IUCLID

Data Set

Existing Chemical	:	ID: 64-67-5
CAS No.	:	64-67-5
EINECS Name	:	diethyl sulphate
EC No.	:	200-589-6
TSCA Name	:	Sulfuric acid, diethyl ester
Molecular Formula	:	C4H10O4S

Producer related part

Company	:	The Dow Chemical Company
Creation date	:	12.09.2003

Substance related part

Company	:	The Dow Chemical Company
Creation date	:	12.09.2003
Status	:	
Memo	:	
Printing date	:	08.11.2006
Revision date	:	
Date of last update	:	08.11.2006
Number of pages	:	54
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	
Name	:	SIBER HEGNER RAW MATERIALS LTD.
Contact person	:	
Date	:	
Street	:	WIESENSTRASSE 8
Town	:	CH-8022 Zurich
Country	:	Switzerland
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	
Source	:	ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston
Flag	:	non confidential

23.10.1995

Type	:	
Name	:	Union Carbide Benelux
Contact person	:	
Date	:	
Street	:	Norderlaan 147
Town	:	2030 Antwerpen
Country	:	Belgium
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	
Source	:	ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston
Flag	:	non confidential

23.10.1995

Type	:	
Name	:	Whyte Chemicals Ltd
Contact person	:	
Date	:	
Street	:	322 Regents Park Road
Town	:	N3 2UA London
Country	:	United Kingdom
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	
Source	:	ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston
Flag	:	non confidential

23.10.1995

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type :
Substance type : organic
Physical status : liquid
Purity : > 99 % w/w
Colour :
Odour :

Remark : Diethyl Sulfate specification has a purity requirement of 99.5 wt %. The product as normally produced and received into the distribution system in 2002 had an average purity of 99.78 wt %. GC analysis of the storage tank for the year 2002 showed an average purity of 99.77 wt %, with a minimum and maximum purity of 99.65 and 99.87 wt %, respectively.
Source : ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
Flag : non confidential
17.12.2003

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Diethyl Sulphate

Source : SIBER HEGNER RAW MATERIALS LTD. Zurich
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995

ethyl sulfate

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995

ETHYLSULPHATE

Source : Whyte Chemicals Ltd London
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995

sulfuric acid, diethyl ester

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC
Specific limits : no
Symbols : T, , ,
Nota : E, ,
R-Phrases : (45) May cause cancer
(46) May cause heritable genetic damage
(20/21/22) Harmful by inhalation, in contact with skin and if swallowed
(34) Causes burns
S-Phrases : (53) Avoid exposure - obtain special instructions before use
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

Source : ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
Flag : non confidential
23.10.1995

1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC
Class of danger : carcinogenic, category 2
R-Phrases : (45) May cause cancer
Specific limits :

Source : ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
Flag : non confidential
23.10.1995

Classified : as in Directive 67/548/EEC
Class of danger : corrosive
R-Phrases : (34) Causes burns
Specific limits :

Source : ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

Flag : non confidential
23.10.1995

Classified : as in Directive 67/548/EEC
Class of danger : harmful
R-Phrases : (20/21/22) Harmful by inhalation, in contact with skin and if swallowed
Specific limits :

Source : ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
Flag : non confidential
23.10.1995

Classified : as in Directive 67/548/EEC
Class of danger : mutagenic, category 2
R-Phrases : (46) May cause heritable genetic damage
Specific limits :

Source : ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
Flag : non confidential
23.10.1995

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAK (DE)
Limit value : .03 ml/m3

Source : SIBER HEGNER RAW MATERIALS LTD. Zurich
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995

Type of limit : TLV (US)
Limit value :

Remark : 1 ppm-skin: TLV-TWA
Union Carbide recommendation
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)

UNION CARBIDE CORPORATION Houston
23.10.1995

Remark : 1 PPM - SKIN TWA
Source : Whyte Chemicals Ltd London
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Remark : As the quantities of this substance placed on the EU market by Union Carbide Benelux N.V. are normally sourced from the manufacturing facilities of its U.S. parent company, no exposure can arise within the EU from the manufacture of these quantities. The comments below on exposure are restricted to uses for which Union Carbide believes its customers use this substance.

Major use(s): chemical intermediate for dyes, pharmaceuticals etc. always used in closed systems.

Sources of human exposure: negligible assuming appropriate industrial hygiene and personal protection precautions are observed. There are no consumer uses, hence no public exposure.

Sources of environmental exposure: none - this substance is chemically transformed into other substances. Releases to waste water systems hydrolyse to ethanol (inherently biodegradable) and sulphuric acid.

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)

UNION CARBIDE CORPORATION Houston

23.10.1995

Remark : Diethyl Sulfate is used for basic organic synthesis. When handling according to the basic precaution rules (avoid all possible contact with the product) no harm whether to humans nor to the environment are to be expected.

Source : SIBER HEGNER RAW MATERIALS LTD. Zurich
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

16.09.2003

Country : Germany MAK-LIST: Group IIIA2

Source : SIBER HEGNER RAW MATERIALS LTD. Zurich
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995

Remark : DES IS PRODUCED IN A CLOSED PROCESS. THE ONLY POSSIBLE EXPOSURE TO HUMANS AND ENVIRONMENT IS VIA AN ACCIDENTAL RELEASE. NO FURTHER INFORMATION AVAILABLE.

Source : Whyte Chemicals Ltd London
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

16.09.2003

1.11 ADDITIONAL REMARKS

Remark : Disposal: Incinerate in a furnace where permitted under appropriate national and local regulations. May be mixed with solvent (acetone) for ease in burning. In very dilute concentrations (about 10 ppm) in water, it may be amenable to biodegradation in a treatment plant, but the acidity resulting from hydrolysis must be carefully monitored and neutralized.

Transport: Diethyl sulphate is classified as class 6.1 product according the ADR/RID/IMDG/ICAO regulations. Diethyl sulphate is shipped in appropriate road and rail transport units and smaller packages (e.g. drums). The product has to be loaded, unloaded or transloaded with a vapour return line. Every container used for diethyl sulphate shall have no bottom outlets. Only top-loading and unloading is allowed.

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

16.09.2003

Remark : NO ADDITIONAL REMARKS.

Source : Whyte Chemicals Ltd London
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value : = -24.5 °C

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
03.11.2003 (10)

Value : -25 °C

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (37)

Value : -24.4 °C

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (29) (47)

2.2 BOILING POINT

Value : = 208 °C at

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
03.11.2003 (10)

Value : 208 °C at
Decomposition : yes
Method :
Year :
GLP :
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (29)

Value : 209.5 °C at
Decomposition : yes
Method :
Year :
GLP :
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (37)

Decomposition : yes
Method :
Year :

GLP :
Test substance :

Remark : decomposes to ethyl ether, ethylene and sulphur oxides at temperatures above 100 degrees C.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (47)

2.3 DENSITY

Type : density
Value : = 1.1774 g/cm³ at 20 °C

Reliability : (2) valid with restrictions
03.11.2003 (10)

Type : relative density
Value : 1.1795 at 20 °C
Method :
Year :
GLP : no data
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (47)

Type : relative density
Value : 1.172 at 28 °C
Method :
Year :
GLP : no data
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (37)

Type : density
Value : 1.1803 at °C
Method :
Year :
GLP : no data
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (29)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .19078 hPa at 20 °C

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
03.11.2003 (36)

Value : .13 hPa at 20 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (47)

Value : .25 hPa at 20 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (29)

Value : 1.33 hPa at 47 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (37)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = 1.14 at °C
pH value :
Method : other (calculated): EPIWIN (v 3.11) KOWWIN Submodel (v 1.67)
Year : 2003
GLP :
Test substance :

Remark : The EPIWIN model was run using the following measured physical chemical properties:
Vapor pressure (mm Hg): 0.14344;
Boiling point (deg C): 208.0; and
Melting point (deg C): -24.50.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.12.2003 (40)

Partition coefficient :
Log pow : 1.14 at °C
pH value :
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
07.11.2003 (46)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : = 7000 mg/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.11.2003 (21)

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Insoluble, decomposes at room temperature.
Reliability : (2) valid with restrictions
25.11.2003 (10)

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : 0.7% by weight solubility in water at 20 degrees C. Diethyl sulphate reacts vigorously with water.
Source : Union Carbide Benelux Antwerpen

ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
09.10.2003 (47)

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Practically insoluble in water and gradually decomposed by it. Rapidly decomposition by hot water into monoethyl sulfate and alcohol.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (37)

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Insoluble in water.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (29)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : 104 °C
Type : closed cup
Method : other: Tag Closed Cup (ASTM D 56)
Year :
GLP : no data
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (29) (37) (47)

2.8 AUTO FLAMMABILITY

Value : 436 °C at

Method :
Year :
GLP : no data
Test substance :

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995 (29)

2.9 FLAMMABILITY

Result : other: no data to report

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995

2.10 EXPLOSIVE PROPERTIES

Remark : Flammability limits in air (% by weight):
- lower: 4.1
- upper: not determined

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995 (48)

2.11 OXIDIZING PROPERTIES

Result : other: no data to report

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Remark : vapour density (air = 1): 5.3
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995 (47)

3.1.1 PHOTODEGRADATION

DIRECT PHOTOLYSIS

Halflife t1/2	:	= 6.5 day(s)
Degradation	:	% after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated): EPIWIN (v 3.11) AOP Submodel (v 1.91)
Year	:	2003
GLP	:	
Test substance	:	

Remark : Overall OH rate constant = 1.6422 E-12 cm3/molecule/sec
The EPIWIN model was run using the following measured physical chemical properties:
Vapor pressure (mm Hg): 0.14344;
Boiling point (deg C): 208.0; and
Melting point (deg C): -24.50.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.12.2003 (38)

Remark :
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
06.10.2003

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	= .4 hour(s) at 50 °C
t1/2 pH7	:	= .4 hour(s) at 50 °C
t1/2 pH9	:	= .2 hour(s) at 50 °C
Deg. product	:	yes
Method	:	OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year	:	2006
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : pH 4 - potassium biphthalate buffer
pH 7 - potassium phosphate buffer
pH 9 - sodium borate buffer

Preliminary Study

Nominal concentration DES = 1500 mg/l (pH 4 and 7) and 1520 mg/l (pH 9).
Incubation time - 5 days
Incubation temp - 50ºC

Precisely measured volumes of neat DES were added directly to each sterile buffer solution due to the rapid hydrolysis of DES. The hydrolytic reaction was quenched with acetonitrile at the sampling times.

DES concentrations were determined using a Gas Chromatograph/Mass

Spectrometer.

The concentrations of the degradation products, ethyl sulfuric acid and ethyl sulfate were measured using an ion chromatograph, and ethanol, was measured using a gas chromatograph/flame ionization detector, respectively.

A definitive test was not performed as the half-lives determined were considered to indicate that DES was sufficiently unstable such that further evaluation of the hydrolysis kinetics were not required.

Result : Mean recoveries of parent DES following 2 hour incubation period:

pH 4.0 - 1.8%
pH 7.0 - 1.7%
pH 9.0 - 0.0%

After 5 days, no DES was detected in any of the solutions. Based on the data above, the hydrolysis half-lives for DES at 50ºC were calculated to be 0.35 hours for pH 4 and 7 and 0.19 hours for pH 9. Since the half-life of DES was determined to be less than 2.4 hours at 50ºC, the extrapolated half-life at 25ºC is estimated to be less than 24 hours as per the guideline. These half-lives are sufficiently unstable such that further evaluation of the hydrolysis kinetics is not warranted. Based upon these results, the half-life of DES at 25ºC at pH7 is predicted to be 1.9 hours.

Analytical determinations of ethyl sulfuric acid and ethanol confirmed that one mole of each byproduct was generated for each mole of DES hydrolyzed. After 5 days of incubation at 50ºC, concentrations of both ethyl sulfuric acid and ethanol remained relatively stable and no sulfate formation was detected in the reaction solutions. Therefore, the rapid initial hydrolysis of DES results in the formation of ethyl sulfuric acid and ethanol as stable hydrolysis products (t1/2 < 0.4 hours at 25ºC) and that ethyl sulfuric acid is relatively resistant to hydrolysis (t1/2 > 1 year at 25ºC).

Conclusion : DES decomposes rapidly to ethyl sulfuric acid and gradually to alcohol and sulfuric acid.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

08.11.2006 (8)

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995

12.11.2003 (10)

3.1.3 STABILITY IN SOIL

Remark : Decomposes gradually by reaction with moisture in soil to alcohol and sulfuric acid

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Media : other: air (emissions to compartment = 1000 kg/hr)
Method : Calculation according Mackay, Level III
Year : 2003

Method : Equilibrium Concentration Model (EQC) Level III
Remark : The EPIWIN model was run using the following measured physical chemical properties:
Vapor pressure (mm Hg): 0.14344;
Boiling point (deg C): 208.0; and
Melting point (deg C): -24.50.
Result : Concentration (%):
Air - 77
Water - 15
Soil - 9
Sediment - < 0.1

Level III Fugacity Model (Full-Output):
==========
Chem Name : Sulfuric acid, diethyl ester
Molecular Wt: 154.18
Henry's LC : 8.4e-006 atm-m3/mole (Henry database)
Vapor Press : 0.143 mm Hg (user-entered)
Log Kow : 1.14 (Kowwin program)
Soil Koc : 5.66 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	76.6	143	1000
Water	14.7	360	0
Soil	8.7	360	0
Sediment	0.0274	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	1.01e-010	311	639	31.1	63.9
Water	3.34e-012	23.6	12.3	2.36	1.23
Soil	5.04e-011	14	0	1.4	0
Sediment	2.74e-012	0.011	0.000458	0.0011	4.58e-005

Persistence Time: 83.5 hr
Reaction Time: 240 hr
Advection Time: 128 hr
Percent Reacted: 34.8
Percent Advected: 65.2

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 142.6
Water: 360

Soil: 360
Sediment: 1440
Biowin estimate: 2.858 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.12.2003 (41)

Media : other: water (emissions to compartment = 1000 kg/hr)
Method : Calculation according Mackay, Level III
Year : 2003

Method : Equilibrium Concentration Model (EQC) Level III
Remark : The EPIWIN model was run using the following measured physical chemical properties:
Vapor pressure (mm Hg): 0.14344;
Boiling point (deg C): 208.0; and
Melting point (deg C): -24.50.
Result : Concentration (%):
Air - < 1
Water - 99
Soil - < 0.1
Sediment - < 1

Level III Fugacity Model (Full-Output):
==========

Chem Name : Sulfuric acid, diethyl ester
Molecular Wt: 154.18
Henry's LC : 8.4e-006 atm-m3/mole (Henry database)
Vapor Press : 0.143 mm Hg (user-entered)
Log Kow : 1.14 (Kowwin program)
Soil Koc : 5.66 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.527	143	0
Water	99.2	360	1000
Soil	0.0598	360	0
Sediment	0.185	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	2.8e-012	8.58	17.7	0.858	1.77
Water	9.06e-011	640	333	64	33.3
Soil	1.39e-012	0.386	0	0.0386	0
Sediment	7.44e-011	0.298	0.0124	0.0298	0.00124

Persistence Time: 335 hr
Reaction Time: 516 hr
Advection Time: 957 hr
Percent Reacted: 65
Percent Advected: 35

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 142.6
Water: 360
Soil: 360
Sediment: 1440

Biowin estimate: 2.858 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.12.2003 (41)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other: see Remarks
Contact time : 28 day(s)
Degradation : = 89 (±) % after 28 day(s)
Result : other
Control substance : Aniline
Kinetic : %
%
Deg. product : not measured
Method : OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year : 1992
GLP : no data
Test substance : other TS

Method : This study investigated the biodegradation of the test substance in closed bottles under aerobic conditions for 28 days. Each test vessel contained 300 ml of basal culture medium into which DES was added (final concentration: 100 mg/L). The activated sludge was added so that the concentration of suspended solid reached 30 mg/L. Negative controls (blank), non-sludge controls (test substance and water) and reference controls (aniline: 0.1 g/L) were also prepared. The flasks were incubated at 25 +/- 1°C, while magnetically stirred, for 28 days. After the termination of cultivation, total organic carbon and the test substance in the test solutions were determined. The pH of the test solutions containing test substance were measured.

Remark : Sludge was collected from the following 10 places in Japan: the Fukogawa city sewage plant; the Fukashiba industry sewage plant; the Nakahama city sewage plant; the Ochiai city sewage plant; the Kitakami river; the Shinano river; the Yoshino river; the Lake Biwa; the Hiroshima bay; and the Dookai Bay. Five liters of the filtrate of the supernatant of an activated sludge was mixed with 500 mL of the filtrate of the supernatant of the newly collected sludge and the mixture was cultured at pH 7.0 +/- 1.0 under aerated conditions.

Result : Biodegradation of DES achieved a maximum level of 89% after 28 days. Biodegradation of aniline at 7 and 14 days was greater than 40 and 60%, respectively, indicating that the test condition was valid.

08.12.2005 (4)

Type : aerobic
Inoculum : other: microbial seed
Contact time :
Degradation : 57 (±) % after 20 day(s)
Result :
Kinetic of testsubst. : 5 day(s) 25 %

10 day(s) 30 %
20 day(s) 57 %
%
%

Deg. product :
Method : other: BOD20
Year : 1974
GLP : no
Test substance :

Remark : The test method utilized was: "Standard Methods for the Examination of Water and Wastewater." 1971. 13th edition, Amer. Pub. Health Assn., New York, NY. A settled domestic wastewater was filtered through glass wool and then added (3 ml/bottle) as seed material to clean 300 ml BOD bottles. The dilution water was sparged with pure oxygen to produce an available DO level of 30 to 35 mg/l and added to the seed material to completely fill the bottles. The pure chemical was added to each bottle (3.0 µl/bottle) to provide a concentration of approximately 10 mg/l. At least two of the concentrations were tested in duplicate. Dissolved oxygen content was measured approximately five times throughout the test using a commercial DO meter filled with an agitated probe. When the DO level dropped below 4.0 mg/l, the contents were reaerated. Samples (2 ml) were analyzed routinely for nitrites and nitrates throughout the study because ammonia nitrogen and organic nitrogen contained in the test system could be oxidized to form these two compounds. No attempt was made to inhibit nitrification. Appropriately seeded blanks and glucose standards were prepared during each test run using the same dilution water used for the test samples.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
13.11.2003 (27) (49)

3.6 BOD5, COD OR BOD5/COD RATIO

COD
Method : other
Year :
COD : 1.25 mg/g substance
GLP :

Remark : calculated THOD
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (46)

3.7 BIOACCUMULATION

Remark : Based on the estimated Log Kow of 1.14 and the rapid hydrolysis of DES in water, the bioaccumulation potential is considered to be very low.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
17.12.2003

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 952 measured/nominal
LC50	:	> 952 measured/nominal
Limit test	:	yes
Analytical monitoring	:	yes
Method	:	other: OECD 203, EEC Directive C.1, US EPA TSCA Guideline, 40 CFR 797.1440
Year	:	2005
GLP	:	yes
Test substance	:	other TS

Method : Rainbow trout, Oncorhynchus mykiss, were exposed to ethanesulfuric acid at 0 (water control) and 1000 mg ethanesulfuric acid/l (limit concentration) for 96 hours under static conditions. For the definitive test, test and control solutions were prepared in triplicate (10 fish/replicate) in 17-l glass cylindrical jars with approximately 15 l of test solution. Test solutions were sampled for analytical confirmation of test substance. The target test temperature was 13 +/- 1 C. The photoperiod was 16 hours light/8 hours dark. Mild aeration was applied to each test vessel during the exposure. The fish were observed at 24, 48, 72 and 96 hours for mortality, sublethal and behavioral effects. Dissolved oxygen, pH and temperature were measured daily in each test vessel. Water temperature was constantly monitored in a surrogate test vessel. Light intensity was measured at each test vessel on Day 0. Water quality parameters (hardness, alkalinity, conductivity and residual chlorine) were measured on Day 0 in the control water and the 1000 mg/l ethane sulfuric acid solution. Terminal body weights and total lengths were measured for all surviving fish. Fish were not fed during the test.

Result : The mean measured concentrations were less then the LOQ (47.3 mg/l) for the water control and 952 mg/l for the 1000 mg/l nominal treatment concentration. Test solution temperature remained constant at 13 C. The pH ranged from 7.2-7.7. Dissolved oxygen levels ranged from 8.7-10.6 mg/l. Light intensity ranged from 724-1068 lux. Pooled length and weight means of all surviving fish combined was 4.7 +/- 0.2 cm and 0.850 +/- 0.123 g, respectively. There was no mortality of any fish over the 96 hours. The 24, 48, 72 and 96 hour LC50 values were all >952 mg/l, the mean measured limit concentration tested. The 96 hour NOEC was 952 mg/l, the mean measured limit concentration tested that exhibited no mortality or sublethal effects.

Test substance	:	Hydrolysis product of DES: Ethanesulfuric acid
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

08.11.2006 (20)

Type	:	
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	95
Limit test	:	
Analytical monitoring	:	no data

Remark : test references:
(1) Methods for Measuring the Acute Toxicity of Effluents

to Freshwater and Marine Organisms, EPA/600/4-85/013, March 1985.
(2) Annual Book of ASTM standards, Water and Environmental Technology, Vol. 111.04, (1990).

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

09.12.2003 (50)

Type :
Species : Salmo gairdneri (Fish, estuary, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 20
Limit test :
Analytical monitoring : no data
Method : other
Year : 1988
GLP : no data
Test substance : no data

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

23.10.1995 (25)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : = 914 measured/nominal
EC50 : > 914 measured/nominal
Limit Test : yes
Analytical monitoring : yes
Method : other: OECD 202, EEC Directive C.2, US EPA TSCA Guideline, 40 CFR 797.1300
Year : 2005
GLP : yes
Test substance : other TS

Method : Freshwater juvenile daphnids, Daphnia magna, were exposed to ethanesulfuric acid at 0 (water control) and 1000 mg ethanesulfuric acid/l (limit concentration) for 48 hours under static conditions. For the definitive test, test and control solutions were prepared in triplicate (10 daphnids/replicate) in 250 ml glass beakers with 200 ml of test solution. Test solutions were sampled for analytical confirmation of test substance. The target test temperature was 20 +/- 1 C. The photoperiod was 16 hours light/8 hours dark. The daphnids were observed at 24 and 48 hours for immobility and abnormal behavior/appearance. Dissolved oxygen, pH and temperature were measured from the bulk solutions on Day 0 and in each test vessel at test termination. Water temperature was constantly monitored in a surrogate test vessel. Light intensity was measured at each test vessel on Day 0. Water quality parameters (hardness, alkalinity, conductivity and residual chlorine) were measured on Day 0 in the control water and the 1000 mg/l ethanesulfuric acid solution. The daphnids were not fed during the test.

Result : The mean measured concentrations of DES were less than the LOQ (48.1 mg/l) for the water control and 914 mg/l for the 1000 mg/l nominal

treatment concentration. Test solution temperatures ranged from 19-21 C. The pH ranged from 7.6-7.7. Dissolved oxygen levels ranged from 8.2-8.7 mg/l. Light intensity ranged from 1990-2160 lux. There was no immobility observed in any of the daphnids over the 48 hours. The 24 and 48 hour LC50 values were >914 mg/l, the mean measured limit concentration tested. The 48 hour NOEC was 914 mg/l, the mean measured limit concentration tested that exhibited no immobility or sublethal effects.

Test substance	:	Hydrolysis product of DES: Ethanesulfuric acid
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

08.11.2006 (19)

Type	:	
Species	:	Daphnia sp. (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 742.393 calculated
Method	:	other: EPIWIN (v 3.11) ECOSAR Submodel (v 0.99g)
Year	:	2003
GLP	:	
Test substance	:	

Remark : The EPIWIN model was run using the following measured physical chemical properties:
Vapor pressure (mm Hg): 0.14344;
Boiling point (deg C): 208.0; and
Melting point (deg C): -24.50.

15.12.2003 (39)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: Pseudokirchneriella subcapitata (formerly known as Selenastrum capricornutum)
Endpoint	:	other: growth, biomass and cell density
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	= 247
EC50	:	> 1958
Method	:	other: OECD 201, EEC Directive C.3, US EPA TSCA Guideline, 40 CFR 797.1050
Year	:	2005
GLP	:	yes
Test substance	:	other TS

Method : Freshwater green algae, Pseudokirchneriella subcapitata (formerly known as Selenastrum capricornutum), was exposed to ethanesulfuric acid. in algal assay medium (AAM) at nominal dosages of 0, 62.5, 125, 250, 500, 1000 and 2000 mg/l under static conditions for 72 hr. Controls were exposed to AAM. Three replicate test chambers (250 ml Erlenmeyer flasks) were maintained for each treatment and six replicates were maintained for the control group. Approximately 10,000 algae cells/ml were added to each test bottle. Bottles were positioned on a mechanical shaker to facilitate mixing and placed in an environmental chamber to maintain test temperature. One additional replicate was maintained without algal cultures for pH and test material concentration sampling without algal biomass. Samples from each bottle were collected for pH measurement at test initiation and at test termination (72 hr). Mean measured test concentrations were determined from samples of medium collected from each chamber at test initiation and at the end of the test. At 24, 48 and 72 hours, algal cell densities were determined by electron particle counting

using a Coulter Multisizer 3 and cell counts were also determined. Subsamples were examined microscopically for atypical cell morphology at test termination. Growth inhibition was calculated for each treatment group as a percentage relative to control values. The endpoints analyzed were growth rate (day-1), cell density (cells x 10000/ml) and biomass area (area under the growth curve, mg/l). The data were tested for normality using the Shapiro-Wilk's Test and for homogeneity of variance using the Bartlett's Test. As these assumptions were met, the data were analyzed using ANOVA and Dunnett's test to determine NOEC values.

Result : Mean measured exposure concentrations were 0, 60.1, 118, 247, 504, 1001 and 1958 mg ethanesulfuric acid/l of AAM (95.8 to 104% of nominal concentrations).

No inhibitory effect greater than 50% of the control was noted at any exposure concentration for the three endpoints so EC50 values were not calculated.

Mean cell densities (E04) at 72 hours were 220, 224, 223, 212, 189, 175 and 120 cells/ml for the 0, 60.1, 118, 247, 504, 1001 and 1958 mg/l concentrations, respectively. Response relative to the controls ranged from -2% to 45% inhibition of mean cell density.

Mean specific growth rates at 72 hours were 1.80, 1.80, 1.80 1.79, 1.75, 1.72 and 1.60 day-1 for the 0, 60.1, 118, 247, 504, 1001 and 1958 mg/l, respectively. Response relative to the controls ranged from 0% to 11% inhibition of mean specific growth rate.

Mean biomass areas at 72 hours were 4060, 4082, 4015, 3832, 6411, 3125 and 2125 for the 0, 60.1, 118, 247, 504, 1001 and 1958 mg/l, respectively. Response relative to the controls ranged from 0% to 48% inhibition of mean biomass area.

The NOEC for mean cell density, specific growth rate and biomass areas was determined to be 247 mg/l. The EC50 for mean cell density, specific growth rate and biomass areas was determined to be > 1958 mg/l.

Test substance : Hydrolysis product of DES: Ethanesulfuric acid
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
08.11.2006 (9)

Species : other algae:Green algae
Endpoint :
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 5.192 calculated
Method : other: EPIWIN (v 3.11) ECOSAR Submodel (v 0.99g)
Year : 2003
GLP :
Test substance :

Remark : The EPIWIN model was run using the following measured physical chemical properties:
Vapor pressure (mm Hg): 0.14344;
Boiling point (deg C): 208.0; and
Melting point (deg C): -24.50.
15.12.2003 (39)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	880 mg/kg bw
Species	:	rat
Strain	:	other: Wistar or Sherman
Sex	:	male
Number of animals	:	6
Vehicle	:	other: corn oil
Doses	:	10, 1, 0.1 ... g/kg bw
Method	:	other: acute oral toxicity
Year	:	1949
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Six male Wistar or Sherman strain rats were given a single dose (10% test substance in corn oil solution) by stomach tube of 10, 1, 0.1, etc. g/kg bw. The initial dose was judged by previous experience with this and other similar chemicals. One week later, six more animals were dosed at another concentration. This procedure was repeated until two dosages differing by a multiple of 10 were found, one of which killed all or some of the animals within 14 days and another which killed none or some of the animals in a 14 day period. The LD50 was then estimated on the assumption that the slope of the probit mortality vs. log dosage curve was the same as that of some structurally similar material previously studied.
Result	:	LD 50 = 880 mg/kg bw (95% confidence limits: 760-1010 mg/kg). Clinical observations were not reported.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston
Test substance	:	Test substance administered as a 10% solution in corn oil.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

08.11.2006 (31) (32)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	250 - 500 ppm
Species	:	rat
Strain	:	other: Wistar or Sherman
Sex	:	male
Number of animals	:	12
Vehicle	:	other: data not specified
Doses	:	other: See methods below
Exposure time	:	4 hour(s)
Method	:	other
Year	:	1949
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of six male Wistar or Sherman rats were exposed for two hours to a flowing stream of air saturated with vapors of DES, prepared by passing it through a fritted disc bubbler at room temperature. This procedure was

repeated on naïve rats until two exposures were identified, one that resulted in 100% mortality and a second that resulted in 0% mortality within two weeks after inhalation.

Result : 0/6 killed at 250 ppm; 6/6 killed at 500 ppm.
Clinical observations were not reported. Inhalation of DES resulted in an LC50 between 250 (1275 mg/L) to 500 ppm (3150 mg/L) with no deaths at 250 ppm and 100% mortality at 500 ppm following four hours of exposure.

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

08.11.2006 (31) (32)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : 706 mg/kg bw
Species : rabbit
Strain : other: data not specified
Sex :
Number of animals :
Vehicle : other: data not specified
Doses :
Method : other: acute dermal toxicity
Year : 1951
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Based on previous information on procedures used by the investigators and the year of publication of this acute dermal toxicity study, while not confirmed, the following method is assumed to have been followed. Undiluted test material was applied to the clipped belly of an albino rabbit and the area was observed over 24 hours for necrosis, edema, erythema or congestion of capillaries. Initially, 0.01 ml of test material was applied, however, if a strong primary reaction was elucidated, then the application was repeated on naïve animals with 10, 1.0 or 0.1%, etc. solutions as necessary to identify the lowest concentration causing irritation.

Result : Original data reported as 0.60 ml/kg; 95% confidence for

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

08.11.2006 (44)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50
Value : 350 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Route of admin. : s.c.
Exposure time :

Method	:	no data
Year	:	
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

01.10.2003 (51)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	5
Vehicle	:	
PDII	:	
Result	:	irritating
Classification	:	
Method	:	Draize Test
Year	:	1949
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Application: 11mg (0.01 ml) applied to the clipped abdomen - the application site remained uncovered and was observed 24 hr after application.
Result	:	Necrosis observed.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

08.11.2006 (31) (32)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	irritating
Classification	:	
Method	:	other: USDOT Skin Irritancy Test (Modified)
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Application period: 4hr, 589 mg (0.5ml, undiluted test substance) covered. Both the skin and the gauze patch were moistened with saline before the test substance was applied. Skin reactions were recorded according to the system of Draize at one hour, one day and two days after application.
Result	:	4/6 with ecchymosis and slight to severe edema, 2/6 with erythema and slight to severe edema, none had necrosis.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston
Conclusion	:	not corrosive

04.11.2003 (42)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	
Exposure time	:	
Comment	:	
Number of animals	:	1
Vehicle	:	
Result	:	irritating
Classification	:	risk of serious damage to eyes
Method	:	other
Year	:	1949
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Method: see Carpenter, C.P. and Smyth, H.F.(1946), Am. J. Ophthal. 29:1363-1372; and Smyth, H.F. and Carpenter, C.P.(1944), J. Ind. Hyg. Toxicol. 26:269-273. Volumes installed: 0.001, 0.005, 0.02ml (1.18, 5.9, 23.6 mg) applied directly to the cornea.
Result	:	Severe corneal injury.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

08.11.2006 (31) (32)

5.3 SENSITIZATION

Remark	:	No information available.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

23.10.1995

5.4 REPEATED DOSE TOXICITY

Remark	:	See section 5.7
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

23.10.1995

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Salmonella typhimurium reverse mutation assay
System of testing	:	TA100
Test concentration	:	500, 1000, 2000, and 4000 ug/plate
Cycotoxic concentr.	:	None
Metabolic activation	:	without
Result	:	positive

Method : other
Year : 1992
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : This assay was carried out with S. typhimurium TA100 in the absence of S9 mixture using the preincubation method (Maron, D.M. and B.N. Ames. 1983. Revised methods for the Salmonella mutagenicity test, Mutation Res., 113:173-215). The reaction mixture consisted of 0.5 ml of phosphate buffer, 0.1 ml of a solution of the test substance prepared at gradient concentration, and 0.1 ml of the cell suspension grown for 8 h at 37 C. Dose concentrations ranged from 500 to 4000 µg/plate. Duplicate plates were run at each dose level for the test substance and solvent controls. A confirmatory assay also was conducted. The test was considered positive when the number of revertant colonies (mean value of two plates) was more than twice that of the solvent control in a dose-dependant manner and the reproducibility of the results was confirmed by a second assay.

Result : In this study, the mutagenicity of diethyl sulfate was demonstrated using a preincubation reverse assay in S. typhimurium TA100 without any metabolic activation. The results of the test showed a dose-dependent increase in the number of revertant colonies that was more than twice the solvent control.

Dose (µg/plate)	His+ revertants/plate
0 (solvent control)	136 ± 5
500	138 ± 4
1000	834 ± 1
2000	4801 ± 48
4000	4261 ± 81

Note: results are the mean ± SD of counts from duplicate plates.

Source : UNION CARBIDE CORPORATION Houston
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
17.11.2003 (26)

Type : HGPRT assay
System of testing : Chinese Hamster Ovary (CHO) cells
Test concentration : 0.08% by volume without S9 activation, 0.04% by volume with S9 activation
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1980
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : CHO cells were exposed for 5 hours to five concentrations of diethyl sulfate from 0.08% (by volume) without the addition of an S9 metabolic activation system and from 0.04% to 0.0025% with S9 activation. In a second, repeat test identical concentrations were tested with S9, and one additional, lower concentration (0.0025%) was tested without S9 activation. Dilutions of diethyl sulfate for testing were prepared by either direct addition of the test agent into the cell culture media or by making sequential one-half dilutions in glass distilled DMSO. The surviving fraction was determined at 20 to 24 hours after treatment and the mutant fraction was determined after a 7 to 10 day period to allow "expression" of the mutant phenotype. S9 liver homogenate was prepared from Aroclor 1254-induced Sprague-Dawley male rats. Appropriate positive (ethylmethane-sulfonate [EMS] without metabolic activation and dimethylnitrosamine [DMN] with metabolic

activation), negative (deionized water) and solvent (DMSO) controls were used. The cells were treated with 200 ug/ml of the positive controls.

Result : An apparent dose response effect upon cytotoxicity was observed for the concentrations of test substance tested with or without S9 activation in comparison to the values for the solvent or negative controls; although a slight difference in cytotoxicity was seen in the two experiments. The following table provides the percent survival data for the two independent experiments:

	Experiment 1		Experiment 2	
Concentration	% Survival		% Survival	
(%, v/v)	-S9	+S9	-S9	+S9
0.080	0	(NT)	0	(NT)
0.040	3.0	0.1	14.0	2.1
0.020	18.8	3.0	34.0	39.2
0.010	31.2	11.0	51.5	45.5
0.005	36.0	24.2	55.5	57.5
0.0025	(NT)	31.0	53.2	51.0
DMSO control	45.5	43.8	52.5	47.8
Neg. control	47.8	35.0	37.0	67.0

(NT) = Not Tested

Significant increases in the mutant frequency were obtained which indicated a dose-related induction of the frequency of mutants/10^6 viable cells over the 16-fold range of concentrations tested for potential mutagenic action either with or without the presence of an S9 metabolic activation system. All tested concentrations of diethyl sulfate produced an increase in the mutation frequency which was statistically significant from the concurrent solvent control in the test either with or without S9 activation. These significant mutagenicity data were considered to be a biologically significant indication of a positive effect. The data also indicated the presence of a dose-related increase in the number of mutants induced by treatment which is considered an important criterion of a positive mutagenic response. Diethyl sulfate was considered to be a mutagenic agent based upon the data. The following table provides the mutant frequency results with and without S9 activation:

	Experiment 1		Experiment 2	
Concentration	Mutants (a)		Mutants (a)	
(%, v/v)	-S9	+S9	-S9	+S9
0.08	382.2*	(NT)	TOXIC	(NT)
0.04	1385.9*	663.3*	811.1*	1267.3*
0.02	672.9*	951.2*	1021.8*	770.7*
0.01	525.3*	472.7*	432.7*	699.0*
0.005	332.7*	131.2*	303.4*	598.0*
0.0025	(NT)	289.2*	198.4	273.7*
DMSO control	88.6	50.7	123.4	35.5
Neg. control	170.3*	73.9	18.7	57.5

(a) = Total # mutant colonies per 10^6 cells plated divided by viable fraction.
* Significantly different from DMSO control (p<0.05, Student's t-test)

Source : UNION CARBIDE CORPORATION Houston
08.11.2006 (45)

Type : Sister chromatid exchange assay
System of testing : Chinese Hamster Ovary (CHO) cells
Test concentration : 0.02% to 0.00125%
Cycotoxic concentr. : 0.02%
Metabolic activation : without

Result : positive
Method : other
Year : 1980
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Dilutions of diethyl sulfate for testing, ranging from 0.02% to 0.00125% (by volume), were prepared either by direct addition into the culture medium or by making sequential one-half dilutions of the maximum dose level in DMSO. For determination of direct mutagenic action, CHO cells were exposed to diethyl sulfate and appropriate controls for 5 hours without S9 activation. Indirect mutagenic action requiring metabolic activation by liver S9 homogenate, was not studied because of the highly significant positive responses observed in the experiment without S9. Chemicals which produce a highly significant response by direct action are considered mutagenic regardless of the response obtained with S9. BrdU required to differentiate between the individual "sister" chromatids by SCE staining, was present at a concentration of 3 ug/mL in the growth medium during treatment and during the culture period following exposure. A total of 15 cells/dose level and 5 dose levels, without metabolic activation were examined. Appropriate dose levels of positive, negative (deionized water) and solvent (DMSO) controls were used. Ethylmethanesulfonate was used as the positive control substance without metabolic activation.

Result : A statistically-significant increase in the SCE frequency was produced by two of the dose-levels of diethyl sulfate tested for direct action in the absence of a metabolic activation system. The test without S9 activation was considered a positive indication of potential direct mutagenic action of diethyl sulfate. An increase in the frequency of SCE corresponding to increased dose-levels of diethyl sulfate was readily apparent from 0.00125% to 0.01% which indicated a probable biological significance of these results. The 0.02% concentration was cytotoxic and inhibited the appearance of cells with SCE staining, possibly because of effects of the test agent on cell growth. The sample of diethyl sulfate was classified as a positive mutagenic agent by direct action and testing with an S9 activation system was not performed. Treatments of CHO cells with diethyl sulfate over a 16-fold range of concentrations indicated a significant potential for mutagenic activity in tests of direct mutagenic action without addition of an active S9, metabolic activation system. Evidence of a dose-related effect of diethyl sulfate exposure on the SCE frequency was evident and the test agent was considered to be an active agent in the in vitro assay. Following is a table of results:

Concentration (%, v/v)	Mean number of SCE/chromosome (+/- S.D.)
0.020	0.474 (0.130) @
0.010	2.192 (0.825)*
0.005	1.634 (0.478)*
0.0025	1.032 (0.277)
0.00125	0.868 (0.287)
DMSO control	0.871 (0.304)
Negative control	0.668 (0.125)

@ = Toxic, only 9 analyzable cells found
* = Significantly different from DMSO control ($p<0.05$, Student's t-test).

Source : UNION CARBIDE CORPORATION Houston

Reliability : (1) valid without restriction
11.11.2003 (45)

Type : Unscheduled DNA synthesis
System of testing : rat hepatocyte cells
Test concentration : 100 x 10^-3% to 0.1 x 10^-3% by volume
Cycotoxic concentr. :
Metabolic activation : no data
Result : positive
Method : other
Year : 1980
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Induction of DNA damage in rat liver cells (hepatocytes), resulting in stimulation of Unscheduled DNA Synthesis (UDS), was studied at a minimum of six dose levels which spanned a 1000-fold range of concentrations from 0.0001, 0.001, 0.003, 0.01, 0.03, and 0.1% (v/v). Cells were treated with diethyl sulfate for 2 hours in culture medium containing 3H-thymidine, hydroxyurea and appropriate dilutions of diethyl sulfate prepared in DMSO. Determination of UDS activity was performed by analyses of radioactive incorporation into isolated hepatocytes nuclei or in DNA. Appropriate dose levels of positive, negative (deionized water) and solvent (DMSO) controls were used.

Result : Diethyl sulfate stimulated a significant amount of incorporation of radioactive thymidine in cells treated over a 1000-fold range of all test concentrations. Measurements of radioactive incorporation into either nuclei or DNA isolated and precipitated from aliquots of nuclei from the same populations of treated cells verified the activity of the positive control agents and the significant activity of the diethyl sulfate test sample. Diethyl sulfate was considered an active mutagenic agent in the test with hepatocytes.

% v/v Concentration	Radioactivity % of solvent control
0.1	193
0.03	312
0.01	260
0.003	281
0.001	191
0.0001	321

Source : UNION CARBIDE CORPORATION Houston
Reliability : (1) valid without restriction
13.11.2003 (45)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay
Species : mouse
Sex : male
Strain : other: ddY
Route of admin. : i.p.
Exposure period : one day
Doses : 100, 200, 400 mg/kg bw
Result : positive
Method : other
Year : 1992

GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : 7 week old male ddY mice (12/group) were used after 1 week acclimatization. They were given commercial food pellets and water ad libitum. The doses administered were decided by referring to published LD50s but in some cases by a preliminary dose-finding experiment. Three doses of the test substance were tested with 4 mice per group, by a single intraperitoneal injection, at 100, 200, and 400 mg/kg bw. Peripheral blood (5 µl) was collected from a tail blood vessel. One thousand well-stained reticulocytes/animal were examined. The data at 48 hours were analyzed with Fisher's exact test to test the significance of the frequency of micronucleated reticulocytes (MNRET) at each test dose compared with the control data, which was the total MNRETs of 12 mice at 0 hours (before treatment). The significance level was 0.01.

Result : MNRET induction was observed only at the highest dose of DES (400 mg/kg bw). The following table summarizes the results:

Single dose (mg/kg)	Time (hours) after the last treatment (a) 0	24	48	72
0	0.13 ± 0.06			
100	0.10 ± 0.00	0.20 ± 0.14	0.25 ± 0.17	0.13 ± 0.05
200	0.13 ± 0.05	0.25 ± 0.13	0.28 ± 0.17	0.18 ± 0.10
400	0.15 ± 0.10	0.28 ± 0.06	0.50 ± 0.10*	0.17 ± 0.06

(a) Values represent mean MNRET induction of four mice per dose group ± SD.

* Significantly different from 0 hour, $p < 0.01$.

Source : UNION CARBIDE CORPORATION Houston
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
08.11.2006 (1)

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : other: MS/Ae
Route of admin. : i.p.
Exposure period : 2 days
Doses : 80 and 160 mg/kg
Result : positive
Method : other
Year : 1995
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : The test substance was administered by i.p. injection in olive oil to mice (5/sex/group). Diethyl sulfate was given twice, 24 h apart, to MS/AE mice at 10 ml/kg. Peripheral blood was collected at time 0 (before treatment) and at 6 h intervals, 24 after the second treatment.

Result :

Dose at a time (mg/kg)	Sampling time (h)	# of animals	MN/1000 RET's assessed per animal	Group Mean ± SD (%)
DS (160)	0	5	2 3 2 4 4	3.0 ± 1.0
	24	4	5 9 9 12	8.8 ± 2.9
	30	4	15 20 15 12	15.5 ± 3.3
	36	4	14 13 10 16	13.3 ± 2.5
	42	4	11 12 8 8	9.8 ± 2.1
	48	4	12 7 7 9	8.8 ± 2.4
	54	4	7 8 7 5	6.8 ± 1.3
	60	4	2 2 5 2	2.8 ± 1.5

DS (80)	0	5	3	3	2	6	2	3.2 ± 1.6
	24	5	11	7	9	7	9	8.6 ± 1.7
	30	5	18	8	6	7	6	9.0 ± 5.1
	36	5	10	6	7	5	9	7.4 ± 2.1
	42	5	8	6	4	3	7	5.6 ± 2.1
	48	5	6	2	1	3	2	2.8 ± 1.9
	54	5	2	6	3	0	0	2.2 ± 2.5
	60	5	5	3	0	1	2	2.2 ± 1.9

The test substance showed peak MNRET (immature erythrocyte with a micronucleus) responses at 30 hours.

Source : UNION CARBIDE CORPORATION Houston
08.11.2006 (11)

Type : Dominant lethal assay
Species : mouse
Sex : male
Strain : other: 101/E1 x C3H/E1
Route of admin. : i.p.
Exposure period : single injection
Doses : 0, 100, 200, 300 mg/kg
Result :
Method : other: rodent Dominant lethal test
Year : 1988
GLP : no data
Test substance : no data

Remark : 25 mice/group; animals 80-98 days old at time of treatment and initial mating. Males were caged with individual F1 hybrid females for 4 day intervals for 48 days for a total of 12 mating intervals.
intraperitoneal injection

Result : Positive; significantly increased pre- and post-implantation loss observed in the 200 mg/kg and 300 mg/kg groups. There was a non-significant increase in pre-implantation loss for the 100 mg/kg group.

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
11.11.2003 (7)

Type : Dominant lethal assay
Species : mouse
Sex : male
Strain : C57BL
Route of admin. : other: intrascrotal injection
Exposure period : single injection
Doses : 0, 6.0, 30, 150 mg/kg
Result :
Method : other: rodent dominant lethal test
Year : 1971
GLP : no data
Test substance : no data

Remark : 15 male mice/group (Strain: C57BL/B6); animals 2.5-3.0 months of age. Test substance administered in physiological saline solution. Each male mated with three virgin CBA females immediately after injection; females replaced each week for six weeks. At the sixth week, three to four females were used for the mating. CBA females were killed on days 14-17 of gestation and examined for embryonic lethality. The number of live embryos (A), dead embryos (B) and the number of corpora lutea (C) were counted. The following indices were calculated:

1) death rate before implantation = C - (A+B)/C
2) death rate after implantation = B/A+B
3) survival = A/C.
The relative indices were calculated by dividing the indices of the experimental group by the corresponding index in the control group.
The significance of the differences between the experimental and control indices was determined by the chi square method.

Result : Positive at doses of 6.0 and 150 mg/kg.
The following table summarizes the indices relative to the control values:

Dose mg/kg	Week	Fertile Females (%)	Relative Lethality (%) Before Implantation	Relative Lethality (%) After Implantation	Relative Survival Rate (%)
150	1	31	171.1*	100.0	90.5
	2	67	170.0*	131.3	84.2*
	3	88	138.4	214.0*	86.2
	4	100	132.4	151.4	91.5
	5	118	107.1	153.9	93.5
	6	89	95.1	82.0	102.3
30	1	87	97.4	143.4	96.8
	2	92	109.4	113.7	96.7
	3	118	65.3	140.4	104.5
	4	125	94.3	135.7	98.2
	5	130	80.7	122.4	101.6
	6	99	113.6	134.7	94.3
6	1	91	161.8*	152.6	87.8*
	2	77	178.7*	144.1	79.8*
	3	129	92.2	152.6	95.3
	4	111	128.9	115.7	94.1
	5	118	66.4	189.4*	98.3
	6	99	81.5	134.7	101.2

* Significantly different from control.

The following table summarizes the data for the first five weeks of the study, reflecting the sensitivity of the meiotic and postmeiotic stages of spermatogenesis. Data are represented relative to the control values.

Dose mg/kg	Relative Lethality (%) After Implantation	Relative Survival (%)
150	157.1*	89.0*
30	128.5	100.0
6	157.1*	92.3*

* Significantly different from control.

At these stages, the doses of 6 and 150 mg/kg caused almost the same frequency of dominant lethal mutations. There was no change in the incidence of fertility of the males at the sixth week at any dose level tested.

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

14.11.2003 (18)

Type : Drosophila SLRL test
Species : Drosophila melanogaster
Sex : male
Strain : other: Samarkand
Route of admin. : oral feed
Exposure period : 2.5-3.0 hours
Doses : 10.5%, 0.75% solutions
Result :
Method : other: SLRL test
Year : 1978

GLP	:	no data
Test substance	:	no data
Remark	:	(modified test) Test substance administered to males in 5% glucose feeding solution; males mated to Oregon K virgin females immediately after feeding treatment. After mating, females were allowed to oviposit immediately or were held for 6 days prior to ovipositing. Embryonic lethality was determined by determining the incidence of unhatched eggs after 24 and 48 hours. Post embryonic lethality was determined by scoring the incidence of larval or pupal death in eggs that had hatched.
Result	:	Positive. Dose-dependent increase in embryonic lethality; holding DES-exposed sperm for 6 days prior to oviposition resulted in a marked increase in post-embryonic lethality over controls and non-stored DES-exposed sperm.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

17.12.2003 (22)

Type	:	other: DNA base sequence changes
Species	:	Drosophila melanogaster
Sex	:	male
Strain	:	no data
Route of admin.	:	oral feed
Exposure period	:	3 hours (oral feeding)
Doses	:	10, 15, 25 mM (oral feeding), 6.25 mM (injection)
Result	:	
Method	:	other: postmeiotic germ cell mutation assay in Drosophila melanogaster
Year	:	1993
GLP	:	no data
Test substance	:	no data
Remark	:	oral, injection Test substance administered to males in buffered 5% sucrose feeding solution or injected in 0.7% NaCl vehicle (0.2 ul). F1 and F2 progeny were screened for occurrence of the vermillion (v) mutation. DNA from 1 g flies was isolated and the vermillion gene amplified using polymerase chain reaction (PCR).
Result	:	Base pair substitutions (93%) and deletions (7%) were induced by treatment with diethyl sulphate; 31 transmissible vermillion mutants were recovered in F1 and F2 progeny. The most frequent type of alteration were GC-AT transitions and AT-TA transversions.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

17.09.2003 (30)

5.7 CARCINOGENICITY

Species	:	mouse
Sex	:	male
Strain	:	other: C3H/HeJ
Route of admin.	:	dermal
Exposure period	:	lifespan
Frequency of treatm.	:	3x/week

Post exposure period	:	none
Doses	:	1 brushful per mouse, approximately 7.4 mg/mouse/application
Result	:	positive
Control group	:	yes, concurrent vehicle
Method	:	other: dermal carcinogenicity
Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Three groups of 40 animals each were exposed to the undiluted test substance, vehicle or positive control substance three times per week via non-occluded application to the clipped back. The animals in the test group were exposed to the undiluted test substance at an average dose of 7.4 mg/mouse/application; animals in the vehicle control group were exposed to acetone at an average dose of 12.6 mg/mouse/application and the animals in the positive control group were exposed to methylcholanthrene (as a 0.2% dilution in benzene) at an average dose of 0.033 mg/mouse/application. The test and control substances were applied to each animal with a series 197, number 1 Grumbacher brush. All animals were 8-9 weeks of age at study initiation. Dosing continued until all surviving mice within a group were observed grossly with malignant skin neoplasms or for their lifespan. Dosing was terminated after 22 months in the diethyl sulfate group; after 6 months in the positive control group; and animals in the vehicle control group were dosed for their lifetime.

Result : Repeated dermal application of undiluted diethyl sulphate produced malignant skin neoplasms in 21 mice out of a surviving effective group of 27 animals. Maximum survival time for the test group (22 months) was shorter than that of the vehicle control group (27 months); median latent period for appearance of neoplasms was 15.7 months for the test group, 3.7 months for positive control group; no tumors were observed in the vehicle control group.

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

03.11.2003 (43)

Species	:	rat
Sex	:	no data
Strain	:	other: BD rats
Route of admin.	:	gavage
Exposure period	:	81 weeks
Frequency of treatm.	:	weekly
Post exposure period	:	
Doses	:	25, 50 mg/kg
Result	:	
Control group	:	no
Method	:	other: Carcinogenicity
Year	:	
GLP	:	no data
Test substance	:	no data

Remark : 12 animals/group; animals approximately 100 days old at start of treatment; survivors observed until death.

Result : Benign papillomas of forestomach observed in 6/24 (number per group not specified); 2/24 squamous cell carcinoma of forestomach observed (one per group).

Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston

12.11.2003 (5) (12) (13)

Species	:	rat
Sex	:	
Strain	:	other: BD rat
Route of admin.	:	i.v.
Exposure period	:	day 15 of gestation
Frequency of treatm.	:	once
Post exposure period	:	
Doses	:	85 mg/kg
Result	:	
Control group	:	no
Method	:	other: transplacental carcinogenesis
Year	:	
GLP	:	
Test substance	:	no data
Remark	:	Maternal dose = 25% of fetal LD50. Three pregnant females injected with test substance on day 15 of gestation; test substance solubilized in an unspecified (probably arachis) oil. Offspring observed until death.
Result	:	Neurogenic tumors observed in 3 of 30 surviving offspring.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

12.11.2003 (5) (6) (12) (13)

Species	:	rat
Sex	:	no data
Strain	:	other: BD rats
Route of admin.	:	s.c.
Exposure period	:	49 weeks
Frequency of treatm.	:	weekly
Post exposure period	:	
Doses	:	25, 50 mg/kg
Result	:	
Control group	:	no
Method	:	other: Carcinogenicity
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	12 animals/group; test substance administered as 1.25% or 2.50% solutions in arachis oil. Animals approximately 100 days old at start of treatment; survivors observed until death.
Result	:	Local sarcomas observed at site of injection in 11 of survivors in high dose group with 2 metastases to the lung; there were local tumors in 6/12 rats in the 25 mg/kg group. Historical data indicated that arachis oil did not induce local tumors when injected subcutaneously.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

04.11.2003 (5) (12) (13)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	mouse
Sex	:	female
Strain	:	other: CF-1
Route of admin.	:	inhalation
Exposure period	:	Gestation Days 6-15
Frequency of treatm.	:	daily
Duration of test	:	7 hours/day
Doses	:	5 and 20 mg/m3
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 5 mg/m³
NOAEL teratogen.	:	> 20 mg/m³
Result	:	Not a teratogen.
Method	:	other: not reported
Year	:	1979
GLP	:	no
Test substance	:	other TS: Sulfuric Acid

Result : Little evidence of toxicity was seen in the fetuses. Slight maternal toxicity was observed at 20 mg/m3. Teratogenicity was not observed.

Reliability : (2) valid with restrictions

08.11.2006 (23)

Species	:	rabbit
Sex	:	female
Strain	:	New Zealand white
Route of admin.	:	inhalation
Exposure period	:	Gestation Days 6-18
Frequency of treatm.	:	daily
Duration of test	:	7 hours/day
Doses	:	5 and 20 mg/m3
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 5 mg/m³
NOAEL teratogen.	:	> 20 - mg/m³
Result	:	Not a teratogen.
Method	:	other: not reported
Year	:	1979
GLP	:	no
Test substance	:	other TS: Sulfuric Acid

Result : Little evidence of toxicity was seen in the fetuses. Slight maternal toxicity was observed at 20 mg/m3. Teratogenicity was not observed.

Reliability : (2) valid with restrictions

08.11.2006 (23)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type	:	other
In vitro/in vivo	:	In vivo
Species	:	mouse
Sex	:	female
Strain	:	other: See methods below
Route of admin.	:	i.p.
Exposure period	:	other: See methods below
Frequency of treatm.	:	other: See methods below
Duration of test	:	other: See methods below
Doses	:	Phase I, Phase II & Phase III: 75 mg/kg
Control group	:	yes, concurrent vehicle

Result : other: See results below
Method : other: See methods below
Year : 1997
GLP : no data
Test substance : other TS: Dimethyl Sulfate (DMS: CAS No. 77-78-1)

Method : This study was conducted in three phases. In the first phase, each female mouse (SECxC57BL6, age 10-12 weeks) (35/group) was administered a single intraperitoneal injection of 75 mg DMS/kg in vehicle or a vehicle control. On the morning following the injection, each female was co-housed with an untreated male mouse (C3H/R1xC57BL10, age 10-12 weeks). The breeding cages were checked daily for the presence of newborn mice beginning on the18th day following the mating initiation or the 18th day following the birth of a previous litter. If newborn mice were present, they were removed from the cage, counted and discarded. This process was repeated until Day 347. The 75 mg/kg dose was based on a preliminary 30-Day survival experiment that determined the maximum tolerated dose (MTD). The proportion of females with litters and the mean number of offspring/female were summarized into post-treatment intervals spanning 19 days; resulting in 17, 19-Day intervals over 347 days. Female reproductive performance was evaluated by averaging the total number of litters per female and the total number of offspring per female. These values were statistically compared to the control values to determine an effect. In Phase II, 10 female mice were dosed with 75 mg DMS/kg or a control agent via the intraperitoneal route and sacrificed 15-days post-dose. The ovaries were removed and a histological evaluation of the ovaries was conducted. The ovaries were fixed in Bouin's fixative for 24 hours, followed by 70% ethanol. One ovary was embedded in paraffin, sectioned and stained with eosin and hematoxylin. The slides were then evaluated for the number of small (primordial oocytes and early growing) follicles, medium-sized (growing) follicles and large (antral) follicles. Only follicles with visible oocyte chromatin were counted.
In Phase III, the possible dominant lethal effects of DMS were examined. Approximately 100, 10 to 12 week old female mice (SECxC57BL6) were administered 75 mg DMS/kg or control agent via the intraperitoneal route. The females were caged (2/cage) with untreated male mice (1/cage). Females were checked for sperm plugs every morning. The dominant lethal response was evaluated at post-treatment intervals of: 0.5-3.5, 4.5-7.5 and 24.5-27.5 days. At these intervals, the number of implantations/female, the number of live embryos/female and the percentage of implantations resorbed/pregnant female were evaluated.

Remark : Female reproductive performance was based on the total number of young produced over the 347-day period, the total number of litters produced over the 347-day period and the litter size at each post-treatment interval. The first two parameters were statistically compared using Student's t-test at a 5% significance level. The litter size analysis was performed with the Student's t-test at a 1% significance level and results of adjacent intervals were considered in determining biological relevance. Analysis of variance (ANOVA) methods were used to determine differences in the number of small, medium or large follicles per ovarian section. The dominant lethal test data on the total number of implantations/female, the number of live embryos/female and the percentage of implantations resorbed/pregnant female were evaluated as described by Lockhart et. al, 1992 (Mutat. Res. 272:35-58). The Student's t test was used at each time interval to determine if a difference existed between the control and test groups for each endpoint. The three endpoints were transformed by a Freeman-Tukey transformation or an arcsine square root transformation to adjust for possible variance heterogeneity in count and proportion endpoints.

Result :

DMS Dose (mg/kg)	Number of offspring per female		Number of litters per female	
	Treated	Control*	Treated	Control*

75	94.8**	134.8	12.1**	14.2

* Vehicle control (HSBB)
** Significantly decreased in comparison to control ($p < 0.01$).

DMS treatment resulted in a slight but significant reduction in small follicles in the ovaries. The mean litter size of the DMS treated females was reduced as compared to the control group at each 19-day interval of the 347-day study, although not statistically significant at the first two intervals. The proportion of productive females treated with DMS was sharply reduced at the first two intervals as compared to the control group. By the third interval, the proportion of productive females that were treated with DMS had increased to be comparable to the control and was higher than the control group for intervals 4-6 before decreasing to less than the control group for the remainder of the 347 days.

Due to the significant reductions in reproductive performance from DMS treatment in the first and second post-treatment intervals, DMS was evaluated for a female dominant lethal effect.

DMS Treatment/ (mg/kg) Control	Day Mated	# of Mated Females	# of Pregnant Females	Implant-ations/ female	Live embryos/ female	% resorbed/ female
75/I	0.5-3.5	39	21	10.6	10.3	2.3
75/I	4.5-7.5	44	32	10.5	9.8*	6.2**
75/VIII	24.5-27.5	32	27	10.2	9.9	3.6
I: DMSO	0.5-3.5	40	25	10.4	10.3	1.5
I: DMSO	4.5-7.5	45	33	10.9	10.9	0.3
VIII: Untreated	24.5-27.5	30	22	10.5	10.0	5.3

* Significantly decreased as compared to the control ($p < 0.01$).
** Significantly increased as compared to the control ($p < 0.05$).

Conclusion : Treatment with DMS resulted in slightly, but significantly, smaller litter sizes as compared to the controls at all intervals with the exception of the first two litters in the continuous breeding phase of this study (Phase I).
The lack of difference at the first two intervals was consistent with the results in the dominant lethal study. Based on the reduction of the number of small follicles present in the ovaries of the DMS treated mice (Phase II) and the results from the continuous breeding phase, DMS was determined to affect female reproductive performance through follicular toxicity. The dominant lethal study demonstrated that DMS treatment did not induce dominant lethal effects.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
08.11.2006 (3)

Type : other
In vitro/in vivo : In vivo
Species : rabbit
Sex : female
Strain : other: no data specified
Route of admin. : inhalation
Exposure period : Gestation Days 6-18
Frequency of treatm. : daily
Duration of test : no data specified
Doses : no data specified
Control group : no data specified

Result	:	TCLo = 20 mg/m3
Method	:	other: no data specified
Year	:	
GLP	:	no data
Test substance	:	other TS: Sulfuric acid
Reliability	:	(4) not assignable

08.11.2006 (34)

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark	:	Type: Cohort study. A historical study examined cancer incidence in 335 process workers who had one or more months employment in an isopropanol plant and an ethanol plant between 1950 and 1976. A total of 225 were still alive, 48 were dead and 32 lost to follow-up. The SIR for laryngeal cancer in this cohort was 5.04, based on four cases. In an expanded cohort of 740 male workers, the SIR was 3.2 based on seven cases. Interviews of former and present supervisors indicated there were frequent exposures to diethyl sulphate, sulfur dioxide, and ethyl ether. The authors speculate that diethyl sulphate formed during the strong-acid process of ethanol production, may be the causative agent.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

23.10.1995 (17)

Remark	:	Type: Cohort study A historical control study of the same worker population examined by Lynch found 50 cases of upper respiratory cancer, including 34 laryngeal cancers. It was determined that the greatest incidence of upper respiratory tract cancers occurred in workers exposed to high levels of sulphuric acid. Levels of diethyl sulphate were not measured.
Source	:	Union Carbide Benelux Antwerpen ECB - Existing Chemicals Ispra (VA) UNION CARBIDE CORPORATION Houston

23.10.1995 (33)

Remark	:	Type: Cohort study A mortality study examined the experience of 1031 ethanol and isopropanol production workers from two chemical plants. Workers were employed for one or more months between 1941 and 1978 were followed through 1983. Among workers exposed to the strong-acid process, there were two deaths from laryngeal cancers (SMR 2.00) and three from cancers of the buccal cavity and pharynx (SMR 1.36); the mortality rate for lung cancers was not elevated (SMR 0.94). No cancer deaths were seen among weak-acid process workers.
Source	:	Union Carbide Benelux Antwerpen

ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (35)

Remark : Type: Case control study.
Controls without cancer were individually matched to 17 gliomas deaths who had worked at a petrochemical plant between 1955-77. Possible associations between brain cancer and job title, department, history of chemical exposure, location within the plant, dates of employment, and place of residence were examined. Estimated exposure to diethyl sulphate gave an odds ratio of 2.1; duration of exposure was not related to disease status.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (16)

Remark : Type: Case control study.
Controls without cancer were matched to 21 brain cancer cases; 17 were gliomas previously analyzed of using different controls by Leffingwell et al. The proportion of brain cancer cases exposed to diethyl sulphate was determined to be similar to that of controls.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (2)

Method : A Texas petrochemical plant had elevated standardized mortality ratios for neoplasms of the brain. A case-control study examined possible associations between gliomas of the brain and job title, departmental employment history, chemical exposure history, geographic location within plant, dates of employment, and residence. An earlier case control study had also been conducted on the same plant over the same issue.
Remark : Case-control study of Gliomas of the Brain
Result : No significant differences between cases and controls were apparent in duration of exposure to any of these chemicals, of which many were used simultaneously. The greatest apparent risks were associated with exposure to carbon dioxide, diethyl sulfate, diethylene glycol, ethanol, ethylene, isopropanol, methane, tetraethylene glycol, and vinyl acetate with first employment in the 1940s or early 1950s, and with residence in La Marque, Texas.
Source : UNION CARBIDE CORPORATION Houston
16.09.2003 (28)

Method : Cases consisted of 21 deaths in which the underlying cause was confirmed as a primary brain tumor. Two control groups of 80 employees each were randomly selected from 450 decedents known to the company in June, 1979. Potential exposures while employed were compared between cases and controls for five known or suspect carcinogens. Exposure potentials were also compared for an additional 37 chemicals to which at least four cases were potentially exposed. Overall and 15-year latency analyses were performed.

Remark : Case-control study of Chemical exposures and Brain tumors
Result : 45.5% of the employees were exposed to the test substance of which 40.0% had gliomas. 48.6% and 40.6% were exposed to control 1 and 2, respectively. The proportion of cases exposed to the five potential carcinogenic chemicals were lower than or consistent with the proportion of exposed controls. No statistically significant differences between the proportions of cases and controls exposed to the 37 other chemicals were found. Exposure determinations could not be made for 48% to 57% of the cases and for 56% to 67% of the controls in each group. This was due to the high proportion of UCC Texas City employees who were assigned to maintenance departments where plantwide travel makes exposure to all chemicals theoretically possible, but technically unknown.
Source : UNION CARBIDE CORPORATION Houston
27.07.2000 (2)

5.11 ADDITIONAL REMARKS

Type : Metabolism

Remark : Following a single 1 ml subcutaneous, oral, or intraperitoneal administration of a 5% (v/v) diethyl sulphate solution in arachis oil (59 mg/rat), male rats were housed in metabolism cages and urine collected for 24 hours. Ethylmercapturic acid and a sulfoxide were detected in the urine of DES-treated rats by paper chromatography. The author propose a metabolic pathway involving glutathione conjugation with one ethyl group.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
16.09.2003 (14)

Type : other: DNA extraction and recovery

Remark : Exposure of HeLa cells in culture to 10 mM DES in 3% DMSO for 1 hour resulted in a 39.3% recovery of 3Hthymidine-labelled DNA after cold phenol extraction, when compared to non-treated control cells. Isolated DNA alkylated by DES shows multiple single-strand breaks and denatured DNA. Other techniques were also employed to demonstrate the presence of macromolecular DNA-protein complexes formed after alkylation with DES.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)
UNION CARBIDE CORPORATION Houston
23.10.1995 (15)

Type : other: Toxicity to fertility

Remark : Diethyl sulphate damaged DNA of E. Coli at the concentration of 5umol/l.
The substance damages DNA of Hamster ovary at the concentration of 2.5 mmol/l.
The substance displayed mutagenicity to Hamster gene at the concentration of 1 mmol/l.
Source : Union Carbide Benelux Antwerpen
ECB - Existing Chemicals Ispra (VA)

UNION CARBIDE CORPORATION Houston

16.09.2003 (24)

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT