9	CAS No.: ―	Substance: Organic tin compounds (Dibutyltin compounds)

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

1. General information

Dibutyltin compounds is a generic term for compounds in which two butyl groups are covalently bonded to a tin atom. They include dibutyltin dichloride (DBTC), dibutyltin dilaurate (DBTL), and dibutyltin oxide (DBTO).

The aqueous solubility of DBTC is 320 mg/L (20°C, pH=2.5), and its vapor pressure is 1.2×10^{-3} mmHg (=0.16 Pa) (25°C). The aqueous solubility of DBTL is less than 1.43 mg/L (20°C). DBTO is insoluble in water and its vapor pressure is 3×10^{-8} mmHg (= 4×10^{-6} Pa) (25°C). The biodegradability (aerobic degradation) is characterized by BOD degradation rates of 50% (DBTL) and 0% (DBTO), and bioaccumulation of both DBTL and DBTO is thought to be nonexistent or low.

Organic tin compounds are classified as Class 1 Designated Chemical Substances under the PRTR Law. The main uses of dibutyltin compounds are as follows: DBTC is used as a raw material for dibutyltin compounds; DBTL is used as a polyvinylchloride resin stabilizer, lubricant, and urethane curing catalyst; and DBTO is used as a raw material for polyvinylchloride resin stabilizer and as a catalyst.

The production and import quantity in fiscal 2015 of DBTO was 1,000 t, and that of dibutyltin aliphatic monocarboxylic acid (C=2–31) salts was less than 1,000 t. The production and import quantity of dibutyltin halide (dichloride, dibromide, and iodide) compounds in fiscal 2015 was not disclosed because the number of reporting businesses was less than two. 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 2017 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. Industries 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 less than 0.0038 μg/m^3 (dibutyltin (DBT) 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 0.01 μg/m^3 (DBT equivalent) when businesses highly unlikely to be handling dibutyltin compounds are excluded.

The maximum expected oral exposure was estimated to be less than 0.000037 μg/kg/day (DBT equivalent) based on calculations from data for groundwater, while that based on calculations from data for public freshwater bodies was estimated to be around 0.00016 μg/kg/day (DBT equivalent). 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 1.9 μg/L (DBT equivalent) assuming all reported releases were dibutyltin compounds. This estimated value is significantly higher than the less than 0.0013 μg/L (DBT equivalent) obtained from measurements taken downstream of applicable business sites. For this reason, the maximum expected oral exposure was calculated using the concentration of 0.014 µg/L (DBT equivalent) obtained from downstream of the business establishment where the second highest concentration was estimated to give 0.00056 µg/kg/day (DBT equivalent).

Data related to food could not be obtained. Therefore, recent (fiscal 2005) maximum concentrations for fish species (0.0050 µg/g) and shellfish species (0.015 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 0.0074 µg/kg/day (DBT equivalent). Combining this with the oral exposure estimated from public freshwater body data gives 0.0076 µg/kg/day (DBT equivalent).

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around 0.004 µg/L (DBT equivalent) for public freshwater bodies and around 0.12 µg/L (DBT 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 1.9 µg/L (DBT equivalent) assuming all reported releases were dibutyltin compounds. This estimated value is significantly higher than the less than the 0.0013 µg/L (DBT equivalent) obtained from measurements taken downstream of applicable businesses. For this reason, the concentration of 0.014 µg/L (DBT 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

Dibutyltin oxide (DBTO) is irritating to the eyes, skin and respiratory tract. DBTO causes effects on the central nervous system, which may result in impaired functions. Exposure could cause death. DBTO causes headache, tinnitus, amnesia and disorientation, if inhaled or ingested. Contact with the eyes causes redness and pain. Contact with the skin causes thermal burns and pain, and the substance on the skin may be absorbed to cause symptoms including headache and tinnitus. Dibutyltin dilaurate (DBTL) is irritating to the eyes and causes redness. The findings of the tests in volunteers indicate that dibutyltin diacetate (DBTA), DBTL, dibutyltin maleate (DBTM) and DBTO are not irritants, and that dibutyltin dichloride (DBTC) proved to be positive chemical burns test. In these tests, saturated solution of each dibutyltin compound was administered by a single application to volunteers on the back of their hands.

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

The LOAEL for oral exposure of 2.5 mg/kg/day (based on the effects on the immune system), determined from toxicity tests in rats exposed to DBTC, 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 0.025 mg/kg/day was deemed to be the lowest reliable dose and the value of 0.019 mg/kg/day, obtained by conversion to dibutyltin (DBT) for compatibility with the estimate of the exposure level, was identified as the ‘non-toxic level*’ of the compounds for oral exposure. The ‘non-toxic level*’ for inhalation exposure could not be identified.

With regard to oral exposure, assuming the compounds are absorbed via public freshwater bodies, the predicted maximum exposure level would be 0.00016 µg/kg/day, approximately. The MOE (Margin of Exposure) would be 12,000, when calculated from the predicted maximum exposure level and the ‘non-toxic level*’of 0.019 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 0.00056 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 3,400, when calculated from this 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 0.0076 µg/kg/day, and the MOE calculated from this level would be 250. Therefore, no further work would be required at present to assess the health risk of dibutyltin compounds via oral exposure.

With regard to inhalation exposure, owing to the lack of identified ‘non-toxic level*’, the health risk could not be assessed. Assuming that 100% of the ingested compounds is absorbed, the ‘non-toxic level*’ for inhalation exposure, derived from the conversion of the ‘non-toxic level*’ for oral exposure, would be 0.063 mg/m^3. The MOE would be over 1,700, when calculated from the predicted maximum exposure level of less than 0.0038 µg/m^3, approximately, and the converted ‘non-toxic level*’ for inhalation exposure, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. The maximum concentration (annual mean) in ambient air near the operators releasing large amount of organic tin compounds was estimated to be 0.01 µg/m^3, based on the releases reported in FY 2015 under the PRTR Law. The MOE would be 630, when calculated from this concentration. Therefore, collection of further information would not be required to assess the health risk of dibutyltin 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*’	0.019	mg/kg/day	Rats	The effects on immune system	Drinking water	―	µg/kg/day	MOE	―	×	○
						Public Freshwater bodies	0.00016	µg/kg/day	MOE	12,000	○	
Inhalation	‘Non-toxic level*’	―	mg/m^3	―	―	Ambient air	<0.0038	µg/m^3	MOE	―	×	(○)
						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 23 µg/L for growth inhibition in the diatom *Skeletonema costatum*, a 48-h EC_{50} of 2.2 µg/L for immobilization in the crustacean *Daphnia magna*, and a 48-h LC_{50} of 753 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 0.022 µg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 69.2 µg/L for growth inhibition in the green algae *Desmodesmus subspicatus*, a 21-d NOEC of 12 µg/L for reproductive inhibition in the crustacean *D. magna*, a 30-d NOEC of 345 µg/L for F0-generation growth inhibition in the fish species *Cyprinodon variegatus* (sheepshead minnow), and an up to 191-d NOEC of 345 µg/L for F1-generation embryo mortality for the same species. Accordingly, based on these chronic toxicity values and an assessment factor of 10, a predicted no effect concentration (PNEC) 1.2 µg/L was obtained.

The value of 0.022 µg/L obtained from the acute toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was 0.18 for freshwater bodies and 5 for seawater. Accordingly, these substances are considered to be candidates for detailed assessment. PEC values for freshwater and seawater differ greatly; accordingly, separate assessments for freshwater and seawater should be considered in the future.

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)			
Crustacean *Daphnia magna*	Acute	EC_{50} Immobilization	100	0.022	Freshwater	0.004	0.18	■	■
					Seawater	0.12	5		

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5. Conclusions

		Conclusions	Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	Although risk to human health could not be confirmed, collection of further information would not be required.	(○)
Ecological risk	Candidates for further work.		■

［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.