FOREWORD INTRODUCTION

1,4-DIETHYLBENZENE

CAS N°: 105-05-5

SIDS Initial Assessment Report

(SIAM 2, Paris, 4-6 July 1994)

Chemical Name: 1,4-Diethylbenzene

CAS No: 105-05-5

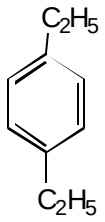
Sponsor Country: Japan

National SIDS Contact Point in Sponsor Country:

Mr. Yasuhisa Kawamura, Ministry of Foreign Affairs, Japan

History: As a high priority chemical for initial assessment, 1,4-Diethylbenzene was selected in the framework of the HPV Programme.
At SIAM-2, conclusion was approved with comments.
Comments at SIAM-2: Rearrangement of the documents.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	105-05-5
Chemical Name	Benezene, 1,4-diethyl-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

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

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Exposure

1,4-Diethylbenzene is a volatile liquid. Its production volume is ca. 1,300 tonnes/year in 1990 - 1992 in Japan and 1,200 tonnes/year were exported to the USA. This chemical is used as a solvent in closed systems. This chemical is stable in neutral, acidic or alkaline solution, and is considered to be "not readily biodegradable" (OECD TG 301C; 0 % by BOD; 02 % by GC after 28 days). Experimental BCF values (OECD TG 305) of the chemical are 320 – 629 in carp after 6 weeks.

PECs have been calculated based on a fugacity level III model considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The estimated environmental concentrations were 1.5×10^{-8} mg/l (air), 4.9×10^{-6} mg/l (water), 5.4×10^{-4} mg/kg (soil), 4.6×10^{-3} mg/kg (sediment).

No monitoring data at the work place or the environment have been reported. The chemical is used in closed systems, and no data for consumer use are available. Based on the physico-chemical properties, the total exposed dose indirectly through the environment was estimated to be 8.8×10^{-4} mg/man/day. Also, the daily intake through drinking water is estimated to be 9.7×10^{-6} mg/man/day and through fish is calculated to be 5.7×10^{-4} mg/man/day.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; 96 h LC_{50} = 1.8 mg/l (acute fish); 24 h EC_{50} = 32 mg/l (acute daphnia); 72 h EC_{50} = 29 mg/l (algae); 21 d NOEC = 0.93 mg/l (long-term daphnia reproduction). As the lowest chronic toxicity result, the 21 d-NOEC (reproduction) for *Daphnia magna* (0.93 mg/l) were adopted. As assessment factor of 100 is applied. Thus the PNEC of 1,4-diethylbenzene is 0.0093 mg/l. Since the PEC is lower than the PNEC, the environmental risk is presumed to be low.

Human Health

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

In a combined repeat dose and reproductive/developmental toxicity screening test (OECD TG 422), increases of liver and kidney weights were observed at the dose level of 750 mg/kg/day and 150 mg/kg/day. In relation to the increase of liver weights, increases of incidence of brown colored livers and enlargement of the livers were observed at the highest dose (750 mg/kg/day) with histopathological findings of swelling of liver cells. For reproductive/developmental toxicity end-points, there were no effects observed concerning mating, fertility and oestrus cycle and also for dams during the pregnancy and lactation period. Therefore, the NOEL was 30 mg/kg/day

for repeated dose toxicity and 750 mg/kg/day for reproductive toxicity.

The total exposure dose indirectly through the environment was estimated to be 8.8×10^{-4} mg/man/day. Also, the daily intake through drinking water is estimated as 9.7×10^{-6} mg/man/day and through fish is calculated as 5.7×10^{-4} mg/man/day. For human health, the margins of safety by indirect exposure from fish or drinking water are very large. Therefore, health risk is presumed to be low.

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

NATURE OF FURTHER WORK RECOMMENDED

This chemical is not a candidate for further work because all SIDS endpoints are sufficient.

FULL SIDS SUMMARY

CAS NO: 105-05-5		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			- 42 °C
2.2	Boiling Point			183 °C (at 1013 hPa)
2.3	Density			4.62 (relative density)
2.4	Vapour Pressure		OECD TG 104	1.054 torr at 25 °C
2.5	Partition Coefficient (Log Pow)		OECD TG 107	4.06 at 25 °C
2.6 A.	Water Solubility		OECD TG 105	17 mg/L at 25 °C
B.	pH			No data available.
	pKa			No data available
2.12	Oxidation: Reduction Potential			No data available.
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		Estimated	Direct photodegradation in water $T_{1/2}$ = 9 y
3.1.2	Stability in Water		OECD TG 111	Stable (pH 4.0, 7.0, 9.0)
3.2	Monitoring Data			No data available.
3.3	Transport and Distribution		Fugacity, level 3 Calculated (MNSEM-147S)	In Air 1.5E-8 mg/L In Water 4.9E-6 mg/L In Soil 5.4E-4 mg/kg In Sediment 4.6E-3 mg/kg
3.5	Biodegradation		OECD TG 301C	not readily biodegradable: 0 % (BOD) in 28 days, 0 - 2% (GC) in 28 days
3.6	Bioaccumulation	Carp	OECD TG 305C	BCF: 320 - 629
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oryzias latipes*	OECD TG 203	LC_{50}(72hr): 2.5 mg/L LC_{50}(96hr): 1.8 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50}(24hr): 32 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	*Selenastrum Capricornutum*	OECD TG 201	EC_{50}(72hr): 29 mg/l
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50}(21d, Mortality): 2.4 mg/l NOEC(21d, Repro): 0.93 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	OECD TG 401	LD_{50} > 2,000 mg/kg
5.1.2	Acute Inhalation Toxicity			No data available.

CAS NO: 105-05-5		SPECIES	PROTOCOL	RESULTS
5.1.3	Acute Dermal Toxicity			No data available.
5.4	Repeated Dose Toxicity	Rat	OECD Combined Test	NOAEL = 30 mg/kg/day
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	*S. .typhimurium* *E. coli*	OECD Guidelines No.471 and 472 and Guidelines for Screening Mutagenicity Testing of Chemicals (Japan)	Negative (With metabolic activation) Negative (Without metabolic activation)
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	CHL cells	OECD Guideline No.473 and Guidelines for Screening Mutagenicity Testing of Chemicals (Japan)	Negative(With metabolic activation) Negative(Without metabolic activation)
5.6	Genetic Toxicity In Vivo			No data available.
5.8	Toxicity to Reproduction	Rat	OECD Combined Test	NOAEL Parental = 750 mg/kg/day NOAEL F1 offspring = 750 mg/kg/day
5.9	Developmental Toxicity/ Teratogenicity	Rat	OECD Combined Test	NOAEL Maternal toxicity = 750 mg/kg/day NOAEL Teratogenicity = 750 mg/kg/day
5.11	Experience with Human Exposure			

SIDS Initial Assessment Report

1. Identity

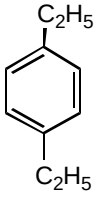
OECD Name: 1,4-Diethylbenzene

Synonym: None

CAS Number: 105-05-5

Empirical Formula: $C_{10}H_{14}$

Structural Formula:



Degree of Purity: 97 %

Major Impurities: 1,3-Diethylbenzene

Essential Additives: None

Physical-chemical Properties:

Melting Point:	-42.85 °C
Boiling Point:	183.75 °C
Density:	4.62
Vapor pressure:	1.054 Torr at 25 °C
Water solubility:	17 mg/L at 25 °C
Log Pow:	4.06 at 25 °C

2. Exposure

2.1 General discussion

1,4-Diethylbenzene is a volatile stable liquid. The production volume was ca. 1,300 tonnes/year in 1990 - 1992 in Japan, and 1,200 tonnes/year were exported to the U.S.A.

This chemical is used as a solvent. Releases to the environment may occur at the production site and specific industrial sites. All disposal wastes are treated by incineration. 1,4-Dethylbenzene seems to be released into water and air from its production sites after biological treatment. No specific monitoring data of the chemical is available. This chemical is stable in neutral, acidic or alkaline solutions, and is classified as "not readily biodegradable".

2.2 Environmental exposure

a) Biodegradability:

If released into water, this substance is not readily biodegraded. In a MITI (I) test, corresponding to the OECD 301C, 0 % degradation during 28 days based on BOD and 0 - 2 % based on GC analysis were measured.

b) Hydrolysis as a function to pH:

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

c) Photodegradability (estimation)

A half-life time of 9 years is estimated for the degradation of 1,4-diethylbenzene in water by direct photodegradation through absorption of UV light (MITI, Japan).

d) Bioaccumulation:

A measured BCF of 320 – 629 in carp (6 weeks at 25 °C) suggests that the potential for bioconcentration in aquatic organisms is low.

e) Estimates of environmental fate, pathway and concentration:

The potential environmental distribution of 1,4-diethylbenzene obtained from a generic fugacity model, Mackay level III, under emission scenarios is shown in Table 1. The results show that when 1,4-diethylbenzene is released into water, the majority of the chemical is likely distributed into soil and sediment

PECs have been calculated based on several models (MNSEM, CHEMCAN, CHEMFRN) considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The estimated concentrations of MNSEM model were 1.5×10^{-8} mg/l (air), 4.9×10^{-6} mg/l (water), 5.4×10^{-4} mg/kg (soil), 4.6×10^{-3} mg/kg (sediment). No monitoring data at work place and environment have been reported. The chemical is used in closed system, and no data for consumer use are available. Based on the physico-chemical properties, the total exposed dose indirectly through the environment was estimated as 8.8×10^{-4}

mg/man/day. Also, the daily intake through drinking water is estimated as 9.7×10^{-6} mg/man/day and through fish is calculated as 5.7×10^{-4} mg/man/day.

Global situation:

Method: MNSEM 147S (Details are shown in Form-1 Annex)
Input data:
Molecular weight: 134.21
Water solubility: 17.00 [mg/l]
Vapor pressure: 1.05 [mmHg]
Log Pow: 4.06
Results: Steady state mass and concentration calculated using MNSEM 147S
Air: 1.5E-08 [mg/l]
Water: 4.9E-06 [mg/l]
Soil: 5.4E-04 [mg/kg dry solid]
Sediment: 4.6E-03 [mg/kg dry solid]
Environmental exposure dose (Concentration in foods)
Inhalation of air: 3.0E-04 [mg/day]
Drinking water: 9.7E-06 [mg/day]
Ingestion of fish: 5.7E-04 [mg/day]
meat: 2.9E-08 [mg/day]
milk: 2.9E-08 [mg/day]
vegetation: 3.5E-06 [mg/day]
Total exposure dose: 8.8E-04 [mg/day]

Table 1: Comparison of calculated environmental concentration using several models.

Model	Air[mg/l]	Water[mg/l]	Soil[mg/kg]	Sediment[mg/kg]
MNSEM	1.5E-08	4.9E-06	5.4E-04	4.6E-03
CHEMCAN2	5.3E-08	3.5E-06	1.0E-04	3.2E-03
CHEMFRAN	5.3E-08	3.6E-06	1.1E-04	3.3E-03

2.3 Consumer Exposure

No data on consumer exposure are available.

2.4 Occupational Exposure

No data on work place monitoring have been reported.

3. Toxicity

3.1 Human Toxicity

a) Acute toxicity

Only one acute toxicity data is available for rat using a limit test according to OECD Test Guideline 401. Rats were administered orally (gavage) at 0 or 2,000 mg/kg.
No deaths occurred for either males or females in the treated groups. As clinical signs, decrease of spontaneous motor activity was observed in both male and female rats and lacrimation was additionally observed in one female rat. No death were observed during the course of the study. All animals gained body weight on day 7 and 14 after administration. No remarkable macroscopical changes were observed in both males and females (MHW, Japan, 1993a). No acute toxicity data are available by inhalation and dermal routes of 1,4-diethylbenzene.

b) Repeated toxicity

There is only one key study on repeated dose toxicity of 1,4-diethylbenzene. This chemical was studied for oral toxicity in rats according to the OECD combined repeated dose and reproductive/developmental toxicity test [OECD TG 422]. As the study was well controlled and conducted according to GLP, this was appropriate to regard as a key study. Male and female SD rats were orally administered (gavage) at doses of 0, 30, 150 and 750 mg/kg/day. In male rats, the administration period was two weeks prior to mating, 2 weeks of mating and 2 weeks after the completion of mating period. In female, in addition to maximum four weeks pre-mating and mating period, they were given through pregnant period until day 3 of post delivery.
The results in clinical observations did not reveal any effects attributable to the administration of test substance and there were no mortality in all groups. Depression of body weight gain observed in both male and female rats receiving 750 mg/kg/day, and food consumption of male rats receiving 750 mg/kg/day was less than those of control until day 7 and thereafter, increases in food consumption were observed in them from Day 28. As a results of hematology, there were no essential effects of test substance.
As the results of blood clinical examination, increases in the BUN and GPT were observed in male rat receiving 150 and 750 mg/kg/day, and increases in total protein, albumin, creatinine and total bilirubin and decrease in glucose were observed in male rats receiving 750 mg/kg/day, suggesting that those changes were due to the effect on kidneys and liver. As the results of organ weight analysis, increases in liver weight were observed in both male and female rats receiving 750 mg/kg/day, moreover increases in kidneys weights were observed in male rats receiving 150 mg/kg/day or more groups. As the gross findings, in relation to increase of liver weights, increases in incidence of brown colored livers or enlargement of the livers were observed in male rats receiving 750 mg/kg/day, and swelling of the liver cells was observed in them, histopathologically. The results described above led to a conclusion that effects of repeated dose toxicity study were considered to appear at 150 mg/kg/day or more in male rats and at 750 mg/kg/day in female rats (MHW, Japan, 1993b). The NOAEL for repeated dose toxicity in rats is considered to be 30 mg/kg/day in males and 150 mg/kg/day in female rats.

c) Reproductive toxicity

1,4-Diethylbenzene was studied for oral toxicity in rats according to the OECD

combined repeated dose and reproductive/developmental toxicity test [OECD TG 422] at doses of 0, 100, 300 and 1,000 mg/kg/day. Although this combined 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 only body weights at day 0 and day 4 after birth, and autopsy findings at day 4.
The results observed in mating, fertility and estrous cycle did not reveal any effects attributable to the administration of test substance. Observation of delivery, all gestation animals delivered of pups, normally and there were not a treatment-related effect throughout the lactation period. The external examination of pups revealed no effects attributable to the administration of test substance. The body weights of fetuses showed the favorably froths until Day 4 of lactation. The necropsy of stillborn, dead pups until Day 4 of lactation and newborns at Day 4 of lactation did not reveal any effects attributable to the administration of test substance. The influences of the test substance on reproductive and developmental toxicity were not observed in both male and female rats receiving 750 mg/kg/day, therefore maximum NOELs were considered to be 750 mg/kg/day in both sexes (MHW, 1993). The NOAEL values for both parental and F_1 offspring in reproductive toxicity are considered to be 750 mg/kg/day. As for developmental toxicity, the NOAEL for F_1 offspring is estimated to be 750 mg/kg/day.

d) Genetic toxicity

Bacterial tests

Reverse gene mutation assays were 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.
1,4-Diethylbenzene showed negative results in *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 and *Escherichia coli* WP2 *uvr*A at concentrations up to 50 ug/plate with or without metabolic activation (MHW, 1993c).

Non-bacterial test *in vitro*

A chromosomal aberration test in line with the 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. The maximum concentration of the chemical was used within no apparent cytotoxic effect in continuous treatment.
Either structural chromosomal aberrations or polyproidy were not recognized up to a maximum concentration of 0.11 and 1.3 mg/ml under conditions of both continuous treatment and short-term treatment, respectively with or without an exogeneous metabolic activation system (MHW, 1993c).

in vivo test

No data are available on *in vivo* genotoxic effects.

e) Other human health related information

None

3.2 Ecotoxicity

1,4-Diethylbenzene 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, 203, 204 and 211]. Acute and chronic toxicity data to test organisms for 1,4-diethylbenzene are summarized in Table 2. No other ecotoxicological data are available.

Various NOEC and LC_{50} values were gained from above tests; LC_{50} = 1.8 mg/l (acute fish); EC_{50} = 32 mg/l (acute daphnia); EC_{50} = 29 mg/l (algae); NOEC = 0.93 mg/l (long-term daphnia reproduction). The lowest chronic toxicity result (21 d-NOEC, reproduction, for Daphnia magna: 0.93 mg/l) was adopted for the calculation of the PNEC. An assessment factor of 100 is applied. Thus the PNEC of 1,4-diethylbenzene is 0.0093 mg/l. Since the PEC is lower than the PNEC the environmental risk is presumed to be low.

Table 2. Acute and chronic toxicity data of 1,4-diethylbenzene to aquatic organisms.

Species	Endpoint[*1]	Conc. (mg/L)	Reference
Selenastrum capricornutum (algae)	Biomass: EC_{50} (72h)	29 mg/L	MOE, Japan. (1992)
Daphnia magna (water flea)	Mor: LC_{50}(24h) Mor: LC_{50}(21d) Rep: EC_{50}(21d) NOEC(21d)	32 mg/L 2.4 mg/L 1.3 mg/L 0.93 mg/L	
Oryzias latipes (fish, Medaka)	Mor: LC_{50}(24h) Mor: LC_{50}(72h) Mor: LC_{50}(96h)	2.5 mg/L 2.5 mg/L 1.8 mg/L	

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

4. Initial assessment

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 1.8 mg/l (acute fish); EC_{50} = 32 mg/l (acute daphnia); EC_{50} = 29 mg/l (acute algae); NOEC = 0.93 mg/l (long-term daphnia reproduction). The lowest chronic toxicity result (21 d-NOEC, reproduction, for Daphnia magna: 0.93 mg/l) was adopted for the calculation of the PNEC. An assessment factor of 100 is applied. Thus the PNEC of 1,4-diethylbenzene is 0.0093 mg/l. Since the PEC is lower than the PNEC the environmental risk is presumably low.

The chemical showed no genotoxic effects in bacteria or chromosomal aberrations *in vitro*. In a combined repeat dose and reproductive/developmental toxicity screening test, increases of liver and kidney weights were observed at the dose level of 750 mg/kg/day and 150 mg/kg/day. In relation to the increase of liver weights, increases of incidence of brown colored livers and enlargement of the livers were observed at the highest dose (750 mg/kg/day) with histopathological findings of swelling of liver cells. For reproductive/ developmental toxicity end-points, there were no effects observed concerning mating, fertility and oestrus cycle and also for dams during the pregnancy and lactation period. Therefore, the NOEL was 30 mg/kg/day for repeated dose toxicity and 750 mg/kg/day for reproductive toxicity. The total exposed dose indirectly through the environment was estimated as 8.8×10^{-4} mg/man/day. Also, the daily intake through drinking water is estimated as 9.7×10^{-6} mg/man/day and through fish is calculated as 5.7×10^{-4} mg/man/day. For human health, the margin of safety by indirect exposure from fish or drinking water are very large. Therefore, health risk is presumed to be low.

5. Overall recommendation and initial assessment

5.1 Conclusion

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

5.2 Recommendation

None

6. REFERENCES

Driesbach, R.R. (1961) Physical Properties of Chemical Compounds. Vol. 3, Am. Chem.Soc., Washington D.C.

EA, Japan (1993) "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)

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

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MHW, Japan (1993c) Unpublished Report on Mutagenicity Test of 1,4-Diethylbenzene. (HPV/SIDS Test conducted by MHW, Japan)

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

MITI, Japan (1993) Unpublished Report (1993) (HPV/SIDS Test conducted by MITI, Japan. Test was performed in Chemicals Inspection and Testing Institute, Japan)

REVISED SIDS DOSSIER ON THE HPV CHEMICAL

1,4-Diethylbenzene

CAS No. 105-05-5

Sponsor Country : Japan

DATE: March 2001

S I D S P R O F I L E

1.01 A.	**CAS No.**	105-05-5
1.01 C.	**CHEMICAL NAME (OECD Name)**	1,4-Diethylbenzene
1.01 D.	**CAS DESCRIPTOR**	Not applicable in this case
1.01 G.	**STRUCTURAL FORMULA**	$C_{10}H_{15}$
	OTHER CHEMICAL IDENTITY INFORMATION	
1.5	**QUANTITY**	In Japan, approx 1,300 tonnes in 1990 - 1992, and 1,200 tonnes were exported to the U. S. A.
1.7	**USE PATTERN**	Solvent (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. 2. Amount released to air from production site is negligible. 3. Information on consumer exposure is not available.
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)		

SIDS SUMMARY

1, 4-Diethylbenzene

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

B. Name *(IUPAC name)* Benzene, 1,4-diethyl-

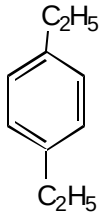
C. Name *(OECD name)* 1,4-Diethylbenzene

D. CAS Descriptor Not applicable

E. EINECS-Number 203-265-2

F. Molecular Formula $C_{10}H_{14}$

G. Structural Formula



H. Substance Group Not applicable

I. Substance Remark None

J. Molecular Weight 134.22

1.02 OECD INFORMATION

A. Sponsor Country: Japan

B. Lead Organisation:

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

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

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

C. Name of responder

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 **[X]**; solid **[ ]**

C. Purity 97 % (weight/weight)

1.2 SYNONYMS

1.3 IMPURITIES Name: 1,3-Diethylbenzene
Value: unknown

1.4 ADDITIVES None

1.5 QUANTITY

Location	Production(tonnes)	Date
Japan	1,300/year	1990-1992
export to U.S.A	1,200/year	1990-1992

Reference: MITI, Japan

1.6 LABELLING AND CLASSIFICATION

Labelling None

Classification None

1.7 USE PATTERN

A. General

Type of Use:	**Category:**
(a) main industry use	Solvent (Closed system) 100 %

Remarks: None

Reference: MITI, Japan

B. Uses in Consumer Products None

Function	Amount present	Physical state

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

None

1.9 SOURCES OF EXPOSURE

Source:	Media of release: Air from a production site Quantities per media: Negligible small
Remarks:	
Reference:	MITI, Japan

1.10 ADDITIONAL REMARKS

A.	**Options for disposal**	Incineration
	Reference:	MITI, Japan
B.	**Other remarks**	None

2. PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT

Value:	- 42.85 °C
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Sublimation:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	None
Reference:	API

2.2 BOILING POINT

Value:	183.75 °C
Pressure:	at 1013 hPa
Decomposition:	Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	None
Reference:	API

2.3 DENSITY (Relative density)

Type:	Bulk density **[ ]**; Density **[ ]**; Relative Density **[X]**
Value:	4.62
Temperature:	Unknown
Method:	Unknown
GLP:	Yes [ ] No **[ ]** ? **[X]**
Remarks:	None
Reference:	ECDIN database

2.4 VAPOUR PRESSURE

Value:	1.054 Torr
Temperature:	25 °C
Method:	calculated **[ ]**; measured **[X]** OECD Test Guideline 104 Static Method
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	
Reference:	Driesbach, R.R. (1961)

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

Log Pow:	4.06
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

(a) **Preferred result**

Value:	17 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:	Unknown
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Remarks:	
Reference:	Company data

B. pH Value, pKa Value

Not applicable

2.7 FLASH POINT

Value:	57 °C
Type of test:	Closed cup **[X]**; Open cup **[ ]**; Other **[ ]**
Method:	Unknown
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Remarks:	
Reference:	Company data

2.8 AUTO FLAMMABILITY

Not applicable

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. ENVIRONMENTAL FATE AND PATHWAYS

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 = 4.70 at 300 nm	
Concentration of Substance:		
Estimated parameter for calculation:		
	Quantum yield	0.01
	Concentration	5×10^{-5} M
	Depth of water body	500 cm
	Conversion rate	6.023×10^{20}
Results:	Degradation rate	1.22×10^{-13} mol/l/s
	Half life	9.00 years
Reference	Lyman, W. J. et al. (1981)	

3.1.2 STABILITY IN WATER

Type:	Abiotic (hydrolysis) **[X]**; biotic (sediment)**[ ]**
Half life:	Not hydrolysed at pH 4, 7 and 9
Method:	OECD TG 111
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	1,4-Diethylbenzene
Reference:	MITI, Japan (1993)

3.1.3 STABILITY IN SOIL

No studies located

3.2 MONITORING DATA (ENVIRONMENT)

No studies located

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENT INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAY

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 [ ]**; Fugacity level IV **[ ]**; Other(calculation) **[X]**;

Other(measurement) **[ ]**

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

Air:	1.5E-08 [mg/l]
Water:	4.9E-06 [mg/l]
Soil:	5.4E-04 [mg/kg dry solid]
Sediment:	4.6E-03 [mg/kg dry solid]

Exposure dose

Inhalation of air:	3.0E-04 [mg/day]
Drinking water:	9.7E-06 [mg/day]
Ingestion of fish:	5.7E-04 [mg/day]
Meat:	2.9E-08 [mg/day]
milk:	2.9E-08 [mg/day]
vegetation:	3.5E-06 [mg/day]
Total exposure dose:	8.8E-04 [mg/day]

Remarks: Input data:

Molecular weight:	134.21
Water solubility:	17.00 [mg/l]
Vapor pressure:	1.05 [mmHg]
Log Pow:	4.06

MNSEM 147S is a slightly revised version of MNSEM 145I.
1. addition of air particle compartment to air phase
2. 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	1.5E-08	4.9E-06	5.4E-04	4.6E-03
CHEMCAN2	5.3E-08	3.5E-06	1.0E-04	3.2E-03
CHEMFRAN	5.3E-08	3.6E-06	1.1E-04	3.3E-03

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]**; activated sludge, 30 mg/l as suspended solid
Concentration of the chemical:	100 mg/l related to COD **[ ]**; DOC **[ ]**; Test substance **[X]**;
Medium:	water **[ ];** water-sediment **[ ];** soil **[ ];** sewage treatment others [X] (Japanese standard activated sludge)
Degradation:	Degree of degradation after 28 days 0, 0 and 0 % from BOD 2, 0 and 0 % from GC analysis
Results:	Readily biodeg. **[ ];** Inherently biodeg. **[ ];** under test condition no biodegradation observed **[X]**, Other **[ ]**

Method:	OECD Test Guideline 301C
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	1,4-Diethylbenzene, purity: > 95 %
Remarks:	None
Reference:	MITI, Japan (1993)

3.6 BOD_5,COD OR RATIO BOD_5/COD

Not applicable

3.7 BIOACCUMULATION

Species:	Carp
Exposure period:	6 weeks
Temperature:	25 °C
Concentration:	(1) 20 µg/l (2) 2 µg/l
BCF:	(1) 362 - 598 (2) 320 - 629
Elimination:	Yes **[ ]** No **[ ]** ? **[ ]**
Method:	OECD TG 305C
Type of test:	**[ ]** calculated; **[X]** measured static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other **[ ]**
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	1,4-Diethylbenzene, Purity: > 95 %
Remarks:	None
Reference:	MITI, Japan (1992)

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 **[X]**; closed-system **[ ]**
Species:	*Oryzias latipes*
Exposure period:	96 hr
Results:	LC_{50} (24h) = 2.5 mg/l (95% confidence level: 1.8-3.4 mg/l) LC_{50} (48h) = 2.5 mg/l (95% confidence level: 1.8-3.4 mg/l) LC_{50} (72h) = 2.5 mg/l (95% confidence level: 1.9-3.2 mg/l) LC_{50} (96h) = 1.8 mg/l (95% confidence level: 1.0-3.2 mg/l) NOEC = LOEC =
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 203 (1981)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,4-Diethylbenzene, Purity = 99.9 %
Remarks:	A group of 10 fishes were exposed to 5 nominal concentrations (0.56-5.6 mg/l), control of Tween 80 (5.6 mg/l) and laboratory water control.
Reference:	EA, Japan (1992)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

Type of test:	static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]**; open-system **[X]**; closed-system **[ ]**
Species:	Daphnia magna
Exposure period:	24 hrs
Results:	EC_{50} (24h) = 32 mg/l (95% confidence level: 28-37 mg/l) EC_{50} (48h) = NOEC = LOEC =
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 202 (1984)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	1,4-Diethylbenzene, purity: = 99.9 %
Remarks:	20 daphnids (4 replicates; 5 organisms per replicate) were exposed to 5 nominal concentrations (10-100 mg/l), control of DMSO:HCO-40 = 9:1 (100 mg/l) and laboratory water control.
Reference:	EA, Japan (1992)

B. Other aquatic organisms

C.

No studies located

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

Species:	Selenastrum capricornutum ATCC 22662
End-point:	Biomass **[X]**; Growth rate **[ ]**; Other **[ ]**
Exposure period:	72 hours
Results:	Biomass: EC_{50} (72h) = 29 mg/l

NOEC =
LOEC =

Analytical monitoring: Yes **[ ]** No **[X]** ? **[ ]**
Method: OECD Test Guideline 201 (1984)
open-system **[**X**]**; closed-system **[ ]**
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: 1,4-Diethylbenzene, purity = 99.9 %
Remarks: The EC_{50} values were calculated based on 4 nominal concentrations (17-100 mg/l), ethanol control (100 mg/l) and laboratory water control.
Reference: EA, Japan (1992)

4.4 TOXICITY TO BACTERIA

No studies located

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1. CHRONIC TOXICITY TO FISH

No studies located

4.5.2. CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type of test: static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other **[ ]**;
End-point: Mortality **[X]**; Reproduction rate **[X]**; Other **[ ]**
Exposure period: 21 days
Results:
Mortality: LC_{50} (24 h) = 7.2 mg/l (95% confidence level: 5.4-9.8 mg/l)
LC_{50} (48 h) = 6.0 mg/l (95% confidence level: 4.5-8.0 mg/l)
LC_{50} (96 h) = 4.2 mg/l (95% confidence level: 3.2-5.4 mg/l)
LC_{50} (7 d) = 3.2 mg/l (95% confidence level: 2.4-4.1 mg/l)
LC_{50} (14 d) = 2.6 mg/l (95% confidence level: 1.9-3.5 mg/l)
LC_{50} (21 d) = 2.4 mg/l (95% confidence level: 1.8-3.2 mg/l)
Reproduction: EC_{50} (14 d) = 1.1 mg/l (95% confidence level: 0.66-1.7 mg/l)
EC_{50} (21 d) = 1.3 mg/l (95% confidence level: 0.97-1.8 mg/l)
NOEC = 0.93 mg/l ($p < 0.05$)
LOEC = 3.0 mg/l ($p < 0.05$)
Analytical monitoring: Yes **[ ]** No **[X]** ? **[ ]**
Method: OECD Test Guideline 202 (1984)
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: 1,4-Diethylbenzene, purity = 99.9 %
Remarks: 40 daphnids (4 replicates; 10 organisms per replicate) were exposed to 5 nominal concentrations (0.3-30 mg/l), control of DMSO:HCO-40 = (:1 (100 mg/l) and laboratory water control.
Reference: EA, Japan (1992)

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No studies located

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

No studies located

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

No studies located

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No studies located

4.8 BIOTRANSFORMATION AND KINETICS IN ENVIRONMENTAL SPECIES

No studies located

4.9 ADDITIONAL REMARKS

None

5. TOXICITY

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

Type : LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rat (Crj:CD(SD))
Value : > 2,000 (mg/kg) for male or female
Method: OECD Test Guideline 401
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: 1,4-Diethylbenzene, purity: 97.2 %
Remarks: As clinical signs, decrease of spontaneous motor activity was observed in both male and female rats and lacrimation was additionally observed in one female rat. No death were observed during the course of the study. All animals gained body weight on day 7 and 14 after administration. No remarkable macroscopical changes were observed in both males and females.
Reference: MHW, Japan (1993a)

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

No studies located

5.2.2 EYE IRRITATION/CORROSION

No studies located

5.3 SKIN SENSITISATION

No studies located

5.4 REPEATED DOSE TOXICITY

Species/strain: Rat (Crj:CD(SD))
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: oral (gavage)
Exposure period: Male: 44 days including 14 days before mating
Female: from 14 days before mating to day 3 of lactation
Frequency of treatment: 7 days/week

Post exposure observation period:
Dose: 0, 30, 150 or 750 mg/kg (12 animals /group)
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**;
Historical **[ ]**
NOEL: 30 mg/kg/day
LOEL: 150 mg/kg/day
Results: The results in clinical observations did not reveal any effects attributable to the administration of test substance and there were no mortality in all groups. Depression of body weight gain observed in both male and female rats receiving 750 mg/kg/day, and food consumption of male rats receiving 750 mg/kg/day was less than those of control until day 7 and thereafter, increases in food consumption were observed in them from Day 28. As a results of hematology, there were no essential effects of test substance. As the results of blood clinical examination, increases in the BUN and GPT were observed in male rat receiving 150 and 750 mg/kg/day, a and increases in total protein, albumin, creatinine and total bilirubin and decrease in glucose were observed in male rats receiving 750 mg/kg/day, suggesting that those changes were due to the effect on kidneys and liver.
As the results of organ weight analysis, increases in liver weight were observed in both male and female rats receiving 750 mg/kg/day, moreover increases in kidneys weights were observed in male rats receiving 150 mg/kg/day or more groups. As the gross findings, in relation to increase of liver weights, increases in incidence of brown colored livers or enlargement of the livers were observed in male rats receiving 750 mg/kg/day, and swelling of the liver cells was observed in them, histopathologically.
The results described above led to a conclusion that effects of repeated dose toxicity study were considered to appear at 150 mg/kg/day or more in male rats and at 750 mg/kg/day in female rats, and maximum NOELs were considered to be 30 mg/kg/day in males and to be 150 mg/kg/day in females.
Method: OECD Combined Repeat dose and Reproductive/Developmental Toxicity Test (1992)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Commercial, purity: 97.2 %
Reference: MHW, Japan (1993b)

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 1539
E. coli WP2 uvrA
Concentration: 0, 2.4 - 78.12 µg/plate
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**;
No data **[ ]**
Results:
Cytotoxicity conc: With metabolic activation: 50 µg/plate
Without metabolic activation: 50 µg/plate
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 **[ ]** ? **[ ]**
Teat substance: Commercial, purity: 97.2 %
Remarks: Procedure: Pre-incubation.
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 (1993c)

B. NON-BACTERIAL IN VITRO TEST

Type : Cytogenetics Assay
System of testing: Species/strain: Chinese hamster CHL cells
Concentration: Incubated with 0, 0.03 - 0.11 mg/ml (-S9)
0, 0.33 - 1.30 mg/ml (+S9)
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results:
Cytotoxicity conc: With metabolic activation: 1.30 mg/ml
Without metabolic activation: 0.11 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 97.2 %
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 (1993c)

5.6 GENETIC TOXICITY IN VIVO

No studies located

5.7 CARCINOGENICITY

No studies located

5.8 TOXICITY TO REPRODUCTION

Type: Fertility **[ ]**; One generation study **[ ]**; Two generation study **[ ]**; Other **[X]**
Species/strain: Rat slc:SD
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: Oral (gavage)
Exposure period: Male: 44 days including 14 days before mating
Female: from 14 days before mating to day 3 of lactation
Frequency of treatment: 7 days/week
Postexposure observation period:
Premating exposure period: male: 14 days, female: 14 days
Duration of the test;
Doses: 0, 30, 150, or 750 mg/kg (12 /animals /sex/ group)

Control group:	Yes **[X]**; No **[ ]**; No data **[ ]**; Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOEL Parental :	= 750 mg/kg/day
NOEL F1 Offspring:	= 750 mg/kg/day
NOEL F2 Offspring:	N/A
Results:	The results observed in mating, fertility and estrous cycle did not reveal any effects attributable to the administration of test substance. Observation of delivery, all gestation animals delivered of pups, normally and there were not a treatment-related effect throughout the lactation period. The external examination of pups revealed no effects attributable to the administration of test substance. The body weights of fetuses showed the favorably froths until Day 4 of lactation. The necropsy of stillborn, dead pups until Day 4 of lactation and newborns at Day 4 of lactation did not reveal any effects attributable to the administration of test substance. The influences of test substance on reproductive and developmental toxicity were not observed in both male and female rats receiving 750 mg/kg/day, therefore maximum NOELs were considered to be 750 mg/kg/day in both sexes.
Method:	OECD Combined Repeated Dose and Reproductive/Developmental toxicity Test
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Commercial, purity 97.2 %
Remarks:	None
Reference:	MHW, Japan (1993b)

5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

No studies located

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

No studies located

B. Toxicodynamics, toxicokinetics

No studies located

5.11 EXPERIENCE WITH HUMAN EXPOSURE

No studies located

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