3-Methyl-4-nitrophenol
CAS N°: 2581-34-2
SIDS Initial Assessment Report

For

SIAM 2

Paris, 4-6 July 1994

1. Chemical Name: 3-Methyl-4-nitrophenol

2. CAS Number: 2581-34-2

3. Sponsor Country: Japan

National SIDS Contact Point in Sponsor Country:
Mr. Yasuhisa Kawamura, Ministry of Foreign Affairs, Japan

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, 3-methyl-4-nitrophenol 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
   Vapour pressure
   Partition coefficient
Environmental fate/Biodegradation
   Photodegradation
   Stability in water
Ecotoxicity
   Acute toxicity to fish
   Acute toxicity to daphnids
   Toxicity to algae
   Chronic toxicity to daphnids
Toxicity
   Preliminary reproductive toxicity

At SIAM 2, the conclusion was 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: March 1994

10. Date of last Update:

11. Comments:
SIDS INITIAL ASSESSMENT PROFILE

<table>
<thead>
<tr>
<th>CAS No.</th>
<th>2581-34-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Name</td>
<td>Phenol, 3-methyl-4-nitro-</td>
</tr>
<tr>
<td>Structural Formula</td>
<td><img src="image" alt="Structural Formula" /></td>
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</tbody>
</table>

CONCLUSIONS AND RECOMMENDATIONS

Potential risk to man is identified due to genotoxicity and thus presumed carcinogenicity, but measures currently in place reduce risks such that the chemical is of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

3-Methyl-4-nitrophenol is a stable solid, and the production volume was 3,300 tonnes/year for 1990 - 1993 in Japan. The substance is used as an intermediate for the synthesis of pesticides. Based on an international information gathering activity on exposure, 3-methyl-4-nitrophenol has been produced in two OECD Member countries, i.e. Japan and Denmark. In Japan, the chemical is manufactured and processed in a closed system, i.e. the product itself and all reagents and solvents for its synthesis are handled in perfectly closed tubes and vessels. The synthesis is operated within the same plant. At the workplace, protective clothing, gloves and goggles are used. No consumer uses are known. Monitoring data in the general environment in Japan (surface water and sediments) are available, but the substance was not detected in 1984. Regarding the Japanese global situation, the predicted worst case concentration in surface water is $1.7 \times 10^{-4}$ mg/l and the predicted indirect exposure to humans through the environment was calculated to be $1.4 \times 10^{-3}$ mg/man/day (i.e. $2.3 \times 10^{-5}$ mg/kg/day). In Denmark, the chemical is produced, but detailed exposure information is not available, except that there is no consumer use.

For the environment, various NOEC and LC₅₀ values were gained from test results; LC₅₀ = 9.8 mg/l (acute fish); EC₅₀ = 9.1 mg/l (acute daphnia); EC₅₀ = 8.6 mg/l (acute algae); NOEC = 0.78 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish, daphnids and algae. The lowest chronic toxicity result, 21 d-NOEC (reproduction) of *Daphnia magna* (0.78 mg/l), was adopted for the calculation of the PNEC, applying an assessment factor of 100. Thus the PNEC of the chemical is 0.0078 mg/l. Since the PEC is lower than the PNEC, the environmental risk is presumably low.

The chemical showed genotoxic effects in a chromosomal aberration test *in vitro* and in an *in vivo* micronucleus test. In a 6 months repeated dose toxicity test, the chemical showed a transient excretion of glucose to urine in the 1500 ppm group, but no other abnormalities were noted. In an OECD preliminary reproductive/developmental toxicity test, the chemical showed no effect on reproductive ability, organ weight, histopathological appearance of reproductive organs, delivery and maternal behaviour of dams, viability, clinical signs, body weight change and autopsy findings for offspring. Also, as repeated dose effect to male rats, decreased locomotor activity, prone position, bradypnea and thrombus in the kidney, heart and lung were observed in the high-dose group (300 mg/kg/day). The NOEL for 6 months repeated dose toxicity was 500 ppm (30.7 mg/kg/day) in both sexes. The NOEL for reproductive toxicity was 300 mg/kg/day and the NOEL for repeat dose toxicity to male rats in the preliminary reproductive test was 100 mg/kg/day.

3-Methyl-4-nitrophenol showed genotoxicity in an *in vitro* chromosomal aberration test. However, this chemical is used as raw material for the synthesis of pesticides in closed systems, and the results from gathering international exposure information showed that the production volume is low, and exposure to the general population from the general environment is currently low. In Japan, the chemical is manufactured and processed in a closed system, i.e. the product itself and all reagents and solvents for its synthesis are handled in perfectly closed tubes and vessels. The synthesis is operated within the same plant. At the workplace, protective clothing, gloves and goggles are used. The
Daily intake of the chemical via the environment was estimated to be $1.4 \times 10^{-3}$ mg/man/day (i.e. $2.3 \times 10^{-5}$ mg/kg/day) from the result of worst-case calculation using the MNSEM 145I exposure model. The concentrations in surface water and sediments were not detectable in a Japanese environmental monitoring program. No consumer uses have been identified. Although no data on work place monitoring have been reported, voluntary exposure reducing procedures are in place in Japan. Occupational exposure seems to be low.

Therefore, 3-methyl-4-nitrophenol is considered as low priority for further work.

| NATURE OF FURTHER WORK RECOMMENDED |
### FULL SIDS SUMMARY

**3-Methyl-4-nitrophenol**

<table>
<thead>
<tr>
<th>CAS NO: 2581-34-2</th>
<th>SPECIES</th>
<th>PROTOCOL</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PHYSICAL-CHEMICAL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1 Melting Point</td>
<td></td>
<td></td>
<td>133 – 133.5 °C</td>
</tr>
<tr>
<td>2.2 Boiling Point</td>
<td></td>
<td></td>
<td>207 °C</td>
</tr>
<tr>
<td>2.3 Density</td>
<td></td>
<td></td>
<td>No data available</td>
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<tr>
<td>2.4 Vapour Pressure</td>
<td></td>
<td>OECD TG 104</td>
<td>&lt; 5.2 x 10^4 hPa at 100 °C</td>
</tr>
<tr>
<td>2.5 Partition Coefficient (Log Pow)</td>
<td></td>
<td>OECD TG 107</td>
<td>2.12 at 25 °C</td>
</tr>
<tr>
<td>2.6 A. Water Solubility</td>
<td>OECD TG 105</td>
<td></td>
<td>13 mg/L at 25 °C</td>
</tr>
<tr>
<td>B. pH</td>
<td></td>
<td></td>
<td>No data available.</td>
</tr>
<tr>
<td></td>
<td>pKa</td>
<td></td>
<td>Not observed.</td>
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<tr>
<td>2.12 Oxidation: Reduction Potential</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **ENVIRONMENTAL FATE AND PATHWAY** |         |          |         |
| 3.1.1 Photodegradation | Estimation | T₁/₂ = 1.35 y (direct photolysis in water) | |
| 3.1.2 Stability in Water | OECD TG 111 | | Stable at pH 4.0, 7.0, 9.0 |
| 3.2 Monitoring Data | In Japanese monitoring study, not detected from surface water and sediment in 1984. | |
| 3.3 Transport and Distribution | Calculated (MNSEM-147S) | | In Air: 1.8E-9 mg/L |
|                  |         | In Water: 1.7E-4 mg/L |
|                  |         | In Soil: 4.1E-3 mg/g |
|                  |         | In Sediment: 6.8E-3 mg/g |
| 3.5 Biodegradation | OECD TG 301C | | Not readily biodegradable: 0% (BOD) in 28 days, 3% (TOC), 6% (UV) in 28 days |
| 3.6 Bioaccumulation | Carp | OECD TG 305C | BCF: 5.2 – 31 |

| **ECOTOXICOLOGY** |         |          |         |
| 4.1 Acute/Prolonged Toxicity to Fish | Oryzias latipes | OECD TG 203 | LC₅₀ (24hr): 11 mg/L |
|                  |         |         | LC₅₀ (96hr): 9.8 mg/L |
| 4.2 Acute Toxicity to Aquatic Invertebrates (Daphnia) | Daphnia magna | OECD TG 202 | EC₅₀ (24hr): 9.1 mg/l |
| 4.3 Toxicity to Aquatic Plants e.g. Algae | Selenastrum capricornutum | OECD TG 201 | EC₅₀ (72hr): 8.6 mg/l |
| 4.5.2 Chronic Toxicity to Aquatic Invertebrates (Daphnia) | Daphnia magna | OECD TG 202 | LC₅₀ (21d, Mortality): 2.9 mg/l |
|                  |         |         | LC₅₀ (21d, Reproduction): 3.9 mg/l |
| 4.6.1 Toxicity to Soil Dwelling Organisms |         |         | NOEC: 5.8 mg/l |
| 4.6.2 Toxicity to Terrestrial Plants |         |         | NOEC (21d, Repro): 0.78 mg/l |
| 4.6.3 Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds) |         |         | No data available. |

<p>| <strong>TOXICOLOGY</strong> |         |          |         |
| 5.1.1 Acute Oral Toxicity | Rat | Unknown | LD₅₀: 1,200 mg/kg (female) |
| 5.1.2 Acute Inhalation Toxicity | | | LD₅₀: 2,300 mg/kg (male) |
| 5.1.3 Acute Dermal Toxicity |         |         | No data available. |
| 5.4 Repeated Dose Toxicity | Rat | Oral (diet) 6 month | NOEL = 30.7 mg/kg/day |</p>
<table>
<thead>
<tr>
<th>CAS NO: 2581-34-2</th>
<th>SPECIES</th>
<th>PROTOCOL</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.5</td>
<td>Genetic Toxicity In Vitro</td>
<td>S. typhimurium</td>
<td>OECD Guidelines No.471 and 472 and Japanese Guidelines</td>
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<tr>
<td>5.5</td>
<td>Genetic Toxicity In Vitro</td>
<td>E. coli</td>
<td>and Japanese Guidelines</td>
</tr>
<tr>
<td>A. Bacterial Test</td>
<td>(Gene mutation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. Non-Bacterial In Vitro Test</td>
<td>CHL cells</td>
<td></td>
<td>Positive (With metabolic activation)</td>
</tr>
<tr>
<td>B. Non-Bacterial In Vitro Test</td>
<td>(Chromosomal aberrations)</td>
<td></td>
<td>Negative (Without metabolic activation)</td>
</tr>
<tr>
<td>5.6</td>
<td>Genetic Toxicity In Vivo</td>
<td>Mouse</td>
<td>Unknown</td>
</tr>
<tr>
<td>5.8</td>
<td>Toxicity to Reproduction</td>
<td>Rat</td>
<td>OECD Preliminary Reproductive Toxicity Test</td>
</tr>
<tr>
<td>5.9</td>
<td>Developmental Toxicity/Teratogenicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.11</td>
<td>Experience with Human Exposure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SIDS Initial Assessment Report

1  IDENTITY

1.1 Identification of the Substance

CAS Number: 2581-34-2  
IUPAC Name: 3-Methyl-4-nitrophenol  
Molecular Formula: C₇H₇NO₃  
Structural Formula:  

Syonyms: 4-Nitro-m-cresol

1.2 Purity/Impurities/Additives

Degree of Purity: ca. 90 %  
Major Impurities: 3-Methyl-6-nitrophenol  
3-Methyl-4, 6-dinitrophenol  
3-Methyl-2, 4-dinitrophenol  
Essential Additives: No additives

1.3 Physico-Chemical properties

Melting Point: 133-133.5 °C  
Boiling Point 207 °C  
Vapour Pressure < 5.2 x 10⁻⁴ hPa at 100 °C  
Partition Coefficient LogKow 2.12  
Water Solubility 13 mg/l at 25 °C

2  GENERAL INFORMATION ON EXPOSURE

3-Methyl-4-nitrophenol is a stable solid, and the production volume was 3,300 tonnes/year for 1990 – 1993 in Japan. It is used as an intermediate for the synthesis of pesticides. Based on an international information gathering activity on exposure, 3-methyl-4-nitrophenol was produced in 2 OECD member countries, i.e. Japan and Denmark. In Japan, the chemical is manufactured and processed in a closed system, i.e. the product itself and all reagents and solvents for its synthesis are handled in perfectly closed tubes and vessels. The synthesis is operated within the same plant. At the work place, protective clothing, gloves and goggles are used. No consumer uses are known. All disposal wastes are treated by incineration. 3-methyl-4-nitrophenol seems to be released into water and air from its production sites after biological treatment. This chemical is stable in neutral, acidic
or alkaline solutions, and is classified as "not readily biodegradable". Monitoring data in the general environment (surface water and sediments) are available, but the substance was not detected in 1984 in Japan. Regarding the Japanese global situation, the predicted worst case concentration in surface water is $1.7 \times 10^{-4}$ mg/l and the predicted indirect exposure to humans through the environment was calculated to be $1.4 \times 10^{-3}$ mg/man/day (i.e. $2.3 \times 10^{-5}$ mg/kg/day). In Denmark, the chemical is produced, but detailed exposure information is not available, except no consumer use.

2.1 Environmental Exposure and Fate

2.1.1 Photodegradation (estimation)

The half-life time of 1.35 years is estimated for the degradation of 3-methyl-4-nitrophenol in water by direct photodegradation (Lyman et al., 1981).

2.1.2 Stability in Water

The chemical is stable in water at pH 4, 7 and 9 (OECD TG 111).

2.1.3 Biodegradation

If released into water, this substance is not readily biodegraded (MITI (I), corresponding to the OECD 301C: 0 % degradation during 28 days based on BOD, 3 % based on TOC and 6 % based on UV analysis).

2.1.4 Bioaccumulation

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

2.1.5 Estimates of environmental fate, pathway and concentration:

Global situation:

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

Input data:

- Molecular weight: 153.14
- Water solubility: 2.00 [mg/l]
- Vapor pressure: 2.34E-06 [mmHg]
- Log Pow: 2.12

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

- Air: 1.8E-09 [mg/l]
- Water: 1.7E-04 [mg/l]
- Soil: 4.1E-03 [mg/kg dry solid]
- Sediment: 6.8E-03 [mg/kg dry solid]
Exposure dose

<table>
<thead>
<tr>
<th>Source</th>
<th>Dosage [mg/day]</th>
<th>(i.e. [mg/kg/day])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation of air</td>
<td>3.5E-05</td>
<td></td>
</tr>
<tr>
<td>Drinking water</td>
<td>3.3E-04</td>
<td>5.5E-06</td>
</tr>
<tr>
<td>Ingestion of fish</td>
<td>3.2E-04</td>
<td>5.3E-06</td>
</tr>
<tr>
<td>Meat</td>
<td>1.6E-08</td>
<td></td>
</tr>
<tr>
<td>Milk</td>
<td>2.1E-08</td>
<td></td>
</tr>
<tr>
<td>Vegetation</td>
<td>7.1E-04</td>
<td></td>
</tr>
<tr>
<td>Total exposure</td>
<td>1.4E-03</td>
<td>2.3E-05</td>
</tr>
</tbody>
</table>

Comparison of calculated environmental concentration 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>1.8E-09</td>
<td>1.7E-04</td>
<td>4.1E-03</td>
<td>6.8E-03</td>
</tr>
<tr>
<td>CHEMCAN2</td>
<td>3.4E-09</td>
<td>1.7E-04</td>
<td>9.4E-04</td>
<td>5.6E-04</td>
</tr>
<tr>
<td>CHEMFRAN</td>
<td>2.5E-10</td>
<td>1.7E-04</td>
<td>6.5E-05</td>
<td>5.6E-04</td>
</tr>
</tbody>
</table>

2.2 Human Exposure

2.2.1 Occupational Exposure

No data on work place monitoring have been reported.

2.2.2 Consumer Exposure

No data on consumer exposure are available.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Acute Toxicity

LD₅₀ values from an acute oral toxicity study in rats were reported as 2,300 mg/kg for males and 1,200 mg/kg for females. LC₅₀ values for acute inhalation toxicity are not available.

3.1.2 Repeated Dose Toxicity

In a 6 months oral repeated dose toxicity test with Wistar rats at doses of 0, 150, 500 and 1,500 ppm, the chemical showed a transient excretion of glucose to urine in the 1500 ppm group, but no other abnormalities were noted. The NOEL for 6 months repeated dose toxicity was 500 ppm (30.7 mg/kg) in both sexes.
In an OECD preliminary reproductive/developmental toxicity test in rats at doses of 0, 30, and 300 mg/kg/day, the chemical showed decreased locomotor activity, prone position, bradypnea and thrombus in the kidney, heart and lung were observed in the high-dose group (300 mg/kg/day) as repeated dose effect to male rats. NOEL for repeated dose toxicity to male rats in the preliminary reproductive toxicity test was 100 mg/kg/day.

3.1.3 Mutagenicity

In vitro Studies

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.

3-Methyl-4-nitrophenol showed negative results in *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 and *Escherichia coli* WP2 uvrA at concentrations up to 1.5 mg/plate with or without a metabolic activation system (MHW, 1993).

Non-bacterial test

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. This study was well controlled and regarded as a key study. Although 3-methyl-4-nitrophenol showed negative results without metabolic activation, positive results were obtained with metabolic activation (MHW, 1993).

In vivo Studies

In a micronucleus test in mice, a positive result was reported. However, detailed data are not available.

3.1.4 Toxicity for Reproduction

3-Methyl-4-nitrophenol was studied for oral toxicity in rats according to the OECD Preliminary reproductive toxicity test at doses of 0, 30, 100 and 300 mg/kg/day. Although this 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 body weights at day 0 and day 4 after birth, and autopsy findings at day 4.

Effects of the repeated administration on both sexes:

No effects of 3-methyl-4-nitrophenol treatment were revealed in body weight changes, food consumption or autopsy. One male of the 300 mg/kg group died, and decrease in spontaneous activity, prone position and bradypnea were noted in the dead animal and two surviving females of the 300 mg/kg group. On the basis of these findings, NOEL of this chemical was considered to be 100 mg/kg/day for repeated administration toxicity of both sexes in this study.

In effects on reproduction of both sexes and development of the next generation, no effects of this chemical were detected in reproductive ability, organ weights or histopathological examination of the reproductive organs of both sexes, delivery or maternal behavior of dams, viability, general appearance, body weight changes or autopsy of pups. On the basis of these findings, the NOEL of this chemical was considered to be 300 mg/kg/day for reproductive/developmental toxicity of both parent animals and offspring in this study.
3.2 Initial Assessment for Human Health

3-Methyl-4-nitrophenol is a stable solid, and the production volume was 3,300 tonnes/year for 1990 - 1993 in Japan. The substance is used as an intermediate for the synthesis of pesticides. Based on an international information gathering activity on exposure, 3-methyl-4-nitrophenol was produced in 2 OECD member countries, i.e. Japan and Denmark.

In Japan, the chemical is manufactured and processed in a closed system, i.e. the product itself and all reagents and solvents for its synthesis are handled in perfectly closed tubes and vessels. The synthesis is operated within the same plant. There are cases where the feeding to tanks and the filling are under opened systems, but in these cases protective mask, gloves and goggles are used. Although no data on work place monitoring have been reported, the chemical is voluntary managed occupationally in Japan. Occupational exposure seems to be low. No consumer uses are known.

The worst case indirect exposure level through the environment was estimated to be $1.4 \times 10^{-3}$ mg/man/day (i.e. $2.3 \times 10^{-5}$ mg/kg/day). The daily intake through drinking water is estimated to be $5.5 \times 10^{-6}$ mg/kg/day and through fish is calculated as $5.3 \times 10^{-6}$ mg/kg/day.

The chemical showed genotoxic effects in a chromosomal aberration test in vitro and an in vivo micronucleus test. In a 6 months repeated dose toxicity test, the chemical showed a transient excretion of glucose to urine in the 1500 ppm group, but no other abnormalities were noted. In OECD preliminary reproductive/developmental toxicity test, the chemical showed no effect on reproductive ability, organ weight, histopathological appearance of reproductive organs, delivery and maternal behaviour of dams, viability, clinical signs, body weight change and autopsy findings for offspring. Also, as repeated dose effect to male rats, decreased locomotor activity, prone position, bradypnea and thrombus in the kidney, heart and lung were observed in the high-dose group (300 mg/kg/day). The NOEL for 6 months repeated dose toxicity was 500 ppm (30.7 mg/kg) in both sexes. The NOEL for reproductive toxicity was 300 mg/kg/day and the NOEL for repeated dose toxicity to male rats in a preliminary reproductive test was 100 mg/kg/day.

3-Methyl-4-nitrophenol showed genotoxicity in an in vitro chromosomal aberration test. However, this chemical is used as a raw material for the synthesis of pesticides in closed systems, and the results from international exposure information gathering showed production volume is low, and exposure to the general population from the general environment is currently low. In Japan, the chemical is manufactured and processed in a closed system, i.e. the product itself and all reagents and solvents for its synthesis are handled in perfectly closed tubes and vessels. The synthesis is operated within the same plant. At the work place, protective clothing, gloves and goggles are used. The worst case daily intake of the chemical via the environment was estimated to be $1.4 \times 10^{-3}$ mg/man/day (i.e. $2.3 \times 10^{-5}$ mg/kg/day) from a calculation using the MNSEM 145I exposure model. The concentrations in surface water and sediments were not detectable in a Japanese environmental monitoring program. No consumer uses have been identified. Although no data on work place monitoring have been reported, voluntary exposure reducing procedures are in place in Japan. Occupational exposure seems to be low.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

3-Methyl-4-nitrophenol 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, 203]. Acute and chronic toxicity data to test organisms for 3-methyl-4-nitrophenol are summarized in Table 1.
Various NOEC and LC50 values were gained from these tests; 72h-LC50 = 9.8 mg/l (acute fish); 24h-EC50 = 9.1 mg/l (acute daphnia); 72h-EC50 = 8.6 mg/l (acute algae); NOEC= 5.8 (algae); 21d-NOEC = 0.78 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish, daphnids and algae. As the lowest chronic toxicity result, the 21 d-NOEC (reproduction) of *Daphnia magna* (0.78 mg/l) was adopted. An assessment factor of 100 is applied. Thus the PNEC of 3-methyl-4-nitrophenol is 0.0078 mg/l. Since the PEC is lower than the PNEC, the environmental risk is presumably low.

**Table 1.** Acute and chronic toxicity data of 3-methyl-4-nitrophenol to aquatic organisms.

<table>
<thead>
<tr>
<th>Species</th>
<th>Endpoint*1</th>
<th>Conc. (mg/L)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Selenastrum capricornutum</em> (algae)</td>
<td>Biomass: EC50 (72h) NOEC</td>
<td>8.6 mg/L 5.8 mg/L</td>
<td></td>
</tr>
<tr>
<td><em>Daphnia magna</em> (water flea)</td>
<td>Imm: EC50(24h) Mor: LC50(21d) Rep: EC50(21d) NOEC(21d)</td>
<td>9.1 mg/L 2.9 mg/L 3.9 mg/L 0.78 mg/L</td>
<td>EA, Japan. (1992)</td>
</tr>
<tr>
<td><em>Oryzias latipes</em> (fish, Medaka)</td>
<td>Mor: LC50(24h) Mor: LC50(96h)</td>
<td>11 mg/L 9.8 mg/L</td>
<td></td>
</tr>
</tbody>
</table>

Notes: *1 Mor; mortality, Rep; reproduction, Imm; immobility

### 4.2 Initial Assessment for the Environment

3-Methyl-4-nitrophenol is a stable solid, and the production volume was 3,300 tonnes/year for 1990 - 1993 in Japan. The substance is used as an intermediate for the synthesis of pesticides. Based on an international information gathering activity on exposure, 3-methyl-4-nitrophenol was produced in 2 OECD member countries, i.e. Japan and Denmark.

Monitoring data in the general environment in Japan (surface water and sediments) are available, but the substance was not detected in 1984 in Japan. PECs have been calculated based on several models considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The worst case estimated concentrations were $1.8 \times 10^{-9}$ mg/l (air), $1.7 \times 10^{-4}$ mg/l (water), $4.1 \times 10^{-3}$ mg/kg (soil), $6.8 \times 10^{-3}$ mg/kg (sediment).

For the environment, various NOEC and LC50 values were gained from test results; 72h-LC50 = 9.8 mg/l (acute fish); 24h-EC50 = 9.1 mg/l (acute daphnia); 72h-EC50 = 8.6 mg/l (acute algae); 21d-NOEC = 0.78 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish, daphnids and algae. As the lowest chronic toxicity result, the 21 d-NOEC (reproduction) of *Daphnia magna* (0.78 mg/l), was adopted. As assessment factor of 100 is applied. Thus the PNEC of the chemical is 0.0078 mg/l. Since the PEC is lower than the PNEC, the environmental risk is presumably low.

### 5 RECOMMENDATIONS

Potential risk to man is identified due to genotoxicity and thus presumed carcinogenicity, but measures currently in place reduce risks such that the chemical is of low priority for further work.
6 REFERENCES

Bringmann, G. & Kuhn, R. (1977a) Z. fur Wasser- und Abwasser-Forschung, 10(3,4), 87-98
Bringmann, G. & Kuhn, R. (1977b) Z. fur Wasser- und Abwasser-Forschung, 10(5), 161-166
Bringmann, G. et al. (1980b) A. Wasser Forsch., 13(5), 170
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 and MITI, Japan)
Kodama et al. (1975) "Subchronic toxicity Studies of Sumithion, Sumioxon and p-nitro-cresol in rats and 92 week feeding study of Sumithion with special reference to change of cholinesterase activity ", Botyu-Kagaku 40, 38-48
MHW, Japan (1993a) Unpublished Report on Preliminary Reproductive Toxicity Test of 3-Methyl-4-nitrophenol. (HPV/SIDS Test conducted by MHW, Japan)
MHW, Japan (1993b) Unpublished Report on Mutagenicity Test of 3-Methyl-4-nitrophenol. (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 (HPV/SIDS Test conducted by MITI, Japan. Test was performed in Chemicals Inspection and Testing Institute, Japan)


Unpublished company report (1988) "Primary eye and skin irritation tests with 3-methyl-4-nitrophenol in rabbits", unpublished report.
SIDS DOSSIER

3-Methyl-4-nitrophenol

CAS No. 2581-34-2

Sponsor Country: Japan
### 3-METHYL-4-NITROPHENOL

#### SIDS PROFILE

<table>
<thead>
<tr>
<th>1.01 A.</th>
<th>CAS No.</th>
<th>2581-34-2</th>
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</thead>
<tbody>
<tr>
<td>1.01 C.</td>
<td>CHEMICAL NAME (OECD Name)</td>
<td>3-Methyl-4-nitrophenol</td>
</tr>
<tr>
<td>1.01 D.</td>
<td>CAS DESCRIPTOR</td>
<td>Not applicable in this case</td>
</tr>
<tr>
<td>1.01 G.</td>
<td>STRUCTURAL FORMULA</td>
<td><img src="https://example.com/structure.png" alt="Structural formula" /></td>
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</tbody>
</table>

#### OTHER CHEMICAL IDENTITY INFORMATION

| 1.5 | QUANTITY | In Japan 3,300 tonnes in 1990 - 1993. |
| 1.7 | USE PATTERN | Non dispersive use in chemical industry as an intermediate in synthesis of pesticide (100 %) |

#### SOURCES AND LEVELS OF EXPOSURE

1. Amount released from production site to water is negligible in Japan. All leaks and spills are contained and cleaned up in an appropriate manner, i.e., water treatment or incineration. Waste water treated at production site is treated again at sewage treatment plant. Concentration at the first treatment is less than 0.01 %.

2. Information on consumer exposure is not available.

#### ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)

<p>| |</p>
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
</table>
3-Methyl-4-nitrophenol

CAS NO: 2581-34-2

<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>Y</td>
</tr>
<tr>
<td>2.2</td>
<td>Boiling Point</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>2.3</td>
<td>Density</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>2.4</td>
<td>Vapour Pressure</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Y</td>
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<tr>
<td>2.5</td>
<td>Partition Coefficient</td>
<td>N</td>
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<td></td>
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<td>Y</td>
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<td>2.6</td>
<td>Water Solubility</td>
<td>N</td>
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<td></td>
<td></td>
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<td>Y</td>
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<tr>
<td></td>
<td>pH and pKa values</td>
<td>N</td>
<td></td>
<td></td>
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OTHER P/C STUDIES RECEIVED

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<tr>
<th>ENVIRONMENTAL FATE and PATHWAY</th>
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</thead>
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<tr>
<td>3.1.2 Stability in water</td>
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<td>3.2 Monitoring data</td>
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<tr>
<td>3.3 Transport and Distribution</td>
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<td>3.5 Biodegradation</td>
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<td>3.6 Bioaccumulation</td>
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<th>ECOTOXICITY</th>
</tr>
</thead>
<tbody>
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<td>4.1 Acute toxicity to Fish</td>
</tr>
<tr>
<td>4.2 Acute toxicity to Daphnia</td>
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<tr>
<td>4.3 Toxicity to Algae</td>
</tr>
<tr>
<td>4.5.2 Chronic toxicity to Daphnia</td>
</tr>
<tr>
<td>4.6.1 Toxicity to Soil dwelling organisms</td>
</tr>
<tr>
<td>4.6.2 Toxicity to Terrestrial plants</td>
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<tr>
<td>4.6.3 Toxicity to Birds</td>
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OTHER ECOTOXICITY STUDIES RECEIVED

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

OTHER TOXICITY STUDIES RECEIVED
1.01 SUBSTANCE INFORMATION

A. CAS-Number 2581-34-2
B. Name (IUPAC name) Phenol, 3-methyl-4-nitro-
C. Name (OECD name) 3-Methyl-4-nitrophenol
D. CAS Descriptor Not applicable
E. EINECS-Number 219-952-5
F. Molecular Formula C₇H₇NO₃
G. Structural Formula

H. Substance Group Not applicable
I. Substance Remark
J. Molecular Weight 154.14

1.02 OECD INFORMATION

A. Sponsor Country: Japan
B. Lead Organisation:
   Name of Lead Organization: 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 [X]; organometallic [ ]; petroleum product [ ]
B. Physical State gaseous [ ]; liquid [ ]; solid [X]
C. Purity ca. 90 %
1.2 SYNONYMS
4-Nitro-m-cresol

1.3 IMPURITIES
3-Methyl-6-nitrophenol
3-Methyl-2-nitrophenol
3-Methyl-4,6-dinitrophenol
3-Methyl-2,4-dinitrophenol
Moisture, Not less than 10 %

1.4 ADDITIVES
None

1.5 QUANTITY
Location Production (tonnes) Data
Japan 3,300 1990-1993

Reference: MITI, Japan

1.6 LABELLING AND CLASSIFICATION
Labelling None
Classification None

1.7 USE PATTERN
A. General
Type of Use: main industry use
Category: Intermediate for pesticide

Reference: MITI, Japan

B. Uses in Consumer Products
None

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE
Source Number of workers Frequency & duration Emission Date
Maintenance Several 1 time/ 3 days Slight smell 1990

Reference: MITI, Japan

1.9 SOURCES OF EXPOSURE
Source: Media of release: Water from a production site
Quantities per media: Negligible small
Remarks: Wastes water treated at production site is treated again at sewerage treatment plant. Concentration at the first treatment is less than 0.01 %.

Reference: MITI, Japan

1.10 ADDITIONAL REMARKS
## 1. GENERAL INFORMATION

### A. Options for disposal
- **Incineration**

Reference: MITI, Japan

### B. Other remarks
- None
2.1 MELTING POINT

Value: 133 - 133.5 °C
Decomposition: Yes [X] No [ ] Ambiguous [ ]
Sublimation: Yes [ ] No [X] Ambiguous [ ]
Method: Unknown
GLP: Yes [ ] No [X] ? [ ]
Remarks: None
Reference: Fujio et al. (1975)

2.2 BOILING POINT

Value: 207 °C
Pressure: Unknown
Decomposition: Yes [ ] No [X] Ambiguous [ ]
Method: Unknown
GLP: Yes [X] No [ ] ? [X]
Remarks: None
Reference: Company's MSDS

2.3 DENSITY (Relative density)

No studies located

2.4 VAPOUR PRESSURE

Value: < 5.2 x 10^4 hPa
Temperature: 100 °C
Method: calculated [ ]; measured [X]
OECD Test Guideline 104 (Dynamic method)
GLP: Yes [X] No [ ] ? [X]
Remarks: None
Reference: MITI, Japan (1993)

2.5 PARTITION COEFFICIENT log_{10}P_{ow}

Log Pow: 2.12
Temperature: 25 °C
Method: calculated [ ]; measured [X]
OECD Test Guideline 107
GLP: Yes [X] No [ ] ? [X]
Remarks: None
Reference: MITI, Japan (1993)

2.6 WATER SOLUBILITY

A. Solubility

Value: 13 mg/l
Temperature: 25 °C
Description: Miscible [ ]; Of very high solubility [ ]; Of high solubility [ ]; Soluble [ ]; Slightly soluble [ ];
OECD SIDS 3-METHYL-4-NITROPHENOL
2. PHYSICO-CHEMICAL DATA
ID: 2581-34-2

Of low solubility [ ]; Of very low solubility [X]; Not soluble [ ]
Method: OECD Test Guideline
GLP: Yes [ ] No [ ] ? [X]
Remarks: Unpublished Company Data
Reference: 

B. pH Value, pKa Value Not applicable

2.7 FLASH POINT Not applicable

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 (Kd) No studies located

B. Other data None
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: \( \epsilon = 7790 \) at 300 nm
Concentration of Substance: 
Estimated parameter for calculation:
  - Quantum yield: 0.0001
  - Concentration: \( 5 \times 10^{-5} \) M
  - Depth of water body: 500 cm
  - Conversion rate: \( 6.023 \times 10^{20} \)

Results:
  - Degradation rate: \( 8.14 \times 10^{-13} \) mol/l/s
  - Half life: 1.35 years

Reference: Lyman, W. J. et al. (1981)

3.1.2 STABILITY IN WATER

Type: Abiotic (hydrolysis) [X]; biotic (sediment)[ ]
Half life: Stable at pH 4, 7 and 9 at 25 °C
Method: OECD Test Guideline 111
GLP: Yes [X] No [ ] ? [ ]
Remarks: None
Reference: MITI, Japan (1993)

3.1.3 STABILITY IN SOIL

No studies located

3.2 MONITORING DATA (ENVIRONMENT)

(a)
Type of Measurement: Background [ ]; At contaminated site [ ]; Other [X]
Media: Surface water
Results: ND (Detection limits: 0.06-0.2 µg/l) in 7 areas in Japan as of 1984
Remarks: 
Reference: EA, Japan (1987)

(b)
Type of Measurement: Background [ ]; At contaminated site [ ]; Other [X]
Media: Sediment
Results: ND (Detection limits: 0.006-0.028 mg/l) in 7 areas in Japan as of 1984
Remarks: 
Reference: EA, Japan (1987)

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: 1.8E-09 [mg/l]
  - Water: 1.7E-04 [mg/l]
  - Soil: 4.1E-03 [mg/kg dry solid]
  - Sediment: 6.8E-03 [mg/kg dry solid]

**Exposure dose**
- Inhalation of air: 3.5E-05 [mg/day]
- Drinking water: 3.3E-04 [mg/day]
- Ingestion of fish:
  - meat: 1.6E-08 [mg/day]
  - milk: 2.1E-08 [mg/day]
  - vegetation: 7.1E-04 [mg/day]

**Total exposure dose:** 1.4E-03 [mg/day]

**Remarks:**
- Input data:
  - Molecular weight: 153.14
  - Water solubility: 2.00 [mg/l]
  - Vapor pressure: 2.34E-06 [mmHg]
  - Log Pow: 2.12

MNSEM 147S is a slightly revised version of MNSEM 145I.
addition of air particle compartment to air phase
equation 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>1.8E-09</td>
<td>1.7E-04</td>
<td>4.1E-03</td>
<td>6.8E-03</td>
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<tr>
<td>CHEMCAN2</td>
<td>3.4E-09</td>
<td>1.7E-04</td>
<td>9.4E-04</td>
<td>5.6E-04</td>
</tr>
<tr>
<td>CHEMFRAN</td>
<td>2.5E-10</td>
<td>1.7E-04</td>
<td>6.5E-04</td>
<td>5.6E-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];
### 3. ENVIRONMENTAL FATE AND PATHWAYS

**Concentration of the chemical:** 100 mh/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
  0 % from BOD
  3 % from TOC analysis
  6 % from UV analysis

**Results:** Readily biodeg. [ ]; Inherently biodeg. [ ]; under test condition no biodegradation observed [X], Other [ ]

**Method:** OECD Test Guideline 301C

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

**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 mg/l
  2. 0.03 mg/l

**BCF:**
  1. 5.2 - 31
  2. 6.0 - 17

**Elimination:** Yes [ ] No [ ] ? [ ]

**Method:** OECD Test Guideline 305C

**Type of test:** calculated [ ]; measured [X]; static [ ]; semi-static [ ]; flow-through [X]; other [ ]

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

**Remarks:** None

**Reference:** MITI, Japan (1992)

#### 3.8 ADDITIONAL REMARKS

**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\textsubscript{50} (24h) = 11 mg/l (95% confidence level: 3.3-36 mg/l)
- LC\textsubscript{50} (48h) = 9.8 mg/l (95% confidence level: 5.8-16 mg/l)
- LC\textsubscript{50} (72h) = 9.8 mg/l (95% confidence level: 5.8-16 mg/l)
- LC\textsubscript{50} (96h) = 9.8 mg/l (95% confidence level: 5.8-16 mg/l)

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


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

Test substance: 3-Methyl-4-nitrophenol, purity = > 98 %

Remarks: A group of 10 fishes were exposed to 5 nominal concentrations (1.8-18 mg/l) and laboratory water control.

Reference: EA, Japan (1992) (HPV/SIDS Test conducted by EA)

(b)

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

Species: Oryzias latipes

Exposure period: 48 hrs

Results: LC\textsubscript{50} (48h) = 8.4 mg/l

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


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

Remarks: Miyamoto, J. et al. (1978)

Reference: EA, Japan (1992)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

(a)

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

Species: Daphnia magna

Exposure period: 24 hrs

Results: EC\textsubscript{50} (24h) = 9.1 mg/l (95% confidence level: 7.9-11 mg/l)
- EC\textsubscript{50} (48h) =
- NOEC =
- LOEC =

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


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

Test substance: 3-Methyl-4-nitrophenol, purity = > 98 %

Remarks: 20 daphnids (4 replicates; 5 organisms per replicate) were exposed to 5 nominal concentrations (3.2-32 mg/l) and laboratory water control.

Reference: EA, Japan (1992)
(b) Type of test: static [X]; semi-static [ ]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]
Species: *Daphnia magna*
Exposure period: 24 hrs
Results: 
- EC₅₀(24h) = 33 mg/l
- EC₅₀(48h) =
- EC₀ (24h) = 18 mg/l
- EC₁₀₀(24h)= 50 mg/l
- EC₀ (48h) =
Analytical monitoring: Yes [ ] No [ ] ? [X]
Method: Method according to Bringmann & Kuhn
GLP: Yes [ ] No [ ] ? [X]

(c) Type of test: static [ ]; semi-static [ ]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]
Species: *Daphnia magna*
Exposure period: 24 hrs
Results: 
- EC₅₀(24h) = 7.8 mg/l
- EC₅₀(48h) =
- EC₀ (24h) = 4.5 mg/l
- EC₁₀₀(24h)= 16 mg/l
Analytical monitoring: Yes [ ] No [ ] ? [X]
Method: Standard method DIN 38412 Part II (draft)
GLP: Yes [ ] No [ ] ? [X]

**B. OTHER AQUATIC ORGANISMS**

(a) Type of test: static [X]; semi-static [ ]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]
Species: *Crangon septemspinosa* (sand shrimp)
Exposure period: 
Results: 
- LC₅₀(96h) = 6.8 mg/l
- NOEC =
- LOEC =
Analytical monitoring: Yes [ ] No [ ] ? [X]
Method: 
GLP: Yes [ ] No [ ] ? [X]
Test substance: 3-Methyl-4-nitrophenol
Remarks: 
Reference: Mcleese, D.W. et al. (1979)

(b) Type of test: static [ ]; semi-static [ X]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]
4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

(a) Species: *Selenastrum capricornutum* ATCC 22662
End-point: Biomass [X]; Growth rate [X]; Other [ ]
Exposure period: 72 hrs
Results: Biomass: EC50(72h) = 8.6 mg/l
NOEC = 5.8 mg/l (p < 0.05)
LOEC = [ ]
Analytical monitoring: Yes [ ] No [ ] ? [X]
open-system [X]; closed-system [ ]
GLP: Yes [ ] No [X] ? [ ]
Test substance: 3-Methyl-4-nitrophenol, purity = >98%
Remarks: The EC50 values were calculated based on 7 nominal concentrations (0.6-19.0 mg/l) and laboratory water control.
Reference: EA, Japan (1992)

(b) Species: *Scenedesmus quadricauda*
End-point: Biomass [ ]; Growth rate [ ]; Other [ ]
Exposure period: 24 hrs
Results: PGR (24h) = 7.0 mg/l
NOEC = [ ]
LOEC = [ ]
Analytical monitoring: Yes [ ] No [ ] ? [X]
Method: open-system [ ]; closed-system [ ]
GLP: Yes [ ] No [X] ? [X]
Test substance: 3-Methyl-4-nitrophenol
Remarks: [ ]
Reference: Bringmann, G. et al. (1978)

(c) Species: *Scenedesmus quadricauda*
End-point: Biomass [ ]; Growth rate [ ]; Other [ ]
Exposure period: 7 days
Results: PGR (7d) = 6.8 mg/l
NOEC = [ ]
LOEC = [ ]
Analytical monitoring: Yes [ ] No [ ] ? [X]
Method: 27 °C, pH 7.0
open-system [ ]; closed-system [ ]
## 4. ECOTOXICITY

### 4.4 TOXICITY TO BACTERIA

**Type:** Aquatic [ ]; Field [ ]; Soil [ ]; Other [ ]

**Species:** *Pseudomonas putida*

**Exposure period:** 16 hrs

**Results:**
- EC₃ (16hrs) = 6 mg/l

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

**Method:** According to Bringmann & Kuhn

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

**Test substance:** 3-Methyl-4-nitrophenol

**Remarks:** Effect growth inhibition

**Reference:** Bringmann, G. & Kuhn, R. (1977a)

### 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) = 19 mg/l (95% confidence level: 12-71 mg/l)
  - LC₅₀ (48 h) = 12 mg/l (95% confidence level: 8.6-26 mg/l)
  - LC₅₀ (96 h) = 5.6 mg/l (95% confidence level: 4.7-7.0 mg/l)
  - LC₅₀ (7 d) = 4.4 mg/l (95% confidence level: 3.7-5.2 mg/l)
  - LC₅₀ (14 d) = 4.1 mg/l (95% confidence level: 3.5-4.9 mg/l)
  - LC₅₀ (21 d) = 2.9 mg/l (95% confidence level: 2.4-3.5 mg/l)

- NOEC
- LOEC

- Reproduction:
  - EC₅₀ (14 d) = 4.1 mg/l (95% confidence level: 3.5-4.7 mg/l)
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EC_{50} (21 d) = 3.9 mg/l (95% confidence level: 3.6-4.3 mg/l)  
NOEC = 0.78 mg/l (p < 0.05)  
LOEC = 2.5 mg/l (p < 0.05)

Analytical monitoring: Yes [ ] No [X] ? [ ]
GLP: Yes [ ] No [X] ? [ ]
Test substance: 3-Methyl-4-nitrophenol, Purity > 98 %
Remarks: 40 daphnids (4 replicates; 10 organisms per replicate) were exposed to 5 nominal concentration (1-10 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

No studies located
5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(a) Type: LD₅₀ [ ]; LD₅₀₀ [ ]; LD₅₀ [X]; LDL₀ [ ]; Other [ ]
Species/strain: Rat (Wistar)
Value: 2,300 (mg/kg) Male
1,200 (mg/kg) Female
Method: 5-10 animals/dose 14 day observation period
GLP: Yes [ ] No [ ] ? [X]
Test substance: 3-Methyl-4-nitrophenol, purity 99.7 %
Remarks:

(b) Type: LD₅₀ [ ]; LD₅₀₀ [ ]; LD₅₀ [X]; LDL₀ [ ]; Other [ ]
Species/strain: Mouse (DD)
Value: 250 (mg/kg)
Method: Unknown
GLP: Yes [ ] No [ ] ? [X]
Test substance: 3-Methyl-4-nitrophenol
Remarks:

5.1.2 ACUTE INHALATION TOXICITY

No studies located

5.1.3 ACUTE DERMAL TOXICITY

No studies located

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

No studies located

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

Species/strain: New Zealand white rabbit
Results: Highly corrosive [ ]; Corrosive [ ]; Highly irritating [ ]; Irritating [ ]; Moderate irritating [ ]; Slightly irritating [ ]; Not irritating [ ]
Classification: Highly corrosive (causes severe burns) [ ]; Corrosive (caused burns) [ ]; Irritating [ ]; Not irritating [ ]
Method: 3 rabbits, (2 males and 1 female, the same rabbit were used for unwashed group in the eye irritation test), 4-hour-exposure period, 72-hour-observation period application: 0.5 g/ rabbit
GLP: Yes [ ] No [ ] ? [X]
Test substance: Purity 82.6 %
Remarks:
### 5.2.2 EYE IRRITATION/CORROSION

**Species/strain:** New Zealand white rabbit  
**Results:**  
- Highly corrosive [X]; Corrosive [ ]; Highly irritating [ ]; Irritating [ ]; Moderate irritating [ ]; Slightly irritating [ ]; Not irritating [ ]  
**Classification:** Irritating [ ]; Not irritating [ ]; Risk of serious damage to eyes [ ]  
**Method:**  
3 rabbits/unwashed group (2 males and 1 female, the same rabbits were used for the skin irritation test), 3 rabbits/washed of (1 male and 2 females). 96 hour-observation period, application: 0.1 g/rabbit; In the case of washed group, the treated eyes were flushed for 1 minute with ca. 300 ml water 30 seconds after application.  
**GLP:** Yes [X] No [ ]? [ ]  
**Test substance:** purity 82.6 %  
**Remarks:** 54.3 scores after 48 hrs, unwashed group (Extremely irritating)  
**Reference:** Unpublished company report (1988)

### 5.3 SKIN SENSITISATION

No studies located

### 5.4 REPEATED DOSE TOXICITY

(a)  
**Species/strain:** Rat (Wistar)  
**Sex:** Female [ ]; Male [ ]; Male/Female [X]; No data [ ]  
**Route of Administration:** oral (Diet)  
**Exposure period:** 6 months  
**Frequency of treatment:**  
**Post exposure observation period:**  
**Dose:** 0, 150, 500 or 1500 ppm  
**Control group:** Yes [X]; No [ ]; No data [ ]; Concurrent no treatment [ ]; Concurrent vehicle [X]; Historical [ ]  
**NOEL:** 500 ppm (30.7 mg/kg/day)  
**LOEL:**  
**Results:** A transient excretion of glucose into urine was observed in the rats fed 1500 ppm. No other abnormalities were noted.  
**Method:**  
**GLP:** Yes [ ] No [X] ? [ ]  
**Test substance:** Commercial, purity: 99.5 %  
**Reference:** Botyu-Kagaku 40, 38-48 (1975)

### 5.5 GENETIC TOXICITY IN VITRO

#### A. BACTERIAL TEST

(a)  
**Type:** Bacterial reverse mutation assay  
**System of testing:**  
**Species/strain:**  
- *S. typhimurium* TA 98, TA 100, TA 1535, TA 1537, TA 1538  
- *E. coli* WP2 uvrA  
**Concentration:** 78.12 - 2500 µg/plate  
**Metabolic activation:** With [ ]; Without [ ]; With and Without [X]; No data [ ]
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Results:
Cytotoxicity conc: With metabolic activation: 1500 µg/plate
Without metabolic activation: 1500 µg/plate
Precipitation conc:
Genotoxic effects: + ? -
With metabolic activation: [X] [ ] [ ]
Without metabolic activation: [ ] [ ] [X]

Method:
GLP: Yes [X] No [ ] ? [ ]
Test substance: Commercial, purity: 99.9 %
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) (HPV/SIDS Test conducted by MHW, Japan.)

B. NON-BACTERIAL IN VITRO TEST

Type: Cytogenetics Assay
System of testing:
Species/strain: Chinese hamster CHL cells
Concentration: Incubated with 0, 124, 500, 1000 or 2500 µg/plate
Metabolic activation: With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:
Cytotoxicity conc: With metabolic activation: 0.04-0.15 mg/ml
Without metabolic activation: 0.006-0.023 mg/ml
Precipitation conc:
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: Commercial, purity: 99.9 %
Remarks: Plates/test: 2
Activation system: S-9 fraction from the liver of Phenobarbital and 5,6-Benzoflavone induced male SD derived rats with NADPH-generating system
No. replicates: 1
Reference: MHW, Japan (1993b) (HPV/SIDS Test conducted by MHW, Japan.)

5.6 GENETIC TOXICITY IN VIVO

Type:
Species/strain: CFLP strain mice
Sex: Female [ ]; Male [ ]; Male/Female [ ]; No data [ ]
Route of Administration:
Exposure period:
Doses: 25 mg/kg ten times (once a week)
Results:
Effect on mitotic index or P/N ratio:
Genotoxic effects: + ? -
[X] [ ] [ ]
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Method:
GLP: Yes [X] No [ ] ?
Test substance:
Remarks:
Reference: M. Nehèz et al. (1985a,b,c)

5.7 CARCINOGENICITY

No studies located

5.8 TOXICITY TO REPRODUCTION

Type: Fertility [ ]; One generation study [ ]; Two generation study [ ]; Other [X]
Species/strain: Rat (Crj:CD(SD))
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration: oral (gavage)
Exposure period: Male: 46 days including 14 days before mating
Female: from 14 days before mating to day 3 of lactation
Duration of the test;
Doses: 0, 30, 100 or 300 mg/kg (12/animals /sex/ group)
Control group: Yes [X]; No [ ]; No data [ ];
Concurrent no treatment [ ]; Concurrent vehicle [X];
Historical [ ]
NOEL Parental : 300 mg/kg/day
NOEL F1 Offspring: 300 mg/kg/day
NOEL F2 Offspring: N/A

Results:
1. Effects of the repeated administration on both sexes.
   (1) In the 300 mg/kg group, one male died on day 1 of administration. This animal showed decrease in spontaneous activity, prone position and bradypnea before death. Histopathological examination on this animal revealed thrombus formation in the kidney, heart and lungs. General appearance mentioned above was noted on day 20 or 21 of gestation in two surviving females of the 300 mg/kg group. In both sexes excluding the dead animal of 3-methyl-4-nitrophenol groups, yellow urine was noted in all animals during the administration period, which was thought to result from the light yellowish brown appearance of the test compound.

   (2) No effects of 3-methyl-4-nitrophenol treatment were revealed in body weight changes, food consumption or autopsy.

   (3) In conclusion, one male of the 300 mg/kg group died, and decrease in spontaneous activity, prone position and bradypnea were noted in the dead animal and two surviving females of the 300 mg/kg group. On the basis of these findings, NOEL of this chemical was considered to be 100 mg/kg/day for repeated administration toxicity of both sexes in this study.

2. Effects on reproduction of both sexes and development of the next generation. (1) No effects of this chemical were detected in reproductive ability, organ weights or histopathological examination of the reproductive organs of both sexes, delivery or maternal behavior of dams, viability, general appearance, body weight changes or autopsy of pups. (2) On the basis of these findings, NOEL of this chemical was considered to be 300
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mg/kg/day for reproductive/developmental toxicity of both sexes in this study.

Method: OECD Preliminary Reproductive Toxicity Test
GLP: Yes [X] No [ ] ? [ ]
Test substance: Commercial, purity 98.5 %
Remarks: None
Reference: MHW, Japan (1993a) (HPV/SIDS Test conducted by MHW, Japan)

5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

Species/strain: CFLP strain female mice
Sex: Female [ ]; Male [ ]; Male/Female [ ]; No data [ ]
Route of Administration:
Duration of the test: Mice were administered orally at a dose of 25mg/kg on the 7th, 9th and 11th day: and on the 18th day of pregnancy.
Exposure period:
Frequency of treatment:
Doses: 25 mg/kg
Control group: Yes [ ]; No [ ]; No data [ ]; Concurrent no treatment [ ]; Concurrent vehicle [ ]; Historical [ ]

NOEL Maternal Toxicity:
NOEL teratogenicity :
Results: No effect (Number of embryos/pregnant females, Weight of embryos, Postimplantation loss, Malformations)
Method: OECD Preliminary Reproductive Toxicity Test
GLP: Yes [ ] No [ ] ? [ ]
Test substance: Commercial, purity 98.5 %
Remarks: None
Reference: M.Nehèz et al. (1985d)

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

No studies located

B. Toxicodynamics, toxicokinetics

No studies located

5.11 EXPERIENCE WITH HUMAN EXPOSURE

No data available
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