FOREWORD INTRODUCTION

2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4-methyl-2-sulfophenyl)azo]-, calcium salt

CAS N°: 5281-04-9

SIDS Initial Assessment Report

For

SIAM 2

Paris, France, 4-6 July 1994

1. Chemical Name: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt (D & C Red No. 7)

2. CAS Number: 5281-04-9

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, D & C Red No. 7 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
- Water solubility

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

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

Toxicity
- Repeated dose toxicity

Reproductive toxicity
Gene mutation
Chromosomal aberration

The original report was already circulated in August 1995, and the report was revised according to the comments from member countries. At SIAM-2, the conclusion was approved with comments. Comments at SIAM-2: Rearrangement of the documents.

7. Review Process Prior to the SIAM:

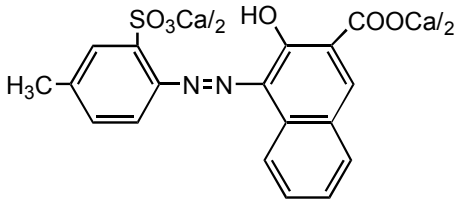
8. Quality check process:

9. Date of Submission: March 1994

10. Date of last Update:

11. Comments:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	5281-04-9
Chemical Name	2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt (D & C Red No.7)
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

D & C Red No.7 is a stable solid. Its production volume was ca. 4,400 tonnes/year in 1990 – 1992 in Japan. This chemical is used in printing inks and plastic industries in open and closed systems. This chemical is stable in neutral, acidic or alkaline solutions, and is considered as "not readily biodegradable".

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 estimated concentrations were 6.6×10^{-9} mg/l (air), 1.0×10^{-4} mg/l (water), 5.2×10^{-7} mg/kg (soil), and 1.1×10^{-3} mg/kg (sediment). Neither monitoring data in the workplace nor consumer exposure data have been reported. Based on the physico-chemical properties, the level of indirect exposure through the environment was estimated as 3.7×10^{-4} mg/man/day (i.e. 6.2×10^{-6} mg/kg/day. The daily intake through drinking water is estimated as 3.3×10^{-6} mg/kg/day and through fish is calculated as 6.0×10^{-7} mg/kg/day. No data on occupational exposure are available.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 33 mg/l (acute fish); EC_{50} = 280 mg/l (acute daphnia); EC_{50} = 190 mg/l (acute algae); NOEC = 3.0 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be slightly toxic to fish. The lowest chronic toxicity result for daphnids [21d-NOEC (reproduction) of *Daphnia magna* (3.0 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 0.03 mg/l in the present report. The PEC is lower than the PNEC, therefore the environmental risk is presumably low.

Human Health

The chemical showed no genotoxic effects in bacteria and chromosomal aberration tests *in vitro*. In a combined repeat dose and reproductive/developmental toxicity screening test, increases of kidney weights and decreases of thymus weights were observed in parental animals at the highest dose (1000 mg/kg/day). At the terminal necropsy, gross changes included a small thymus up to the lowest dose (100 mg/kg/day). In the histopathological examinations, regenerated renal tubular epitheliums were also seen at the middle dose (300 mg/kg/day) and at the highest. Regarding reproductive/developmental end-points, there were no effects observed related to mating,

fertility and the oestrus cycle and there were no effects observed in dams during the pregnancy and lactation period. Therefore, the NOEL was less than 100 mg/kg/day for repeated dose toxicity and than 1000 mg/kg/day for reproductive toxicity.

As for indirect exposure via the environment, the daily intake through drinking water is estimated as 3.3×10^{-6} mg/kg/day and through fish is calculated as 6.0×10^{-7} mg/kg/day. For human health, although NOEL is estimated as less than 100 mg/kg/day for repeated dose and 1,000 mg/kg/day for reproductive toxicity, the margin of safety is very large. Therefore, the health risk through the environment, in general, is considered to be presumably low due to the chemical's 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: 5281-04-9		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			357.5 °C
2.2	Boiling Point			No data available
2.3	Density			No data available
2.4	Vapour Pressure		OECD TG 104	< 130 Pa at 25 °C
2.5	Partition Coefficient (Log Pow)		OECD TG 117	pH3: 2.5 pH7: 1.1 at 25 °C
2.6 A.	Water Solubility		OECD TG 105	8.9 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		estimation	Half-life: 0.049 years in water
3.1.2	Stability in Water		OECD TG 111	Stable at pH 4.0, 7.0 and 9.0.
3.2	Monitoring Data			No data available
3.3	Transport and Distribution		Calculated (Fugacity Level III)	In Air 6.6 E-09 mg/L In Water 1.0E-04 mg/L In Soil 5.2E-07 mg/kg dw In Sediment 1.1E-03 mg/kg dw
3.5	Biodegradation		OECD TG 301C	Not readily biodegradable: 9-12 % (BOD) in 28 days, 0 % (HPLC) in 28 days
3.6	Bioaccumulation	Carp	OECD TG 305C	BCF: 0.7 – 1.8
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oryzias latipes*	OECD TG 203	LC_{50} (24hr): 170 mg/L LC_{50}(96hr): 33 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (24hr): 280 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	*Selenastrum capricornutum*	OECD TG 201	EC_{50} (72hr): 190 mg/l NOEC: 5.8 mg/l
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (21d, Mortality): 9.7 mg/l EC_{50} (21d, Reproduction): 9.1 mg/l NOEC (21d, Repro): 3.0 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

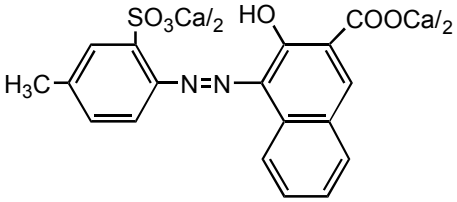
CAS NO: 5281-04-9		SPECIES	PROTOCOL	RESULTS
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	OECD TG 401	LD_{50} > 5,000 mg/kg
5.1.2	Acute Inhalation Toxicity			No data available.
5.1.3	Acute Dermal Toxicity			No data available
5.4	Repeated Dose Toxicity	Rat	OECD Combined Test	NOEL: < 100 mg/kg/day
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	*S. .typhimurium* *E. coli*	OECD Guidelines No.471 and 472 and Japanese	Negative in all bacterial strain with and without metabolic activation
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	CHL cells	OECD Guideline No.473 and Japanese	Negative with and without metabolic activation
5.6	Genetic Toxicity In Vivo			No data available
5.8	Toxicity to Reproduction	Rat	OECD Combined Test	NOEL Parental = 1,000 mg/kg/day NOEL F1 offspring = 1,000 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: 5281-04-9
Chemical Name: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt (D & C Red No. 7)
Molecular Formula: $C_{18}H_{12}N_2O_5Ca$
Structural Formula:



Synonyms: C.I. Pigment Red 57-1
Lithol Rubine Calcium Salts
Briliant Carmine 6B

1.2 Purity/Impurities/Additives

Degree of Purity: 95 - 97 %

Major Impurities: Sodium chloride, Calcium chloride

Essential Additives: No additives

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value
Melting point	357.5 °C
Vapour pressure	< 130 Pa at 25 °C
Water solubility	8.9 mg/l
Partition coefficient n-octanol/water (log value)	1.1 at pH 7 (2.5 at pH 3 and 2.4 at pH 4)

2 GENERAL INFORMATION ON EXPOSURE

D & C Red No. 7 is a stable solid. Its production volume was ca. 4,400 tonnes/year in 1990 - 1992 in Japan. This chemical is used in printing inks and plastic industries in open and closed systems. The chemical seems to be released into water and air from its production sites after biological treatment. No specific monitoring data of the chemical is available. This chemical is stable in neutral, acidic or alkaline solutions, and is considered as “not readily biodegradable”.

2.1 Environmental Exposure and Fate

2.1.1 Photodegradation

The half-life time of 0.049 years is estimated for the degradation of the chemical in water by direct photolysis. (W.J. 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: 9-12 % degradation during 28 days based on BOD and 0 % based on HPLC analysis).

2.1.4 Bioaccumulation

BCF= 0.7 – 1.8 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

Input data:

Molecular weight:	424.45
Water solubility:	8.90 [mg/l]
Vapor pressure:	1.00 [mmHg]
Log Pow:	1.10

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

Air:	6.6E-09 [mg/l]
Water:	1.0E-04 [mg/l]
Soil:	5.2E-07 [mg/kg dry solid]
Sediment:	1.1E-03 [mg/kg dry solid]

Exposure dose

Inhalation of air:	1.3E-04 [mg/day]	
Drinking water:	2.0E-04 [mg/day]	(i.e. 3.3E-06 mg/kg/day)
Ingestion of fish:	3.6E-05 [mg/day]	(i.e. 6.0E-07 mg/kg/day)
meat:	7.0E-13 [mg/day]	
milk:	9.9E-13 [mg/day]	
vegetation:	3.5E-07 [mg/day]	
Total exposure dose:	3.7E-04 [mg/day]	(i.e. 6.2E-06 mg/kg/day)

Comparison of calculated environmental concentrations of D & C Red No.7 using several models.

Model	Air[mg/l]	Water[mg/l]	Soil[mg/kg]	Sediment[mg/kg]
MNSEM	6.6E-09	1.0E-04	5.2E-07	1.1E-03
CHEMCAN2	7.6E-07	6.6E-05	7.6E-08	2.0E-05
CHEMFRAN	7.5E-07	6.6E-05	7.8E-08	2.0E-05

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} in acute oral toxicity studies in rats were reported as > 5,000 mg/kg. LC_{50} and LD_{50} values from acute inhalation and dermal toxicity studies are not available.

3.1.2 Repeated Dose Toxicity

There is only one key study on repeated dose toxicity of D & C Red No. 7. This chemical was studied for oral toxicity in rats according to the OECD combined repeated dose and reproductive/developmental toxicity test [OECD TG 422]. As the study was well controlled and conducted under GLP, it was appropriate to regard as a key study. Male and female SD rats were orally administered (gavage) at doses of 0, 100, 300 and 1,000 mg/kg/day. All animals survived to the end of the study. No clinical findings indicative of chemical toxicity were observed; red-stained feces of exposed animals were due to contact with D & C Red No.7 and were not indicative of toxicity. The mean body weight gains and food consumptions of the dosed group, in both sexes, were comparable to those in the control groups throughout the study. No biologically significant changes in hematological parameters were noted in any dosed male groups. Male rats that received 300 mg/kg or greater showed significantly decreased levels for serum calcium and phosphorus. Significant decreases in serum potassium and total cholesterol levels, and significant increases in chloride and GOT levels were also shown in the males that received 1000 mg/kg. No other significant differences in clinical parameters were observed in the dosed male groups. Male rats that received 1000 mg/kg showed a significant increase in relative kidney weights, and females that received 100 or 1000 mg/kg showed decreases in thymus weights in comparison with the controls. No other significant differences in organ weights were observed in both the males and females. At the terminal necropsy, gross pathological changes included a small thymus in 2 and 5 female rats that received 100 and 1000 mg/kg, respectively; no marked changes were noted in the dosed males. In the histopathological examinations, predominant alterations occurred in the kidney suggesting effects of D & C Red No. 7 in dosed rats. The lesions included regenerated renal tubular epithelium in male rats receiving 300 mg/kg or greater, and those with necrotic or foamy tubular epithelial cells in the dosed females. These lesions were of greater severity and/or occurred with an increased incidence in the higher dose groups.

There were no histopathological changes in the sexual organs of the females that showed no evidence of the copulation, pregnancy or parturition. Under the conditions of this study, the NOEL of this chemical for repeated dose toxicity was than 300 and 100 mg/kg/day on males and females, respectively.

3.1.3 Mutagenicity

Bacterial test

A reverse gene mutation assay was conducted in line with the 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. D & C Red No. 7 showed negative results in Salmonella typhimurium TA100, TA1535, TA98, TA1537, TA1538 and Escherichia coli WP2 uvrA at concentrations up to 5 mg/plate with or without a Metabolic activation system (MHW, 1993b).

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 with no apparent cytotoxic effect in the continuous treatment. In the short term treatment, it was set to 2.5 mg/ml because the concentration was equivalent to ca. 10 mM as required in the test guidelines.

No structural chromosomal aberrations or polyproidy were recognized up to a maximum concentration of 3.5 mg/ml under conditions of both continuous treatment and short-term treatment with or without an exogeneous metabolic activation system (MHW, Japan, 1993b).

in vivo test

No data are available.

3.1.4 Toxicity for Reproduction

D & C Red No. 7 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. Pertinent pregnancy and offspring parameters, e.g. mating performance, duration of gestation, pup viability, body weight and sex distribution, and gross anomalies, were determined. No treatment-related adverse effects were detected. Under the conditions of this study, the NOEL for reproductive/ developmental toxicity of the rats was 1,000 mg/kg/day.

3.2 Initial Assessment for Human Health

Neither monitoring data in the workplace nor consumer exposure data have been reported. Based on the physico-chemical properties, the level of indirect exposure through the environment was estimated as 3.7×10^{-4} mg/man/day (i.e. 6.2×10^{-6} mg/kg/day . The daily intake through drinking water is estimated as 3.3×10^{-6} mg/kg/day and through fish is calculated as 6.0×10^{-7} mg/kg/day. No data on occupational exposure are available.

The chemical showed no genotoxic effects in bacteria and chromosomal aberration tests *in vitro*. In a combined repeat dose and reproductive/developmental toxicity screening test, increases of kidney weights and decreases of thymus weights were observed in parental animals at the highest dose (1000 mg/kg/day). At the terminal necropsy, gross changes included a small thymus up to the

lowest dose (100 mg/kg/day). In the histopathological examinations, regenerated renal tubular epitheliums were also seen at the middle dose (300 mg/kg/day) and at the highest. Regarding reproductive/developmental end-points, there were no effects observed related to mating, fertility and the oestrus cycle and there were no effects observed in dams during the pregnancy and lactation period. Therefore, the NOEL was less than 100 mg/kg/day for repeated dose toxicity and than 1000 mg/kg/day for reproductive toxicity.

As for indirect exposure via the environment, the daily intake through drinking water is estimated as 3.3 x 10^{-6} mg/kg/day and through fish is calculated as 6.0 x 10^{-7} mg/kg/day. For human health, although NOEL is estimated as less than 100 mg/kg/day for repeated dose and 1,000 mg/kg/day for reproductive toxicity, the margin of safety is very large. Therefore, the health risk through the environment, in general, is considered to be presumably low due to the chemical's use pattern and exposure.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

D & C Red No. 7 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 and 203]. Acute and chronic toxicity data to test organisms for D & C Red No. 7 are summarized in Table 2. No other ecotoxicological data are available. Various NOEC and LC_{50} values were gained from the above tests; 96h LC_{50} = 33 mg/l (acute fish); 24h LC_{50} = 280 mg/l (acute daphnia); 72h NOEC = 5.8 mg/l (algae); 21d NOEC = 3.0 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to daphnids and algae and slightly toxic to fish. The lowest chronic toxicity data for daphnia [21 d-NOEC (reproduction) of *Daphnia magna* (3.0 mg/l)] were adopted. An assessment factor of 100 was applied. Thus the PNEC of D & C Red No. 7 is 0.03 mg/l. Since the PEC is lower than the PNEC, the environmental risk is presumably low.

Table 2. Acute and chronic toxicity data of D & C Red No. 7 to aquatic organisms.

Species	Endpoint[*1]	Conc. (mg/L)	Reference
Selenastrum capricornutum (algae)	Biomass: EC50 (72h) NOEC	190 mg/L 5.8 mg/L	EA, Japan (1992)
Daphnia magna (water flea)	Imm: EC50(24h) Mor: EC50(21d) Rep: EC50(21d) NOEC(21d)	280 mg/L 9.7 mg/L 9.1 mg/L 3.0 mg/L	
Oryzias latipes (fish, Medaka)	Mor: LC50(24h) Mor: LC50(72h) Mor: LC50 (96h)	170 mg/L 44 mg/L 33 mg/L	

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

4.2 Initial Assessment for the Environment

D & C Red No.7 is a stable solid. Its production volume was ca. 4,400 tonnes/year in 1990 – 1992 in Japan. This chemical is used in printing inks and plastic industries in open and closed systems.

This chemical is stable in neutral, acidic or alkaline solutions, and is considered as "not readily biodegradable".

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 estimated concentrations were 6.6×10^{-9} mg/l (air), 1.0×10^{-4} mg/l (water), 5.2×10^{-7} mg/kg (soil), and 1.1×10^{-3} mg/kg (sediment).

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 33 mg/l (acute fish); EC_{50} = 280 mg/l (acute daphnia); EC_{50} = 190 mg/l (acute algae); NOEC = 3.0 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be slightly toxic to fish. The lowest chronic toxicity result for daphnids [21d-NOEC (reproduction) of *Daphnia magna* (3.0 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 0.03 mg/l in the present report. The PEC is lower than the PNEC, therefore the environmental risk is presumably low.

5 RECOMMENDATIONS

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

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

6 REFERENCES

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

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

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

MHW, Japan (1993a) Unpublished Report on Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of D & C Red No 7. (HPV/SIDS Test conducted by MHW, Japan)

MHW, Japan (1993b) Unpublished Report on Mutagenicity Test of D & C Red No 7. (HPV/SIDS Test conducted by MHW, Japan)

MITI, Japan : Unpublished data

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

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

NPIRI Raw Material Data Handbook, Vol.4. Pigments.

Pigment Handbook, Vol. 1, 2nd Ed.

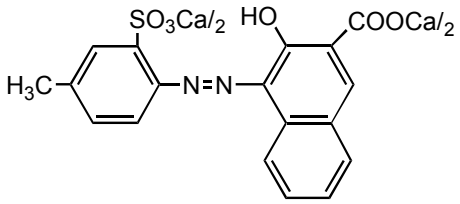
SIDS DOSSIER

D & C Red No. 7

CAS No. 5281-04-9

Sponsor Country: Japan

S I D S P R O F I L E

1.01 A.	**CAS No.**	5281-04-9
1.01 C.	**CHEMICAL NAME (OECD Name)**	D & C Red No. 7
1.01 D.	**CAS DESCRIPTOR**	Not applicable
1.01 G.	**STRUCTURAL FORMULA**	 $C_{18}H_{12}N_2O_6Ca$
	OTHER CHEMICAL IDENTITY INFORMATION	
1.5	**QUANTITY**	In Japan approx 4,400 tonnes in 1990 - 1992.
1.7	**USE PATTERN**	(a) main industry use: Printing ink industry (Open system) 90 - 95 % (b) main industry use: Plastic processing (open or closed system) 5 - 10%
1.9	**SOURCES AND LEVELS OF EXPOSURE**	1. Media of release: Water from a production site Quantities per media: < 10 kg/year 2. Media of release: Air from a production site Quantities per media: < 1 kg/year 3. Information on consumer exposure is not available.
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)		

S I D S S U M M A R Y

D & C Red No. 7

CAS NO: 5281-04-9		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	N						Y
5.5	Genetic Toxicity *in vitro*							
	. Gene mutation	N						Y
	. Chromosomal aberration	N						Y
5.6	Genetic Toxicity *in vivo*	N						N
5.8	Reproduction Toxicity	N						Y
5.9	Development / Teratogenicity	N						Y
5.11	Human experience	N						N
OTHER TOXICITY STUDIES RECEIVED								

1.01 SUBSTANCE INFORMATION

A. CAS-Number 5281-04-9

B. Name *(IUPAC name)* 2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4-methyl-2-sulfophenyl)azo]-, calcium salt

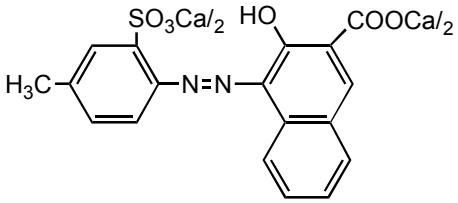
C. Name *(OECD name)* D & C Red No. 7

D. CAS Descriptor Not applicable

E. EINECS-Number 226-109-5

F. Molecular Formula $C_{18}H_{12}N_2O_6Ca$

G. Structural Formula



H. Substance Group Not applicable

I. Substance Remark

J. Molecular Weight 424.45

1.02 OECD INFORMATION

A. Sponsor Country: Japan

B. Lead Organisation:

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

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

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

C. Name of responder Same as above contact person

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element **[ ]**; inorganic **[ ]**; natural substance **[ ]**;
organic **[X]**; organometallic **[ ]**; petroleum product **[ ]**

B. Physical State

gaseous **[ ]**; liquid **[ ]**; solid **[X]**

C. Purity 95 - 97 %

1.2 SYNONYMS

C.I. Pigment Red 57-1
Lithol Rubine Calcium Salts
Briliant Carmine 6B

1.3 IMPURITIES Water, Sodium chloride and Calcium chloride

1.4 ADDITIVES None

1.5 QUANTITY

Location	Production (tonnes)	Data
Japan	4,400	1990-1992

Export (tonnes)	1993	1992	1991	1990
German	350	350	360	260
France	110	70	40	40
England	20	70	100	100
others	420	290	260	260

* Export data was obtained from one company

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	Printing ink industry (Open or closed system) 90 - 95 %
(b) main industry use	Plastic processing (Open or closed system) 5 - 10 %

Reference: MITI, Japan

B. Uses in Consumer Products

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Source	Number of workers exposed	Frequency & duration of exposure	Emission data
Grinding	1 – 3	15 - 600 min/day	0.002-1.4 mg/m^3
Packing	1 – 7	1 - 10 hrs/day	0.005-0.4 mg/m^3

1.9 SOURCES OF EXPOSURE

(a)
Source: Media of release: Water from a production site
Quantities per media: < 10 kg/year

(b)
Source: Media of release: Air from a production site
Quantities per media: < 1 kg/year

Reference: MITI, Japan

1.10 ADDITIONAL REMARKS

A. Options for disposal

Unknown

B. Other remarks None

2.1 MELTING POINT

Value: 357.5 °C
Decomposition: Yes **[X]** No **[ ]** Ambiguous **[ ]**
Sublimation: Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method: Unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks: None
Reference: Unpublished company data

2.2 BOILING POINT

No studies located

2.3 DENSITY (Relative density)

No studies located

2.4 VAPOUR PRESSURE

Value: < 130 Pa
Temperature: 25 °C
Method: calculated **[ ]**; measured [X]
OECD Test Guideline 104 (Static method)
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Remarks:
Reference: MITI, Japan (1993)

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

Log Pow: 2.5 at pH 3
2.4 at pH 4
1.1 at pH 7
Temperature: 25 °C
Method: calculated **[ ]**; measured **[**X**]**
OECD Test Guideline 117 (HPLC method)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Remarks: None
Reference: MITI, Japan (1993)

2.6 WATER SOLUBILITY

A. Solubility

Value: 8.9 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 105
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Remarks:
Reference: MITI, Japan (1993)

B. pH Value, pKa Value Not applicable

2.7 FLASH POINT

No studies located

2.8 AUTO FLAMMABILITY

No studies located

2.9 FLAMMABILITY

Value:	575 - 590 °C
Results:	Extremely flammable**[ ]**;Extremely flammable-liquified gas**[]**; Highly Flammable **[ ]**; Flammable **[ ]**; Non flammable **[ ]**; Spontaneously flammable in air **[ ]**; Contact with water liberates highly flammable gases **[ ]**; Other **[ ]**
Method:	
GLP:	Yes **[ ]** No **[ ]** ? **[ ]**
Remarks:	It only smokes below 575 °C without flame.
Reference:	Unpublished company data

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 = 4240 at 300 nm	
	epsilon = 6790 at 330 nm	
	epsilon = 21600 at 525 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	2.25×10^{-11}mol/l/s
	Half-life	0.049 years
Reference	W. J. Lyman 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 Test Guideline 111
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	D & C Red No. 7
Remarks:	None
Reference:	MITI, Japan (1993)

3.1.3 STABILITY IN SOIL

No studies located

3.2 MONITORING DATA (ENVIRONMENT)

No studies located

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

3.3.1 TRANSPORT

No studies located

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

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

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

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

Air : 6.6E-09 [mg/l]
Water: 1.0E-04 [mg/l]
Soil: 5.2E-07 [mg/kg dry solid]
Sediment: 1.1E-03 [mg/kg dry solid]

Exposure dose

Inhalation of air: 1.3E-04 [mg/day]
Drinking water: 2.0E-04 [mg/day]
Ingestion of fish: 3.6E-05 [mg/day]
meat: 7.0E-13 [mg/day]
milk: 9.9E-13 [mg/day]
vegetation: 3.5E-07 [mg/day]

Total exposure dose: 3.7E-04 [mg/day]

Remarks: Input data:

Molecular weight: 424.45
Water solubility: 8.90 [mg/l]
Vapor pressure: 1.00 [mmHg]
Log Pow: 1.10

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	6.6E-09	1.0E-04	5.2E-07	1.1E-03
CHEMCAN2	7.6E-07	6.6E-05	7.6E-08	2.0E-05
CHEMFRAN	7.5E-07	6.6E-05	7.8E-08	2.0E-05

Reference: EA and MITI, Japan (1993)

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

No studies located

3.5 BIODEGRADATION

Type: aerobic **[X]**; anaerobic **[ ]**
Inoculum: adapted **[ ]**; non-adapted **[X]**;
Concentration of the chemical: 100 mg/l related to COD **[ ]**; DOC **[ ]**; Test substance **[X]**;
Medium: water **[ ];** water-sediment **[ ];** soil **[ ];** sewage treatment others **[X]** (Japanese standard activated sludge)
Degradation: Degree of degradation after 28 days
12, 9 and 9 % from BOD
0, 0 and 0 % from HPLC 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:	D & C Red No. 7
Remarks:	None
Reference:	MITI, Japan (1993)

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 µg/l
	(2) 0.03 µg/l
BCF:	(1) < 0.7 - 1.8
	(2) < 6.9
Elimination:	Yes **[ ]** No **[ ]** ? **[ ]**
Method:	OECD Test Guideline 305C
Type of test:	**[ ]** calculated; **[X]** measured
	static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other **[ ]**
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	D & C Red No. 7
Remarks:	None
Reference:	MITI, Japan (1992)

3.8 ADDITIONAL REMARKS None

A. Sewage treatment

B. Other information

4.1 ACUTE/PROLONGED TOXICITY TO FISH

(a)

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) = 170 mg/l
LC_{50} (48h) = 98 mg/l (95% confidence level: 80-120 mg/l)
LC_{50} (72h) = 44 mg/l (95% confidence level: 30-66 mg/l)
LC_{50} (96h) = 33 mg/l (95% confidence level: 11-98 mg/l)
NOEC =
LOEC =
Analytical monitoring: Yes **[ ]** No **[X]** ? **[ ]**
Method: OECD Test Guideline 203 (1981)
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: D & C Red No. 7, Purity = 87 %
Remarks: A group of 10 fishes were exposed to 5 nominal concentrations (17.1-180 mg/l), DMSO control (0.5 mg/l) and laboratory water control.
Reference: EA, Japan (1992)

(b)

Type of test: static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other **[ ]**
open-system **[ ]**; closed-system **[ ]**
Species: *Oryzias latipes* (Orange killifish)
Exposure period: 96 hr
Results: LC_{50} (24h) =
LC_{50} (48h) = 50 mg/l
LC_{50} (72h) =
LC_{50} (96h) =
NOEC =
LOEC =
Analytical monitoring: Yes **[ ]** No **[ ]** ? **[X]**
Method: Japanese Industrial Standard (JIS K 0102-1986-71)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: D & C Red No. 7
Remarks: None
Reference: MITI, Japan (1992)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

(a)

Type of test: static **[X]**; semi-static **[ ]**; flow-through **[ ]**; other **[ ]**;
open-system **[**X**]**; closed-system **[ ]**
Species: *Daphnia magna*
Exposure period: 24 hr
Results: EC_{50} (24h) = 280 mg/l (95% confidence level: 150-490 mg/l)
EC_{50} (48h) =
NOEC =
LOEC =
Analytical monitoring: Yes **[ ]** No **[X]** ? **[ ]**
Method: OECD Test Guideline 202 (1984)

GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: D & C Red No. 7, purity: = 87 %
Remarks: 20 daphnids (4 replicates; 5 organisms per replicate) were exposed to 5 nominal concentrations (90-940 mg/l), control of DMSO:HCO-40 = 9:1 (100 mg/l) and laboratory water control.
Reference: EA, Japan (1992)

B. Other aquatic organisms

No studies located

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

Species: *Selenastrum capricornutum* ATCC 22662
End-point: Biomass **[X]**; Growth rate **[ ]**; Other **[ ]**
Exposure period: 72 hr
Results: Biomass: EC_{50} (24h) =
EC_{50} (72h) = 190 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: D & C Red No. 7, purity = 87 %
Remarks: The EC_{50} values were calculated based on 13 nominal concentrations (1.0-1000 mg/l) and laboratory 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 **[ ]**;
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) = 210 mg/l (95% confidence level: 160-300 mg/l)
LC_{50} (48 h) = 43 mg/l (95% confidence level: 31-58 mg/l)
LC_{50} (96 h) = 18 mg/l (95% confidence level: 14-24 mg/l)
LC_{50} (7 d) = 13 mg/l (95% confidence level: 10-17 mg/l)
LC_{50} (14 d) = 10 mg/l (95% confidence level: 7.8-13 mg/l)
LC_{50} (21 d) = 9.7 mg/l (95% confidence level: 7.7-12 mg/l)
NOEC =
LOEC =

Reproduction:	EC_{50} (14 d) = 4.4 mg/l (95% confidence level: 3.1-5.8 mg/l) EC_{50} (21 d) = 9.1 mg/l NOEC = 3.0 mg/l ($p < 0.05$) LOEC = 9.4 mg/l ($p < 0.05$)
Analytical monitoring:	Yes **[ ]** No **[X]** ? **[ ]**
Method:	OECD Test Guideline 202 (1984)
GLP:	Yes **[ ]** No **[X]** ? **[ ]**
Test substance:	D & C Red No.7, purity = 87 %
Remarks:	40 daphnids (4 replicates; 10 organisms per replicate) were exposed to 5 nominal concentrations (3-300 mg/l), Control of DMSO:HCO-40 = 9:1 (100 mg/kg) 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

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(a)
Type : LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rat
Value : > 5,000 (mg/kg)
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: D & C Red No 7, purity: Unknown
Remarks:
Reference: Pigment Handbook

(b)
Type : LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Mouse (CFLP)
Value : > 16,000 (mg/kg)
Method: unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: D & C Red No 7, purity: Unknown
Remarks:
Reference: Unpublished Company data

5.1.2 ACUTE INHALATION TOXICITY

No studies located

5.1.3 ACUTE DERMAL TOXICITY

Type : LD_0 **[X]**; LD_{100} **[ ]**; LD_{50} **[ ]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Mouse
Value:
Method:
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance:
Comments:
Remarks: The repeated application of 0.1 ml contg. 1.0% dye did not increase the incidence of neoplasia when compared to control in any of the groups receiving application of the 14 dyes.
Reference: Cutaneous Ocul. Toxicol., 3(4) 357-70

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

No studies located

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

(a)
Species/strain: 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:
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance:
Remarks: Not irritating; average score for redness or swelling 0.5 (maximum primary skin irritation score=8°)
Reference: NPIRI Raw Material Data Handbook

(b)
Species/strain: 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 **[X]**
Method:
GLP: Yes **[ ]** No **[ ]** ? **[ ]**
Test substance:
Remarks: Non-irritant to rabbit skin
Reference: Company data

5.2.2 EYE IRRITATION/CORROSION

Species/strain: 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:
GLP: Yes **[ ]** No **[ ]** ? **[ ]**
Test substance:
Remarks: Not eye irritant; no ulceration, corneal opacity or iris inflammation, no or slight redness or swelling.
Reference: NPIRI Raw Material Data Handbook

5.3 SKIN SENSITISATION

No studies located

5.4 REPEATED DOSE TOXICITY

Species/strain: Rat (Crj:CD(SD))
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: oral (gavage)
Exposure period: Males: 42 days including 14 days before mating
Females: from 14 days before mating to day 3 of lactation
Frequency of treatment: 7 days/week
Post exposure observation period:
Dose: 0, 100, 300 or 1,000 mg/kg (13 animals /group)
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**;
Historical **[ ]**
NOEL: < 100 mg/kg/day
LOEL: 100 mg/kg/day

Results: All animals survived to the end of the studies. No clinical findings indicative of chemical toxicity were observed; red-stained feces of exposed animals were due to contact with D & C Red No.7 and were not indicative of toxicity. The mean body weight gains and food consumptions of the dosed group, in both sexes, were comparable to those in the control groups throughout the study. No biologically significant changes in hematological parameters were noted in any dosed male groups. Male rats that received 300 mg/kg or greater showed significantly decreased levels for serum calcium and phosphorus. Significant decreases in serum potassium and total cholesterol levels, and significant increases in chloride and GOT levels were also shown in the males that received 1000 mg/kg. No other significant differences in clinical parameters were observed in the dosed male groups. Male rats that received 1000 mg/kg showed a significant increase in relative kidney weights, and females that received 100 or 1000 mg/kg showed decreases in thymus weights in comparison with the controls. No other significant differences in organ weights were observed in both the males and females. At the terminal necropsy, gross pathological changes included a small thymus in 2 and 5 female rats that received 100 and 1000 mg/kg, respectively; no marked changes were noted in the dosed males. In the histopathological examinations, predominant alterations occurred in the kidney suggesting effects of D & C Red No. 7 in dosed rats. The lesions included regenerated renal tubular epithelium in male rats receiving 300 mg/kg or greater, and those with necrotic or foamy tubular epithelial cells in the dosed females. These lesions were of greater severity and/or occurred with an increased incidence in the higher dose groups. There were no histopathological changes in the sexual organs of the females that showed no evidence of the copulation, pregnancy or parturition. Under the conditions of this study, the NOEL of this chemical for repeated dose toxicity was doses of less than 300 and 100 mg/kg/day on males and females, respectively.

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

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

Test substance: Commercial, purity: 98 %

Reference: MHW, Japan (1993a)

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 uvrA

Concentration: 0, 50, 250, 1000 or 5000 µg/plate

Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**

Results:

Cytotoxicity conc: With metabolic activation: 5000 µg/plate
Without metabolic activation: 5000 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: 98 %
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 (1993b)

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:
Without metabolic activation:
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 98 %
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)

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: 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, 100, 300, or 1,000 mg/kg (13 animals/sex/group)
Control group:	Yes **[X]**; No **[ ]**; No data **[ ]**; Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOEL Parental :	= 1,000 mg/kg/day
NOEL F1 Offspring:	= 1,000 mg/kg/day
NOEL F2 Offspring:	N/A
Results:	Pertinent pregnancy and offspring parameters, e.g. mating performance, duration of gestation, pup viability, body weight and sex distribution, and gross anomalies, were determined. No treatment-related adverse effects were detected. Under the conditions of this study, NOEL for reproductive/ developmental toxicity of the rats was 1,000mg/kg/day.
Method:	Combined Repeated Dose and Reproductive/Developmental toxicity Screening Test
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	Commercial, purity 98 %
Remarks:	None
Reference:	MHW, Japan (1993a)

5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

No studies located

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

No studies located

B. Toxicodynamics, toxicokinetics

No studies located

5.11 EXPERIENCE WITH HUMAN EXPOSURE

None

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

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