015 was 3,056 t.

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2. Exposure assessment

Total release of organic tin compounds to the environment in fiscal 2015 under the PRTR Law was 5.4 t, of which approximately 5.4 t or 99% were reported. The majority of reported releases were to atmosphere. In addition, 0.019 t was transferred to sewage and 36 t was transferred to waste materials.

Industry types with large reported releases were ceramics and soil and stone product manufacturing for the atmosphere, and transportation equipment manufacturing for public water bodies. The largest release among releases to the environment, including those unreported, was to the atmosphere. A prediction of distribution proportions by individual media was not carried out because the physicochemical properties required for predicting these distribution proportions were lacking.

The maximum expected concentration of exposure to humans via inhalation, based on general environmental atmospheric data, was around 0.0068 μg/m^3 (monobutyltin (MBT) equivalent). The mean annual value for the atmospheric concentration in fiscal 2015 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 1.1 μg/m^3 (MBT equivalent).

The maximum expected oral exposure was estimated to be around 0.0056 μg/kg/day (MBT equivalent) based on calculations from data for public freshwater bodies. In contrast, when releases to public freshwater bodies in fiscal 2015 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 1.4 μg/L (MBT equivalent). This estimated value is significantly higher than the less than 0.0027 μg/L (MBT equivalent) obtained from measurements taken downstream of applicable business sites. For this reason, the maximum expected oral exposure was calculated using the concentration of 0.011 μg/L (MBT equivalent) obtained from downstream of the business establishment where the second highest concentration was estimated to give 0.00044 μg/kg/day (DBT equivalent).

Data related to food could not be obtained. Therefore, recent (fiscal 2005) maximum concentrations for fish species (0.0022 μg/g) and shellfish species (0.030 μg/g) were used along with average daily intakes (66.6 g/capita/day for fish species and 2.4 g/capita/day for shellfish species to calculate an exposure by intake from an environmental medium via food of 0.0044 μg/kg/day (MBT equivalent). Combining this with the oral exposure estimated from public freshwater body data gives 0.010 μg/kg/day (MBT equivalent).

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be

around 0.14 μg/L (MBT equivalent) for public freshwater bodies and around 0.028 μg/L (MBT equivalent) for seawater. When releases to public freshwater bodies in fiscal 2015 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 1.4 μg/L (MBT equivalent) assuming all reported releases were monobutyltin compounds. This estimated value is significantly higher than the less than 0.0027 μg/L (MBT equivalent) obtained from measurements taken downstream of applicable businesses. For this reason, the concentration of 0.011 μg/L (MBT equivalent) obtained from downstream of the business establishment where the second highest concentration was estimated was adopted.

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3. Initial assessment of health risk

No information was available on acute symptoms in humans. Monobutyltin trichloride (MBTC) is severely irritating to the skin and eyes in rabbits. The massive hemorrhages in the gastric and intestinal walls were observed in the mice sacrificed 24 hours after a single dose of 4,000 mg/kg of MBTC by gavage administration.

As sufficient information on the carcinogenicity of monobutyltin compounds was not available, the initial assessment was conducted on the basis of information on their non-carcinogenic effects.

The NOAEL for oral exposure of 96 mg/kg/day (based on the increase in relative weight of the liver, increase in the number of reticulocytes, etc.), determined from toxicity tests in rats exposed to MBTC, was divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 9.6 mg/kg/day was deemed to be the lowest reliable dose and the value of 6.0 mg/kg/day, obtained by conversion to monobutyltin (MBT) for compatibility with the estimate of the exposure level, was identified as the 'non-toxic level*' of the compounds for oral exposure.

The LOAEL for inhalation exposure of 2.4 mg/m^3 (based on edema in the lungs), determined from toxicity tests in rats exposed to MBTC, was adjusted according to exposure conditions to obtain 0.43 mg/m^3 and subsequently 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 0.0043 mg/m^3 was deemed to be the lowest reliable dose, and the value of 0.0027 mg/m^3, obtained by conversion to MBT for compatibility with the estimate of the exposure concentration, was identified as the 'non-toxic level*' of the compounds for inhalation exposure.

With regard to oral exposure, assuming the compounds are absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.0056 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 110,000, when calculated from the predicted maximum exposure level and the 'non-toxic level*' of 6.0 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. In addition, the maximum exposure level was calculated to be 0.00044 μg/kg/day. This value derives from the estimated concentration in the effluents from the high discharging plants, according to the releases of the organic tin compounds reported in FY 2015 under the PRTR Law. The MOE would be 1,400,000, when calculated from this level and the 'non-toxic level*'. Furthermore, assuming the compounds are absorbed via public freshwater bodies and seafood in the context of unidentified exposure level via food, the maximum exposure level would be 0.010 μg/kg/day, and the MOE calculated from this level would be 60,000. Therefore, no further work would be required at present to assess the health risk of monobutyltin compounds via oral exposure.

With regard to inhalation exposure, the predicted maximum exposure concentration in ambient air was 0.0068 μg/m^3, approximately. The MOE would be 40, when calculated from the predicted maximum exposure concentration and the 'non-toxic level*'of 0.0027 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. In addition, the maximum concentration (annual mean) in ambient air near the operators releasing large amount of organic tin compounds was estimated to be 1.1 μg/m^3 based on the releases reported in FY 2015 under the PRTR Law. The MOE would be 0.2, when calculated from this concentration. Therefore, collection of information

would be required to assess the health risk of monobutyltin compounds via inhalation in 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*' 6.0 mg/kg/day	Rats	Increase of relative weight of liver, increase of the number of reticulocytes, etc.	Drinking water	— μg/kg/day	MOE	—	×	○
				Public Freshwater bodies	0.0056 μg/kg/day	MOE	110,000	○	
Inhalation	'Non-toxic level*' 0.0027 mg/m^3	Rats	Edema in the lungs	Ambient air	0.0068 μg/m^3	MOE	40	▲	▲
				Indoor air	— μg/m^3	MOE	—	×	×

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 190 μg/L for growth inhibition in the green algae *Desmodesmus subspicatus*, a 24-h EC_{50} of 30,500 μg/L for immobilization in the crustacean *Daphnia magna*, and a 48-h LC_{50} of 23,700 μg/L for the fish species *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 1.9 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 7.5 μg/L for growth inhibition in the green algae *D. subspicatus*. Accordingly, based on this chronic toxicity value and an assessment factor of 10, a predicted no effect concentration (PNEC) 0.75 μg/L was obtained.

The value of 0.75 μg/L obtained from the chronic toxicity to the algae was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.19 for freshwater bodies and 0.04 for seawater. Accordingly, efforts to collect data are needed. Regarding these substances, efforts are needed to understand trends in production and import quantities as well as in PRTR data, and the necessity of conducting a survey of prevalent concentrations in public water bodies should be considered. Further, there is a need to consider developing more comprehensive chronic toxicity data.

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	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)			
Green algae	Chronic	NOEC Growth inhibition	10	0.75	Freshwater	0.14	0.19	▲	▲
					Seawater	0.028	0.04		

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5. Conclusions

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