7	CAS No.: ―	Substance: Organic tin compounds (Dioctyltin compounds)

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

1. General information

Dioctyltin compounds is a generic term for compounds in which two octyl groups are covalently bonded to a tin atom. They include dioctyltin oxide (DOTO), dioctyltin dichloride (DOTC) and dioctyltin maleate (DOTM).

The aqueous solubility of DOTO is less than 0.0152 mg/L (20°C, pH=6.26), and the vapor pressure is less than 3.2×10^{-6} mmHg (=4.2×10^{-4} Pa) (25°C). The aqueous solubility of DOTC is 1,000 mg/L, and the vapor pressure is 9.8×10^{-7} mmHg (=1.3×10^{-4} Pa) (25°C). The biodegradability (aerobic degradation) of DOTM is characterized by a BOD degradation rate of 3%, and bioaccumulation 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 DOTO are as a raw material for polyvinylchloride resin stabilizers and as catalysts. The main use of DOTC is as an intermediate for polyvinylchloride resin stabilizers. The main use of DOTM is as a polyvinylchloride resin stabilizer.

The production and import quantity of di-*n*-octyltin dihalide (C1, Br, I) compounds and di-*n*-octyl tin dihalide maleate 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 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 the 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 could not be obtained. 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 0.014 µg/m^3 (dioctyltin (DOT) equivalent) when business sites considered highly unlikely to be handling dioctyltin compounds are excluded.

The maximum expected oral exposure was estimated to be around 0.00038 µg/kg/day (DOT 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 2.9 µg/L (DOT equivalent), assuming all reported releases were dioctyltin compounds. Calculating oral exposure to humans by using this estimated river concentration gave 0.12 µg/kg/day (DOT equivalent).

Data related to food could not be obtained. Therefore, recent (fiscal 2008) maximum concentrations for fish species (0.038 µg/g) and shellfish species (0.0003 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 0.051 µg/kg/day (DOT equivalent). Combining this with the oral exposure estimated from public freshwater body data gives 0.051 µg/kg/day (DOT equivalent).

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around 0.0096 μg/L (DOT equivalent) for public freshwater bodies and around 0.0007 μg/L (DOT 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 2.9 μg/L (DOT equivalent), assuming all reported releases were dioctyltin compounds.

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3 Initial assessment of health risk

No information was available on acute symptoms in humans. Convulsions, respiratory depression and dyspnea were observed in mice exposed to dioctyltin bis(2-ethylhexyl maleate), dioctyltin bis(2-ethylhexylmercaptoacetate) (DOT(EHTG)) or dioctyltin bis(butylmaleate) by ingestion. Somnolence, dyspnea and diarrhea were observed in rats and mice exposed to dioctyltin diacetate by ingestion. Fatty liver degeneration and changes in blood vessels or in circulation of kidneys were observed in mice exposed to dioctyltin bis(dodecylmercaptide) by ingestion.

As sufficient information on the carcinogenicity of dioctyltin 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 0.47 mg/kg/day (based on lymphocyte depletion in the thymus), determined from toxicity tests in rats exposed to the mixture of dioctyltin dichloride (DOTC) and monooctyltin trichloride (MOTC), 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 0.0047 mg/kg/day was deemed to be the lowest reliable dose, and the value of 0.0039 mg/kg/day, obtained by conversion to dioctyltin (DOT) 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 0.00038 μg/kg/day, approximately. The MOE (Margin of Exposure) would be 1,000, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 0.0039 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans. For comparison, the maximum exposure level was calculated to be 0.12 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, 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 0.051 μg/kg/day, and the MOE calculated from this level would be 8. Therefore, collection of further information would be required to assess the health risk of dioctyltin compounds via oral exposure.

With regard to inhalation exposure, owing to the lack of identified 'non-toxic level*' and exposure concentrations, 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 0.013 mg/m^3. The maximum concentration (annual mean) in ambient air near the operators releasing large amount of organic tin compounds was estimated to be 0.014 μg/m^3 based on the releases reported in FY 2015 under the PRTR Law. The MOE would be 93, when calculated from this concentration 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. Therefore, collection of further information would be required to assess the health risk of dioctyltin compounds via inhalation in ambient air.

<table>
<tr><th colspan="4">Toxicity</th><th colspan="2">Exposure assessment</th><th colspan="3" rowspan="2">Result of risk assessment</th><th rowspan="2">Judgment</th></tr>
<tr><th>Exposure Path</th><th>Criteria for risk assessment</th><th>Animal</th><th>Criteria for diagnoses (endpoint)</th><th>Exposure medium</th><th>Predicted maximum exposure dose and concentration</th></tr>
<tr><td rowspan="2">Oral</td><td rowspan="2">‘Non-toxic level*’ 0.0039 mg/kg/day</td><td rowspan="2">Rats</td><td rowspan="2">Lymphocyte depletion in the thymus</td><td>Drinking water</td><td>－ µg/kg/day</td><td>MOE</td><td>－</td><td>×</td><td rowspan="2">(▲)</td></tr>
<tr><td>Public Freshwater bodies</td><td>0.00038 µg/kg/day</td><td>MOE</td><td>1,000</td><td>○</td></tr>
<tr><td rowspan="2">Inhalation</td><td rowspan="2">‘Non-toxic level*’ － mg/m³</td><td rowspan="2">－</td><td rowspan="2">－</td><td>Ambient air</td><td>－ µg/m³</td><td>MOE</td><td>－</td><td>×</td><td>(▲)</td></tr>
<tr><td>Indoor air</td><td>－ µg/m³</td><td>MOE</td><td>－</td><td>×</td><td>×</td></tr>
</table>

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 more than 1.1 µg/L for growth inhibition in the green algae *Desmodesmus subspicatus*, a 48-h EC_{50} of 78 µg/L for immobilization in the crustacean *Daphnia magna*, and a 96-h LC_{50} of 86 µg/L for the fish species *Danio rerio* (zebrafish). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of more than 0.011 µg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 72-h NOEC of 0.62 µg/L for growth inhibition in the green algae *D. subspicatus*, and a 21-d NOEC of 131 µg/L for reproductive inhibition in the crustacean *D. magna*. Accordingly, based on these chronic toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) 0.0062 µg/L was obtained.

The value of 0.0062 µg/L obtained from the chronic toxicity to the algae was used as the PNEC for this substance.

The PEC/PNEC ratio was 1.5 for freshwater bodies and 0.11 for seawater. Accordingly, these substances are considered to be candidates for detailed assessment. 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 2.9 µg/L (DOT equivalent), assuming all reported releases were dioctyltin compounds. The ratio of this value and PNEC is 467.

<table>
<tr><th colspan="3">Hazard assessment (basis for PNEC)</th><th rowspan="2">Assessment coefficient</th><th rowspan="2">Predicted no effect concentration PNEC (µg/L)</th><th colspan="2">Exposure assessment</th><th rowspan="2">PEC/ PNEC ratio</th><th rowspan="2">Judgment based on PEC/PNEC ratio</th><th rowspan="2">Assessment result</th></tr>
<tr><th>Species</th><th>Acute/ chronic</th><th>Endpoint</th><th>Water body</th><th>Predicted environmental concentration PEC (µg/L)</th></tr>
<tr><td rowspan="2">Green algae</td><td rowspan="2">Chronic</td><td rowspan="2">NOEC Growth inhibition</td><td rowspan="2">100</td><td rowspan="2">0.0062</td><td>Freshwater</td><td>0.0096</td><td>1.5</td><td rowspan="2">■</td><td rowspan="2">■</td></tr>
<tr><td>Seawater</td><td>0.0007</td><td>0.11</td></tr>
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5. Conclusions

<table>
<tr><th></th><th colspan="2">Conclusions</th><th>Judgment</th></tr>
<tr><td rowspan="2">Health risk</td><td>Oral exposure</td><td>Further information collection would be required.</td><td>(▲)</td></tr>
<tr><td>Inhalation exposure</td><td>Although risk to human health could not be confirmed, further information collection would be required.</td><td>(▲)</td></tr>
<tr><td>Ecological risk</td><td colspan="2">Candidates for further work.</td><td>■</td></tr>
</table>

［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.	