2,2,4-Trimethyl-1,3-pentanediol diisobutyrate
CAS N°: 6846-50-0
SIDSI Initial Assessment Report

For

SIAM 3

Williamsburg, Virginia, 13-15 February 1995

1. Chemical Name: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate
2. CAS Number: 6846-50-0
3. Sponsor Country: Japan
   National SIDS Contact Point: Mr. Yasuhisa Kawamura, Ministry of Foreign Affairs
4. Shared Partnership with:
5. Roles/Responsibilities of the Partners:
   • Name of industry sponsor /consortium
   • Process used
6. Sponsorship History
   • How was the chemical or category brought into the OECD HPV Chemicals Programme?
     As a high priority chemical for initial assessment, 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate was selected in the framework of the OECD HPV Chemicals Programme. SIDS Dossier and Testing Plan were reviewed at a SIDS Review Meeting in 1993, where the following SIDS Testing Plan was agreed.
     No testing ( )
     Testing (X)
     Physical-Chemical Properties
     Melting point
     Vapour pressure
     Partition coefficient
     Water solubility
     Environmental fate/Biodegradation
     Biodegradation
     Photodegradation
     Stability in water
     Ecotoxicity
     Acute toxicity to fish
     Acute toxicity to daphnids
     Toxicity to algae
     Chronic toxicity to daphnids
Toxicity

Repeated dose toxicity
Reproductive toxicity
Gene mutation
Chromosomal aberration

At SIAM-2, the conclusions were approved with comments. Comments at SIAM-2: Rearrangement of the documents.

7. Review Process Prior to the SIAM:

8. Quality check process:

9. Date of Submission: December 1994

10. Date of last Update:

11. Comments:
SIDS INITIAL ASSESSMENT PROFILE

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>2,2,4-Trimethyl-1,3-pentanediol diisobutyrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural Formula</td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

2,2,4-Trimethyl-1,3-pentanediol diisobutyrate is stable liquid and the production volume is ca. 1,200 tonnes/year in 1990 - 1993 in Japan. This chemical is used as additives to plastic (plasticizer). This chemical is stable in neutral and acidic solutions, and is considered as “inherently biodegradable”.

PECs have been calculated based on an emission and effluent scenario and a dilution factor. PECs\textsubscript{local} for the aquatic compartment were $5.1 \times 10^{-11}$ and $1.3 \times 10^{-8}$ mg/l.

For the environment, various NOEC and LC\textsubscript{50} values were gained from test results; $LC_{50} = 18$ mg/l (acuteness); $EC_{50} = 8.0$ mg/l (acute algae); NOEC = 5.3 mg/l (acute algae); NOEC = 3.2 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to algae and daphnids, and slightly toxic to fish. The lowest chronic toxicity data to daphnia, 21d-NOEC (reproduction) of *Daphnia magna* (3.2 mg/l) was adopted for the calculation of PNEC. An assessment factor of 100 was used to both acute and chronic toxicity data to determine PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, PNEC of the chemical is 0.032 mg/l. The PEC is lower than the PNEC, therefore the environmental risk is presumably low.

Neither monitoring data at work place nor consumer exposure have been reported. Based on the physico-chemical properties and a calculation model, the level exposed indirectly through the environment was estimated as $9.3 \times 10^{-4}$ mg/man/day. The daily intake through drinking water is estimated as $4.2 \times 10^{-7}$ mg/kg/day and through fish is calculated as $1.5 \times 10^{-5}$ mg/kg/day.

The chemical showed no genotoxic effects in bacteria and chromosomal aberration test *in vitro*.

In a combined repeat dose and reproductive/developmental toxicity screening test, increase of liver and kidney weights were observed in parental animals from the middle dose level (150 mg/kg/day). In the histopathological examinations, increases in grade of basophilic change of renal tubular epithelium and degeneration of hyaline droplet were observed from the same level. In addition, necrosis and other renal effects were also observed. From the view point of reproductive/developmental end-points, there were no effects observed related to mating, fertility and oestrous cycle and also for dams during the pregnancy and lactation period and for pups after their birth. Therefore, NOEL was 30 mg/kg/day for repeated dose toxicity as well as 750 mg/kg/day for reproductive toxicity.

As for indirect exposure via the environment, the daily intake through drinking water is estimated as $4.2 \times 10^{-7}$ mg/kg/day and through fish is calculated as $1.5 \times 10^{-5}$ mg/kg/day. The margin of safety is very large. Therefore, health risk through the environment, in general, is considered to be presumably low due to its use pattern and...
exposure situation.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED
### PHYSICAL-CHEMICAL

<table>
<thead>
<tr>
<th>SPECIES</th>
<th>PROTOCOL</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Melting Point</td>
<td></td>
<td>&lt; -10 °C</td>
</tr>
<tr>
<td>2.2 Boiling Point</td>
<td></td>
<td>280 °C at 1,013 hPa</td>
</tr>
<tr>
<td>2.3 Density</td>
<td></td>
<td>No data available</td>
</tr>
<tr>
<td>2.4 Vapour Pressure</td>
<td>OECD TG 104</td>
<td>8.8 x 10⁻² Pa at 25 °C</td>
</tr>
<tr>
<td>2.5 Partition Coefficient (Log Pow)</td>
<td>OECD TG 107</td>
<td>&gt; 4.11 at 25 °C</td>
</tr>
<tr>
<td>2.6 A. Water Solubility</td>
<td>OECD TG 105</td>
<td>15 mg/l at 25 °C</td>
</tr>
<tr>
<td>B. pH</td>
<td></td>
<td>No data available</td>
</tr>
<tr>
<td>pKa</td>
<td></td>
<td>No data available</td>
</tr>
<tr>
<td>2.12 Oxidation: Reduction Potential</td>
<td></td>
<td>No data available</td>
</tr>
</tbody>
</table>

### ENVIRONMENTAL FATE AND PATHWAY

<table>
<thead>
<tr>
<th>SPECIES</th>
<th>PROTOCOL</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1.1 Photodegradation</td>
<td></td>
<td>Half-life: 90.7 years</td>
</tr>
<tr>
<td>3.1.2 Stability in Water</td>
<td>OECD TG 111</td>
<td>Stable at pH 4.0 and 7.0.</td>
</tr>
<tr>
<td>3.2 Monitoring Data</td>
<td></td>
<td>Half-life: 178 days at pH 9.</td>
</tr>
<tr>
<td>3.3 Transport and</td>
<td>Calculated</td>
<td>100% released to water,</td>
</tr>
<tr>
<td>Distribution</td>
<td>(Fugacity Level III)</td>
<td>In Air 3.4E-10 mg/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In Water 1.2E-05 mg/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In Soil 7.4E-06 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In Sediment 3.2E-03 mg/kg</td>
</tr>
<tr>
<td>3.5 Biodegradation</td>
<td>OECD TG 301C</td>
<td>Inherently biodegradable: 4-82 % (BOD) in 28 days, 2-84% (TOC), 3-100 % (GC) in 28 days</td>
</tr>
<tr>
<td>3.6 Bioaccumulation</td>
<td>Carp</td>
<td>OECD TG 305C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BCF: 5.2 – 31</td>
</tr>
</tbody>
</table>

### ECOTOXICOLOGY

<table>
<thead>
<tr>
<th>SPECIES</th>
<th>PROTOCOL</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1 Acute/Prolonged Toxicity to Fish</td>
<td>OECD TG 203</td>
<td>LC₅₀ (24hr): 18 mg/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LC₅₀ (96hr): 18 mg/L</td>
</tr>
<tr>
<td>4.2 Acute Toxicity to Aquatic Invertebrates (Daphnia)</td>
<td>OECD TG 202</td>
<td>EC₅₀ (24hr): 300 mg/l</td>
</tr>
<tr>
<td>4.3 Toxicity to Aquatic Plants e.g. Algae</td>
<td>OECD TG 201</td>
<td>EC₅₀ (72hr): 8.0 mg/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NOEC: 5.3 mg/l</td>
</tr>
<tr>
<td>4.5.2 Chronic Toxicity to Aquatic Invertebrates (Daphnia)</td>
<td>OECD TG 202</td>
<td>EC₅₀ (21d, Mortality): 12 mg/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC₅₀ (14d, Reproduction): 5.6 mg/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NOEC (21d, Repro): 3.2 mg/l</td>
</tr>
<tr>
<td>4.6.1 Toxicity to Soil Dwelling Organisms</td>
<td></td>
<td>No data available.</td>
</tr>
<tr>
<td>4.6.2 Toxicity to Terrestrial Plants</td>
<td></td>
<td>No data available.</td>
</tr>
<tr>
<td>CAS NO: 6846-50-0</td>
<td>SPECIES</td>
<td>PROTOCOL</td>
</tr>
<tr>
<td>-------------------</td>
<td>--------------</td>
<td>------------------------</td>
</tr>
<tr>
<td><strong>TOXICOLOGY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.1.1 Acute Oral Toxicity</td>
<td>Rat</td>
<td>OECD TG 401</td>
</tr>
<tr>
<td>5.1.2 Acute Inhalation Toxicity</td>
<td>Rat</td>
<td>Unknown</td>
</tr>
<tr>
<td>5.1.3 Acute Dermal Toxicity</td>
<td>Guinea pig</td>
<td>Unknown</td>
</tr>
<tr>
<td>5.4 Repeated Dose Toxicity</td>
<td>Rat</td>
<td>OECD Combined Test</td>
</tr>
<tr>
<td>5.5 Genetic Toxicity In Vitro Bacterial Test (Gene mutation)</td>
<td>S. typhimurium E. coli</td>
<td>OECD TG 471 and 472 and Japanese Guidelines</td>
</tr>
<tr>
<td>5.6 Genetic Toxicity In Vivo Non-Bacterial In Vitro Test (Chromosomal aberrations)</td>
<td>CHL cells</td>
<td>OECD TG 473 and Japanese Guidelines</td>
</tr>
<tr>
<td>5.8 Toxicity to Reproduction</td>
<td>Rat</td>
<td>OECD Combined Test</td>
</tr>
<tr>
<td>5.9 Developmental Toxicity/Teratogenicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.11 Experience with Human Exposure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1 IDENTIFICATION

1.1 Identification of the Substance

CAS Number: 6846-50-0
Chemical Name: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate
Molecular Formula: C_{16}H_{30}O_{4}
Structural Formula:

\[
\begin{align*}
\text{H}_3\text{C} & - \text{C} - \text{O} \\
\text{H}_3\text{C} & - \text{CH}_2 - \text{O} - \text{C} - \text{CH}_3 \\
\text{H}_3\text{C} & - \text{CH} - \text{CH}_2 - \text{O} - \text{C} - \text{CH}_3 \\
\text{H}_3\text{C} & - \text{CH}_2 - \text{O} - \text{C} - \text{CH}_3
\end{align*}
\]

1.2 Purity/Impurities/Additives

Degree of Purity: > 99 %
Major Impurities: 2,2,4-Trimethyl-1,3-pentanediol monoisobutyrate
Essential Additives: No additives

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting point</td>
<td>&lt; -10 °C</td>
</tr>
<tr>
<td>Boiling point</td>
<td>280 °C</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>(8.8 \times 10^{-2}) Pa at 25 °C</td>
</tr>
<tr>
<td>Water solubility</td>
<td>15 mg/l</td>
</tr>
<tr>
<td>Partition coefficient n-octanol/water (log value)</td>
<td>&gt; 4.11</td>
</tr>
</tbody>
</table>

2 GENERAL INFORMATION ON EXPOSURE

2.1 General discussion

2,2,4-Trimethyl-1,3-pentanediol diisobutyrate is a stable liquid and the production volume is ca. 1,200 tonnes/year in 1990 - 1993 in Japan. This chemical is used as an additive for plastic (plasticizer). All disposal wastes are treated by incineration. The chemical seems to be released into water and air from its production sites after biological treatment. No specific monitoring data of the chemical is available. This chemical is stable in neutral and acidic solutions, and is considered to be “inherently biodegradable”.

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8 UNEP PUBLICATIONS
2.2 Environmental exposure

2.2.1 Biodegradability:
If released into water, this substance is inherently biodegraded (MITI (I), corresponding to the OECD 301C: 4-82 % during 28 days based on BOD and 2-84 % based on TOC and 3-100 % based on GC analysis).

2.2.2 Hydrolysis as a function to pH:
The chemical is stable in water at pH 4 and 7 (OECD TG 111). The half-life at pH 9 is 178 days.

2.2.3 Photodegradability (estimation)
A half-life time of 90.7 years is estimated for the direct photodegradation of the chemical in water (MITI, Japan).

2.2.4 Bioaccumulation:
BCF= 5.2 – 31 in carp (6 weeks at 25 °C) suggests that the potential for bioconcentration in aquatic organisms is low.

2.2.5 Estimates of environmental fate, pathway and concentration:
Global situation:

Method: MNSEM 147S (Details are shown in Form-1 Annex)
Input data:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>286.41</td>
</tr>
<tr>
<td>Water solubility</td>
<td>10.00 [mg/l]</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>7.5E-04 [mmHg]</td>
</tr>
<tr>
<td>Log Pow</td>
<td>4.32</td>
</tr>
</tbody>
</table>

Results: Steady state mass and concentration calculated using MNSEM 147S

<table>
<thead>
<tr>
<th>Environment</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>3.4E-10 [mg/l]</td>
</tr>
<tr>
<td>Water</td>
<td>1.2E-05 [mg/l]</td>
</tr>
<tr>
<td>Soil</td>
<td>7.4E-06 [mg/kg dry solid]</td>
</tr>
<tr>
<td>Sediment</td>
<td>3.2E-03 [mg/kg dry solid]</td>
</tr>
</tbody>
</table>

Exposure dose

<table>
<thead>
<tr>
<th>Exposure route</th>
<th>Concentration [mg/day]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation of air</td>
<td>6.8E-06</td>
</tr>
<tr>
<td>Drinking water</td>
<td>2.5E-05</td>
</tr>
<tr>
<td>Ingestion of fish</td>
<td>9.0E-04</td>
</tr>
<tr>
<td>meat</td>
<td>2.9E-10</td>
</tr>
<tr>
<td>milk</td>
<td>3.0E-10</td>
</tr>
<tr>
<td>vegetation</td>
<td>6.9E-08</td>
</tr>
<tr>
<td>Total exposure dose</td>
<td>9.3E-04</td>
</tr>
</tbody>
</table>

= 1.1E-07 [mg/kg/day]
= 4.2E-07 [mg/kg/day]
= 1.5E-05 [mg/kg/day]
= 4.8E-12 [mg/kg/day]
= 5.0E-12 [mg/kg/day]
= 1.1E-09 [mg/kg/day]
= 1.5E-05 [mg/kg/day]

Comparison of calculated environmental concentration of 2,2,4-trimethyl-1,3-pentanediol diisobutyrate using several models.

<table>
<thead>
<tr>
<th>Model</th>
<th>Air[mg/l]</th>
<th>Water[mg/l]</th>
<th>Soil[mg/kg]</th>
<th>Sediment[mg/kg]</th>
</tr>
</thead>
<tbody>
<tr>
<td>MNSEM</td>
<td>3.4E-10</td>
<td>1.2E-05</td>
<td>7.4E-06</td>
<td>3.2E-03</td>
</tr>
<tr>
<td>CHEMCAN2</td>
<td>1.9E-09</td>
<td>1.3E-05</td>
<td>2.3E-04</td>
<td>3.9E-04</td>
</tr>
<tr>
<td>CHEMFRAN</td>
<td>1.0E-09</td>
<td>1.3E-05</td>
<td>4.5E-05</td>
<td>4.3E-04</td>
</tr>
</tbody>
</table>
Local exposure assessment (1):

1. Production volume: 450 tonnes/year
2. Emission Volume:  
   - to water: 18 kg/year
   - to air: negligible
   - waste materials: none
3. Calculation of PEC<sub>local</sub>
   
   \[ PEC_{\text{local}} = \frac{W}{Q} x \left( \frac{100-P}{100} \right) x \left( \frac{1}{D} \right) = 5.1 \times 10^{-8} \text{ mg/l} \]
   
   - W: 18 kg/year
   - Q: 35,000,000 m³/year
   - P: 90%
   - D: 1000 assuming the dilution with sea water.
   
   The actual dilution rate must be much higher because the treated waste water is directly released to the Tokyo Bay

Local exposure assessment (2):

1. Production volume: 680 tonnes/year
2. Emission Volume:  
   - to water: < 26 kg/year
   
   (Substance is not detected in treated waste water (5400 m³/day) with a detection limit of 0.013 ug/ml)
   - to air: negligible
   - waste materials: none
3. Calculation of PEC<sub>local</sub>
   
   \[ PEC_{\text{local}} = \frac{< W}{Q} x 1/D = 1.3 \times 10^{-5} \text{ mg/l} \]
   
   - W: < 26 kg/year
   - Q: 197,100 m³/year
   - D: 1000 assuming the dilution with sea water.
   
   The actual dilution rate must be much higher because the treated waste water is directly released to the Tokyo Bay

2.3 Consumer Exposure

No data on consumer exposure are available.

2.4 Occupational Exposure

No data on work place monitoring have been reported.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Acute Toxicity

LD<sub>50</sub> values in acute oral toxicity studies in rats were reported as > 3,200 mg/kg. LC<sub>50</sub> and LD<sub>50</sub> values in acute inhalation (rats) and dermal (guinea pigs) toxicity studies are 453 ppm and > 20 ml/kg, respectively.

3.1.2 Repeated Dose Toxicity

There is only one key study on repeated dose toxicity of 2,2,4-trimethyl-1,3-pentanediol diisobutyrate. This chemical was studied for oral toxicity in rats according to the OECD combined repeated dose and reproductive/developmental toxicity test [OECD TG 422]. As the study was well
controlled and conducted under GLP, it was appropriate to regard this as a key study. Male and female SD rats were orally administered (gavage) at doses of 0, 30, 150 and 750 mg/kg/day. In male rats, the administration period was two weeks prior to mating, 2 weeks of mating and 2 weeks after the completion of the mating period. In females, in addition to a maximum of four weeks pre-mating and mating period, they were administered throughout the pregnant period until day 3 of post delivery.

The results in clinical observations did not reveal any effects attributable to the administration of test substance, and there was no mortality in any group. Depressions of body weight gain were observed in male rats receiving 750 mg/kg/day, and food consumption of female rats receiving 750 mg/kg/day was greater than those of control. Hematology results show that there were no essential effects of test substance. In blood clinical examination, increases in creatinine and total bilirubin were observed in rats receiving 150 and 750 mg/kg/day, and increases in total protein were observed in male rats receiving 750 mg/kg/day, suggesting that those changes were due to the effect on kidneys and liver. In organ weight analysis, increases in liver weight were observed in male rats receiving 150 and 750 mg/kg/day, moreover increases in kidneys weights were observed in male rats receiving 750 mg/kg/day. Gross findings indicate an increase in incidence of brown colored livers in male rats receiving 750 mg/kg/day. Histopathological findings indicate increases in the grade of basophilic changes of the renal tubular epithelium and degeneration of hyaline droplet in male rats receiving 150 mg/kg/day or more. Moreover, necrosis and fibrosis of the proximal tubule, dilatation of the distal tubule, decreased fatty changes and swelling of the liver cells were observed in male rats receiving 750 mg/kg/day. The NOAEL for repeated dose toxicity in rats is considered to be 30 mg/kg/day.

3.1.3 Mutagenicity

Bacterial test

A reverse gene mutation assay was conducted in line with Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Test Guidelines 471 and 472, using the pre-incubation method. This study was well controlled and regarded as a key study.

2,2,4-Trimethyl-1,3-pentanediol diisobutyrate showed negative results in Salmonella typhimurium TA100, TA1535, TA98, TA1537 and Escherichia coli WP2 uvrA at concentrations up to 5 mg/plate with or without a metabolic activation system (MHW, 1993).

Non-bacterial test in vitro

A chromosomal aberration test in line with Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Test Guideline 473 was conducted using cultured Chinese Hamster lung (CHL/IU) cells. Neither structural chromosomal aberrations nor polypoidy were recognized up to a maximum concentration of 0.04 mg/ml under conditions of both continuous treatment and short-term treatment with or without an exogeneous metabolic activation system (MHW, 1998).

In vivo test

No data are available on in vivo genotoxic effects.

3.1.4 Toxicity for Reproduction

2,2,4-Trimethyl-1,3-pentanediol diisobutyrate was studied for oral toxicity in rats according to the OECD combined repeated dose and reproductive/developmental toxicity test [OECD TG 422] at doses of 0, 30, 150 and 750 mg/kg/day. Although this combined study was designed to investigate reproductive capability in parental generation as well as development in F₁ offspring, parameters to
evaluate developmental toxicity were limited to only body weights at day 0 and day 4 after birth, and autopsy findings at day 4.

The results observed in mating, fertility and the estrous cycle did not reveal any effects attributable to the administration of the test substance. Observation at delivery, all gestation animals delivered pups, normally and there was not a treatment-related effect throughout the lactation period. The external examination of pups revealed no effects attributable to the administration of the test substance. The body weights of pups showed favorable growths until day 4 of lactation. The necropsy of stillborn, dead pups until day 4 of lactation and newborns at day 4 of lactation did not reveal any effects attributable to the administration of the test substance. The NOAEL values for both parental and F1 offspring in reproductive toxicity are considered to be 750 mg/kg/day.

3.2 Initial Assessment for Human Health

Neither monitoring data in the workplace nor consumer exposure has been reported. Based on the physico-chemical properties and a calculation model, the level exposed indirectly through the environment was estimated as $9.3 \times 10^{-4}$ mg/man/day. The daily intake through drinking water is estimated to be $4.2 \times 10^{-7}$ mg/kg/day and through fish is calculated to be $1.5 \times 10^{-5}$ mg/kg/day.

The chemical showed no genotoxic effects in bacteria and chromosomal aberration tests in vitro.

In a combined repeated dose and reproductive/developmental toxicity screening test, increased liver and kidney weights were observed in parental animals from the middle dose level (150 mg/kg/day). In the histopathological examinations, increases in grade of basophilic changes of renal tubular epithelium and degeneration of hyaline droplet were observed from the same level. In addition, necrosis and other renal effects were also observed. From the viewpoint of reproductive/developmental end-points, there were no effects observed related to mating, fertility and the oestrus cycle, as well as for dams during the pregnancy and lactation period and for pups after their birth. Therefore the NOEL was 30 mg/kg/day for repeated dose toxicity and 750 mg/kg/day for reproductive toxicity.

As for indirect exposure via the environment, the daily intake through drinking water is estimated to be $4.2 \times 10^{-7}$ mg/kg/day and through fish, $1.5 \times 10^{-5}$ mg/kg/day. The margin of safety is very large. Therefore, health risk through the environment, in general, is considered to be presumably low due to its use pattern and exposure situation.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

2,2,4-Trimethyl-1,3-pentanediol diisobutyrate has been tested in a limited number of aquatic species (Selenastrum capricornutum, Daphnia magna and Oryzias latipes), under OECD test guidelines [OECD TG 201, 202 (part I and II) and 203,]. Acute and chronic toxicity data to test organisms for 2,2,4-trimethyl-1,3-pentanediol diisobutyrate are summarized in Table 2. No other ecotoxicological data are available. Various NOEC and LC50 values were gained from above tests; 96h LC50 = 18 mg/l (acute fish); 24h EC50 = 300 mg/l (acute daphnia); 72h NOEC = 5.3 mg/l (algae); NOEC = 3.2 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to daphnids and algae, and slightly toxic to fish. The lowest chronic toxicity data to daphnia (21d-NOEC (reproduction) for Daphnia magna of 3.2 mg/l) was adopted for the derivation of a PNEC. An assessment factor of 100 is applied. Thus the PNEC of 2,2,4-trimethyl-1,3-pentanediol diisobutyrate is 0.032 mg/l. Since the PEC is lower than the PNEC, the environmental risk is presumably low.
Table 2  Acute and chronic toxicity data of 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate to aquatic organisms.

<table>
<thead>
<tr>
<th>Species</th>
<th>Endpoint</th>
<th>Conc. (mg/L)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selenastrum capricornutum (algae)</td>
<td>Biomass: EC50 (72h) NOEC</td>
<td>8 mg/L 5.3 mg/L</td>
<td></td>
</tr>
<tr>
<td>Daphnia magna (water flea)</td>
<td>Mor: LC50(24h) Mor: LC50(21d) Rep: EC50(21d) NOEC(21d)</td>
<td>300 mg/L 12 mg/L 5.6 mg/L 3.2 mg/L</td>
<td>EA, Japan. (1992)</td>
</tr>
<tr>
<td>Oryzias latipes (fish, Medaka)</td>
<td>Mor: LC50(24h) Mor: LC50(72h) Mor:LC50(96h)</td>
<td>18 mg/L 18 mg/L 18 mg/L</td>
<td></td>
</tr>
</tbody>
</table>

Notes: *1 Mor; mortality, Rep; reproduction.

4.2 Initial Assessment for the Environment

2,2,4-Trimethyl-1,3-pentanediol diisobutyrate is a stable liquid and the production volume was ca. 1,200 tonnes/year in 1990 - 1993 in Japan. This chemical is used as an additive to plastic (plasticizer). This chemical is stable in neutral and acidic solutions, and is considered “inherently biodegradable”.

PECs have been calculated based on an emission and effluent scenario and a dilution factor. PEC_{local} for aquatic compartments were $5.1 \times 10^{-11}$ and $1.3 \times 10^{-5}$ mg/l for Tokyo Bay.

For the environment, various NOEC and LC_{50} values were gained from test results; 96h LC_{50} = 18 mg/l (acute fish); 24h EC_{50} = 300 mg/l (acute daphnia); 72h EC_{50} = 8.0 mg/l (acute algae); NOEC = 5.3 mg/l (acute algae); 21d NOEC = 3.2 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to algae and daphnids, and slightly toxic to fish. The lowest chronic toxicity data to daphnids (21d-NOEC (reproduction) for *Daphnia magna* of 3.2 mg/l) was adopted for the derivation of a PNEC. The assessment factors of 100 were used for both acute and chronic toxicity data to determine a PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.032 mg/l. The PEC is lower than the PNEC, therefore environmental risk is presumably low.

5 RECOMMENDATIONS

The chemical is currently considered of low potential risk and low priority for further work.

No further testing is needed at present considering its toxicity and exposure levels.
6 REFERENCES


EA, Japan (1992) "Investigation on the Ecotoxicological Effects of OECD High Production Volume Chemicals", Office of Health Studies, Environmental Health Department, Environment Agency, Japan (HPV/SIDS Test conducted by EA, Japan)

EA and MITI, Japan (1993) Unpublished Report on Exposure Estimation (HPV/SIDS Test conducted by EA and MITI, Japan)


MHW, Japan (1993a) Unpublished Report on Combined Repeat Dose and Reproductive/developmental Toxicity Screening Test of 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate. (HPV/SIDS Test conducted by MHW, Japan)

MHW, Japan (1993b) Unpublished Report on Mutagenicity Test of 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate. (HPV/SIDS Test conducted by MHW, Japan)

MITI, Japan: Unpublished data

MITI, Japan (1992) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Edit CITI, Japan

MITI, Japan (1993) Unpublished Report (Test was performed in Chemicals Inspection and Testing Institute, Japan)
SIDS DOSSIER

2,2,4-Trimethyl-1, 3-pentanediol diisobutyrate

CAS No. 6846-50-0

Sponsor Country: Japan
<table>
<thead>
<tr>
<th>SIDS PROFILE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.01 A.</td>
</tr>
<tr>
<td>1.01 C.</td>
</tr>
<tr>
<td>1.01 D.</td>
</tr>
<tr>
<td>1.01 G.</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1.5</td>
</tr>
<tr>
<td>1.7</td>
</tr>
<tr>
<td>ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)</td>
</tr>
</tbody>
</table>
### SIDS SUMMARY

**CAS NO:** 105-05-5

<table>
<thead>
<tr>
<th>STUDY</th>
<th>Information</th>
<th>OECD Study</th>
<th>GLP</th>
<th>Other Study</th>
<th>Estimation Method</th>
<th>Acceptable</th>
<th>SIDS Testing Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Melting Point</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>2.2</td>
<td>Boiling Point</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>2.3</td>
<td>Density</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>Vapour Pressure</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>Partition Coefficient</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>2.6</td>
<td>Water Solubility</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>pH and pKa values</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**OTHER P/C STUDIES RECEIVED**

**ENVIRONMENTAL FATE and PATHWAY**

| 3.1.1 | Photodegradation | N |     |     |     | Y |
| 3.1.2 | Stability in water | N |     |     |     | Y |
| 3.2   | Monitoring data   | N |     |     |     | N |
| 3.3   | Transport and Distribution | N |     |     |     | N |
| 3.5   | Biodegradation    | N |     |     |     | Y |
| 3.6   | Bioaccumulation   | Y | Y | Y | N | N | Y |

**OTHER ENV FATE STUDIES RECEIVED**

**ECOTOXICITY**

| 4.1   | Acute toxicity to Fish | N |     |     |     | Y |
| 4.2   | Acute toxicity to Daphnia | N |     |     |     | Y |
| 4.3   | Toxicity to Algae      | N |     |     |     | Y |
| 4.5.2 | Chronic toxicity to Daphnia | N |     |     |     | Y |
| 4.6.1 | Toxicity to Soil dwelling organisms | N |     |     |     | N |
| 4.6.2 | Toxicity to Terrestrial plants | N |     |     |     | N |
| 4.6.3 | Toxicity to Birds      | N |     |     |     | N |

**OTHER ECOTOXICITY STUDIES RECEIVED**

**TOXICITY**

| 5.1.1 | Acute Oral | Y | N | N | Y | N | Y | N |
| 5.1.2 | Acute Inhalation | Y | N | N | Y | N | Y | N |
| 5.1.3 | Acute Dermal | Y | N | N | Y | N | Y | N |
| 5.4   | Repeated Dose   | N |     |     |     |     |     | Y |
| 5.5   | Genetic Toxicity in vitro |  |   |   |   |   |   |   |
|       | . Gene mutation | N |     |     |     |     |     | Y |
|       | . Chromosomal aberration | N |     |     |     |     |     | Y |
| 5.6   | Genetic Toxicity in vivo | N |     |     |     |     |     | N |
| 5.8   | Reproduction Toxicity | N |     |     |     |     |     | Y |
| 5.9   | Development / Teratogenicity | N |     |     |     |     |     | Y |
| 5.11  | Human experience | N |     |     |     |     |     | N |

**OTHER TOXICITY STUDIES RECEIVED**
1.01 SUBSTANCE INFORMATION

A. CAS-Number 6846-50-0

B. Name (IUPAC name) 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate

C. Name (OECD name) 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate

D. CAS Descriptor Not applicable

E. EINECS-Number 229-934-9

F. Molecular Formula $C_{16}H_{30}O_{4}$

G. Structural Formula

H. Substance Group Not applicable

I. Substance Remark

J. Molecular Weight 286.41

1.02 OECD INFORMATION

A. Sponsor Country: Japan

B. Lead Organisation:
   Name of Lead Organisation:
   Ministry of Health and Welfare (MHW)
   Ministry of International Trade and Industry (MITI)
   Environment Agency (EA)

   Contact person: Mr. Yasuhisa Kawamura
   Director
   Second International Organization Bureau
   Ministry of Foreign Affairs

   Address: 2-2-1 Kasumigaseki, Chiyoda-ku
   Tokyo 100, Japan
   TEL 81-3-3581-0018
   FAX 81-3-3503-3136

C. Name of responder Same as above contact person
1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

- element
- inorganic
- natural substance
- organic
- organometallic
- petroleum product

B. Physical State

- gaseous
- liquid
- solid

C. Purity

> 99%

1.2 SYNONYMS

Isobutyric acid, 1-isopropyl-2,2-dimethyltrimethylene

1.3 IMPURITIES

2,2,4-Trimethyl-1,3-pentanediol monoisobutyrate

1.4 ADDITIVES

None

1.5 QUANTITY

<table>
<thead>
<tr>
<th>Location</th>
<th>Production (tonnes)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>1,200</td>
<td>1990-1993</td>
</tr>
<tr>
<td>Thailand</td>
<td>145</td>
<td>167 197 127</td>
</tr>
<tr>
<td>Formosa</td>
<td>61</td>
<td>107 132 35</td>
</tr>
<tr>
<td>Korea</td>
<td>0</td>
<td>30 61 2</td>
</tr>
</tbody>
</table>

Reference: MITI, Japan

1.6 LABELLING AND CLASSIFICATION

None

1.7 USE PATTERN

A. General

- Type of Use: main industry use
- Category: Additive to plastic (Plasticizer) 97%

MITI, Japan

B. Uses in Consumer Products

None

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Data are not available.

1.9 SOURCES OF EXPOSURE

(a) Source: Media of release: Water from a production site
Quantities per media: Negligible small

(b)
Source: Media of release: Air from a production site
Quantities per media: Negligible small

Reference: MITI, Japan

1.10 ADDITIONAL REMARKS

A. Options for disposal

   Incineration
   Reference: MITI, Japan

B. Other remarks None
2.1 MELTING POINT

Value: $<-10 ^{\circ}C$
Decomposition: Yes [ ] No [X] Ambiguous [ ]
Sublimation: Yes [ ] No [X] Ambiguous [ ]
Method: Unknown
GLP: Yes [ ] No [ ] ? [X]
Remarks: None
Reference: Unpublished company data

2.2 BOILING POINT

Value: 280 $^{\circ}C$
Pressure: at 1013 hPa
Decomposition: Yes [ ] No [X] Ambiguous [ ]
Method: GLP: Yes [ ] No [ ] ? [X]

2.3 DENSITY (Relative density)

No studies located

2.4 VAPOUR PRESSURE

Value: $8.8 \times 10^{-2}$ Pa
Temperature: 25 $^{\circ}C$
Method: calculated [ ]; measured [X]
OECD Test Guideline 104 (Dynamic Method)
GLP: Yes [X] No [ ] ? [ ]

2.5 PARTITION COEFFICIENT $\log_{10}Pow$

Log Pow: $>4.11$
Temperature: 25 $^{\circ}C$
Method: calculated [ ]; measured [X]
OECD Test Guideline 107
GLP: Yes [X] No [ ] ? [ ]
Remarks: None
Reference: MITI, Japan (1993)

2.6 WATER SOLUBILITY

A. Solubility

Value: ca. 15 mg/l
Temperature: 25 $^{\circ}C$
Description: Miscible[ ]; Of very high solubility [ ]; Of high solubility [ ]; Soluble [ ]; Slightly soluble [ ]; Of low solubility [ ]; Of very low solubility [X]; Not soluble [ ]
Method: Unknown
GLP: Yes [ ] No [ ] ? [X]
Remarks: Unpublished company data

B. **pH Value, pK_a Value** Not applicable

2.7 **FLASH POINT**

Value: 140 °C
Type of test: Closed cup [ ]; Open cup [X]; Other [ ]
Method: JIS K2265-1980
GLP: Yes [ ] No [ ] ? [X]
Remarks: Unpublished company data

2.8 **AUTO FLAMMABILITY**

No studies located

2.9 **FLAMMABILITY**

No studies located

2.10 **EXPLOSIVE PROPERTIES**

No studies located

2.11 **OXIDIZING PROPERTIES**

No studies located

2.12 **OXIDATION: REDUCTION POTENTIAL**

No studies located

2.13 **ADDITIONAL DATA**

A. **Partition co-efficient between soil/sediment and water (K_d)**

No studies located

B. **Other data**

No studies located
3.1 STABILITY

3.1.1 PHOTODEGRADATION

Type: Air [ ]; Water [X]; Soil [ ]; Other [ ]
Light source: Sun light [X]; Xenon lamp [ ]; Other [ ]
Light spectrum: 
Relative intensity: 
Spectrum of substance: \( \varepsilon = 2.58 \text{ at } 300 \text{ nm} \)
Concentration of Substance: 
Estimated parameter for calculation:
- Quantum yield: 0.01
- Concentration: \( 5 \times 10^{-5} \text{ M} \)
- Depth of water body: 500 cm
- Conversion rate: \( 6.023 \times 10^{20} \)

Results:
- Degradation rate: \( 1.21 \times 10^{-14} \text{ mol/l/s} \)
- Half life: 90.7 years


3.1.2 STABILITY IN WATER

Type: Abiotic (hydrolysis) [X]; biotic (sediment)[ ]
Half life: Stable at pH 4, and 7 at 25 °C
Half life time: 178 days at ph 9 at 25 °C
Method: OECD Test Guideline 111
GLP: Yes [X], No [ ] ? [ ]
Test substance: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate
Remarks: None
Reference: MITI, Japan (1993)

3.1.3 STABILITY IN SOIL

No studies located

3.2 MONITORING DATA (ENVIRONMENT)

No studies located

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

3.3.1 TRANSPORT

No studies located

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Media: Air-biota [ ]; Air-biota-sediment-soil-water [ ]; Soil-biota [ ]; Water-air [ ]; Water-biota [ ]; Water-soil [ ]; Other [X] (Air-soil-water-sediment)
Method: Fugacity level I [ ]; Fugacity level II [ ]; Fugacity level III [X];
Fugacity level IV [ ]; Other(calculation) [ ]; Other(measurement) [ ]

Results: Steady state mass and concentration calculated using MNSEM 147S

- Air: 3.4E-10 [mg/l]
- Water: 1.2E-05 [mg/l]
- Soil: 7.4E-06 [mg/kg dry solid]
- Sediment: 3.2E-03 [mg/kg dry solid]

Exposure dose

- Inhalation of air: 6.8E-06 [mg/day]
- Drinking water: 2.5E-05 [mg/day]
- Ingestion of fish: 9.0E-04 [mg/day]
  - meat: 2.9E-10 [mg/day]
  - milk: 3.0E-10 [mg/day]
  - vegetation: 6.9E-08 [mg/day]

Total exposure dose: 9.3E-04 [mg/day]

Remarks: Input data:
- Molecular weight: 286.41
- Water solubility: 10.00 [mg/l]
- Vapor pressure: 7.5E-04 [mmHg]
- Log Pow: 4.32

MNSEM 147S is a slightly revised version of MNSEM 145I. 
addition of air particle compartment to air phase 
execution of calculation on a spreadsheet program

Comparison of calculated environmental concentration using several methods (Japanese environmental conditions are applied to the calculations.)

<table>
<thead>
<tr>
<th>Model</th>
<th>Air [mg/l]</th>
<th>Water [mg/l]</th>
<th>Soil [mg/kg]</th>
<th>Sediment [mg/kg]</th>
</tr>
</thead>
<tbody>
<tr>
<td>MNSEM</td>
<td>3.4E-10</td>
<td>1.2E-05</td>
<td>7.4E-06</td>
<td>3.2E-03</td>
</tr>
<tr>
<td>CHEMCAN2</td>
<td>1.9E-09</td>
<td>1.3E-05</td>
<td>2.3E-04</td>
<td>3.9E-04</td>
</tr>
<tr>
<td>CHEMFRA2</td>
<td>1.0E-09</td>
<td>1.3E-05</td>
<td>4.5E-05</td>
<td>4.3E-04</td>
</tr>
</tbody>
</table>

Reference: EA and MITI, Japan (1993)

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

No studies located

3.5 BIODEGRADATION

Type: aerobic [X]; anaerobic [ ]

Inoculum: adapted [ ]; non-adapted [X];

Concentration of the chemical: 100 mg/l related to COD [ ]; DOC [ ]; Test substance [X];

Medium: water [ ]; water-sediment [ ]; soil [ ]; sewage treatment others [X] (Japanese standard activated sludge)

Degradation: Degree of degradation after 28 days
- 5, 82 and 4 % from BOD
- 2, 84 and 3 % from TOC analysis
- 4, 100 and 3 % from GC analysis
3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 6846-50-0

Results: Readily biodeg. [ ]; Inherently biodeg. [X]; under test condition no biodegradation observed [ ], Other [ ]
Method: OECD Test Guideline 301C
GLP: Yes [X] No [ ] ? [ ]
Test substance: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate
Remarks: None
Reference: MITI, Japan (1992)

3.6 BOD₅, COD OR RATIO BOD₅/COD

No studies located

3.7 BIOACCUMULATION

Species: Carp
Exposure period: 6 weeks
Temperature: 25 °C
Concentration: 
  (1) 0.3 µg/l
  (2) 0.03 µg/l
BCF:
  (1) 5.2 - 31
  (2) 6.0 - 17
Elimination: Yes [ ] No [ ] ? [ ]
Method: OECD Test Guideline 305C
Type of test: [ ] calculated; [X] measured
  static [ ]; semi-static [ ]; flow-through [ ]; other [ ]
GLP: Yes [X] No [ ] ? [ ]
Test substance: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate
Remarks: None
Reference: MITI, Japan (1992)

3.8 ADDITIONAL REMARKS

None

A. Sewage treatment

B. Other information
4.1 **ACUTE/PROLONGED TOXICITY TO FISH**

Type of test: static [ ]; semi-static [X]; flow-through [ ]; other [ ]
open-system [X]; closed-system [ ]

Species: *Oryzias latipes*

Exposure period: 96 hr

Results:
- \( LC_{50} (24h) = 18 \text{ mg/l} \) (95% confidence level: 8.0-40 mg/l)
- \( LC_{50} (48h) = 18 \text{ mg/l} \) (95% confidence level: 11-29 mg/l)
- \( LC_{50} (72h) = 18 \text{ mg/l} \) (95% confidence level: 11-29 mg/l)
- \( LC_{50} (96h) = 18 \text{ mg/l} \) (95% confidence level: 11-29 mg/l)

NOEC =

LOEC =

Analytical monitoring: Yes [X] No [ ] ? [ ]


GLP: Yes [ ] No [X] ? [ ]

Test substance: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate, purity > 98%

Remarks: A group of 10 oryzias latipes were exposed to 5 nominal concentrations (9.5-100 mg/l), DMSO control (0.5 mg/l) and laboratory control.

Reference: EA, Japan (1992)

4.2 **ACUTE TOXICITY TO AQUATIC INVERTEBRATES**

A. **Daphnia**

Type of test: static [X]; semi-static [ ]; flow-through [ ]; other [ ];
open-system [X]; closed-system [ ]

Species: *Daphnia magna*

Exposure period: 24 hr

Results:
- \( EC_{50} (24h) = 300 \text{ mg/l} \) (95% confidence level:190-550 mg/l)
- \( EC_{50} (48h) = \)

NOEC =

LOEC =

Analytical monitoring: Yes [ ] No [X] ? [ ]


GLP: Yes [ ] No [X] ? [ ]

Test substance: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate, purity = > 98%

Remarks: 20 daphnids (4 replicates; 5 organisms per replicate) were exposed to 11 nominal concentrations (3.2-1000 mg/l) and laboratory control.

Reference: EA, Japan (1992)

B. **Other aquatic organisms**

No studies located

*4.3 **TOXICITY TO AQUATIC PLANTS e.g. Algae**

Species: *Selenastrum capricornutum* ATCC 22662

End-point: Biomass [X]; Growth rate [ ]; Other [ ]

Exposure period: 72 hr

Results:
- Biomass: \( EC_{50} (24h) = \)
- \( EC_{50} (72h) = 8.0 \text{ mg/l} \)
- NOEC = 5.3 mg/l (p < 0.05)
- LOEC =
4. ECOTOXICITY

4.4 TOXICITY TO BACTERIA

No studies located

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1. CHRONIC TOXICITY TO FISH

No studies located

(*)4.5.2. CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type of test: static [ ]; semi-static [X]; flow-through [ ]; other [ ]; open-system [X]; closed-system [ ]
Species: Daphnia magna
End-point: Mortality [X]; Reproduction rate [X]; Other [ ]
Exposure period: 21 day
Results:
Mortality: LC₅₀ (24 h) = > 32 mg/l
LC₅₀ (48 h) = 45 mg/l (95% confidence level: 31-110 mg/l)
LC₅₀ (96 h) = 20 mg/l (95% confidence level: 15-29 mg/l)
LC₅₀ (7 d) = 13 mg/l (95% confidence level: 9.9-16 mg/l)
LC₅₀ (14 d) = 12 mg/l (95% confidence level: 9.0-16 mg/l)
LC₅₀ (21 d) = 12 mg/l (95% confidence level: 7.9-19 mg/l)
NOEC =
LOEC =
Reproduction: EC₅₀ (14 d) = 5.6 mg/l (95% confidence level: 2.5-16 mg/l)
EC₅₀ (14 d) = 7.3 mg/l (95% confidence level: 4.9-12 mg/l)
NOEC = 3.2 mg/l (p < 0.05)
LOEC = 1.0 mg/l (p < 0.05)
Analytical monitoring: Yes [ ] No [X] ? [ ]
GLP: Yes [ ] No [X] ? [ ]
Test substance: 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate, purity = > 98 %
Remarks: 40 daphnids (4 replicates; 10 organisms per replicate) were exposed to 5 nominal concentrations (0.32-32 mg/l) and laboratory water control.
Reference: EA, Japan (1992)

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No studies located

4.6.2 TOXICITY TO TERRESTRIAL PLANTS
No studies located

4.6.3 TOXICITY TO OTHER NON MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

No studies located

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No studies located

4.8 BIOTRANSFORMATION AND KINETICS IN ENVIRONMENTAL SPECIES

No studies located

4.9 ADDITIONAL REMARKS

None
5. **ACUTE TOXICITY**

### 5.1 ACUTE ORAL TOXICITY

(a)

- **Type:** LD$_0$ []; LD$_{100}$ [ ]; LD$_{50}$ [X]; LD$_{L0}$ [ ]; Other [ ]
- **Species/strain:** Rat
- **Value:** > 3,200 (mg/kg)
- **Method:** Unknown
- **GLP:** Yes [ ] No [X] ? [ ]
- **Test substance:** 2,2,4-trimethyl-1,3-pentanediol diisobutyrate
- **Remarks:**
- **Reference:** Aetill B.D. et al. (1972)

(b)

- **Type:** LD$_0$ [ ]; LD$_{100}$ [ ]; LD$_{50}$ [X]; LD$_{L0}$ [ ]; Other [ ]
- **Species/strain:** Mouse
- **Value:** > 6,400 (mg/kg)
- **Method:** Unknown
- **GLP:** Yes [ ] No [X] ? [ ]
- **Test substance:** 2,2,4-trimethyl-1,3-pentanediol diisobutyrate
- **Remarks:**
- **Reference:** Aetill B.D. et al. (1972)

### 5.2 CORROSIVENESS/IRRITATION

No studies located
5.2.1 SKIN IRRITATION/CORROSION

(a)
Species/strain: Guinea pig
Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [ ]; Irritating [ ]; Moderate irritating [X]; Slightly irritating [ ]; Not irritating [ ]
Classification: Highly corrosive (causes severe burns) [ ]; Corrosive (caused burns) [ ]; Irritating [ ]; Not irritating [ ]
Method:
GLP: Yes [ ] No [ ] ? [X]
Test substance: 2,2,4-trimethyl-1,3-pentanediol diisobutyrate
Remarks: 5 mg/kg (Mild)
Reference: Aetill B.D. et al. (1972)

5.2.2 EYE IRRITATION/CORROSION
No studies located

5.3 SKIN SENSITISATION
No studies located

*5.4 REPEATED DOSE TOXICITY
Species/strain: Rat (Crj:CD(SD))
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: Oral (gavage)
Exposure period: Males: 44 days including 14 days before mating
Females: from 14 days before mating to day 3 of lactation
Frequency of treatment: 7 days/week
Post exposure observation period:
Dose: 0, 30, 150 or 750 mg/kg (12 animals/group)
Control group: Yes [X]; No [ ]; No data [ ]; Concurrent no treatment [ ]; Concurrent vehicle [X]; Historical [ ]
NOEL: 30 mg/kg/day
LOEL: 150 mg/kg/day
Results: The results in clinical observations did not reveal any effects attributable to the administration of test substance, and there were no mortality in all groups. Depressions of body weight gain were observed in male rats receiving 750 mg/kg/day, and food consumption of female rats receiving 750 mg/kg/day was greater than those of control. As the results of hematology, there were no essential effects of test substance. In blood clinical examination, increases in creatinine and total bilirubin were observed in rats receiving 150 and 750 mg/kg/day, and increases in total protein were observed in male rats receiving 750 mg/kg/day, suggesting that those changes were due to the effect on kidneys and liver. In organ weight analysis, increases in liver weight were observed in male rats receiving 150 and 750 mg/kg/day, moreover increases in kidneys weights were observed in male rats receiving 750 mg/kg/day. As the results of gross findings, increases in incidence of brown colored livers were observed in male rats receiving 750 mg/kg/day. As the results of histopathological findings, increases in grade of
basophilic change of the renal tubular epithelium and degeneration of hyaline droplet were observed in male rats receiving 150 mg/kg/day or more. Moreover, necrosis and fibrosis of the proximal tubule, dilatation of the distal tubule, decreased fatty change and swelling of the liver cells were observed in male rats receiving 750 mg/kg/day.

Method: OECD Combined Repeat dose and Reproductive/Developmental Screening Toxicity Test (1992)

GLP: Yes [X] No [ ] ? [ ]
Test substance: Purity: 99.7 %
Reference: MHW, Japan (1993a)

*5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

(a) Type: Bacterial reverse mutation assay
System of testing: S. typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Species/strain: E. coli uvrA
Concentration: 0, 312.5, 625, 1250, 2500 or 5000 µg/plate
Metabolic activation: With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:
- Cytotoxicity conc: With metabolic activation: 5000 µg/plate
- Precipitation conc: 1250 µg/plate
- Genotoxic effects: + ? -
  - With metabolic activation: [ ] [ ] [X]
  - Without metabolic activation: [ ] [ ] [X]
Method: Japanese Guideline for Screening Mutagenicity testing of chemicals
GLP: Yes [X] No [ ] ? [ ]
Test substance: Purity: 99.7 %
Remarks: Procedure: Plate method
Plates/test: 3
Activation system: Liver S-9 fraction from Phenobarbital and 5,6-Benzoflavone pretreated male SD rats with NADPH-generating system
Media: Histidine selective
No. replicates: 2
Reference: MHW, Japan (1993b)

B. NON-BACTERIAL IN VITRO TEST

Type: Cytogenetics Assay
System of testing: Species/strain: Chinese hamster CHL cells
Concentration: With [ ]; Without [ ]; With and Without [X]; No data [ ]
Metabolic activation: With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:
- Cytotoxicity conc: With metabolic activation: 0.018 mg/ml
- Precipitation conc: 0.04 mg/ml
- Genotoxic effects: + ? -
  - With metabolic activation: [ ] [ ] [X]
  - Without metabolic activation: [ ] [ ] [X]
Method: Japanese Guideline for Screening Mutagenicity testing of chemicals

Reference: MHW, Japan (1993b)
5. TOXICITY

ID: 6846-50-0

5.6 GENETIC TOXICITY IN VIVO

No studies located

5.7 CARCINOGENICITY

No studies located

*5.8 TOXICITY TO REPRODUCTION

Type: Fertility [X]; One generation study [ ]; Two generation study [ ]; Other [X]
Species/strain: Rat (sla:SD)
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: Oral (gavage)
Exposure period: Males: 44 days including 14 days before mating
Females: from 14 days before mating to day 3 of lactation.
Frequency of treatment: 7 days/week
Postexposure observation period:
Premating exposure period: male: 14 days, female: 14 days
Duration of the test;
Doses: 0, 30, 150, or 750 mg/kg (12 animals/sex/group)
Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment [ ]; Concurrent vehicle [X];
Historical [ ]
NOEL Parental: 750 mg/kg/day
NOEL F1 Offspring: 750 mg/kg/day
NOEL F2 Offspring: N/A
Results: The results observed in mating, fertility and estrous cycle did not reveal any effects attributable to the administration of test substance. Observation at delivery, gestation animals delivered of pups, normally and there were not a treatment-related effect throughout the lactation period. The external examination of pups revealed no effects attributable to the administration of test substance. The body weights of pups showed the favorably growths until day 4 of lactation. The necropsy of stillborn, dead pups until day 4 of lactation and newborns at day 4 of lactation did not reveal any effects attributable to the administration of test substance.
Method: Combined Repeated Dose and Reproductive/Developmental toxicity Screening Test

GLP: Yes [X] No [ ] ? [ ]
Test substance: Purity 99.7 %
Remarks: None
Reference: MHW, Japan (1993a)

*5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

No studies located
5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities
   No studies located

B. Toxicodynamics, toxicokinetics
   No studies located

* 5.11 EXPERIENCE WITH HUMAN EXPOSURE
   None
EA, Japan (1992) "Investigation on the Ecotoxicological Effects of OECD High Production Volume Chemicals", Office of Health Studies, Environmental Health Department, Environment Agency, Japan (HPV/SIDS Test conducted by EA, Japan)
EA and MITI, Japan (1993) Unpublished Report on Exposure Estimation (HPV/SIDS Test conducted by EA and MITI, Japan)
MHW, Japan (1993a) Unpublished Report on Combined Repeat Dose and Reproductive/developmental Toxicity Screening Test of 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate. (HPV/SIDS Test conducted by MHW, Japan)
MHW, Japan (1993b) Unpublished Report on Mutagenicity Test of 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate. (HPV/SIDS Test conducted by MHW, Japan)
MITI, Japan: Unpublished data
MITI, Japan (1992) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Edit CITI, Japan
MITI, Japan (1993) Unpublished Report (Test was performed in Chemicals Inspection and Testing Institute, Japan)