IUCLID

Data Set

Existing Chemical	:	ID: 1115-20-4
CAS No.	:	1115-20-4
EINECS Name	:	3-hydroxy-2,2-dimethylpropyl 3-hydroxy-2,2-dimethylpropionate
EC No.	:	214-222-2
TSCA Name	:	Propanoic acid, 3-hydroxy-2,2-dimethyl-, 3-hydroxy-2,2-dimethylpropyl ester
Molecular Formula	:	C10H20O4

Producer related part

Company	:	PCA Services, Inc
Creation date	:	16.10.2005

Substance related part

Company	:	PCA Services, Inc
Creation date	:	16.10.2005
Status	:	
Memo	:	
Printing date	:	21.11.2006
Revision date	:	16.10.2005
Date of last update	:	21.11.2006
Number of pages	:	61
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

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

IUPAC Name	:	Propanoic acid, 3-hydroxy-2,2-dimethyl-, 3-hydroxy-2,2-dimethylpropyl ester
Smiles Code	:	O=C(OCC(CO)(C)C)C(CO)(C)C
Molecular formula	:	C10 H20 O4
Molecular weight	:	204.27
Petrol class	:	
Reliability	:	(1) valid without restriction

30.10.2006

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	organic
Physical status	:	solid
Purity	:	>= 97.5 % w/w
Colour	:	
Odour	:	

30.10.2006 (4)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

3-(Hydroxypivaloyloxy)-2,2-dimethylpropanol

30.10.2006

3-Hydroxy-2,2-dimethylpropyl hydroxypivalate

30.10.2006

Esterdiol 204

30.10.2006

HPHP

30.10.2006

Hydroxyneopentyl hydroxypivalate

30.10.2006

Hydroxypivalic acid neopentyl glycol ester

30.10.2006

Hydroxypivalyl hydroxypivalate

30.10.2006

Neopentyl glycol monohydroxypivalate

30.10.2006

1.3 IMPURITIES

Purity :
CAS-No : 7732-18-5
EC-No : 231-791-2
EINECS-Name : water
Molecular formula :
Value : <= .3 % w/w

29.10.2006 (5)

1.4 ADDITIVES

Remark : No intentional additives.
30.10.2006

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial
Category : Chemical industry: used in synthesis

29.10.2006 (4)

1.7.1 DETAILED USE PATTERN

Industry category : 3 Chemical industry: chemicals used in synthesis
Use category : 33 Intermediates
Extra details on use category :

Emission scenario document : available
Product type/subgroup :
Tonnage for Application :
Year :
Fraction of tonnage for application :
Fraction of chemical in formulation :
Production : :
Formulation : :
Processing : :
Private use :
Recovery :

29.10.2006 (4)

1.7.2 METHODS OF MANUFACTURE

Origin of substance : Synthesis
Type : Production

29.10.2006

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

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

Type : EINECS
Additional information :

29.10.2006

Type : TSCA
Additional information :

29.10.2006

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= 48 - 54.9 °C
Sublimation	:	
Method	:	other: according to BASF standard test procedure
Year	:	
GLP	:	no
Test substance	:	other TS
Test substance	:	CAS No. 1115-20-4 of 98.3% purity.
Reliability	:	(2) valid with restrictions Conducted with acceptable method on highly pure test sample
Flag	:	confidential, Critical study for SIDS endpoint

30.10.2006 (17)

Value	:	= 54.6 °C
Sublimation	:	
Method	:	other: measured
Year	:	
GLP	:	no
Test substance	:	other TS
Test substance	:	3-Hydroxy-2,2-dimethylpropyl 3-hydroxy-2,2-dimethylpropionate, purity 96.9 mol% (DSC)
Reliability	:	(2) valid with restrictions Discrepancy between documented test parameters and standard methods, but scientifically acceptable
Flag	:	confidential

12.11.2006 (18)

Value	:	= 46 - 50 °C
Sublimation	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS
Test substance	:	Hydroxy Pivalic Acid, Neopentyl glycol ester, no further data.
Reliability	:	(4) not assignable Manufacturer/producer data without documentation.
Flag	:	non confidential

28.10.2006 (11)

Value	:	= 49.6 °C
Sublimation	:	
Method	:	other: measured
Year	:	
GLP	:	no
Test substance	:	other TS
Test substance	:	Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability	:	(4) not assignable Incomplete documentation.

28.10.2006 (8)

Value	:	= 49.8 °C
Sublimation	:	
Method	:	other: according to BASF standard
Year	:	

GLP : no
Test substance : other TS

Test condition : Solidification temperature measuring equipment, type BASF
Test substance : Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability : (2) valid with restrictions
Scientifically acceptable method.
Flag : confidential
28.10.2006 (7)

Value : = 50 °C
Sublimation :
Method : other: unknown
Year :
GLP : no data
Test substance : other TS

Test substance : CAS No. 1115-20-4 of 98.7% purity.
Reliability : (4) not assignable
No documentation
01.11.2006 (48)

2.2 BOILING POINT

Value : = 283.2 °C at 1013 hPa
Decomposition :
Method : other: measured
Year :
GLP : no
Test substance : other TS

Test substance : 3-hydroxy-2,2-dimethylpropyl 3-hydroxy-2,2-dimethyl propionate, purity 99.76 area %
Reliability : (2) valid with restrictions
scientifically acceptable method, using purified test sample.
Flag : confidential, Critical study for SIDS endpoint
28.10.2006 (16)

Value : = 283.5 °C at 1013.25 hPa
Decomposition :
Method : other: Calculated (regression)
Year :
GLP : no
Test substance : other TS

Test condition : Dynamic vapour pressure measurement with argon. Calculated value based on measured data
Test substance : 3-hydroxy-2,2-dimethylpropyl
3-hydroxy-2,2-dimethylpropionate, purity 96.6 area %.
Reliability : (2) valid with restrictions
Calculated value in accordance with generally accepted standard methods.
Flag : confidential
28.10.2006 (10)

Value : = 292 °C at
Decomposition :
Method : other
Year :
GLP : no
Test substance : other TS

Test substance : Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability : (4) not assignable
Manufacturer/producer data without documentation.
Flag : non confidential
28.10.2006 (11)

Value : = 303.7 °C at 1013 hPa
Decomposition :
Method : other: estimated
Year : 2006
GLP : no
Test substance : other TS

Test condition : Program inputs were CAS No. 1115-20-4, melting point of 54.6 degrees C, and boiling point of 283.2 degrees C.
Test substance : Theoretical 100% material
Reliability : (2) valid with restrictions
Recognized estimation method
10.11.2006 (36)

2.3 DENSITY

Type : density
Value : = 1.015 g/cm³ at 67 °C
Method : other: according to BASF standard
Year :
GLP : no
Test substance : other TS

Test substance : 3-hydroxy-2,2-dimethylpropyl
3-hydroxy-2,2-dimethylpropionate, purity 98.3 weight %.
Reliability : (2) valid with restrictions
Scientifically acceptable method, but not GLP or by current protocol.
Flag : confidential, Critical study for SIDS endpoint
28.10.2006 (17)

Type : density
Value : = 1.0143 g/cm³ at 60 °C
Method : other
Year :
GLP : no
Test substance : other TS

Test substance : Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability : (4) not assignable
Manufacturer/producer data without documentation.
28.10.2006 (11)

Type : bulk density
Value : = 400 - 600 kg/m3 at °C
Method : other
Year :
GLP : no
Test substance : other TS

Test substance : Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability : (4) not assignable
Manufacturer/Producer data without documentation.
Flag : non confidential

20.11.2006 (11)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 1 hPa at 115.2 °C
Decomposition :
Method : other (measured): dynamic with argon
Year : 1989
GLP : no
Test substance : other TS

Result : Temperature (°C) vapour pressure (hPa)

Temperature (°C)	vapour pressure (hPa)
115.17	1.00
126.23	2.00
133.16	3.00
142.35	5.00
148.81	7.00
155.94	10.00
170.89	20.00
180.12	30.00
192.44	50.00
201.1	70.00
209.8	100.0
229.0	200.0

Test substance : 3-hydroxy-2,2-dimethylpropyl 3-hydroxy-2,2-dimethylpropionate, purity 96.6 area %.
Reliability : (2) valid with restrictions
Scientifically acceptable method, but non-current protocol or GLP.
Flag : confidential, Critical study for SIDS endpoint
30.10.2006 (10)

Value : = .03 hPa at 20 °C
Decomposition :
Method : other (measured)
Year :
GLP : no
Test substance : other TS

Test substance : Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability : (4) not assignable
Manufacturer/producer data without sufficient documentation.
Flag : non confidential
20.11.2006 (11)

Value : = .00016 hPa at 20 °C
Decomposition :
Method : other (calculated)
Year : 2006
GLP : no
Test substance : other TS

Test condition : Program inputs were CAS No. 1115-20-4, melting point of 54.6 degrees C, and boiling point of 283.2 degrees C.
Test substance : Theoretical 100% material
Reliability : (2) valid with restrictions
Recognized estimation method

10.11.2006 (36)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = .858 at 25 °C
pH value :
Method : OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask shaking Method"
Year : 1988
GLP : no data
Test substance : other TS

Result : 3 testings with slightly different HPN-concentration were carried out:

	Octanol 1	HPN	Water	log P(OW)
1	24.9561 g	0.1163 g	20.9337 g	0.865
2	20.9353 g	0.3329 g	24.9228 g	0.859
3	20.9452 g	0.6318 g	24.7819 g	0.848

Test condition : GC conditions:

Diethylpolysiloxan capillary

film thickness	1.0 micro m
internal diameter	.32 mm
length	30 m
oven temperature	200°C
initial temperature	250 °C
detector temperature	250°C
carrier gas	nitrogen, 1.75 bar
injected quantity	1 microliter
total flow	68 ml/min

Test substance : Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability : (2) valid with restrictions
Standard protocol, but no data on purity or GLP.
Flag : Critical study for SIDS endpoint
28.10.2006 (6)

Partition coefficient : octanol-water
Log pow : = 1.07 at 20 °C
pH value : = 7
Method : other (calculated)
Year : 2006
GLP :
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Data obtained using an approved model.
28.10.2006 (35)

Partition coefficient : octanol-water
Log pow : = .884 at °C
pH value :
Method : other (calculated): Incremental method by Rekker with computer program of the firm CompuDrug Ltd.
Year : 1989

GLP	:	
Test substance	:	other TS: theoretically pure CAS No. 1115.20-4.
Reliability	:	(2) valid with restrictions Scientifically acceptable method of calculation.

02.11.2006 (3)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 270 g/l at 25 °C
pH value	:	= 3.8
concentration	:	100 g/l at 20 °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS
Test substance	:	Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability	:	(2) valid with restrictions Manufacturer/producer data.
Flag	:	Critical study for SIDS endpoint

10.11.2006 (11)

Solubility in	:	Water
Value	:	= 18440 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: calculated
Year	:	2006
GLP	:	no
Test substance	:	other TS
Test condition	:	Program input was CAS No. 1115-20-4
Test substance	:	Theoretical 100% material
Reliability	:	(2) valid with restrictions Recognized estimation method

10.11.2006 (37)

2.6.2 SURFACE TENSION

Test type	:	
Value	:	= 29.3 mN/m at 70 °C
Concentration	:	
Method	:	other: According to BASF standard test procedure.
Year	:	1981

GLP : no data
Test substance : other TS

Test substance : 3-hydroxy-2,2-dimethylpropyl 3-hydroxy-2,2-dimethylpropionate, purity 98.3 weight%.
Reliability : (2) valid with restrictions
Scientifically acceptable method, but little documentation.
30.10.2006 (17)

2.7 FLASH POINT

Value : = 161 °C
Type : closed cup
Method : other: DIN 51 758. Pensky-Martens
Year : 1974
GLP : no
Test substance : other TS

Test substance : Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability : (2) valid with restrictions
Scientifically acceptable method, but purity of test substance not given.
30.10.2006 (12)

2.8 AUTO FLAMMABILITY

Value : = 340 °C at
Method : other: DIN 51 794
Year : 1974
GLP : no
Test substance : other TS

Remark : Auto-Ignition Temperature.
Test substance : Hydroxy Pivalic Acid, Neopentyl Glycol Ester, no further data.
Reliability : (2) valid with restrictions
Scientifically acceptable method, but purity of test sample not given.
30.10.2006 (12)

Result : No self heating because of low melting point
Reliability : (2) valid with restrictions
Expert Judgment.
28.10.2006 (14)

2.9 FLAMMABILITY

Result : other: not highly flammable
Method : Directive 84/449/EEC, A.10 "Flammability (solids)"
Year : 1994
GLP : no data
Test substance : other TS: no purity given

Reliability : (2) valid with restrictions
Discrepancy between documented test parameters and standard methods, but scientifically acceptable.
02.11.2006 (15)

2.10 EXPLOSIVE PROPERTIES

Result : not explosive

Remark : The molecule does not have a chemical structure or functionality that has any correlation with known explosive materials.

Reliability : (2) valid with restrictions
Expert judgment, based on knowledge of chemical structures and their properties.

28.10.2006 (14)

2.11 OXIDIZING PROPERTIES

Result : no oxidizing properties

Remark : Judgment about oxidizing properties is based on the chemical structure, which has no oxidizing groups.

Reliability : (2) valid with restrictions
Expert judgment based on knowledge of chemical structures and functionality.

28.10.2006 (14)

2.12 DISSOCIATION CONSTANT

01.11.2006

2.13 VISCOSITY

Value : = 52.78 - mPa s (dynamic) at 69.9 °C
Result :
Method : other: BASF standard procedure
Year :
GLP : no
Test substance : other TS

Test substance : 3-hydroxy-2,2-dimethylpropyl
3-hydroxy-2,2-dimethylpropionate, purity 98.3 weight %,

Reliability : (2) valid with restrictions
Scientifically acceptable method, but non GLP and not a guideline method with documentation.

28.10.2006 (17)

2.14 ADDITIONAL REMARKS

Memo : Dust Explosion

Reliability : (2) valid with restrictions
Discrepancy between documented test parameters and standard methods, but scientifically acceptable.

28.10.2006 (13)

Memo : Explosion Limits: Lower 9 vol % (measured at 144°C); Upper 37.7 vol % (measured at 201°C)

Reliability : (2) valid with restrictions
Scientifically acceptable test method, but little documentation.

28.10.2006 (12)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	Sun light
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .000000000010829 cm³/(molecule*sec)
Degradation	:	= 50 % after 11.9 hour(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	2006
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Model input was 12 hours of light/day.
Reliability	:	(2) valid with restrictions Values were estimated using an approved model.
Flag	:	Critical study for SIDS endpoint

30.10.2006 (33)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	ca. 113.7 year at 20 °C
t1/2 pH9	:	at °C
t1/2 pH 8	:	ca. 11.4 year at 20 °C
Deg. product	:	
Method	:	other (calculated)
Year	:	2006
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Fragment(s) on this compound are NOT available from the fragment library for EPIWIN HYDROWIN. Substitute(s) have been used. In general, carboxylic esters are known to be subject to hydrolysis. The rate of hydrolysis is normally very slow under neutral ambient conditions in the absence of catalysts. Esters can be rapidly hydrolyzed at high pHs (in the presence of strong base). CAS No. 1115-20-4 is expected to hydrolyze more slowly than most aliphatic esters, because of its highly branched structure.
Reliability	:	(2) valid with restrictions Values were calculated using an approved model.

12.11.2006 (34)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	other: air, water, soil and sediment
Air	:	.424 % (Fugacity Model Level I)
Water	:	37.1 % (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	.0726 % (Fugacity Model Level II/III)
Soil	:	62.4 % (Fugacity Model Level II/III)
Method	:	other: calculated
Year	:	2006
Result	:	A Henry's Law Constant of 1.70 E-09 atm m3/mol was estimated by EPIWIN HENRY (v3.10)(bond estimate). A soil sediment partition coefficient of Koc of 10 was estimated by EPIWIN PCKOC (v1.66). Fugacity Level III half-lives in various media were estimated to be: air = 23.7 hours, water = 360 hours, soil = 720 hours, and sediment = 3240 hours. A Bioconcentration factor BCF = 3.162 (log BCF = 0.5) was estimated by EPIWIN BCF Program (v2.15).
Test condition	:	Inputs to the model run were CAS No. 1115-20-4, melting point 54.6 deg C, boiling point 283.2 deg C, vapor pressure 0.0225 mm Hg, water solubility 270,000 mg/L, and Log Pow 0.86. Normal default emission rates were used.
Reliability	:	(2) valid with restrictions Data were calculated using an approved model.
Flag	:	Critical study for SIDS endpoint

20.11.2006 (38)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Concentration	:	34 mg/l related to Test substance 20 mg/l related to DOC (Dissolved Organic Carbon)
Contact time	:	28 day(s)
Degradation	:	= 90 - 100 (±) % after 28 day(s)
Result	:	readily biodegradable
Kinetic of testsubst.	:	7 day(s) < 0 % 10 day(s) = 18 % 14 day(s) = 66 % 17 day(s) = 98 % 21 day(s) = 99 %
Control substance	:	Aniline
Kinetic	:	3 day(s) = 29 % 5 day(s) = 94 %
Deg. product	:	
Method	:	OECD Guide-line 301 A (new version) "Ready Biodegradability: DOC Die Away Test"

Year : 2003
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : The test substance is readily biodegradable according to OECD criteria.

- duration of the adaptation phase (lag-phase): ca. 7 days

- duration of the degradation phase (log-phase): ca. 10 days

- physico-chemical (abiotic) elimination assay: < 10 % (DOC) at the end of the test

- adsorption control: < 10 % (DOC) after 5 days

- inhibition assay: 98 % (DOC) after 28 days

Reference control:

- reference substance: aniline
- concentration: 20 mg/l related to DOC
- kinetic of reference substance:
1 day -2 % DOC-elimin.
3 day(s) 29 % DOC-elimin.
5 day(s) 94 % DOC-elimin.
14 day(s) 94 % DOC-elimin.
21 day(s) 94 % DOC-elimin.
28 day(s) 94 % DOC-elimin.

Inhibition control:

- substances: aniline + test substance
- concentration: aniline: 20 mg/l related to DOC
test subst.: 20 mg/l related to DOC
- kinetic of inhibition control:
1 day(s) -2 % DOC-elimin.
3 day(s) 13 % DOC-elimin.
7 day(s) 45 % DOC-elimin.
14 day(s) 97 % DOC-elimin.
21 day(s) 98 % DOC-elimin.
28 day(s) 97 % DOC-elimin.

Assay to examine physico-chemical (abiotic) elimination:

- concentration: 20 mg/l related to DOC
- w/o inoculum, w mercury chloride to avoid microbial biodegradation
- kinetic of physico-chemical elimination:
1 day(s): -2 % DOC-elimin.
7 day(s): -4 % DOC-elimin.
14 day(s): 6 % DOC-elimin.
21 day(s): -9 % DOC-elimin.
28 day(s): -15 % DOC-elimin.

Adsorption control:

- concentration: 20 mg/l related to DOC
- w inoculum, w mercury chloride to avoid microbial biodegradation
- kinetic of adsorption control:
1 day(s): -7 % DOC-elimin.

5 day(s): -2 % DOC-elimin.

Test condition : Test device:

- 2-l Erlenmeyer flasks, liquid volume: 1000 ml

Incubation:

- on a laboratory shaker, approx. 120 rpm
- temperature: 22 +- 2 °C

Number of replicates:

- test substance (TS): 2
- reference substance (RS): 1
- blank (BC): 2
- inhibition control (IH): 1
- assay to examine physico-chemical (abiotic) elimination (PC): 1
- adsorption control (AC): 1

Inoculum:

- source: activated sludge, domestic (sludge from laboratory wastewater treatment plants fed with municipal sewage)

Test substance : Purity: 98.7 %
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
27.10.2006 (24)

Type : aerobic
Inoculum : domestic sewage
Concentration : 50 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time : 28 day(s)
Degradation : = 100 (±) % after 28 day(s)
Result : inherently biodegradable
Kinetic of testsubst. : 1 day(s) = 1.5 %
9 day(s) = 13.5 %
13 day(s) = 53 %
22 day(s) = 97 %
28 day(s) = 100 %
Control substance : Benzoic acid, sodium salt
Kinetic : 3 day(s) = 95 %
28 day(s) = 97 %
Deg. product : not measured
Method : OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year : 1995
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Protocol Deviations: The address and room numbers listed in the SOPs were not current, due to relocation. The test material was dissolved in sparged MNS (not sparged distilled H2O as stated in the protocol). Although the protocol stated that all study documentation would be transferred to the Sponsor, they were maintained by the laboratory conducting the study. None of these deviations affected the integrity of the study.
Result : Starting DOC levels of the two test and single positive control solutions were 44.7 ppm. 44.0 ppm and 43.1 ppm, respectively. On Day 28, the

DOC levels in these solutions were -0.1 ppm, -0.7 ppm and 1.2 ppm, respectively. These values represent a loss of 101% (average) and 97% for the test material and positive control.

Starting pH values for the MNS, positive control and test material stock solutions were 7.538, 7.621 and 7.635, respectively. At the end of the test, the pH values for the blank, positive control and two test solutions were 7.049, 7.359, 7.070 and 7.054, respectively. The dissolved oxygen (DO) content of the MNS at the beginning of the test was 9.1 mg/l, and the DO content of the blank, positive control and two test solutions at the end of the test were 9.2 mg/l, 9.1 mg/l, 9.0 mg/l and 9.0 mg/l, respectively.

The test was valid, since the DOC removal in the positive control was >= 70% within 14 days.

Test condition : Date of Study Initiation: Oct 17, 1994
Date of Study Completion: Feb 10, 1995

Inoculum: Microorganisms were obtained from mixed liquor suspended solids (MLSS) from Van Lare Waste Water Treatment Plant, Rochester, New York. Viability of the microorganisms was confirmed after inoculation of the test solutions and activity was checked with a positive control.

Sludge was washed with laboratory dilution water, then spun in a centrifuge at 7000 rpm for 15 min. The supernatant was then decanted. The washing procedure was repeated twice. A small amount of the washed sludge was weighed, oven dried (200 degrees F, 4 min), and reweighed. The amount of wet sludge required to obtain a MLSS concentration of 2.0 g/l (final concentration of 0.2 - 1.0 g/l in the test medium) was measured out, homogenized for 2 min in a blender and aerated until use. The inoculum was used on the day of collection.

Test solutions: Stock solutions A (8.50 g KH2PO4, 21.75 g K2HPO4, 33.40 g Na2HPO4.2H2O, and 0.50 g NH4Cl in 1000 ml distilled H20), B (27.50 g CaCl2 in 1000 ml distilled H20), and C (22.50 g MgSO4.7H2O in 1000 ml distilled H20) were made in advance, filter sterilized through 0.45 micron membranes, and refrigerated for up to 6 months. Stock solution D (25.0 mg FeCl3.6H2O in 1000 ml distilled H20) was prepared on the day of the study. Mineral nutrient solution (MNS, pH 7.4 +/- 0.2) (10 ml of stock solution A, and 1.0 ml each of stock solutions B, C made up to 1 liter with distilled water) was prepared immediately before use. It was sparged for 30 min with CO2-free air obtained by passing air through a NaOH (8.0 g/l) trap. The test material and positive control materials were dissolved in MNS to achieve theoretical concentrations of 50 mg DOC/L. The pHs of the stock solutions were not adjusted since they were within the required range (6.5 - 8.0).

Test conduct: Test and positive control stock solutions (500 ml) were placed into 2-liter Erlenmeyer flasks. Duplicate flasks were prepared for the test material. Sparged MNS (400 ml) was added to each flask. A negative control containing 900 ml MNS also was prepared. Inoculum (100 ml) was then added to each vessel.

Test solutions were covered with aluminum foil and stirred on stir plates (21 - 23 degrees C). Aeration was accomplished by inserting a 5-ml glass pipette approximately 1 cm above the bottom of the test vessel). The pH and dissolved oxygen concentration were measured on sampling days (see below) and were not adjusted since they were within the required ranges. Sparged, distilled water was added weekly to replace that which had been lost due to evaporation. Amounts added ranged from 20-25 ml.

10-ml Samples were taken in triplicate at the start of the test and on Days 1, 3, 6, 9, 13, 16, 19, 22, 27 and 28. Samples were filtered through 0.22

micron membranes and the first 7 ml of filtrate was discarded. Two hundred microliters of the remaining 3 ml of each sample was injected into a Dohrmann DC-180 Carbon analyzer that had been previously calibrated using a 10 ppm organic carbon standard. The DOC content of each sample (plus the average and standard deviation), sample size and date of analysis were recorded on a printer.

Method of calculating DOC concentrations: Lotus 1-2-3 was used to calculate and graphically present the % DOC removal with respect to the material. Values were corrected for background levels of DOC. Data were not analyzed statistically. All raw data and summaries were to be retained for at least 10 years.

Test substance : The structure of the test material was confirmed on May 27, 1994, using GC/MS. Initial and final purity (confirmed by GC/FID) of the test material were 98.6% and 98.7%, respectively. The purity of sodium benzoate (positive control) was 100%.

Reliability : (1) valid without restriction
Guideline study

12.11.2006 (45)

Type : aerobic
Inoculum : activated sludge
Contact time :
Degradation : = 90 - 100 (±) % after 7 day(s)
Result :
Deg. product :
Method : OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year :
GLP :
Test substance :

Method : (CSB)
Remark : Easily eliminated from water, biodegradable.
Reliability : (3) invalid
original reference not available

27.10.2006 (27)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 1024 measured/nominal
LC50	:	> 1024 measured/nominal
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other: OECD 203 and EEC/Annex VC.1
Year	:	1995
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Protocol Deviations: In disagreement with the protocol, the length of the minnows was not determined at the test start. A GC column containing DB-5 (rather than DB-1) was used. Minnows were examined after the first 5 (rather than 6) hours of exposure. Samples were diluted 1:1 with acetone (rather than analyzed neat). Additionally, although the protocol stated that all study documentation would be transferred to the Sponsor, they were maintained by the laboratory conducting the study. None of these deviations affected the integrity of the study.
Result	:	Nominal concentrations: 95.0, 171.5, 308.5, 555.5 and 1000.0 mg/l Measured concentrations: 97.1, 176.3, 307.8, 586.4 and 1023.9 mg/l for first series; 99.5, 179.1, 323.5, 546.0 and 1030.9 mg/l for second series. Percent loss: The analyzed percent loss of test material ranged from -7.1% to 8.6%. Biological observations: No abnormal effects were noted in any controls or exposed fish. Mortality: None of the organisms died during the study. Element value: The 24-, 48-, 72- and 96-hour LC50 values were > 1023.9 mg/l for the first series and > 1030.9 mg/l for the second series. No effects were noted at the highest concentrations tested. Observations: No particulates, surface slicks of precipitates were observed in the test solutions. Remarks: The study was considered to be valid since the control mortality was not greater than 10%, the dissolved O2 concentration did not fall below 60% of the initial O2 level and there were no deviations that could have affected the outcome of the test.
Test condition	:	Date of Study Initiation: June 8, 1994 Date of Study Completion: March 3, 1995 Test fish: Juvenile fathead minnow used in the test were obtained from Eco-Chem Testing Group Minnow Breeding Facility, Eastman Kodak Company, Rochester, NY. They hatched on March 31, 1994. All fish were acclimated to study water for at least 2 weeks prior to use. Dilution water source: The water was pumped from Lake Ontario by a water treatment facility into a large underground storage reservoir located near the testing facility. This water was pumped into the laboratory, and passed through 1) 3-micron polypropylene filter tubes; 2) powdered,

activated carbon filter tubes; and 3) another set of 3-micron polypropylene filter tubes. The filtered water stream was then injected with 150 ppb of Na2S2O3 (to reduce residual chlorine). The water was then tempered to 20 +/- 2 degrees C, and cascaded through a column degassing unit into an open aeration basin for seasoning.

Dilution water chemistry: Representative values for hardness and total alkalinity (both as CaCO3) during the study were 120 mg/l and 92 mg/l, respectively.

Stock and test solution preparation: All exposure solutions (0, 95.0, 171.5, 308.5, 555.5 and 1000.0 mg/l, nominal) were prepared by directly adding the test material to test vessels containing 20 L of diluent water. The solutions in each vessel were stirred with a hand-held mixer. All test solutions and controls were prepared in duplicate. They were analyzed at the beginning and end of the study for concentration of test material.

Analysis of test material concentration: Solutions were analyzed for concentrations of test material using GC/FID. Time 0 samples were analyzed as received (i.e. in diluent water). The 96 hour samples were diluted 1:1 with acetone. Standards were prepared in 1:1 acetone:diluent water. A 0.2 ml aliquot of an internal standard solution of ethylene glycol in acetone (0.2 g/10 ml) was added to each sample and standard.

Exposure vessel type: Fish were exposed in seamless, Pyrex 30.5-cm cuboidal chromatography jars. The light/dark cycle was 16 hours on/8 hours off, with a 20-min transition period.

Number of replicates/fish per replicate: Ten fish were randomly allocated to each test vessel. Biological loading was kept to below 1.0 g wet weight/liter test solution. The average wet weights of fish in the two control vessels were 0.42 g and 0.36 g. The test was performed in duplicate.

Study conduct: Fish were observed for mortality and signs of stress at 0, 5, 24, 48, 72 and 96 hours. Temperature, dissolved O2 and pH were measured at 0, 24, 48, 72 and 96 hours.

Water chemistry in test: The pH and dissolved O2 concentration ranged from 7.3 - 8.2 and 7.0 - 9.0 mg/l, respectively.

Test temperature range: The temperature in all vessels remained at 22 +/- 1 degrees C during the test.

Statistical methods: The LC50 values and confidence intervals were calculated by the binomial method, using a computer program inputted with the concentration of the test material (nominal or measured), number of organisms exposed, and number of organisms that died. Data for control vessels were not entered.

Data storage: All study documents were maintained by the laboratory that conducted the study.

Test substance : The structure of the test material was confirmed on May 27, 1994, using GC/MS. Initial and final purity (confirmed by GC/FID) of the test material were 98.2% and 98.6%, respectively.

Reliability : (1) valid without restriction
Guideline study with analytical monitoring

Flag : Critical study for SIDS endpoint

12.11.2006 (41)

Type : static

Species : Leuciscus idus (Fish, fresh water)

Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 1000 measured/nominal
LC0	:	= 2150 measured/nominal
LC50	:	= 3160 measured/nominal
LC100	:	= 4640 measured/nominal
Limit test	:	no
Analytical monitoring	:	no
Method	:	other: following German Industrial Standard DIN 38412, Part 15
Year	:	1987
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The 96 hour median lethal concentration (LC50) was estimated according to OECD guideline 203 (1992) by calculating the geometric mean of the maximum concentration causing no mortality and the minimum concentration causing 100 % mortality.
Result	:	Effect concentrations related to nominal values:

No observed effect concentration: 1000 mg/l
Maximum concentration causing no mortality: 2150 mg/l
Minimum concentration causing 100 % mortality: 4640 mg/l
96-h LC50 (geometric mean): 3160 mg/l

Mortality:

Concentration (mg/l)	No. of fish introduced	No. of dead fish after 1h	4h	24h	48h	72h	96h
Control	10	0	0	0	0	0	0
1000	10	0	0	0	0	0	0
2150	10	0	0	0	0	0	0
4640	10	0	10	10	10	10	10
10000	10	10	10	10	10	10	10
10000*	10	10	10	10	10	10	10

* neutralized

Symptoms observed:

- tumbling (after 24 h, 48 h, and 72 h in 2150 mg/l)
- narcotic like state (after 1 h in 4640 mg/l)

Physico-chemical parameters:

- pH values:

Concentration (mg/l)	Test start	24h	48h	72h	96h
Control	7.4	7.9	7.9	7.9	7.8
1000	7.2	7.7	7.8	7.7	7.7
2150	7.0	7.6	7.7	7.7	7.7
4640	6.6				
10000	5.7				
10000*	7.4				

* neutralized

- oxygen values (mg/l):

Concentration (mg/l)	Test start	24h	48h	72h	96h
Control	7.5	8.4	8.5	8.6	8.4
1000	7.7	8.3	8.4	8.5	8.5
2150	7.7	8.4	8.4	8.6	8.6
4640	8.1				
10000	8.5				
10000*	8.4				

* neutralized

The temperature was 20 °C in all vessels tested at all observation times.

Test condition **:** Test conditions:

- fish species:
Leuciscus idus L., golden variety (golden orfe)

(During the 3-months housing period, fish were treated twice with 0.05 mg/l malachite green chloride and once with 10 mg/l tetracycline hydrochloride.)

- body length:
5.1 cm (range: 4.8 - 5.7 cm)

- body weight:
1.8 g (range: 1.4 - 2.7 g)

- corpulence factor:
1.4

- positive control of animals conducted with chloroacetamide:
LC50 (48 h): approx. 32 mg/l (corresponds to the normal sensitivity)

- test water:
Reconstituted freshwater was prepared from fully demineralized tap water according to DIN 38 412, Part 11 (1982). The water was resalted by the addition of 294.0 mg/l CaCl2*2H2O, 123.3 mg/l MgSO4*7H2O, 64.8 mg/l NaHCO3 and 5.8 mg/l KCl.

- specifications of test water:
total hardness: 2.5 mmol/l, acid capacity: 0.8 mmol/l, ratio Ca/Mg ions: 4:1, ratio Na/K ions: 10:1, pH: about 7.9

- liquid volume/aquarium:
10 l

- aeration:
slight

- photoperiod:
16 h light and 8 h darkness

- No. of animals per test concentration:
10

- loading (g fish body weight / l test water):
1.8

- test vessels:
all-glass aquaria (30 * 22 * 24 cm)

- temperature:
20 °C

- withdrawal of food:
1 day before and during exposure

- duration of adaptation to test water and test temperature:
3 days

- nominal test concentrations:
0, 1000, 2150, 4640, and 10000 mg/l; the 10000 mg/l concentration was additionally set up after neutralization

- preparation of the concentrations:
The chemical was added to the test water without any pretreatment. Subsequently the fish were placed into the aquaria.

Observations/measurements:

- mortalities after 1, 4, 24, 48, 72, and 96 h
- pH at beginning and after 24, 48, 72, and 96 h
- O2 content at beginning and after 24, 48, 72, and 96 h

Test substance : Purity: 98 %

Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions (exposure concentrations in the test and the stability of the test item were not confirmed by chemical analysis)

12.11.2006 (21)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= 560 measured/nominal
EC50	:	> 560 measured/nominal
Limit Test	:	no
Analytical monitoring	:	yes
Method	:	other: OECD 202 and EEC/Annex VC.2
Year	:	1995
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Protocol Deviations: In disagreement with the protocol, daphnids were inspected after the first 5 (rather than 6) hours of exposure. Additionally, although the protocol stated that all study documentation would be transferred to the Sponsor, they were maintained by the laboratory conducting the study. Neither of these deviations affected the integrity of the study.

Result : Nominal concentrations: 95.0, 171.5, 308.5, 555.5 and 1000.0 mg/l

Measured concentrations: 96.0, 175.8, 290.3, 568.5 and 1125.8 mg/l for first series; 98.0, 173.3, 342.6, 559.6 and 1048.8 mg/l for second series.

Percent loss: The analyzed percent loss of test material ranged from -21.7% to 11.3%.

Biological observations: In the first experiment, 1/10 daphnids exposed to 1125.8 mg/l were immobile at 24 hours. 1/10 controls, 1/10 exposed to

175.8 mg/l and 1/10 exposed to 1125.8 mg/l were immobile at 48 hours. In the second experiment, 1/10 daphnids exposed to 173.3 mg/l, 1/10 exposed to 342.6 mg/l and 2/10 exposed to 1048.8 mg/l were immobile at 48 hours.

Element value: The 24- and 48-hour EC50 values were > 1125.8 mg/l for the first series and > 1048.8 and > 559.6 mg/l (respectively) for the second series. The 24- and 48-hour NOEC values were 1125.8 mg/l for the first series and 1048.8 and 559.6 mg/l (respectively) for the second series.

Observations: No particulates, surface slicks of precipitates were observed in the test solutions.

Remarks: The study was considered to be valid since the control mortality was not greater than 10%, the dissolved O2 concentration did not fall below 60% of the initial O2 level, there were no deviations that could have affected the outcome of the test, and test daphnids in the control groups were not trapped at the surface of the water.

Test condition **:** Date of Study Initiation: June 8, 1994
Date of Study Completion: Feb. 9, 1995

Test organisms: Adult Daphnia magna were reared in 100-L stainless steel culturing tanks located within the Eco-Chem Testing Group, Eastman Kodak Company, Rochester, NY. The same water used in the study was supplied continuously to the rearing tanks. Gravid daphnids used to produce test organisms remained in the tanks for at least 2 weeks. Filtered air was dispensed into rearing tanks through dual 2.5-cm diameter air stones. While in the tanks, Daphnids were fed a blended diet of staple flake fish diet, spinach, cod liver oil and a yeast mix, plus a 50/500 mix of 1 x 10E6 cells/ml of Selenastrum capricornutum and Antistrodesmus braunii.

Approximately 100 gravid daphnids were transferred by net into two 20-cm diameter bowls containing 1 liter of diluent water and 5 ml food. All adults were removed 18 hours later. Neonates (6 - 24 hours old) used in the study were harvested 6 hours later.

Dilution water source: The water was pumped from Lake Ontario by a water treatment facility into a large underground storage reservoir located near the testing facility. This water was pumped into the laboratory, and passed through 1) 3-micron polypropylene filter tubes; 2) powdered, activated carbon filter tubes; and 3) another set of 3-micron polypropylene filter tubes. The filtered water stream was then injected with 150 ppb of Na2S2O3 (to reduce residual chlorine). The water was then tempered to 20 +/- 2 degrees C, and cascaded through a column degassing unit into an open aeration basin for seasoning.

Dilution water chemistry: Representative values for hardness and total alkalinity (both as CaCO3) during the study were 120 mg/l and 92 mg/l, respectively.

Stock and test solution preparation: All exposure solutions (0, 95.0, 171.5, 308.5, 555.5 and 1000.0 mg/l, nominal) were prepared by directly adding the test material to test vessels containing 20 L of diluent water. The solutions in each vessel were stirred with a hand-held mixer. Prior to addition of organisms, aliquots (200 ml) of each exposure solution were transferred to the 250-ml exposure vessels. All test solutions and controls were prepared in duplicate. They were analyzed at the beginning and end of the study for concentration of test material.

Analysis of test material concentration: Solutions were analyzed for concentrations of test material using GC/FID. Time 0 samples were analyzed as received (i.e. in diluent water). The 96 hour samples were

diluted 1:1 with acetone. Standards were prepared in 1:1 acetone:diluent water. A 0.2 ml aliquot of an internal standard solution of ethylene glycol in acetone (0.2 g/10 ml) was added to each sample and standard.

Exposure vessel type: Daphnids were exposed in 250-ml Pyrex glass beakers. The light/dark cycle was 16 hours on/8 hours off, with a 20-min transition period.

Number of replicates/daphnids per replicate: Neonatal daphnids were collected by pipet and randomly transferred into exposure vessels (10 per vessel).

Study conduct: Daphnids were observed for immobility and stress at 0, 5, 24, and 48 hours. The temperature, dissolved O2 and pH of each exposure solution were measured at 0 and 48 hours. Dead organisms were removed from vessels when found.

Water chemistry in test: The pH and dissolved O2 concentration ranged from 8.0 - 8.3 and 8.3 - 9.0 mg/l, respectively.

Test temperature range: The temperature in all vessels remained at 20 +/- 2 degrees C during the test.

Statistical methods: The EC50 values (within 95% confidence intervals) were calculated by the binomial method, using a computer program inputted with the concentration of the test material (nominal or measured), number of organisms exposed, and number of organisms immobilized. Data for control vessels were not entered.

Data storage: All study documents were maintained by the laboratory that conducted the study.

Test substance : The structure of the test material was confirmed on May 27, 1994, using GC/MS. Initial and final purity (confirmed by GC/FID) of the test material were 98.2% and 98.6%, respectively.

Reliability : (1) valid without restriction
Guideline study with analytical monitoring.

Flag : Critical study for SIDS endpoint
12.11.2006 (40)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC0 : = 500 measured/nominal
EC50 : > 500 measured/nominal
EC100 : > 500 measured/nominal
Analytical monitoring : no
Method : other: Directive 79/831/EEC, Annex V, Part C
Year : 1988
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : Effect values (nominal concentrations):

	24 h	48 h
EC0 :	500 mg/l	500 mg/l
EC50 :	> 500 mg/l	> 500 mg/l
EC100 :	> 500 mg/l	> 500 mg/l

Daphnid mobility:

Mobile daphnids (n) at

Concentration (mg/l)	0 h	3 h	6 h	24 h	48 h
0 (control)	20	20	20	20	20
7.81	20	20	20	20	20
15.6	20	20	20	19	19
31.2	20	20	20	20	20
62.5	20	20	20	20	20
125.0	20	20	20	20	19
250.0	20	20	20	20	20
500.0	20	20	20	19	18

pH:

Concentration (mg/l)	0 h	48 h
0 (control)	7.62	8.14
7.81	7.75	7.88
15.6	7.73	7.88
31.2	7.74	7.89
62.5	7.72	7.9
125.0	7.71	7.88
250.0	7.66	7.85
500.0	7.61	7.92

Oxygen content (mg/l):

Concentration (mg/l)	0 h	48 h
0 (control)	8.40	8.5
7.81	8.70	8.5
15.6	8.50	8.5
31.2	8.70	8.3
62.5	8.50	8.5
125.0	8.20	8.5
250.0	8.70	8.3
500.0	8.60	8.4

Test condition **:** Test conditions:

- test organisms:
Daphnia magna STRAUS

- dilution water:
source: tap water; pretreatment steps: (1) 6 µm- and charcoal-filtration; (2) H_2SO_4 was added to reduce alkalinity up to pH 4.3; (3) distilled water was added to reduce water-hardness; (4) water was aerated (oil-free air) until saturated with oxygen; (5) water was stored for at least 24 h for stabilization.

- specifications of test water at test start:
water-hardness: 2.52 mmol/l, alkalinity up to pH 4.3: 0.85 +/- 0.1 mmol/l, pH: 7.95, conductivity: 625 µS/cm, ratio Ca:Mg: 4:1, ratio Na:K 10:1

- water solubility of the test substance:
> 500 mg/l

- illumination:
artificial light, day/night rhythm = 16/8 h

- light intensity:
ca. 5 µE/(m^2*s) at a wave length of 400-750 nm

- temperature:
19 °C

- test volume:
10 ml

- test vessels:
test tubes (glass) with flat bottom

- replicates:
4 per concentration

- volume/animal:
2 ml

- number of animals/vessel:
5

- total number of animals/concentration:
20

- age of animals:
2-24 h

- observation times:
visually after 0, 3, 6, 24 and 48 h

- observed/measured parameters:
swimming ability, pH, oxygen

- nominal test concentrations:
0 (control), 7.81, 15.6, 31.2, 62.5, 125, 250, 500 mg/l

Test substance : Purity: not stated

Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions (exposure concentrations in the test and the stability of the test item were not confirmed by chemical analysis)

27.10.2006 (22)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: Desmodesmus subspicatus (formerly Scenedesmus)
Endpoint	:	biomass
Exposure period	:	72 hour(s)
Unit	:	mg/l
EC10	:	= 650 measured/nominal
EC50	:	= 1600 measured/nominal
EC90	:	= 3900 measured/nominal
Limit test	:	
Analytical monitoring	:	no
Method	:	other: following German Industrial Standard DIN 38412, Part 9
Year	:	1989
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Result : Effect values (as given in the report)

Biomass reduction (mg/l):
Evaluation: graphical computerized

72-h EbC10:	650	--
72-h EbC50:	1600	1600
72-h EbC90:	3900	4900

Growth rate inhibition (mg/l):

Evaluation:	graphical	computerized
72-h ErC10	1000	870
72-h ErC50:	2000	3170
72-h EbC90:	--	--

All values refer to nominal concentrations of the test item. No chemical analysis of the test substance was carried out.

During the 72 h exposure, cell densities (relative fluorescence values) were as follows (average of 4 – 6 replicates):

Nominal test concentration	Cell density (fluorescence)			
(mg/l)	0 h	24 h	48 h	72 h
0	0.11	0.36	1.56	2.37
200	0.11	0.36	1.36	2.36
400	0.12	0.37	1.46	2.36
800	0.11	0.36	1.28	2.26
1600	0.12	0.32	0.88	1.31
3200	0.12	0.23	0.28	0.34
6400	0.12	0.18	0.14	0.12

Biomass, growth rate and their inhibition were given as follows:

Nominal test concentration	Biomass		Growth rate	
(mg/l)	B	% inh.	µ	% inh.
0	2.82	--	1.02	--
200	2.61	7.4	1.01	0.1
400	2.72	3.6	1.01	0.9
800	2.48	12.2	1.00	1.6
1600	1.57	44.4	0.81	20.2
3200	0.39	86.3	0.35	65.6
6400	0.07	97.5	-1.46	100.0

pH
--

Nominal test concentration	pH after	
(mg/l)	0 h	72 h
0	8.1	9.6
6400	7.9	8.6

Test condition **:** Test conditions:

- species:
Scenedesmus subspicatus (renamed to Desmodesmus subspicatus)

- medium:
DIN-medium (pH 8.2 +/- 1.0)

- temperature:
20 +/- 1 °C

- test flasks:
glass test tubes

- test volume:
10 ml

- No. of algae in test flasks at test start:
10000 exponentially-growing cells

- stock solution of test substance:
concentration: 12800 mg/l (no solvent used)

- test concentrations:
0 (control), 200, 400, 800, 1600, 3200, 6400 mg/l

- replicates:
4 per concentration and 8 for control

- incubation:
tubes were incubated in an incubation chamber for 72 h at 20 +/- 1 °C

- flasks were shaken twice daily to hold cells in suspension

- illumination:
permanent artificial light (10 000 lx / 120 µE)

- samples were taken at regular intervals (24, 48, and 72h)

- measurements:
cell density (growth) by means of a fluorimeter, pH-values

- test evaluation:
biomass (b), growth rate (µ); each graphically and computerized

Test substance : Purity: not stated
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions (exposure concentrations in the test and the stability of the test item were not confirmed by chemical analysis)
Flag : Critical study for SIDS endpoint
27.10.2006 (23)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : other bacteria: activated sludge from laboratory waste water
Exposure period : 30 minute(s)
Unit : mg/l
EC50 : > 1000 measured/nominal
EC20 : > 1000 measured/nominal
EC80 : > 1000 measured/nominal
Analytical monitoring : no
Method : OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year : 2003
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : The EC20 in the activated sludge respiration inhibition test is > 100 mg/l. Disturbances in the biodegradation process of activated sludge are not to be expected, if the substance is correctly introduced into adapted wastewater treatment plants at low concentrations.

Result :

	Oxygen consumption (mg O2/l*h)	Inhibition (% of blank control)

Blank (mean value)	18	-
Test substance (TS):		
1000 mg/l	16	89
Reference substance:		
1 mg/l (RS1)	18	100
10 mg/l (RS2)	10	56
100 mg/l (RS3)	3	17

Effect concentrations for the reference substance:
EC20 (30 min): ca. 2.9 mg/l
EC50 (30 min): ca. 15 mg/l
EC80 (30 min): ca. 85 mg/l

pH-values

Before adding inoculum	BC1	BC2	BC3	TS	RS1	RS2	RS3
before correction:	6.8	6.8	6.8	6.8	6.8	6.8	6.9
after correction:	7.1	7.2	7.3	7.2	7.2	7.4	7.1
After adding inoculum							
at test end (30 min):		7.7					

Test condition **:** - incubation time:
30 min

- temperature:
20 +-2 °C

- test vessels:
Erlenmeyer-flasks (nominal volume: 250 ml)

- test volume:
250 ml

- synthetic medium:
8 ml/flask 100-fold concentrated OECD-medium

- oxygen concentration during aeration:
> 2.5 mg/l

- oxygen concentration immediately before measurement:
> 6.5 mg/l

- duration of the measurement of oxygen consumption:
8-10 min

- reference substance:
3,5-dichlorophenol

- reference substance concentration:
100, 10, 1 mg/l

- test substance concentration:
1001 mg/l (nominal)

- inoculum:
concentration: 1 g/l dry substance;
source: activated sludge from laboratory waste water plant treating municipal sewage

- replicates:
blank control (BC): 3
test substance (TC): 1

reference substance (RS): 1
Test substance : Purity: 98.7 %
Reliability : (1) valid without restriction
12.11.2006 (25)

Type :
Species : Pseudomonas putida (Bacteria)
Exposure period : 17 hour(s)
Unit : mg/l
EC10 : = 2500
Method : other: Cell growth inhibition test
Year :
GLP :
Test substance :

Reliability : (3) invalid
original reference not available
27.10.2006 (26)

Type :
Species : other bacteria: waste water microorganisms
Exposure period :
Unit : mg/l
EC0 : = 2000
Method : other: Modified Warburg Method (DEV/L2)
Year :
GLP :
Test substance :

Remark : No inhibition effect on the respiration activity of waste water microorganisms up to the tested concentration of 2000 mg/L.
27.10.2006 (27)

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

In Vitro/in vivo : In vivo
Type :
Species : rat
Number of animals
Males : 7
Females :
Doses
Males : 0.125 mmol/Kg
Females :
Vehicle :
Route of administration : i.v.
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method : other
Year : 2003
GLP : yes
Test substance : other TS

Result : Following intravenous administration of isobutyl isobutyrate, blood collection were done as fast as possible due to the rapid metabolism of the test article. Analysis of these blood samples demonstrated an extremely rapid hydrolysis of isobutyl isobutyrate to form isobutanol and isobutyric acid. The estimated T1/2 (from a simple one-compartment model with bolus input and first-order output) was 11.1 seconds. Peak isobutyl isobutyrate levels were found in the less than 15 seconds sampling time period with mean values of 1045 micromolar. The isobutyl isobutyrate levels decreased very quickly (by 46 seconds, they were at 43 micromolar) and could not be detected 166 seconds after dose administration. Isobutanol levels increased to the 78-220 micromolar range within the 15 seconds required for the first sample and stayed in this range until the end of sampling at 240 seconds. Isobutyric acid levels increased up to 304 micromolar within the 31-45 seconds time point and remained above 100 micromolar until 196 seconds. Isobutyric acids were consistently higher than the isobutanol levels suggesting formation of isobutyric acid from the further metabolism of isobutanol. This study demonstrates an extremely rapid hydrolysis of isobutyl isobutyrate, with a half-life measured in seconds. It also demonstrates the rapid appearance of the down stream metabolites, isobutanol and isobutyric acid.

Isobutyl isobutyrate, isobutanol and isobutyric acid blood levels found following isobutyl isobutyrate intravenous injection.

Sampling Time (seconds)	Isobutyl isobutyrate*	Isobutanol	Isobutyric acid*
0	Nd**	Nd	Nd
<15	1045	103	129
16-30	405	209	268
31-45	115	218	304
46-60	43	196	295

61-75	18	163	252
76-90	12	153	225
91-105	8	135	188
106-120	6	115	161
121-135	6	128	162
136-150	3	97	126
151-165	6	103	126
166-180	Nd	98	122
181-195	Nd	87	107
196-210	Nd	78	95
211-225	Nd	82	98
226-240	Nd	96	107

*mean µM whole blood, **Nd = not detected

Test condition : Preliminary studies were conducted to select dose levels, dose formulations, and sampling times for the definitive studies. Isobutyl isobutyrate in saline with 1% Tween 20 was administered individually to seven male, Sprague Dawley rats via an indwelling femoral vein catheter. Serial blood samples were collected from an indwelling jugular vein catheter and immediately deproteinized to halt enzymatic activity. All catheters were made of Teflon as the test material adhered to the other types of plastic catheter materials. Extensive methods development was conducted to insure the test material was delivered into the systemic circulation and that the sampling times would provide useful metabolism/toxicokinetic data. The entire sampling period lasted only 240 seconds. Concentrations of isobutyl isobutyrate as well as down stream metabolites (isobutanol and isobutyric acid) were assayed by an internal standard GC-MS selected ion monitoring method.

Test substance : isobutyl isobutyrate purity > 99%

Reliability : (2) valid with restrictions
Accepted scientific methodology

21.11.2006 (29)

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : = 8000 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 20
Vehicle : water
Doses : 4640 and 10000 mg/kg bw
Method : other: Similar to OECD 401
Year : 1974
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Data have been compiled using the unpublished raw data
Result : Mortalities:
Deaths occurred within 4 h after dosing. Mortalities within the 7-d observation period were as follows. The combined LD50 was 8000 mg/kg bw.

Dose (mg/kg bw)	Mortalities males	females
4640	0/5	1/5
10000	3/5	4/5

		Clinical signs: No signs were seen in low dose animals. Signs in high dose animals included dyspnea, abdominal and lateral posture, apathy, cyanosis, red encrusted noses. Pathology: Heart dilatation, darkened liver, some cases of splenomegaly.
Test condition	:	Animals: Species: rat Strain: Sprague-Dawley (Gassner) Sex: 5 per sex and dose level Body weight range: 180-205g (males), 160-170g (females) Treatment: Application: oral gavage Solvent: water Concentration of TS: 35% Dose levels: 4640 and 10000 mg/kg bw Observation: Clinical signs of toxicity, mortalities within 7 days Terminal necropsy Observation period: 7 days
Test substance	:	Purity 100%
Reliability	:	(2) valid with restrictions Comparable to guideline study with acceptable restrictions. Restrictions: observation period only 7 days.
Flag	:	Critical study for SIDS endpoint
27.10.2006		(19)

Type	:	LD50
Value	:	= 3200 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	
Year	:	1971
GLP	:	no
Test substance	:	other TS

Test substance	:	Neopentyl glycol (CAS No. 126-30-7).
Reliability	:	(4) not assignable Non-GLP, secondary reference.
21.11.2006		(31)

Type	:	LD50
Value	:	> 6400 mg/kg bw
Species	:	
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	
Year	:	1956
GLP	:	no
Test substance	:	other TS

Remark	:	This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20. Weakness, and ataxia were observed in the animal receiving 12800 mg/kg. The time of death was the 2nd day following dosing.
Test condition	:	The test material was administered undiluted to seven animals at dose levels ranging from 200 to 12800 mg/kg. One rat was used at each dose level. The animals were observed for 14 days following dosing and no necropsies were performed.
Test substance	:	isobutyl isobutyrate
Reliability	:	(2) valid with restrictions Acceptable w/restrictions

21.11.2006 (44)

Type	:	LD50
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: EPA (TSCA) Health Effects Testing Guidelines 40 CFR Part 798 (Subpart B, Section 798.1175:acute oral toxicity; and 1987 OECD Guidelines for Testing of Chemicals (Section 4: Health Effects; 401:acute oral toxicity).
Year	:	1993
GLP	:	yes
Test substance	:	other TS

Remark	:	This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20. In preliminary testing, 1 female rat was dosed with 2000 mg/kg of isobutanol and 1 female rat was dosed with 8000 mg/kg (20% w/v emulsions in 0.25% aqueous methyl cellulose solution). The rat receiving 8000 mg/kg died. In the definitive test, the peroral LD50 for female rats dosed with the test substance (emulsions in 0.25% aqueous methyl cellulose solution) was 3350 mg/kg. None of 3 male rats died after receiving peroral doses of 2830 mg/kg of isobutano1 (a comparison dose that produced 0 of 5 female deaths), although signs were apparent. Signs of toxicity included sluggishness, unsteady gait, lacrimation, piloerection, slow breathing, prostration and a trace to large amount of blood in urine (positive by HEMASTIX. Reagent Strips). Several females exhibited a slight weight loss within 7 to 14 days. Deaths occurred within 2 hours to 1 day. Survivors recovered within 0.5 hour to 6 days. Necropsy of animals that died revealed discolored and/or mottled lungs (bright to dark red), tan to dark maroon and/or mottled livers (in 2), discolored stomachs (gray and/or yellow), 1 liquid-filled stomach, dark red and/or gray areas on the intestines, red to brown kidneys (in 1) and a large amount of blood in the urine of 1 (positive by HEMASTIX. Reagent Strips). There were no gross lesions apparent in any survivor at necropsy. One female survivor dosed with 2830 mg/kg of isobutanol appeared pregnant at necropsy (determined to be a pseudopregnancy during microscopic valuation). The kidneys and urinary bladders from 1 or 2 rats from each dose group (except 1000 mg/kg) were saved and examined microscopically (see Appendix 2). The only kidney lesions evident were single instances of tubular proteinosis, tubular basophilia, mineralization and congestion, which were not considered to be attributable to the test substance. There were no lesions observed in the urinary bladders. In the uterus of the 1 female rat (2830 mg/kg) that appeared pregnant at necropsy, deciduoma of pseudopregnancy were apparent. This

condition is somewhat unusual for animals of this age group. Subsequent investigations revealed that the female rats ordered for this study had undergone vaginal swabbing on the day of shipment at the animal supplier. This female animal (and one other from the acute inhalation study) had pseudopregnancy due to cervical stimulation from the vaginal swabbing procedure. The male rat oral (fasted) LD50 was > 2830 mg/kg bw; 0 of 3 died. The female rat oral (fasted) LD50 was 3350 (2860 to 3920) mg/kg bw. Microscopic kidney lesions were evident but probably not related to treatment.

Result : LD50 > 2830 mg/kg bw (males)
3350 (2860 to 3920) mg/kg bw (females)

Test condition : Rat (Harlan Sprague Dawley) body weights were within +/- 20% of the group mean for each sex. The body weight range on the day of dosing was 281 to 292 g for males and 210 to 259 g for females (including those used for preliminary testing). A total of 3 male and 20 female rats were used for the definitive peroral test. An additional 2 female rats were used for preliminary testing. The animals were acclimated for at least 5 days before dosing. Detailed clinical observations were conducted twice, at the time of receipt and during animal identification and/or dosing. Cage-side observations and mortality checks were conducted at least once daily. Animals considered unacceptable for the study, based on the clinical signs were rejected for use on this study. Each dosing mixture was prepared just prior to administration by diluting the appropriate amount of isobutanol with 0.25% w/v aqueous methyl cellulose solution. All resulting emulsions were mixed for approximately 15 to 30 minutes on a magnetic stirrer. Doses were administered by stomach intubation through a commercial 16-gauge (3-inch) ball-end stainless steel needle attached to a disposable syringe. The exact amounts of test substance and emulsion given to each rat were recorded on the raw data form. The rats were fasted overnight before dosing. Five female rats were included on each of several dose levels in order to determine an LD50. Three male rats were included on an intermediate dose level for comparison. An additional 2 female' rats were used for preliminary peroral toxicity testing. For individual animals, the dosing volume was adjusted according to body weight. Dosed rats were observed frequently for signs of toxicity on the first day of the test and twice a day thereafter (except on weekends or holidays when they were examined for death alone). Weights were recorded on the day of dosing and at 7 and 14 days after dosing or at death. After 14 days, all survivors were sacrificed by CO2 overdose. Necropsies were performed on all animals that died or were sacrificed. Unless tissues were judged to be excessively autolyzed, the following tissues were collected from selected animals and retained in 10% neutral buffered formalin: kidneys, urinary bladder, liver, sciatic nerve, stomach, intestines and spleen. Lungs were also saved because of possible lung damage, based on clinical signs. An LD50 was calculated for female rats, based on the 14-day observation period. It was calculated by the moving average method. An estimate of the slope was made by the formula developed by Weil. During the acute peroral toxicity test, several animals (including survivors) had varying amounts of blood present in the urine. Therefore, histology evaluations were performed on all saved kidney and urinary bladder tissues. One female rat appeared to be pregnant at necropsy and the uterus was saved in order to verify this condition (since the animals are ordered to be non-pregnant).

Test substance : Isobutanol (99.9% purity by capillary GC, GC/MS and NMR used to confirm identity)

Reliability : (1) valid without restriction
GLP guideline study for Isobutanol

21.11.2006 (28)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	other: Inhalation Hazard Test
Value	:	
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	18
Vehicle	:	other: air
Doses	:	
Exposure time	:	8 hour(s)
Method	:	other: Inhalation Hazard test (cf. OECD TG 403)
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Data have been compiled using the unpublished raw data.
Result	:	Mortalities: No death (0/12) was seen during 7 days following the 8h exposure period. The exposure concentration was estimated to be 0.04 mg/l. Symptoms: none were seen. Necropsy: no findings.
Test condition	:	Animals: Species: rat. Strain: Sprague-Dawley. Sex: male and female. Mean body weight: 165g. Inhalation Exposure: Concentration: saturated atmosphere (20°C). Atmosphere generation: Saturation was achieved by pumping air through TS in a gas-washing bottle that was placed in a water bath. Exposure period: 8 h. Analytical measurement of exposure concentration: no data. Concentration was frequently estimated from the amount of TS consumed and the air volume at the time of the study. Observation: Observation period: 7 days. Clinical signs of toxicity, mortalities. Terminal necropsy.
Test substance	:	Purity 100%
Conclusion	:	There was no inhalation hazard noted.
Reliability	:	(2) valid with restrictions Comparable to guideline study with acceptable restrictions. Restriction: observation period 7 days; estimation of exposure concentration.

12.11.2006 (19)

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	LD50
Value	:	= 730 mg/kg bw

Species	:	mouse
Strain	:	NMRI
Sex	:	male/female
Number of animals	:	20
Vehicle	:	water
Doses	:	215, 464, 681, 1000, 2150, and 46440 mg/kg bw
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other: Acute toxicity following i.p.injection.
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Data have been compiled using the unpublished raw data.
Result	:	Mortalities: The combined LD50 was 730 mg/kg bw.

==========

Dose (mg/kg bw)	Mortalities males	females
215	0/5	0/5
464	0/5	0/5
681	1/5	0/5
1000	5/5	4/5
2150	5/5	5/5
4640	5/5	5/5

==========

Clinical signs:
Signs included dyspnea, abdominal and lateral posture, apathy, cyanosis, convulsion.

Necropsy:
No TS noted in the abdominal cavity.

Test condition	:	Animals: Species: mouse Strain: NMRI Sex: 5 per sex and dose level Body weight range: no data Treatment: Application: i.p. injection Solvent: water Concentration of TS: varied from 3% to 35% Dose levels: 215, 464, 681, 1000, 2150, and 46440 mg/kg bw Observation: Clinical signs of toxicity, mortalities within 7 days. Terminal necropsy. Observation period: 7 days.
Test substance	:	Purity 100%
Reliability	:	(3) invalid Unsuitable test system for assessment. Unphysiological route of exposure. However, information may be useful for further research.

12.11.2006 (19)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	80 % active substance
Exposure	:	Occlusive
Exposure time	:	20 hour(s)
Number of animals	:	2
Vehicle	:	water
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	other: similar to OECD TG 404
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Data have been compiled using the unpublished raw data.
Result	:	No effect on dorsal skin was seen at 24 h and 8 days post treatment:

Contact period	Finding 24h	8 d
1 min	none	none
5 min	none	none
15 min	none	none
20 h	none	none

Test condition :

Animals:
2 male rabbits; mean body weight 2.7 kg.

Application:
Application: occlusive; intact skin.
Moistened TS (80% TS, 20% water) was placed on a gauze patch to the clipped dorsal and ear skin.
Contact period with dorsal skin was 1, 5, and 15 minutes, and 20 hours. TS was washed off after indicated contact periods.

Observation:
Skin reactions were examined at 24 hrs and at 8 days post treatment.

Data evaluation:
Skin reactions were scored similar to the table of Draize contained in the OECD TG 404.

Reliability : (4) not assignable
Documentation insufficient for assessment: amount of TS used not stated.

12.11.2006 (19)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	100 % active substance
Dose	:	.05 ml
Exposure time	:	
Comment	:	
Number of animals	:	2
Vehicle	:	
Result	:	irritating
Classification	:	risk of serious damage to eyes
Method	:	other: similar to OECD TG 405
Year	:	1974
GLP	:	no

Test substance : as prescribed by 1.1 - 1.4

Remark : Data have been compiled using the unpublished raw data.
Result : Moderate reddening, edema and corneal opacity developed within 24 h after eye contact and persisted until day 8 post treatment. Based on the experimental experience the lesions were not expected to be reversible.

Finding	Grade 1h	24 h	8 days
Reddening	1	2	1
Edema	2	2	1
Opacity	1	2	2
other	discharge	discharge	
Scar		x	

Test condition : Animals:
2 male rabbits; mean body weight 3.12 kg.

Application:
50 µl of neat TS was placed into the right conjunctival sac of the rabbit's eye.

Observation:
Eye reactions were examined at 1 and 24 hrs and at 8 days post treatment.

Evaluation:
Similar to the table contained in OECD TG 405.

Test substance : Purity 100%
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions.
Restriction: low amount of TS. Acceptable because irreversible eye damage was already seen with the low volume of TS.

12.11.2006 (19)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type :
Species : rat
Sex : male/female
Strain :
Route of admin. : gavage
Exposure period :
Frequency of treatm. :
Post exposure period :
Doses : 100 - 1000 mg/kg/day
Control group :
NOAEL : = 100 mg/kg bw
LOAEL : = 300 mg/kg bw
Method : OECD combined study TG422
Year :

GLP	:	yes
Test substance	:	other TS
Remark	:	"This study is present only as secondary literature; this secondary literature does not mention whether the indicated rat strain is Sprague-Dawley or not. Within male animals of the highest dose group, an increase in albumin, total protein and bilirubin was observed. Within male animals of both of the high dose groups the absolute and relative liver weight was increased. The kidney weight of the 1000 mg/kg males was increased compared to the control group and the kidney weight of the 3000 mg/kg males had a tendency for an increase. Within male animals of the highest dose group, liver hypertrophy and histological evidence of protein cylinders, hyaline drops and basophilic changes within kidney tubuli were observed." (translation of German text found in the "Toxicity to Reproduction" Section of the European Commission IUCLID document for CAS No. 126-30-7 available at http://ecb.jrc.it/IUCLID-Data-Sheet/ 126307.pdf).
Result	:	The no observable effect limit (NOAEL) for systemic toxicity was 100 mg/kg/day. Effects observed at 300 mg/kg/day (in males only) were increased total protein, bilirubin and albumin in blood and increased absolute and relative kidney and liver weights. Additional findings at 1000 mg/kg/day were hypertrophy of the liver of two males (without evidence of histological lesions) and a high incidence of protein casts, hyaline droplets and basophilic changes in the renal tubules of males. Systemic toxicity was not observed in females.
Test condition	:	In an OECD Test Guideline 422 study, Sprague-Dawley rats (x/sex/dose) were administered 0, 100, 300 or 1000 mg/kg/day of the HPHP metabolite NPG (99% pure) by gavage. Males were exposed for 14 days prior to mating and during mating (total of 42 days), and females were exposed for 14 days prior to mating, and during mating, gestation and three days of lactation.
Test substance	:	Neopentyl glycol (CAS No. 126-30-7; 99% pure)
Reliability	:	(1) valid without restriction Guideline study

21.11.2006 (46)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	other: oral gavage as a solution in corn oil
Exposure period	:	18 weeks
Frequency of treatm.	:	7 days/week for 18 weeks
Post exposure period	:	none
Doses	:	0, 10, 100, and 1000 mg/kg
Control group	:	yes
NOAEL	:	= 1000 mg/kg
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	other TS
Remark	:	This study was performed due to the food additive use. This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20.
Result	:	No deaths or abnormal behaviour was noted during the study. No differences in body weight, feed or water consumption, or histological findings were noted. The only change in haematology parameters was a decrease in hemoglobin concentration in the male 100 and 1000 mg/kg bw/day groups after two weeks of exposure. These changes were no accompanied by changes in other red blood cell parameters in these groups, and the female animals were not affected. In addition, similar

findings were not observed at the 6 and 18-week haematology determinations. Kidney function tests and urine examination was normal. The only change in organ weights was an increase (14%) in relative spleen weight (when corrected for body weights) in the 1000 mg/kg bw/day male group. The mean terminal body weights of animals in this group were decreased by 7% compared to the control group (not statistically significant but may explain the increased relative spleen weight). Due to the fact that there were no histological changes in this or any other organ, this finding was considered spurious.

Test condition : The study consisted of male and female animals (15/sex/group) receiving 0, 10, 100, or 1000 mg/kg isobutyl isobutyrate by oral gavage for 18 weeks. The dose volume was 5 ml/kg with the control animals receiving corn oil alone. In addition, groups of five rats of each sex were given the same doses for either 2 or 6 weeks. The animals were weighed on Day 1, 2, 6 and weekly thereafter. Feed and water consumption were determined on a cage basis (5/cage by sex). After the final dose, the animals were fasted for 24 hours and killed under barbiturate anesthesia. Hematology parameters were collected at 3, 6, and 18 weeks into the study. A gross necropsy was performed and brain, heart, liver, spleen, kidney, adrenals, stomach, small intestine, caecum, gonads, pituitary, and thyroid(s) were weighed. Typical organs were collected, fixed in formalin, and processed for histological exam. Urine was collected during week 2, 6, and 18 of treatment and examined. Kidney function tests were also performed during week 6 and 18.

Test substance : isobutyl isobutyrate (>98% pure).

Reliability : (2) valid with restrictions
Accepted scientific methodology

21.11.2006 (30)

Type :
Species : rat
Sex : male/female
Strain : other: CD
Route of admin. : gavage
Exposure period : 90 days
Frequency of treatm. : daily
Post exposure period : N/A
Doses : 0, 100, 316, or 1000 mg/kg/day
Control group : yes
NOAEL : = 316 mg/kg
LOAEL : = 1000 mg/kg
Method : other
Year : 1987
GLP : yes
Test substance : other TS

Remark : This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20.

Analysis of dosing solutions confirmed concentrations and stability. The difference between the presence or absence of acute clinical signs of toxicity (ataxia, hypoactivity) following oral administration between the isobutanol and isobutyl isobutyrate studies is most probably due to the vehicle used. The isobutanol study uses distilled water, a vehicle that would allow rapid absorption of the alcohol while the limited solubility of isobutyl isobutyrate in water necessitated the use of a corn oil vehicle. The corn oil vehicle would allow for a slower absorption of the test article and hence, the lack of acute signs of intoxication.

Result : Treatment-related clinical signs noted in the 1000 mg/kg dose group included hypoactivity, ataxia, salivation, labored respiration, rales, prostration, hypothermia, and emaciation. Hypoactivity and ataxia were the most common clinical signs and these resolved primarily after week 4.

There were no compound related clinical signs in the 100 or 316 mg/kg dose groups. The mortality rate was 1/60, 1/60, 2/60, and 11/60 for the control, 100, 316, and 1000 mg/kg groups, respectively. The only difference in body weights, body weight gain, or feed consumption were during weeks 1 and 2 of the study and were restricted to the 1000 mg/kg/day dose group. In addition, there were no dose-related differences observed in organ weights, gross pathology or histopathological examination. The mortality observed in the different dose groups was due to gavage errors, and was not due to compound administration.

Test condition : Four groups of male and female rats (30/sex/group) were dosed daily by gavage with 0, 100, 316 or 1000 mg/kg/day of isobutanol for either 4 weeks (interim sacrifice; 10/sex/group) or 13 weeks (remaining animals). Dosing solutions of isobutanol in deionized water were used and 10 mL/kg was the constant dosing volume. Body weights and feed consumption were recorded weekly. Clinical signs were recorded daily. Blood and urine were collected for clinical pathology at pre-dose (10 sentinel animals), and at the 4 and 13-week necropsies. Organ weights and results of gross pathology exams were recorded at both the 4 and 13-week necropsies. Histopathological examinations of tissues from the control and 1000 mg/kg groups were conducted as well as examination of hearts, livers, and kidneys from the 100 and 316 mg/kg dose groups.

Test substance : isobutanol (purity 99.9%)

Reliability : (2) valid with restrictions
Standard method with restrictions; conducted with isobutanol

21.11.2006 (2)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Salmonella typhimurium; TA1535, TA100, TA1537, TA1538, and TA98
Test concentration : 4, 20, 100, 500, and 2500 µg/plate
Cytotoxic concentr. : > 2500 µg/plate
Metabolic activation : with and without
Result : negative
Method : other: Similar to OECD TG 471.
Year : 1979
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : The test substance did not increase the number of revertants in any test strain, with or without metabolic activation, in the range 4-2500 µg/plate. There was no cytotoxicity noted at any dose including the highest concentration tested.

The following number of revertants (mean +/- standard deviation) was calculated from the original reference data:

Dose (µg/plate)	S-9	TA98	TA100
0	+	35+/-2	129+/-12
4	+	34+/-3	141+/-12
20	+	32+/-4	148+/-17
100	+	32+/-4	137+/-13
500	+	34+/-2	144+/-16
2500	+	32+/-4	138+/-5

2-AA	+	1812+/-63	3025+/-222
Cyclophos.	+	--	250+/-18
0	-	36+/-4	135+/-19
4	-	35+/-6	138+/-17
20	-	34+/-3	134+/-14
100	-	34+/-7	149+/-19
500	-	34+/-3	139+/-3
2500	-	34+/-4	148+/-24
MNNG	-	1650+/-122	3400+/-245

		TA1535	TA1537	1538
0	+	20+/-2	10+/-3	23+/-3
4	+	18+/-1	11+/-1	22+/-3
20	+	17+/-2	12+/-2	20+/-3
100	+	18+/-3	13+/-5	22+/-5
500	+	19+/-2	11+/-2	21+/-3
2500	+	18+/-3	10+/-2	20+/-3
2-AA	+	183+/-24	153+/-34	1002+/-149
Cyclophos.	+	184+/-24	--	--
0	-	13+/-1	6+/-1	13+/-1
4	-	14+/-3	8+/-2	14+/-2
20	-	14+/-2	7+/-2	15+/-2
100	-	13+/-3	7+/-3	13+/-2
500	-	13+/-3	8+/-3	11+/-2
2500	-	14+/-2	7+/-1	12+/-1
MNNG	-	2925+/-225	48+/-6	--

Test condition : TEST SYSTEM
Ames test: standard plate test.
Metabolic activation: with and without metabolic microsomal enzyme systems (S9-fraction) from Aroclor 1254-induced male Sprague-Dawley rat liver.

Concentrations used:
4, 20, 100, 500, and 2500 µg TS/plate, with and without S9-fraction.
Solvent: water.

Controls: included.
Negative control: solvent only.
Positive control substances:
With metabolic activation: cyclophosphamide (TA100, TA1535) and 2-Aminoanthracene (all tester strains).
Without S9: N-methyl-N'-nitro-N-nitrosoguanidine (MNNG; for TA100, TA98, TA1537, and TA1535).

Number of replicates: 4 plates per test substance dose and per control.

EVALUATION
A substance is considered positive if the following criteria are met:

(i) doubling of the spontaneous mutation rate,
(ii) dose-response relationship,
(iii) reproducibility of results.

Test substance : Purity >97.5%

Conclusion : The test substance did not increase the number of revertants in any test

strain, with or without metabolic activation, in the range 4 to 2500 µg/plate. There was no cytotoxicity noted at any dose including the highest concentration tested.

Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions.
Restriction: TS not tested into cytotoxic range and highest dose less than recommended in the current OECD 471 test guideline.

12.11.2006 (20)

Type : Cytogenetic assay
System of testing : Chinese Hamster Lung Cells
Test concentration : 0.25, 0.50, 1.0 mg/ml
Cytotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: Japanese Guideline
Year :
GLP : yes
Test substance : other TS

Remark : Summary translated from a European IUCLID document for CAS No. 126-30-7 available at http://ecb.jrc.it/IUCLID-Data-Sheet/126307.pdf.
Test substance : 2,2-dimethlypropane-1,3-diol (CAS No. 126-30-7, neopentyl glycol), purity 99.15%
Reliability : (2) valid with restrictions
Guideline study without detailed documentation
Flag : Critical study for SIDS endpoint

21.11.2006 (39)

Type : Ames test
System of testing : Salmonella typhimurium TA100, TA1535, TA98, TA1537, Escherichia coli WP2 uvrA
Test concentration : 312.5, 625, 1250, 2500, 5000 micrograms/plate
Cytotoxic concentr. : > 5000 micrograms/plate
Metabolic activation : with and without
Result : negative
Method : other: Japanese Guideline (plate test)
Year : 1993
GLP : yes
Test substance : other TS

Remark : Summary translated from a European IUCLID document for CAS No. 126-30-7 available at http://ecb.jrc.it/IUCLID-Data-Sheet/126307.pdf. Additional information (cytotoxic dose, positive controls) added from SIDS submission for CAS No. 126-30-7 available at http://cs3-hq.oecd.org/scripts/hpv.
Test condition : Positive controls: without S9: AF-2(TA100, WP2 uvrA, TA98), sodium azide (TA1525) and 9-aminoacridine (TA1537)

with S9: 2-aminoanthracene (all strains)
Test substance : 2,2-dimethlypropane-1,3-diol (CAS No. 126-30-7, neopentyl glycol), purity 99.15%
Reliability : (2) valid with restrictions
Guideline study without detailed documentation

21.11.2006 (39) (49)

Type : Mammalian cell gene mutation assay
System of testing : Chinese Hamster Lung Cells
Test concentration : 0.25, 0.50, 1.0 mg/ml
Cytotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: Japanese Guideline

Year	:	1993
GLP	:	yes
Test substance	:	other TS
Remark	:	Summary translated from a European IUCLID document for CAS No. 126-30-7 available at http://ecb.jrc.it/IUCLID-Data-Sheet/126307.pdf. Additional information (positive control, S9 data, purity) added from SIDS submission for CAS No. 126-30-7 available at http://cs3-hq.oecd.org/scripts/hpv.
Test condition	:	positive control: mitomycin C and cyclophosphamide S-9: induced by phenobarbital and 5,6-benzoflavone
Test substance	:	2,2-dimethlypropane-1,3-diol (CAS No. 126-30-7, neopentyl glycol), purity 99.1%
Reliability	:	(2) valid with restrictions Guideline study without detailed documentation

21.11.2006 (39) (49)

Type	:	Ames test
System of testing	:	Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, Escherichia coli strain WP2uvrA-
Test concentration	:	
Cytotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	
Method	:	
Year	:	2003
GLP	:	yes
Test substance	:	other TS
Remark	:	This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20.
Result	:	Isobutyl isobutyrate was non-mutagenic when tested to a maximum concentration of 5000 micrograms/plate, using the plate incorporation protocol. At least five doses were tested in triplicate, without metabolic activation, and with 10% liver S-9 from rat. Replicate testes were performed after the initial trial to confirm these results.
Test condition	:	Isobutyl isobutyrate was tested as a coded chemical using the plate incorporation method using S. typhimurium tester strains, TA98, TA100, TA1535, and TA1537 and E. coli strain WP2uvrA- in the presence and absence of phenobarbitone/ß-naphthoflavone-induced liver S9 from male Sprague Dawley rats. Test concentrations of isobutyl isobutyrate (up to 5000 µg/plate) were prepared using dimethyl sulphoxide as the solvent; a maximum of 0.1 ml solvent was added to each plate. Each dose was tested in triplicate without activation, and with 10% rat liver S-9. Concurrent positive and solvent controls were run with each trial. Repeat experiments were performed following the initial trial. A material was considered mutagenic if it produced a reproducible, dose-related increase in revertants over the solvent control, under a single metabolic activation condition, in replicate trials. A material was considered questionable if the positive response was elicited at only one concentration, or if the response could not be reproduced. A chemical was designated as non-mutagenic only after it was tested without metabolic activation, and with 10% rat S-9.
Test substance	:	isobutyl isobutyrate, purity >99%
Reliability	:	(1) valid without restriction Guideline study

21.11.2006 (47)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	

Species	:	mouse
Sex	:	male/female
Strain	:	NMRI
Route of admin.	:	gavage
Exposure period	:	
Doses	:	500, 1,000 or 2,000 mg/kg
Result	:	negative
Method	:	other: OECD No. 474 (Proposal for updating, ENV/EPOC (96)4); EPA/TSCA 789.5395 (August 1997); EEC Directive 92/69, B 12 (December 1992)
Year	:	
GLP	:	yes
Test substance	:	other TS
Remark	:	This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20. Both of the positive control chemicals, i.e. cyclophosphamide for clastogenicity and vincristine for spindle poison effects, led to the expected increase in the rate of polychromatic erythrocytes containing small or large micronuclei.
Result	:	Oral gavage dose of 500, 1,000 or 2,000 mg/kg of isobutanol did not have any chromosome-damaging (clastogenic) effect, and there were no indications of any impairment of chromosome distribution in the course of mitosis. There was no effect of isobutanol on the mitotic index or the P/N Ratio. The lowest dose producing toxicity was1000 mg/kg.
Test substance	:	isobutanol
Reliability	:	(1) valid without restriction Guideline study

21.11.2006 (32)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type	:	other: OECD 422
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	Males: 14 days prior to mating and during mating (total of 42 days); Females: 14 days prior to mating, during mating, gestation and three days of lactation.
Frequency of treatm.	:	continuous
Premating exposure period		
Male	:	14 days
Female	:	13 days
Duration of test	:	to Day 3 of lactation
No. of generation studies	:	1
Doses	:	100, 300 or 1000 mg/kg bw
Control group	:	yes
NOAEL parental	:	= 1000 mg/kg bw
NOAEL F1 offspring	:	= 1000 mg/kg bw
Method	:	OECD combined repeated dose and reproductive/developmental toxicity screening test

Year	:	
GLP	:	yes
Test substance	:	other TS
Remark	:	"This study is present only as secondary literature; this secondary literature does not mention whether the indicated rat strain is Sprague-Dawley or not. No substance-caused impact on mating, fertility and estrous cycle was observed. All litters of the animals of the control group were without findings except the litter of one animal. During lactation no substance-caused influences were observed in maternal animals. Within the offspring no substance-induced increased in external anomalies was observed. The offsprings' increase in body weight remained unchanged until Day 4 postnatal. There were no microscopic findings in dead born offspring, offspring that died, or offspring killed on Day 4 postnatal." (translation of German text found in the "Toxicity to Reproduction" Section of the European Commission IUCLID document for CAS No. 126-30-7 available at http://ecb.jrc.it/IUCLID-Data-Sheet/126307.pdf).
Result	:	There was no effect of test material on copulation, fertility, estrus cycle or lactation. Delivery was normal with the exception of one control animal. The NOAELs for teratogenicity and fetal toxicity were also 1000 mg/kg/day. Stillborn, dead pups and pups killed on Day for of lactation showed no abnormal findings attributable to administration of the test material. Body weight gain of treated pups (to Day 4 of lactation) was normal. External examination of the pups revealed no increase in abnormalities in exposed groups.
Test condition	:	Rats were administered 0, 100, 300 or 1000 mg/kg/day of NPG (99% pure) by gavage. Males were exposed for 14 days prior to mating and during mating (total of 42 days), and females were exposed for 14 days prior to mating, and during mating, gestation and three days of lactation.
Test substance	:	Neopentyl glycol (CAS No. 126-30-7; 99% pure)
Reliability	:	(1) valid without restriction Guideline study
Flag	:	Critical study for SIDS endpoint

21.11.2006 (46)

Type	:	Two generation study
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	6 hours/day
Frequency of treatm.	:	7 days/week prior to mating, during mating and gestation; treatment was suspended during lactation days 0-4 and re-initiated on lactation day 5.
Premating exposure period		
Male	:	10 weeks
Female	:	10 weeks
Duration of test	:	
No. of generation studies	:	
Doses	:	0, 500, 1000 and 2500 ppm
Control group	:	yes, concurrent no treatment
NOAEL parental	:	= 2500 ppm
NOAEL F1 offspring	:	= 2500 ppm
NOAEL F2 offspring	:	= 2500 ppm
Method	:	other: Conducted according to US EPA Health Effects Test Guidelines OPPTS 870.3800, Reproduction and Fertility Effects, August 1998.
Year	:	
GLP	:	yes
Test substance	:	other TS
Remark	:	This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20.

		The highest exposure concentration was chosen based upon decreases in reaction to an external stimuli reported in a previous neurotoxicity study (Le, et al., 2001). However, the animals exposed to 2500 ppm in this study did not demonstrate decreases in response to external stimuli as was previously reported.
Result	:	Exposure to isobutanol concentrations up to 2500 ppm did not cause any parental systemic, reproductive, or neonatal toxicity when administered for two generations via whole body exposure.
Test condition	:	Briefly, groups of male and female rats (30/sex/group) were exposed to 0, 500, 1000, or 2500 ppm isobutanol for six hours/day, seven days/week for ten weeks prior to mating. Exposures continued in the male animals until sacrifice. The female animals were exposed thru gestation day 20, with exposure reinitiated on lactation day 5 and continued thru lactation day 28. The F1 pups were weaned on postnatal day 29 and those chosen to represent the next generation started direct inhalation exposures on postnatal day 29. These F1 male and female animals (30/sex/group) were exposed for ten weeks prior to mating. The F1 males continued exposure until sacrifice. The F1 female animals were exposed thru gestation day 20, with exposure reinitiated on lactation day 5 and continued thru lactation day 21. Body weight, feed consumption, exposure parameters, necropsy endpoints, and reproductive and developmental endpoints were collected according to the test guideline.
Test substance	:	isobutanol (>99.9% purity)
Reliability	:	(1) valid without restriction GLP Guideline Study

21.11.2006 (1)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	Males: 14 days prior to mating and during mating (total of 42 days); Females: 14 days prior to mating, during mating, gestation and three days of lactation.
Frequency of treatm.	:	continuous
Duration of test	:	to Day 3 of lactation
Doses	:	100, 300 or 1000 mg/kg bw
Control group	:	yes
NOAEL maternal tox.	:	= 1000 mg/kg bw
NOAEL teratogen.	:	= 1000 mg/kg bw
Method	:	other: OECD 422
Year	:	
GLP	:	yes
Test substance	:	other TS
Remark	:	"This study is present only as secondary literature; this secondary literature does not mention whether the indicated rat strain is Sprague-Dawley or not. No substance-caused impact on mating, fertility and estrous cycle was observed. All litters of the animals of the control group were without findings except the litter of one animal. During lactation no substance-caused influences were observed in maternal animals. Within the offspring no substance-induced increased in external anomalies was observed. The offsprings' increase in body weight remained unchanged until Day 4 postnatal. There were no microscopic findings in dead born offspring, offspring that died, or offspring killed on Day 4 postnatal." (translation of German text found in the "Toxicity to Reproduction" Section of the European Commission IUCLID document for CAS No. 126-30-7

available at http://ecb.jrc.it/IUCLID-Data-Sheet/126307.pdf).

Result	:	There was no effect of test material on copulation, fertility, estrus cycle or lactation. Delivery was normal with the exception of one control animal. The NOAELs for teratogenicity and fetal toxicity were also 1000 mg/kg/day. Stillborn, dead pups and pups killed on Day for of lactation showed no abnormal findings attributable to administration of the test material. Body weight gain of treated pups (to Day 4 of lactation) was normal. External examination of the pups revealed no increase in abnormalities in exposed groups.
Test condition	:	Rats were administered 0, 100, 300 or 1000 mg/kg/day of NPG (99% pure) by gavage. Males were exposed for 14 days prior to mating and during mating (total of 42 days), and females were exposed for 14 days prior to mating, and during mating, gestation and three days of lactation.
Test substance	:	Neopentyl glycol (CAS No. 126-30-7; 99% pure)
Reliability	:	(1) valid without restriction Guideline study

21.11.2006 (46)

Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	inhalation
Exposure period	:	Day 6 thru 15 of gestation
Frequency of treatm.	:	Daily for 6 hours/day
Duration of test	:	10 treatment days/animal
Doses	:	0, 0.5, 2.5, or 10.0 mg/l
Control group	:	yes, concurrent no treatment
NOAEL teratogen.	:	= 10 mg/l
LOAEL Maternal Toxicity	:	= 10 mg/l
Method	:	
Year	:	1990
GLP	:	yes
Test substance	:	other TS
Remark	:	This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20.
Result	:	No treatment related effects on either the dams or the offspring were observed. Therefore, under the conditions of this study, 10 mg/l was considered a No-Observed-Effect Level for both maternal and fetal outcomes. This study corroborates the findings of Nelson, et al., Tox. Ind. Health, 6(314):373-387, 1990.
Test condition	:	Pregnant rats were exposed to isobutanol by whole body inhalation from gestation day 6 thru 15. Body weights, feed consumption, and clinical sign data were collected throughout the study. Chamber concentrations (actual and nominal), temperature, and absolute and relative humidity values were collected.
Test substance	:	isobutanol (purity >99.8%)
Reliability	:	(1) valid without restriction GLP guideline study

21.11.2006 (43)

Species	:	rabbit
Sex	:	female
Strain	:	Himalayan
Route of admin.	:	inhalation
Exposure period	:	Day 7-19 of gestation
Frequency of treatm.	:	6 hours/day
Duration of test	:	Up to Day 29 post-implantation
Doses	:	0.5; 2.51; 10 mg/l
Control group	:	yes
NOAEL maternal tox.	:	= 2.51 mg/l

NOAEL teratogen.	:	= 10 mg/l
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1990
GLP	:	yes
Test substance	:	other TS
Remark	:	This summary was obtained from the robust summary document for CAS No. 97-85-8 presented at SIAM 20.
Result	:	Each control and study group contained 15 pregnant females. A slight (non-significant) retardation in body weight was observed in rabbits of the high-dose group throughout the exposure period. Otherwise, no compound-related effects indicative of maternal toxicity were found. Significantly increased incidences of intraventricular foramen/septum membranaceum (cardiac septal defects) were found for the high-dose group; this finding was not considered to be of biological significance, because by comparison with historical control data, the incidences were found to lie fully within the range of biological variation. Substance related effects on the offspring, indicative of embryo-/fetotoxicity or teratogenicity, were not observed.
Test substance	:	Isobutanol, purity >99.8%
Reliability	:	(1) valid without restriction GLP guideline study

21.11.2006 (9) (42)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

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

(1) "An inhalation two-generation reproductive toxicity study of isobutanol in rats." WIL Research Laboratory Study Number WIL-186013, WIL Research Laboratories, Inc., 1407 George Rd, Ashland, OH 44805-9281, sponsored by the Oxo-Process Panel of the American Chemistry Council, 1300 Wilson Boulevard, Arlington VA 22209.2003, as referenced in the Robust Summary document for CAS No. 97-85-8 presented at SIAM 20, December 2004, available at http://www.chem.unep.ch/irptc/ sids/OECDSIDS/97858.pdf.

(2) "Rat Oral Subchronic Toxicity Study Final Report. Compound: Isobutyl Alcohol." Toxicity Research Laboratories, Ltd. Muskegon, MI. TRL Study #032-002 dated 1987, as referenced in the Robust Summary document for CAS No. 97-85-8 presented at SIAM 20, December 2004, available at http://www.chem.unep.ch/irptc/ sids/OECDSIDS/97858.pdf.

(3) BASF AG (1989), Labor fuer Umweltanalytik; unpublished data, 09 Jan 1989

(4) BASF AG Technical Data Sheet Dated 2005 on line at http://worldaccount.basf.com/wa/NAFTA/Catalog/ChemicalsNAFTA /nfo/BASF/PRD/30036619.

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT