FOREWORD INTRODUCTION

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:

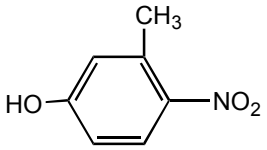
8. Quality check process:

9. Date of Submission: March 1994

10. Date of last Update:

11. Comments:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	2581-34-2
Chemical Name	Phenol, 3-methyl-4-nitro-
Structural Formula	

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 work place, 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 1.7×10^{-4} mg/l and the predicted indirect exposure to humans through the environment was calculated to be 1.4×10^{-3} mg/man/day (i.e. 2.3×10^{-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 LC_{50} values were gained from test results; LC_{50} = 9.8 mg/l (acute fish); EC_{50} = 9.1 mg/l (acute daphnia); EC_{50} = 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 work place, protective clothing, gloves and goggles are used. The

daily intake of the chemical via the environment was estimated to be 1.4 x 10^{-3} mg/man/day (i.e. 2.3 x 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

CAS NO: 2581-34-2		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			133 – 133.5 °C
2.2	Boiling Point			207 °C
2.3	Density			No data available
2.4	Vapour Pressure		OECD TG 104	< 5.2 x 10^{-4} hPa at100 °C
2.5	Partition Coefficient (Log Pow)		OECD TG 107	2.12 at 25 °C
2.6 A.	Water Solubility		OECD TG 105	13 mg/L at 25 °C
B.	pH			No data available.
	pKa			Not observed.
2.12	Oxidation: Reduction Potential			No data available.
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Estimation	$T_{1/2}$ = 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	LC_{50} (24hr): 11 mg/L LC_{50} (96hr): 9.8 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (24hr): 9.1 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	*Selenastrum capricornutum*	OECD TG 201	EC_{50} (72hr): 8.6 mg/l NOEC: 5.8 mg/l
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	LC_{50} (21d, Mortality): 2.9 mg/l LC_{50} (21d, Reproduction): 3.9 mg/l NOEC (21d, Repro): 0.78 mg/l
4.6.1	Toxicity to Soil Dwelling Organisms			No data available.
4.6.2	Toxicity to Terrestrial Plants			No data available.
(4.6.3)	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)			No data available
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	Unknown	LD_{50}: 1,200 mg/kg (female) LD_{50}: 2,300 mg/kg (male)
5.1.2	Acute Inhalation Toxicity			No data available.
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

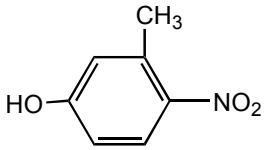
CAS NO: 2581-34-2		SPECIES	PROTOCOL	RESULTS
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	*S.typhimurium* *E. coli*	OECD Guidelines No.471 and 472 and Japanese Guideline	Negative (With metabolic activation) Negative (Without metabolic activation)
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	CHL cells	OECD Guideline No.473 and Japanese Guidelines	Positive (With metabolic activation) Negative (Without metabolic activation)
5.6	Genetic Toxicity In Vivo	Mouse	Unknown	Positive (detailed data are not clear)
5.8	Toxicity to Reproduction	Rat	OECD Preliminary Reproductive Toxicity Test	NOEL Parental = 300 mg/kg/day NOEL F1 offspring = 300 mg/kg/day
5.9	Developmental Toxicity/ Teratogenicity			
5.11	Experience with Human Exposure			

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: $C_7H_7NO_3$
Structural Formula:



Synonyms: 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
Partion 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 1.7×10^{-4} mg/l and the predicted indirect exposure to humans through the environment was calculated to be 1.4×10^{-3} mg/man/day (i.e. 2.3×10^{-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

Inhalation of air:	3.5E-05 [mg/day]	
Drinking water:	3.3E-04 [mg/day]	(i.e. 5.5E-06 mg/kg/day)
Ingestion of fish:	3.2E-04 [mg/day]	(i.e. 5.3E-06 mg/kg/day)
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]	(i.e. 2.3E-05 mg/kg/day)

Comparison of calculated environmental concentration using several models.

Model	Air[mg/l]	Water[mg/l]	Soil[mg/kg]	Sediment[mg/kg]
MNSEM	1.8E-09	1.7E-04	4.1E-03	6.8E-03
CHEMCAN2	3.4E-09	1.7E-04	9.4E-04	5.6E-04
CHEMFRAN	2.5E-10	1.7E-04	6.5E-05	5.6E-04

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

LD_{50} 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. LC_{50} 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 *uvr*A 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 F_1 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 1.4×10^{-3} mg/man/day (i.e. 2.3×10^{-5} mg/kg/day). The daily intake through drinking water is estimated to be 5.5×10^{-6} mg/kg/day and through fish is calculated as 5.3×10^{-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 1.4×10^{-3} mg/man/day (i.e. 2.3×10^{-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 LC_{50} values were gained from these tests; 72h-LC_{50} = 9.8 mg/l (acute fish); 24h-EC_{50} = 9.1 mg/l (acute daphnia); 72h-EC_{50} = 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.

Species	Endpoint[*1]	Conc. (mg/L)	Reference
Selenastrum capricornutum (algae)	Biomass: EC_{50} (72h) NOEC	8.6 mg/L 5.8 mg/L	EA, Japan. (1992)
Daphnia magna (water flea)	Imm: EC_{50}(24h) Mor: LC_{50}(21d) Rep: EC_{50}(21d) NOEC(21d)	9.1 mg/L 2.9 mg/L 3.9 mg/L 0.78 mg/L	
Oryzias latipes (fish, Medaka)	Mor: LC_{50}(24h) Mor: $LC5_0$(96h)	11 mg/L 9.8 mg/L	

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 1.8×10^{-9} mg/l (air), 1.7×10^{-4} mg/l (water), 4.1×10^{-3} mg/kg (soil), 6.8×10^{-3} mg/kg (sediment).

For the environment, various NOEC and LC_{50} values were gained from test results; 72h-LC_{50} = 9.8 mg/l (acute fish); 24h-EC_{50} = 9.1 mg/l (acute daphnia); 72h-EC_{50} = 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

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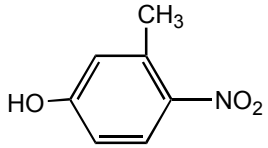
SIDS DOSSIER

3-Methyl-4-nitrophenol

CAS No. 2581-34-2

Sponsor Country: Japan

S I D S P R O F I L E

1.01 A.	**CAS No.**	2581-34-2
1.01 C.	**CHEMICAL NAME (OECD Name)**	3-Methyl-4-nitrophenol
1.01 D.	**CAS DESCRIPTOR**	Not applicable in this case
1.01 G.	**STRUCTURAL FORMULA**	
	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 %)
1.9	**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)		

S I D S S U M M A R Y

3-Methyl-4-nitrophenol

CAS NO: 2581-34-2		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**
PHYSICAL-CHEMICAL DATA								
2.1	Melting Point	Y	N	N	Y	N	Y	N
2.2	Boiling Point	Y	N	N	Y	N	Y	N
2.3	Density	Y	N	N	Y	N	Y	N
2.4	Vapour Pressure	N						Y
2.5	Partition Coefficient	N						Y
2.6	Water Solubility	N						Y
	pH and pKa values	N						N
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	Y	N	N	Y	N	Y	N
3.3	Transport and Distribution	N						N
3.5	Biodegradation	N						Y
3.6	Bioaccumulation	Y	Y	Y	N	N	Y	N
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	N						N
5.1.3	Acute Dermal	N						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*	Y	N	N	Y	N	Y	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**	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**	$C_7H_7NO_3$
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:	**Category:**
main industry use	Intermediate for pesticide 100 %

Reference: MITI, Japan

B. Uses in Consumer Products None

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Source	Number of workers exposed	Frequency & duration of exposure	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

A. **Options for disposal** Incineration

Reference: MITI, Japan

B. **Other remarks** None

2.1 MELTING POINT

Value:	133 - 133.5 °C
Decomposition:	Yes **[ ]** No **[X]** 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:	
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	Unknown
GLP:	Yes **[ ]** 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 **[ ]** ? **[ ]**
Remarks:	
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 **[ ]** ? **[ ]**
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 **[ ]**;

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

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	5×10^{-5} M
	Depth of water body	500 cm
Conversion rate	6.023×10^{20}	
Results:	Degradation rate	8.14×10^{-13}mol/l/s
	Half life	1.35 year
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:	3.2E-04 [mg/day]
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
execution of calculation on a spreadsheet program

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

Model	Air[mg/l]	Water[mg/l]	Soil[mg/kg]	Sediment[mg/kg]
MNSEM	1.8E-09	1.7E-04	4.1E-03	6.8E-03
CHEMCAN2	3.4E-09	1.7E-04	9.4E-04	5.6E-04
CHEMFRAN	2.5E-10	1.7E-04	6.5E-05	5.6E-04

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 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 BOD_5,COD OR RATIO BOD_5/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 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) = 11 mg/l (95% confidence level: 3.3-36 mg/l) LC_{50} (48h) = 9.8 mg/l (95% confidence level: 5.8-16 mg/l) LC_{50} (72h) = 9.8 mg/l (95% confidence level: 5.8-16 mg/l) LC_{50} (96h) = 9.8 mg/l (95% confidence level: 5.8-16 mg/l) NOEC = LOEC =
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 203 (1984)
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_{50} (48h) = 8.4 mg/l
Analytical monitoring:	Yes **[ ]** No **[ ]** ? **[X]**
Method:	
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	
Reference:	Miyamoto, J. et al. (1978)

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_{50} (24h) = 9.1 mg/l (95% confidence level: 7.9-11 mg/l) EC_{50} (48h) = NOEC = LOEC =
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 202 (1984)
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:	EC_{50}(24h) = 33 mg/l EC_{50}(48h) = EC_0 (24h) = 18 mg/l EC_{100}(24h)= 50 mg/l EC_0 (48h) =
Analytical monitoring:	Yes **[ ]** No **[ ]** ? **[X]**
Method:	Method according to Bringmann & Kuhn
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	
Reference:	Bringmann, G. & Kuhn, R. (1977b)

(c)

Type of test:	static **[ ]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]**; open-system **[ ]**; closed-system **[ ]**
Species:	*Daphnia magna*
Exposure period:	24 hrs
Results:	EC_{50}(24h) = 7.8 mg/l EC_{50}(48h) = EC_0 (24h) = 4.5 mg/l EC_{100}(24h)= 16 mg/l
Analytical monitoring:	Yes **[ ]** No **[ ]** ? **[X]**
Method:	Standard method DIN 38412 Part II (draft)
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	
Reference:	Bringmann, G. & Kuhn, R. (1982)

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:	LC_{50}(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 **[ ]**

Species: *Procambarus clarkii* (Red Swamp Crayfish)
Exposure period: 48 hrs (Renewal at 24 hrs)
Results:
NOEC = 400 mg/l
Analytical monitoring: Yes **[ ]** No **[ ]** ? **[X]**
Method:
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: 3-Methyl-4-nitrophenol
Remarks: A range finding test was carried out and resulted that the highest no observable effect concentration was 400 mg/l exposed one male and one female to the chemical for 24 hours at the concentration of 0.1-400 mg/l.
Reference: Foster, G.D. & Crosby, D.G. (1986)

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]** ? **[ ]**
Method: OECD Test Guideline 201 (1984)
open-system **[X]**; closed-system **[ ]**
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: 3-Methyl-4-nitrophenol, purity = >98%
Remarks: The EC_{50} 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]**
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 **[ ]**

GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: 3-Methyl-4-nitrophenol
Remarks:
Reference: Bringmann, G. et al. (1980a)

(d)
Species: *Chilomonas paramecium*];
End-point: Biomass **[ ]**; Growth rate **[ ]**; Other **[ ]**
Exposure period:
Results: PGR (h) = 5.5 mg/l
NOEC =
LOEC =
Analytical monitoring: Yes **[ ]** No **[ ]** ? **[X]**
Method: 20 °C, pH 6.9
open-system **[ ]**; closed-system **[ ]**
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: 3-Methyl-4-nitrophenol
Remarks:
Reference: Bringmann, G. et al. (1980b)

4.4 TOXICITY TO BACTERIA

Type: Aquatic **[ ]**; Field **[ ]**; Soil **[ ]**; Other **[ ]**
Species: *Pseudomonas putida*
Exposure period: 16 hrs
Results: EC_3 (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: LC_{50} (24 h) = 19 mg/l (95% confidence level: 12-71 mg/l)
LC_{50} (48 h) = 12 mg/l (95% confidence level: 8.6-26 mg/l)
LC_{50} (96 h) = 5.6 mg/l (95% confidence level: 4.7-7.0 mg/l)
LC_{50} (7 d) = 4.4 mg/l (95% confidence level: 3.7-5.2 mg/l)
LC_{50} (14 d) = 4.1 mg/l (95% confidence level: 3.5-4.9 mg/l)
LC_{50} (21 d) = 2.9 mg/l (95% confidence level: 2.4-3.5 mg/l)
NOEC
LOEC
Reproduction: EC_{50} (14 d) = 4.1 mg/l (95% confidence level: 3.5-4.7 mg/l)

	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]** ? **[ ]**
Method:	OECD Test Guideline 202 (1984)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	3-Methyl-4-nitrophenol, Purity > 98 %
Remarks:	40 daphnids (4 replicates; 10 organisms per reolicate) 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 :	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; 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:	
Reference:	Unpublished company report (1974)

(b)

Type :	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Mouse (DD)
Value :	250 (mg/kg)
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	3-Methyl-4-nitrophenol
Remarks:	
Reference:	Unpublished company report (1974)

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 **[X]**
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:	
Reference:	Unpublished company report (1988)

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 **[ ]**

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 **[ ]** ? **[ ]**
Teat 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] [ ] [ ]

Method:
GLP: Yes **[ ]** No **[X]** ? **[ ]**
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
Frequency of treatment:
Postexposure observation period:
Premating exposure period: male: 14 days, female: 14 days
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

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:
GLP: Yes **[ ]** No **[ ]** ? **[ ]**
Test substance:
Remarks:
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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