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CAS No.: 26471-62-5 (Mixed isomers)
584-84-9 (4-Methyl isomer, hereinafter 2,4-TDI)
91-08-7 (2-Methyl isomer, hereinafter 2,6-TDI)

Substance: Methyl-1,3-phenylene diisocyanate

| Chemical Substances Control Law Reference No.: | 3-2214 (Diisocyanate toluene) |
| PRTR Law Cabinet Order No.: | 1-298 (Tolylene diisocyanate) |
| Molecular Formula: | C₉H₆N₂O₂ |
| Molecular Weight: | 174.16 |
| Structural Formula: |

Mixed isomers  
2,4-TDI  
2,6-TDI

1. General information

The aqueous solubility and partition coefficient (1-octanol/water) (log K<sub>ow</sub>) of this substance was not calculated using a model because the substance hydrolyzes. The vapor pressure is 0.023 mmHg (3 Pa) (25°C) (2,4-TDI). Biodegradability (aerobic degradation) is judged to be difficult (2,4-TDI), and bioaccumulation is thought to be nonexistent (2,4-TDI). The half-life for hydrolysis (2,4-TDI) is less than 0.5 h (27°C, initial concentration: 10 mg/L), 0.5 h (27°C, initial concentration: 100 mg/L), approximately 0.7 h (27°C, initial concentration: 1,000 mg/L), and approximately 1.6 h (27°C, initial concentration: 10,000 mg/L).

1,3-Diisocyanate (methyl) benzene is designated as a Priority Assessment Chemical Substance, and tolylene diisocyanate is designated as 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). This substance is a key raw material for polyurethane. The production and import quantity in fiscal 2013 was 225,653 t. The production and import category under the PRTR Law is more than 100 t as tolylene diisocyanate.

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2. Exposure assessment

Total release to the environment in fiscal 2013 under the PRTR Law was approximately 2.1 t, of which approximately 2.0 t or 93% of overall releases were reported. The major destination of reported releases was the atmosphere. In addition, approximately 55 t was transferred to waste materials. Industry types with large reported releases were the plastic product manufacturing industry and the chemical industry for the atmosphere, and the chemical industry for public water bodies. The largest release among releases to the environment including those unreported was to the atmosphere.

A multi-media distribution prediction was not carried out because the required physicochemical properties could not be obtained.

The maximum expected concentration of exposure to humans via inhalation, based on general environmental atmospheric data, was less than around 0.0011 µg/m³. The mean annual value for the atmospheric concentration in fiscal 2013 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 0.083 µg/m³. The maximum expected oral exposure to humans could not be obtained. However, when releases to public freshwater bodies in fiscal 2013 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 0.041 µg/L, and calculating oral exposure to humans by using this estimated river concentration gave 0.0016 µg/kg/day. However, taking into account this substance’s high hydrolyzability, the value is likely to be less than 0.0016 µg/kg/day.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, could not be set because water quality data could not be obtained. When releases to public freshwater bodies in fiscal 2013 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 0.041 µg/L. However, taking into account this substance’s high hydrolyzability, the value is likely to be less than 0.041µg/L.

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### 3. Initial assessment of health risk

The isomers of the substance are irritating to the eyes, skin and respiratory tract. Inhalation exposure to the isomers causes abdominal pain, coughs, nausea, shortness of breath, sore throat and vomiting, and may cause asthma-like reactions, chemical bronchitis, pneumonitis and lung edema. Oral exposure to the isomers causes diarrhea in addition to the symptoms of inhalation.

Contact with the eyes causes redness, pain and blurred vision, and contact with skin causes redness, burning sensation and pain.

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

The LOAEL of 23 mg/kg/day for oral exposure (based on limitation of body weight gain, reduction of survival rate and bronchopneumonia), determined from medium-term and long-term toxicity tests in rats, was adjusted for exposure conditions to obtain 16 mg/kg/day, and subsequently divided by a factor of 10 to account for uncertainty in using LOAEL. The obtained value of 1.6 mg/kg/day was deemed to be the lowest reliable dose and was identified as the ‘non-toxic level*’ of the mixture of the isomers for oral exposure.

The NOAEL of 0.0009 ppm for inhalation exposure (based on declines in respiratory function), determined from effects in humans, was adjusted for exposure conditions. The obtained value of 0.00018 ppm (0.0013 mg/m³) was deemed to be the lowest reliable concentration and was identified as the ‘non-toxic level*’ of the mixture of the isomers for inhalation exposure.

With regard to oral exposure to the mixture, owing to lack of identified exposure level, the health risk could not be assessed.

For comparison, the maximum exposure level was calculated to be 0.0016 µg/kg/day. This value derives from the concentration in the effluents from the high discharging plants, estimated according to the emissions data reported in FY 2013 under the PRTR Law. The MOE (Margin of Exposure) would be 20,000, when calculated from this level and the ‘non-toxic level*, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and another factor of 5 to account for carcinogenicity. Since exposure to the isomers in environmental media via food is presumed to be limited, its inclusion in the calculation would not change the MOE significantly. Therefore, collection of further information would not be required to assess the health risk of the mixture via oral exposure.

With regard to inhalation exposure, the predicted maximum exposure concentration in ambient air was less than 0.0011 µg/m³, approximately. The MOE would be over 240, when calculated from the predicted maximum exposure concentration and the ‘non-toxic level*of 0.0013 mg/m³, and subsequently divided by a factor of 5 to account for carcinogenicity. In addition, the maximum concentration (annual mean) in ambient air near the operators releasing large amount of the mixture to ambient air was estimated to be 0.083 µg/m³ on the basis of the data reported in FY 2013 under the PRTR Law. The MOE would be 3, when using this value and the...
non-toxic level* of 0.0013 mg/m³. Therefore, collection of information on inhalation exposure would be required to assess the health risk of the mixture via inhalation in ambient air.

<table>
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<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>
<th>Result of risk assessment</th>
<th>Judgment</th>
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<tr>
<td>Oral</td>
<td>'Non-toxic level*' 1.6 mg/kg/day</td>
<td>Rat</td>
<td>Limitation of body weight gain, reduction of survival rate and bronchopneumonia</td>
<td>Drinking water</td>
<td>— µg/kg/day</td>
<td>MOE — ×</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Groundwater</td>
<td>— µg/kg/day</td>
<td>MOE — ×</td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td>'Non-toxic level*' 0.0013 mg/m³</td>
<td>Human</td>
<td>Declines in lung function</td>
<td>Ambient air</td>
<td>&lt;0.0011 µg/m³</td>
<td>MOE &gt;240 ○</td>
<td>(▲)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Indoor air</td>
<td>— µg/m³</td>
<td>MOE — ×</td>
<td></td>
</tr>
</tbody>
</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.

4. Initial assessment of ecological risk

This substance is used as a raw material for polyurethane. Total release to the environment reported under the PRTR law was approximately 2.1 t, with approximately 2.0 t released to the atmosphere and 0.0015 t to public water bodies. When releases to public freshwater bodies in fiscal 2013 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 0.041 μg/L. The possibility of detecting releases of this substance to the atmosphere in public water bodies is considered to be low, given its high hydrolyzability (half-life of less than several hours) and measured concentrations in typical atmospheric environments.

Release of this substance to the environment from the quantity transferred to waste materials (i.e., 55 t shipped from factories that handle the substance) is unclear. However, the likelihood of exposure to this substance by intake from an environmental medium is considered nonexistent for normal activities when taking into consideration the high hydrolyzability of this substance (half-life of less than several hours).

In addition, the toxicity value for this substance obtained from toxicity test findings for aqueous organisms is thought to indicate the toxicity of its hydrolysis products, and not reflect the actual toxicity of the substance.

Accordingly, an initial assessment of ecological risk to aqueous organisms for this substance was not conducted.

A separate evaluation of the need for an initial assessment of the ecological risk of this substance’s hydrolysis products is considered necessary. Furthermore, among the hydrolysis products of this substance, an initial assessment of ecological risk was conducted for toluene-2,4-diamine (also called 2,4-Diaminotoluene; CAS No.: 95-80-7) in the sixth revision. This indicated that “the need for further work is considered low at this point in time” (PNEC of 52 μg/L obtained from the NOEC for reproductive inhibition in the crustacean Daphnia magna was adopted).

5. Conclusions

<table>
<thead>
<tr>
<th>Health risk</th>
<th>Conclusions</th>
<th>Judgment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral exposure</td>
<td>No need for further work at present.</td>
<td>○</td>
</tr>
<tr>
<td>Inhalation exposure</td>
<td>Further information collection would be required for risk characterization.</td>
<td>(▲)</td>
</tr>
<tr>
<td>Ecological risk</td>
<td>Initial assessment of ecological risk to aqueous organisms for this substance was not carried out. Another evaluation of the need for an initial assessment of ecological risk of substance’s hydrolysis products considered necessary.</td>
<td></td>
</tr>
</tbody>
</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.