FOREWORD INTRODUCTION

BENZENE, 1,4-DICHLORO-2-NITRO-

CAS N°: 89-61-2

SIDS Initial Assessment Report

For

SIAM 4

Tokyo, Japan, 20-22 May 1996

1. Chemical Name: Benzene, 1,4-dichloro-2-nitro-

2. CAS Number: 89-61-2

3. Sponsor Country: Japan

National SIDS Contact Point in the 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, 2,5-dichloronitrobenzene was selected for assessment in the framework of the HPV Programme.

7. Review Process Prior to the SIAM:

SIDS Dossier and Testing Plan were reviewed at a SIDS Review Meeting in 1994, where the following SIDS Testing Plan was agreed:

no testing [ ]

testing [X]

Physical Chemical Properties
- Vapour Pressure
- Partition Coefficient
- Water solubility

Environmental fate / Biodegradation
- Photodegradation
- Stability in water
- Biodegradation

Ecotoxicity
- Acute toxicity to fish
- Acute toxicity to daphnids
- Acute toxicity to algae
- Chronic toxicity to daphnids

Toxicity
- Reproductive/developmental toxicity
- Gene mutation test
- Chromosomal aberration in vitro

At SIAM-4, the conclusions of the Report were approved with comments. Comments at SIAM-4: The documents should be rearranged. The original report was already circulated in March 1996, and was revised according to the comments from member countries.

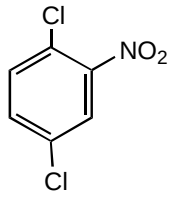
8. Quality check process:

9. Date of Submission: 30 April 1996

10. Date of last Update:

11. Comments:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	89-61-2
Chemical Name	Benzene, 1,4-dichloro-2-nitro- (2,5-Dichloronitrobenzene)
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

A potential hazard to man due to genotoxicity is identified, but exposure is low in the sponsor country.

Unless further information on exposure in other Member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Exposure

The production volume of 2,5-dichloronitrobenzene in Japan was ca. 200 - 1,200 tonnes/year in 1988 – 1992, and 2,400 - 2,800 tonnes/year in Germany. This chemical is used as an intermediate for pigments, pesticides and UV absorbents in closed systems in Japan. This chemical is stable in neutral, acidic or alkaline solutions, and is considered as “not readily biodegradable”.

The potential environmental distribution of the chemical obtained from a generic fugacity model (Mackey level III) showed that the chemical would be distributed mainly to water and soil. The Predicted Environmental Concentration (PEC_{local}) of this chemical was estimated as 8.0×10^{-4} mg/l in a Japanese local exposure scenario

As 2,5-dichloronitrobenzene is produced in a closed system, exposure during synthesis may be excluded. Workers wear personal protective equipment (e.g. a chemical cartridge respirator with an organic vapour cartridge) when filling barrels with the product. Therefore, the exposure in the workplace is considered to be negligible in the present situation. In addition, this chemical is not contained in consumer products, because it is an intermediate in industrial use. As for indirect exposure via the environment, the daily intake through drinking water is estimated to be 2.6×10^{-5} mg/kg/day and through fish is calculated as 1.2×10^{-3} mg/kg/day.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; 96h-LC_{50} = 5.4 - 8.5 mg/l (acute fish); 24h-EC_{50} = 8.0 mg/l (acute daphnia); 72h-EC_{50} = 5.0 mg/l (acute algae); 72h-NOEC = 2.0 mg/l (algae); 21d-NOEC = 1.0 mg/l (long-term daphnia reproduction). The lowest chronic toxicity result for daphnia [21d-NOEC (reproduction) of *Daphnia magna* (1.0 mg/l)] was used with an assessment factor of 100 to determine the PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.01 mg/l. The PEC is lower than the PNEC. The environmental risk is presumed to be low.

Human Health

The chemical showed genotoxic effects in the Ames test and the chromosomal aberration test *in vitro*. In a repeated dose toxicity test, a slight effect to the liver (e.g. increased liver weight) and damage in the reproductive system (e.g.

necrosis of germ epithelium, azoospermia) were observed. The NOEL was 10 mg/kg/day. In a preliminary reproductive/ developmental screening toxicity test, one dam, receiving 60 mg/kg/day, delivered dead pups. In the highest dose group (200 mg/kg/day), one dam died on day 20 of the pregnancy, one during the delivery period and four during the lactation period. A lack of care behaviour was also found in dams at the highest dose level. At that level, many pups died during the lactation period and a reduced body weight of the pups was observed. In this study, suppression of body weight gains and food consumption and an effect to the testes were also observed in adult rats at the highest dose. The NOEL for reproductive toxicity was 20 mg/kg/day.

For human health, the NOEL is estimated as 10 mg/kg/day for repeated dose and 20 mg/kg/day for reproductive toxicity. As for indirect exposure via the environment, the PEC was estimated as 8.0×10^{-4} mg/l in a local exposure scenario. The daily intake through drinking water is estimated as 2.6×10^{-5} mg/kg/day and through fish is calculated as 1.2×10^{-3} mg/kg/day. The margin of safety is large. Therefore, the health risk through the environment, in general, is considered to be low due to its use pattern and exposure.

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

NATURE OF FURTHER WORK RECOMMENDED

FULL SIDS SUMMARY

CAS NO: 89-61-2		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			54.6 °C
2.2	Boiling Point			261 °C at 1,013 hPa
2.3	Density			1.669 at 22°C
2.4	Vapour Pressure		OECD TG 104	0.51 Pa at 25 °C
2.5	Partition Coefficient (Log Pow)		OECD TG 107	2.93 at 25 °C
2.6 A.	Water Solubility		OECD TG 105	95 mg/L at 25 °C
B.	pH			6.9 (80 mg/l water) at 20°C
	pKa			No data available
2.12	Oxidation: Reduction Potential			No data available.
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		AOP Win v 1.86	$T_{1/2}$ = 9.32 x 10^{-2} y (sensitizer: OH radical)
3.1.2	Stability in Water		OECD TG 111	Stable at pH 4.0, 7.0, 9.0 at 25°C
3.2	Monitoring Data			Not detected from surface water and Sediment in Japan in 1982.
3.3	Transport and Distribution		Calculated (Fugacity Level III)	100% released to water, In Air 0.85% In Water 91.27% In Soil 5.60% In Sediment 2.28%
3.5	Biodegradation		OECD TG 301C	Not readily biodegradable: 0 – 8% (BOD) in 28 days, 0 - 1% (HPLC) in 28 days
3.7	Bioaccumulation	Guppy		BCF: 820
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oryzias latipes*	OECD TG 203	LC_{50} (72hr): 7.0 mg/L LC_{50} (96hr): 5.4 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (24hr): 8.0 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	*Selenastrum capricornutum*	OECD TG 201	EC_{50} (72hr): 5.0 mg/l NOEC: 2.0 mg/l
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (21d, Immobility): 2.3 mg/l EC_{50} (21d, Reproduction): 2.5 mg/l NOEC (21d, Repro): 1.0 mg/l

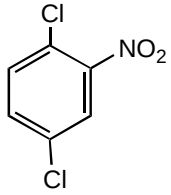
CAS NO: 89-61-2		SPECIES	PROTOCOL	RESULTS
4.6.1	Toxicity to Soil Dwelling Organisms			No data available.
4.6.2	Toxicity to Terrestrial Plants			No data available.
(4.6.3)	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)			No data available.
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat		LD_{50} : 2,503 mg/kg
5.1.2	Acute Inhalation Toxicity			No data available.
5.1.3	Acute Dermal Toxicity	Rat		LD_{50} : > 2,000 mg/kg
5.4	Repeated Dose Toxicity	Rat	28-days Repeated Toxicity Test Oral (gavage)	NOEL = 10 mg/kg/day
5.5	Genetic Toxicity *in vitro*			
A.	Bacterial Test (Gene mutation)	*S. typhimurium* *E. coli*	OECD TG 471 and 472 and Japanese Guidelines	TA 100: Positive with and without metabolic activation TA 1535: Positive without metabolic activation Other bacterial strains: Negative (With and without metabolic activation)
B.	Non-Bacterial *in vitro* Test (Chromosomal aberrations)	CHL cells	OECD TG 473 and Japanese Guidelines	Positive (Without metabolic activation) Negative (With metabolic activation)
5.6	Genetic Toxicity *in vivo*			No data available
5.8	Toxicity to Reproduction	Rat	OECD Preliminary Reproductive Toxicity Test	NOEL Parental = 20 mg/kg/day NOEL F1 offspring = 60 mg/kg/day
5.9	Developmental Toxicity/ Teratogenicity			See 5.8
5.11	Experience with Human Exposure			

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 89-61-2
IUPAC Name: Benzene, 1,4-dichloro-2-nitro-
Molecular Formula: $C_6H_3Cl_2NO_2$
Structural Formula:



Synonyms: 2,5-Dichloronitrobenzene

1.2 Purity/Impurities/Additives

Degree of Purity: 98 %

Major Impurities: Unknown

Essential Additives: None

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value
Melting point	56.6 ºC
Boiling point	261 ºC
Vapour pressure	0.51 Pa at 25 ºC
Water solubility	95 mg/l at 25 ºC

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

The production volume of 2,5-dichloronitrobenzene in Japan was ca. 200 - 1,200 tonnes/year in 1988 - 1992. The majority of this amount was sold and handled in Japan. This chemical is used as an intermediate for pigments, pesticides and UV absorbents in closed systems in Japan. This chemical is stable in neutral, acidic or alkaline solutions, and is considered to be “not readily biodegradable”. Direct photodegradation is expected because 2,5-dichloronitrobenzene absorbs UV light. The half-life is estimated to be about a week.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

The potential environmental distribution of 2,5-dichloronitrobenzene obtained from a generic level III fugacity model is shown in Table 2. The results show that if 2,5-dichloronitrobenzene is released mainly to water and soil, it is unlikely to distribute into other compartments. But, if 2,5-dichloronitrobenzene is released mainly to air, it is likely to be transported both to water and soil.

Table 2: Environmental distribution of 2,5-dichloronitrobenzene using a generic level III fugacity model.

Compartment	Release: 100% to air	Release: 100% to water	Release: 100% to soil
Air	12.16%	0.85%	0.12%
Water	7.68%	91.27%	2.61%
Soil	79.97%	5.60%	97.21%
Sediment	0.19%	2.28%	0.07%

Local exposure

According to a Japanese manufacturer, 8000 kg/year (estimated) of 2,5-dichloronitrobenzene are released with 1.0×10^{7} t/y of effluent into a bay. The local predicted environmental concentration (PEC_{local}) is 8.0×10^{-4} mg/l, employing the following calculation model. In this case, the dilution factor is estimated to be 1000.

$$\frac{\text{Amount of release } (8.0 \times 10^{9} \text{ mg/y})}{\text{Volume of effluent } (1.0 \times 10^{10} \text{ l/y}) \times \text{Dilution factor } (1000)}$$

2.3 Human Exposure

The highest exposure to the general population via the environment would be expected through drinking water processed from surface water. Based on the physical chemical properties of 2,5-dichloronitrobenzene, a significant removal during processing is not expected. Although PEC_{global} cannot be estimated, the concentration in drinking water is assumed to be 8.0×10^{-4} mg/l, as the worst case.

2.3.1 Occupational Exposure

As 2,5-dichloronitrobenzene is produced in a closed system, exposure during synthesis may be excluded. This chemical is used as an intermediate for pigments, pesticides and UV absorbents. Workplace exposure is possible when the product is filled into barrels, with inhalation uptake considered to be the main exposure route. Skin contact plays a minor role. Workers wear a chemical cartridge respirator with an organic vapour cartridge during the filling process. Therefore, the exposure to workers is estimated to be negligibly small in the present situation.

2.3.2 Consumer Exposure

2,5-Dichloronitrobenzene is not contained in consumer products because this substance is used as an intermediate for pigments, pesticides and UV absorbents. No further information on consumer use is available.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Acute Toxicity

Oral and dermal LD_{50} values of 2,5-dichloronitrobenzene for male rats was reported to be 2,503 mg/kg and > 2,000 mg/kg, respectively.

3.1.2 Irritation

Two reports on irritation tests are available. The results were that 2,5-dichloronitrobenzene was not irritating to the skin and eyes of rabbits.

3.1.3 Repeated Dose Toxicity

An Oral 28-Days repeated dose study of 2,5-Dichloronitrobenzene in Wistar rats at doses of 0, 10, 50, 250 mg/kg/day was reported (Hoechst AG, 1990). Impairment of body weight gain, increased hepatic weight and bilirubin value, and damaging of the forestomach were observed in the 50 mg/kg or more groups. The high dose group showed distinct increases of water consumption and clinical symptoms (salivation, crouching position, crural walk). Also, hepatocellular hypertrophy and testicle damage (necrosis of germ epithelium, azoospermia, depression of spermatogenesis) were observed in the high dose group. The NOEL for 28 days repeated dose toxicity was considered to be 10 mg/kg/day from this study.

3.1.4 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. Although 2,5-dichloronitro benzene showed positive results in *S. typhimurium* TA 100 with and without metabolic activation and TA 1535 without metabolic activation, negative results were obtained in TA98, TA 1537 and *Escherichia coli* WP2 *uvr*A with and without metabolic activation at concentrations up to 5 mg/plate (MHW, 1994b).

Non-bacterial test in vitro

A chromosomal aberration test in line with the Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and the 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. The maximum concentration of the chemical was used with no apparent cytotoxic effect in continuous treatment. The chemical showed positive results in Chinese hamster CHL cells without metabolic activation. (MHW, 1994b).

In vivo Studies

No data are available on *in vivo* mutagenicity tests.

3.1.5 Toxicity for Reproduction

2,5-Dichloronitrobenzene was studied for its oral toxicity in rats in an OECD preliminary reproductive toxicity test at doses of 0, 6, 20, 60, 200 mg/kg/day (MHW, 1994a). One dam receiving 60 mg/kg delivered only dead pups. In the 200 mg/kg group, one dam died on day 20 of pregnancy, one during the delivery period and four during the lactation period. A lack of care behaviour was also found in seven dams receiving 200 mg/kg. A lower value for the viability index on day 4 of lactation was obtained with 200 mg/kg because many pups died during the lactation period. With the pups of the 200 mg/kg group, reduced body weight values were obtained for both sexes on day 0 and 4 of lactation. It is concluded that the chemical exerts effects on dams during the perinatal period at 60 mg/kg or more and the dams during the lactation period at 200 mg/kg. In addition, there are indications that the chemical affects growth of new born pups at 200 mg/kg.

Regarding repeated dose toxicity, the chemical exhibited influence on general signs (yellowish urine and salivation at 60 mg/kg or more, and perigenital soiling, decrease in locomoter activity and extension of the hind limbs at 200 mg/kg in both sexes), suppressed body weight gains in both sexes at 200 mg/kg, and lower values for food consumption in females at 200 mg/kg. Degeneration of seminiferous epithelium in the testes and debris in ducts of the epididymides were found at 200 mg/kg. Atrophy of the thymus and decreased cellularity of white pulps in the spleen were found in surviving females, whereas atrophy/hemorrhage in the thymus, lymphoid atrophy and decreased cellularity of the marginal zone in the spleen, congestion in the lungs and liver, and glandular stomach ulcers were found in females receiving 200 mg/kg which died. The NOEL for reproductive toxicity was considered to be 200 mg/kg/day and 20 mg/kg/day for reproductive performance of male and females, respectively, and 60 mg/kg/day for development of pups.

3.2 Initial Assessment for Human Health

2,5-Dichloronitrobenzene showed genotoxic effects in the Ames test and the chromosomal aberration test *in vitro* using CHL cells. The NOEL is estimated to be 10 mg/kg/day for repeated dose toxicity and 20 mg/kg/day for reproductive toxicity. As for indirect exposure via the environment, the PEC was estimated to be $8.0 \times 10^{-4.}$ mg/l in a local exposure scenario. The daily intake through drinking water is estimated to be 2.6×10^{-5} mg/kg/day and through fish is calculated as 1.2×10^{-3} mg/kg/day. The margin of safety is large. Therefore, the health risk through the environment, in general, is considered to be low due to its use pattern and exposure.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute and ChronicToxicity Test Results

2,5-Dichloronitrobenzene has been tested in a limited number of aquatic species (*Selenastrum capricornutum*, *Daphnia magna* and *Oryzias latipes*) according to OECD test guidelines [OECD TG 201, 202 (part I and II), and 203]. Acute and chronic toxicity data to test organisms for the chemical are summarized in Table 3. No other ecotoxicological data are available. Various NOEC and LC_{50} values were gained from the above tests; LC_{50} (96h) = 5.4 mg/l (acute fish); EC_{50} (24h) = 8.0 mg/l (acute daphnia); EC_{50} (72h) = 5.0 mg/l (acute algae); NOEC (72h) = 2.0 mg/l; EC_{50} (21d) = 2.5 mg/l (long-term daphnia reproduction); NOEC (21d) = 1.0 mg/l. Therefore, the chemical is considered to be moderately toxic to, fish, daphnids and algae. The lowest chronic toxicity result [21d-NOEC (reproduction) of *Daphnia magna* (1.0 mg/l)] was used with an assessment factor of 100 to determine the PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.01 mg/l. The PEC is lower than the PNEC. The environmental risk is presumed to be low.

Table 3: Acute and chronic toxicity results of 2,5-dichloronitrobenzene with aquatic organisms.

Species	Endpoint[*1]	Conc. (mg/L)	Reference
Selenastrum capricornutum (algae)	Biomass: EC_{50} (72h) Biomass: NOEC	5.0 mg/L 2.0 mg/L	MOE, Japan. (1992)
Daphnia magna (water flea)	Imm: EC_{50}(24h) Imm: LC_{50}(21d) Rep: EC_{50}(21d) Imm: NOEC(21d)	8.0 mg/L 2.3 mg/L 2.5 mg/L 1.0 mg/L	
Oryzias latipes (fish, Medaka)	Mor: LC_{50}(48h) Mor: LC_{50}(72h) Mor: LC_{50}(96h)	8.2 mg/L 7.0 mg/L 5.4 mg/L	

Notes: [*1] Mor = mortality; Rep = reproduction.

4.2 Initial Assessment for the Environment

Various NOEC and LC_{50} values were gained from test results; LC_{50} = 5.4 - 8.5 mg/l (acute fish); EC_{50} = 8.0 mg/l (acute daphnia); EC_{50} = 5.0 mg/l (acute algae); NOEC = 2.0 mg/l (acute algae); NOEC = 1.0 mg/l (long-term daphnia reproduction). The lowest chronic toxicity result [21d-NOEC (reproduction) of *Daphnia magna* (1.0 mg/l)] was used with an assessment factor of 100 to determine the PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.01 mg/l. The PEC is lower than the PNEC. The environmental risk is presumed to be low.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

A potential hazard to man due to genotoxicity is identified, but exposure is low in the sponsor country.

Unless further information on exposure in other Member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

6 REFERENCES

EA, Japan (1994) "Investigation of 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 & MITI, Japan (1993) Unpublished Report on Exposure Estimation (HPV/SIDS Test conducted by EA and MITI, Japan)

EA, Japan (1985) Chemicals in the Environment: Report on Environmental Survey and Wildlife Monitoring in F.Y. 1982 and 1983, and Chemicals in the Environment: Report on Environmental Survey and Wildlife Monitoring in F.Y. 1984 and 1985. (Test was conducted by Office of Health Studies, Environmental Health Department, EA, Japan)

ECDIN database (1994)

Hanna, P.J., Bull. Environm. Contam. Toxicol., 28, 29-32 (1982)

Lange's Handbook of Chemistry (11th edition)

Lyman, W.J, W. F. Reehl and D. H. Rosenblatt (1981) "Handbook of Chemical Property Estimation Method", McGraw Hill Book Co.

MHW, Japan (1994a) Unpublished Report on Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 2,5-dichloronitrobenzene. (HPV/SIDS Test conducted by MHW, Japan)

MHW, Japan (1994b) Unpublished Report on Mutagenicity Test of 2,5-dichloronitrobenzene. (HPV/SIDS Test conducted by MHW, Japan)

MITI, Japan (1994a): Unpublished data

MITI, Japan (1994b) Unpublished Report (HPV/SIDS Test conducted by MITI, Japan. Test was performed in Chemicals Inspection and Testing Institute, Japan)

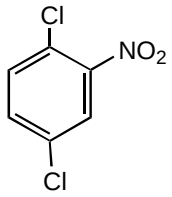
SIDS DOSSIER

Benzene, 1,4-dichloro-2-nitro-

CAS No. 89-61-2

Sponsor Country: Japan

S I D S P R O F I L E

1.01 A.	**CAS No.**	89-61-2
1.01 C.	**CHEMICAL NAME (OECD Name)**	Benzene, 1,4-dichloro-2-nitro-
1.01 D.	**CAS DESCRIPTOR**	Not applicable
1.01 G.	**STRUCTURAL FORMULA**	
	OTHER CHEMICAL IDENTITY INFORMATION	
1.5	**QUANTITY**	In Japan, 200-1,200 tonnes/year in 1988 - 1992.
1.7	**USE PATTERN**	Intermediate for pigments, pesticides and UV absorbents.
1.9	**SOURCES AND LEVELS OF EXPOSURE**	In Japan, Amount released from production site to water is 8 tonnes/year. All of the waste water is incinerated.
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)		

S I D S S U M M A R Y

CAS NO: 89-61-2		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	N						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	Y	N	N	Y	N	Y	N
5.4	Repeated Dose	Y	N	N	Y	N	Y	N
5.5	Genetic Toxicity *in vitro*							
	. Gene mutation	N						Y
	. Chromosomal aberration	N						Y
5.6	Genetic Toxicity *in vivo*	N						N
5.8	Reproduction Toxicity	N						Y
5.9	Development / Teratogenicity	N						Y
5.11	Human experience	N						N
OTHER TOXICITY STUDIES RECEIVED								

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

A. CAS-Number 89-61-2

B. Name (IUPAC name) 1,4-Dichloro-2-nitrobenzene

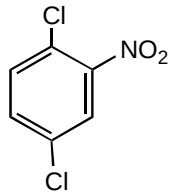
C. Name *(OECD name)* Benzene, 1,4-dichloro-2-nitro

D. CAS Descriptor Not applicable

E. EINECS-Number 201-923-3

F. Molecular Formula $C_3H_9Cl_2NO_2$

G. Structural Formula



H. Substance Group Not applicable

I. Substance Remark None

J. Molecular Weight 192.00

1.02 OECD INFORMATION

A. Sponsor Country: Japan

B. Lead Organisation:

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

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

Address: 2-2-1 Kasumigaseki, Chiyoda-ku
Tokyo 100, Japan
TEL 81-3-3581-0018
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C. Name of responder

Name: 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** 98 %

1.2 **SYNONYMS** 2,5-Dichloronitrobenzene

1.3 **IMPURITIES** Unknown

1.4 **ADDITIVES** Unknown

1.5 **QUANTITY**

Location	Production (tonnes)	Date
Japan	200-1,200/year	1988-1992

Reference: MITI, Japan (1994a)

1.6 **LABELLING AND CLASSIFICATION**

None

1.7 **USE PATTERN**

A. **General**

Type of Use:	**Category:**
Industry use	Intermediate for pigments, Pesticides and UV absorbents

Reference: MITI, Japan (1994a)

B. **Uses in Consumer Products**

None

1.8 **OCCUPATIONAL EXPOSURE LIMIT VALUE**

None

1.9 **SOURCES OF EXPOSURE**

Source: Media of release: Water from a production site
Quantities per media: 8 tonnes/year

Reference: MITI, Japan (1994a)

1.10 **ADDITIONAL REMARKS**

A. **Options for disposal** Incineration

Reference: MITI, Japan (1994a)

B. **Other remarks** None

2. PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT

(a)

Value:	54.6 °C
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Reference:	MITI (1992)

(b)

Value:	52.8 °C
Decomposition:	Yes [ ] No **[ ]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method:	
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Reference:	Company (Hoechst) data (1889)

2.2 BOILING POINT

(a)

Value:	261.3-261.7 °C
Pressure:	1013 hPa
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Reference:	MITI (1994b)

(b)

Value:	267 °C
Pressure:	1013 hPa
Decomposition:	Yes **[ ]** No **[ ]** Ambiguous **[ ]**
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	None
Reference:	Company (Hoechst) data (1989)

2.3 DENSITY (Relative density)

Type:	Bulk density **[ ]**; Density **[X]**; Relative Density **[ ]**
Value:	1.669
Temperature:	22 °C
Method:	Unknown
GLP:	Yes [ ] No **[ ]** ? **[ ]**
Remarks:	None
Reference:	ECDIN Database (1994)

2.4 VAPOUR PRESSURE

(a)

Value:	0.51 Pa
Temperature:	25°C

Method:	calculated **[ ]**; measured **[X]**
	OECD Test Guideline 104 Dynamic method
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Reference:	MITI, Japan (1994b)

(b)

Value:	< 0.7 hPa
Temperature:	20°C
Method:	calculated **[ ]**; measured **[X]**
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Reference:	Company (Hoechst) data (1989)

2.5 PARTITION COEFFICIENT $log_{10}P_{ow}$

(a)

Log Pow:	2.93
Temperature:	25 °C
Method:	calculated **[ ]**; measured **[X]**
	OECD Test Guideline 107
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Reference:	MITI (1994b)

(b)

Log Pow:	3.3
Temperature:	
Method:	calculated **[X]**; measured **[ ]**
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Reference:	Company (Hoechst) data (1991)

2.6 WATER SOLUBILITY

A. Solubility

(a)

Value:	95 mg/l
Temperature:	25 °C
Description:	Miscible **[ ]**; Of very high solubility **[ ]**;
	Of high solubility **[ ]**; Soluble **[ ]**;Slightly soluble **[ ]**;
	Of low solubility **[X]**; Of very low solubility **[ ]**;
	Not soluble **[ ]**
Method:	OECD Test Guideline 105
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Reference:	MITI, Japan (1994b)

(b)

Value:	0.83 mg/l
Temperature:	20 °C
Description:	Miscible **[ ]**; Of very high solubility **[ ]**;
	Of high solubility **[ ]**; Soluble **[ ]**;Slightly soluble **[ ]**;
	Of low solubility **[ ]**; Of very low solubility **[X]**;
	Not soluble **[ ]**
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Reference:	Company (Hoechst) data (1991)

B. pH Value, pKa Value

Value:	pH 6.9 (80 mg/l water)
Temperaturre:	20 °C
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Reference:	Company (Hoechst) data (1991)

2.7 FLASH POINT

No data available

2.8 AUTO FLAMMABILITY

No data available

2.9 FLAMMABILITY

No data available

2.10 EXPLOSIVE PROPERTIES

No data available

2.11 OXIDIZING PROPERTIES

No data available

2.12 OXIDATION: REDUCTION POTENTIAL

No data available

2.13 ADDITIONAL DATA

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

No data available

B. Other data None

3. ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY

3.1.1 PHOTODEGRADATION

Type:	Air **[ ]**; Water **[X]**; Soil; Other **[ ]**	
Light source:	Sunlight **[X];** Xenon lamp **[ ];** Other **[ ]**	
Spectrum of substance:	epsilon = 1.26 x 10-3 at 300 nm	
Estimated parameter for calculation:		
	Quantum yield 0.01	
	Concentration	5×10^{-5} M
	Depth of water body	500 cm
	Conversion constant	6.023×10^{20}
Result:	Degradation rate	1.18×10^{-11} mol / l / s
	Half life	9.32×10^{-2} years
Reference:	W. J. Lyman, W. F. Reehl and D. H. Rosenblatt, "Handbook of Chemical Property Estimation Method", McGraw Hill Book Co., 1981.	

3.1.2 STABILITY IN WATER

Type:	Abiotic (hydrolysis) **[X]**; biotic (sediment)**[ ]**
Result:	Stable at pH 4, 7 and 9 at 25 °C
Method:	OECD Test guideline 111
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	2,5-Dichloronitrobenzene
Reference:	MITI, Japan (1994b)

3.1.3 STABILITY IN SOIL

No data available

3.2 MONITORING DATA (ENVIRONMENT)

(a)

Type of Measurement:	Background [ ], At contaminated Site [ ], Other [X]
Media:	Surface water
Results:	ND (Detection limits:0.02 ug/ml) in 21 areas in Japan as of 1982
Remarks:	None
Reference:	EA, Japan (1985)

(b)

Type of Measurement:	Background [ ], At contaminated Site [ ], Other [ ]
Media:	Sediment
Results:	ND (Detection limits: 0.001 ug/ml) in 21 areas in Japan as of 1982
Remarks:	None
Reference:	EA, Japan (1985)

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

3.3.1 TRANSPORT

No data available

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

The potential environmental distribution of 2,5-dichloronitrobenzene obtained from a generic level III fugacity model is shown in Table. The results show that if 2,5-dichloronitrobenzene is released mainly to water or soil, it is unlikely to distribute into other compartments. But, if 2,5-dichloronitrobenzene is released mainly to air, it is likely to be transported both to water and soil.

Environmental distribution of 2,5-dichloronitrobenzene using a generic level III fugacity model.

Compartment	Release: 100% to air	Release: 100% to water	Release: 100% to soil
Air	12.16%	0.85%	0.12%
Water	7.68%	91.27%	2.61%
Soil	79.97%	5.60%	97.21%
Sediment	0.19%	2.28%	0.07%

Reference: EA & MITI, Japan (1994)

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

No data available

3.5 BIODEGRADATION

Type:	aerobic **[X]**; anaerobic **[ ]**
Inoculum:	adapted **[ ]**; non-adapted **[X]**;
Concentration of the chemical:	100 mg/l related to Test Substance **[X]**
Medium:	water **[ ];** water-sediment **[ ];**soil **[ ];**sewage treatment **[ ]** other **[**Japanese standard activated sludge**]**
Degradation:	Degree of degradation after 28 days 8, 4 and 0 % from BOD 0.1, and 1 % from HPLC analysis
Results:	Readily biodeg. **[ ];** Inherently biodeg. **[ ]**; under test condition no biodegradation observed **[X]**
Method:	OECD Test Guideline 301 C
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	2,5-Dichloronitrobenzene
Reference:	MITI (1994b)

3.6 BOD_5,COD OR RATIO BOD_5/COD

Not applicable

3.7 BIOACCUMULATION

Species:	Guppy

Exposure period:

Temperature:	21-23 °C
Concentration:	1 mg/l
BCF:	820
Method:	
Type of test:	calculated **[ ]**; measured **[X]** static **[ ]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]**
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	Purity 98 %
Reference:	Denner, J.W. et al., Aquit. Toxicol. 10, 115 - 129 (1987)

3.8 ADDITIONAL REMARKS

A. Sewage treatment None

B. Other information None

4. ECOTOXICOLOGICAL DATA

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type of test:	static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other **[ ]** open-system **[ ]**; closed-system **[X]**
Species:	*Oryzias latipes*
Exposure period:	96 hrs
Results:	LC_{50} (24h) = 8.5 mg/l (95% confidence limits: 7.2-10 mg/l) LC_{50} (48h) = 8.2 mg/l (95% confidence limits: 6.8-9.8 mg/l) LC_{50} (72h) = 7.0 mg/l (95% confidence limits: 5.1-10 mg/l) LC_{50} (96h) = 5.4 mg/l (95% confidence limits: 4.5-6.6 mg/l) NOEC = mg/l LOEC = mg/l
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 203 (1981)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,4-Dichloro-2-nitrobenzene, purity = 98 %
Remarks:	A group of 10 fish were exposed to each of 5 nominal concentrations (3.0-15 mg/l). Stock solution was prepared with Tween 80:acetone = 1:1 (100 mg/l). Controls with and without this vehicle were taken for the test. The vessel was sealed with a Parafilm.
Reference:	EA, Japan (1994)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]**; open-system **[**X**]**; closed-system **[ ]**
Species:	*Daphnia magna*
Exposure period:	24 hr
Results:	EC_{50} (24h) = 8.0 mg/l (95% confidence limits:6.1-11 mg/l)
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 202 (1984)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,4-Dichloro-2-nitrobenzene, purity: = 98 %
Remarks:	20 daphnids (4 replicates; 5 organisms per replicate) were exposed to each of 7 nominal concentrations (1.0-32 mg/l). Stock solution was prepared with DMSO:HCO = 9:1 (1000 mg/l). Controls with and without this vehicle were taken for the test.
Reference:	EA, Japan (1994)

B. Other aquatic organisms

No data available

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

Species:	*Selenastrum capricornutum* ATCC 22662
End-point:	Biomass **[X]**; Growth rate **[ ]**; Other **[ ]**
Exposure period:	72 hours
Results:	Biomass: EC_{50} (72h) = 5.0 mg/l NOEC = 2.0 mg/l ($p<0.05$) LOEC =
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	open-system **[**X**]**; closed-system **[ ]** OECD Test Guideline 201 (1984)

GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,4-Dichloro-2-nitrobenzene, purity = 98 %
Remarks:	The EC_{50} values for biomass were calculated based on 5 nominal concentrations (2-10 mg/l). Stock solution was prepared with DMSO (1000 mg/l). Controls with and without this vehicle were taken for the test.
Reference:	EA, Japan (1994)

4.4 TOXICITY TO BACTERIA

No studies located

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1. CHRONIC TOXICITY TO FISH

Test species:	*Poecilia reticulata* (guppy)
Test method:	
Type of test:	static **[ ]**, semi-static **[ ],** flow-through **[ ]** Other (e.g., field test) **[X]**
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test results:	LC_{50}: 4.9 mg/l
Test substance:	purity: 98 %
Remarks:	
Reference:	Denner. J.W. et al., Aquat. Toxicol. 10, 115-129 (1987)

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 **[ ]**; Reproduction rate **[X]**; Other **[X]**
Exposure period:	21 day
Results:	
Immobility:	LC_{50} (48 h) = 17 mg/l (95% confidence limits: 12-66 mg/l) LC_{50} (21 d) = 2.3 mg/l (95% confidence level: 730-860 mg/l) NOEC = LOEC =
Reproduction:	EC_{50} (21 d) = 2.5 mg/l (95% confidence level: 2.1-3.1 mg/l) NOEC = 1.0 mg/l ($p < 0.05$) LOEC = 3.2 mg/l ($p < 0.05$)
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 202 (1984)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,4-Dichloro-2-nitrobenzene, purity = 98 %
Remarks:	40 daphnids (4 replicates; 10 organisms per replicate) were exposed to each of 5 nominal concentrations (0.10-10 mg/l). Stock solution was prepared with DMSO:HCO-40=9:1 (500 mg/l). Controls with and without this vehicle were taken for the test.
Reference:	EA, Japan (1994)

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

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 AVIAN)

No data available

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No studies located

4.8 BIOTRANSFORMATION AND KINETICS IN ENVIRONMENTAL SPECIES

No data available

4.9 ADDITIONAL REMARKS

None

5. TOXICITY

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
Value :	2,503 mg/kg
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	purity: Unknown
Remarks:	None
Reference:	Company data (Hoechst AG)

5.1.2 ACUTE INHALATION TOXICITY

No data available

5.1.3 ACUTE DERMAL TOXICITY

Type :	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rat
Value :	> 2,000 mg/kg
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	purity: Unknown
Remarks:	None
Reference:	Company data (Hoechst AG, 1988)

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

No data available

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

(a)

Species/strain:	Rabbit
Method:	Barail-test
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Results:	No irritation
Test substance:	purity: Unknown
Remarks:	None
Reference:	Company data (Hoechst AG, 1968)

(b)

Species/strain:	Rabbit
Method:	Patch-test, semi-okkulusive
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Results:	No irritation
Test substance:	purity: Unknown
Remarks:	None
Reference:	Company data (Hoechst AG, 1989)

5.2.2 EYE IRRITATION/CORROSION

(a)

Species/strain:	Rabbit
Method:	
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Results:	No irritation
Test substance:	purity: Unknown
Remarks:	None
Reference:	Company data (Hoechst AG, 1968)

(b)

Species/strain:	Rabbit
Method:	Standard Draized method
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Results:	100 mg/24 h Moderate
Test substance:	purity: Unknown
Remarks:	None
Reference:	RTECS Database

5.3 SKIN SENSITISATION

Species/strain:	Guinea Pigs
Method:	Maximization test
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Results:	No sensitization
Test substance:	purity: Unknown
Remarks:	None
Reference:	Company data (Hoechst AG, 1968)

5.4 REPEATED DOSE TOXICITY

Species/strain:	Rat (Wistar)
Sex:	Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration:	oral gavage
Exposure period:	28 days
Frequency of treatment:	
Post exposure observation period:	
Dose:	0, 10, 50 or 250 mg/kg
Control group:	Yes **[X]**; No **[ ]**; No data **[ ]**; Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOEL:	10 mg/kg/day
LOEL:	50 mg/kg/day
Results:	Impair pf body weight gain, increased hepatic weight and bilirubin value, and damaging of the forestomach were observed in the 50 mg/kg or more groups. High dose group showed distinct increases of water consumption and clinical symptoms (salivation, crouching position, crural walk). Also, hepatocellular hypertrophy and testicle damaging (necrosis of germ epithelium, azoospermia, depression of spermatogenesis) were observed in the high dose group.
Method:	not described
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	Commercial, purity: Unknown
Reference:	Company data (Hoechst AG, 1990)

5.5 GENETIC TOXICITY *IN VITRO*

A. BACTERIAL TEST

Type :	Bacterial reverse mutation assay
System of testing:	
Species/strain:	*S. typhimurium* TA 98, TA 100, TA 1535, TA1537 *E.coli* WP2 uvrA
Concentration:	0, 78.13, 156.3, 312.5, 625, 1250, 2500, 5000 µg/plate
Metabolic activation:	With **[ ]**;Without **[ ]**;With and Without **[X]**;No data **[ ]**
Results:	
Cytotoxicity conc:	With metabolic activation: 1250 µg/plate Without metabolic activation: 1250 µg/plate
Precipitation conc:	
Genotoxic effects:	

	+	?	-
S. typhimurium TA 100			
With metabolic activation:	**[X]**	**[ ]**	**[ ]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**
S. typhimurium TA 1535			
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**
S. typhimurium TA 98 and TA1537			
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**
E. coli WP2 uvrA			
With metabolic activation:	**[ ]**	**[ ]**	**[X]**
Without metabolic activation:	**[ ]**	**[ ]**	**[X]**

Method:	Japanese Guideline for Screening Mutagenicity testing of chemicals
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Teat substance:	Commercial, purity: > 99.5 %
Remarks:	Procedure: Plate incorporation 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 (1994)

B. NON-BACTERIAL *IN VITRO* TEST

Type :	Cytogenetics Assay
System of testing:	
Species/strain:	Chinese hamster lung (CHL/IU) cells
Concentration:	-S9 (continuous treatment) 0, 0.04, 0.08, 0.15 mg/ml -S9 (short-term treatment) 0, 0.024, 0.047, 0.094 mg/ml +S9 (short-term treatment) 0, 0.024, 0.047, 0.094 mg/ml
Metabolic activation:	With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results:	
Cytotoxicity conc:	With metabolic activation:

	Without metabolic activation: 0.15 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 Media: RPMI 1640 medium *plus* 10% foetal calf serum *plus* phytohaemagglutinin No. replicates: 1
Reference:	MHW, Japan (1994b)

5.6 GENETIC TOXICITY *IN VIVO*

No data available

5.7 CARCINOGENICITY

No data available

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:	Males: 42 days including 14 days before mating Females: from 14 days before mating to day 3 of lactation.
Frequency of treatment:	7 days/week
Postexposure observation period:	
Premating exposure period: male: 14 days, female: 14 days	
Duration of the test;	
Doses:	0, 6, 20, 60 or 200 mg/kg (12 animals/sex/group)
Control group:	Yes **[X]**; No **[ ]**; No data **[ ]**; Corn oil Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOEL Parental:	20 mg/kg/day
NOEL F1 Offspring:	60 mg/kg/day
NOEL F2 Offspring:	N/A
Results:	One dam receiving 60 mg/kg delivered only dead pups. In the 200 mg/kg group, one dam died on Day 20 of pregnancy, one during the delivery period and four during the lactation period. A lack of care behaviour was also found in seven dams receiving 200 mg/kg. A lower value for the viability index on Day 4 of lactation was obtained with 200 mg/kg because many pups died during the lactation period. With the pups of the 200 mg/kg group, reduced body weight values were obtained for both sexes on Day 0 and 4 of lactation. It is concluded that the chemical exerts effects on dams during the perinatal period at 60 mg/kg or more and the dams during the lactation period at 200 mg/kg. In addition, there are indications that the chemical affects growth of new born pups at 200 mg/kg. With the repeated dose toxicity, the chemical exhibited influence on general signs (yellowish urine and salivation at 60 mg/kg or more, and perigenital soiling, decrease in locomoter activity and extension of the hind limbs at 200 mg/kg in both sexes), suppressed body weight gains in both sexes at 200 mg/kg, and lower values for food

consumption in females at 200 mg/kg. Degeneration of seminiferous epithelium in the testes and debris in the ducts of the epididymides were found at 200 mg/kg. Atrophy of the thymus and decreased cellularity of white pulps in the spleen were found in surviving females, whereas atrophy/hemorrhage in the thymus, lymphoid atrophy and decreased cellularity of the marginal zone in the spleen, congestion in the lungs and liver, and glandular stomach ulcers were found in females receiving 200 mg/kg which died.

Method: OECD Preliminary Reproductive Toxicity Test (1992)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Purity > 99.5 %
Remarks:
Reference: MHW, Japan (1994b)

5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

See 5.8

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

No data available

B. Toxicodynamics, toxicokinetics

No data available

5.11 EXPERIENCE WITH HUMAN EXPOSURE

None

6. REFERENCES

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