I U C L I D

Data Set

Existing Chemical	:	ID: 107-88-0
Memo	:	HPV
CAS No.	:	107-88-0
EINECS Name	:	butane-1,3-diol
EC No.	:	203-529-7
Molecular Weight	:	90.12
Structural Formula	:	CH3CHOHCH2CH2OH
Molecular Formula	:	C4H10O2

Producer related part

Company	:	Celanese Ltd
Creation date	:	30.10.2001

Substance related part

Company	:	Celanese Ltd
Creation date	:	30.10.2001

Status	:	
Memo	:	
Printing date	:	14.07.2003
Revision date	:	
Date of last update	:	14.07.2003
Number of pages	:	31
Chapter (profile)	:	Chapter: 1.0.1, 1.2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6.1, 3.1.1, 3.1.2, 3.3.1, 3.3.2, 3.5, 4.1, 4.2, 4.3, 4.4, 5.1.1, 5.1.2, 5.1.3, 5.1.4, 5.4, 5.5, 5.6, 5.7, 5.8.1, 5.8.2
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

RECEIVED
OPPT CBIC

2003 JUL 15 PM 2:10

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	other:
Name	:	
Contact person	:	
Date	:	
Street	:	
Town	:	
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

31.12.2002

1.2 SYNONYMS AND TRADENAMES

2.1 MELTING POINT

Value : = -77 °C

Remark : Handbook Data
Reliability : (2) valid with restrictions
Handbook values are assigned a reliability of 2

24.09.2002 (24)

2.2 BOILING POINT

Value : = 207.5 °C at 1013 hPa

Remark : Also listed as 207.5 C in Merck Index (Thirteenth Edition) and in manufacturer's product description sheet.
Reliability : (2) valid with restrictions
Handbook values are assigned a reliability of 2

27.11.2001 (24)

2.3 DENSITY

Type : density
Value : = 1.0059 g/cm³ at 20 °C

Remark : Handbook Value
Reliability : (2) valid with restrictions
Handbook values are assigned a reliability of 2

24.09.2002 (28)

2.4 VAPOUR PRESSURE

Value : = .08 hPa at 20 °C

Remark : Converted from 0.06 mm Hg as listed in handbook
Handbook Data
Test substance : 1,3-Butylene glycol (CASNO 107-88-0)
Reliability : (2) valid with restrictions
Handbook values are assigned 2

06.11.2002 (27)

Value : = .027 hPa at 25 °C

Remark : Handbook Value
Reliability : (2) valid with restrictions
Published value from secondary literature

24.09.2002 (6)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	
Log pow	:	= -.29 at °C
pH value	:	
Method	:	other (calculated)
Year	:	2001
GLP	:	
Test substance	:	
Reliability	:	(2) valid with restrictions Calculated by an acceptable method

26.11.2001 (55)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	miscible
Stable	:	
Reliability	:	(2) valid with restrictions Handbook value
Flag	:	Critical study for SIDS endpoint

24.09.2002 (34)

Solubility in	:	Water
Value	:	at °C
pH value	:	= 6 - 7
concentration	:	1 vol% at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	miscible
Stable	:	
Reliability	:	(2) valid with restrictions 2 Handbook Value

24.09.2002 (22) (51)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .0000000000142 cm³/(molecule*sec)
Degradation	:	= 50 % after .8 day(s)
Deg. product	:	
Method	:	
Year	:	2001
GLP	:	
Test substance	:	

Method : Calculated using AOP version 1.90. Based on 12-hour day and the current EPA default of 1,500,000 hydroxyl radicals per cc.

Remark : AOP Program (v1.90) Results:
==========
SMILES : CC(O)CCO
CHEM : 1,3-Butanediol
MOL FOR: C4 H10 O2
MOL WT : 90.12
---------- SUMMARY (AOP v1.90): HYDROXYL RADICALS --------
Hydrogen Abstraction = 13.9529 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 0.2800 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings = 0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant = 14.2329 E-12 cm3/molecule-sec
HALF-LIFE = 0.751 Days (12-hr day; 1.5E6 OH/cm3)
HALF-LIFE = 9.018 Hrs

Reliability : (2) valid with restrictions
Calculated by an acceptable method

16.12.2002 (2)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Degradation	:	< 1 % after 1 year at pH and °C
Deg. product	:	
Method	:	
Year	:	2001
GLP	:	
Test substance	:	

Remark : Glycols of this type are considered resistant to hydrolysis as they contain no hydrolysable group. Experience in the synthesis and use of this material is also consistent with it being resistant to hydrolysis.
Source : Celanese Ltd
Reliability : (2) valid with restrictions
Estimated by an accepted method

26.11.2001 (29)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : volatility
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: calculated
Year :

Remark : The Henry's Law constant indicates that this compound is essentially non-volatile from water.
Result : Henry's Law constant: 0.00000023 Pa x m3 x mol-1
Source : Hoechst Celanese NV Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

31.05.1995 (21) (30)

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level III
Year : 2001

Method : Calculated using MacKay level III model in EPIWIN 3.05 using highest measured vapour pressure value.
Result : Level III Fugacity Model (Full-Output):

==========

Chem Name : 1,3-Butanediol
Molecular Wt: 90.12
Henry's LC : 2.3e-007 atm-m3/mole (Henrywin program)
Vapor Press : 0.06 mm Hg (user-entered)
Log Kow : -0.29 (Kowwin program)
Soil Koc : 0.21 (calc by model)

	Concent. (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	2.96	18	1000
Water	49.7	208	1000
Soil	47.3	208	1000
Sediment	0.074	832	0

	Fugacity (atm)	Reaction (percent)	Advection (percent)
Air	4.66e-011	22	5.74
Water	3.69e-012	32.1	9.63
Soil	1.28e-010	30.5	0
Sediment	2.75e-012	0.012	0.000288

Persistence Time: 194 hr
Reaction Time: 229 hr
Advection Time: 1.26e+003 hr
Percent Reacted: 84.6
Percent Advected: 15.4

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 18.04
Water: 208.1
Soil: 208.1
Sediment: 832.3
Biowin est: 3.320 (days-weeks)

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

Reliability : (2) valid with restrictions
26.11.2001 (11)

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, domestic, non-adapted
Concentration : 10 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time : 29 day(s)
Degradation : = 81 (±) % after 29 day(s)
Result : readily biodegradable
Kinetic of testsubst. : 4 day(s) = 28 %
10 day(s) = 56 %
14 day(s) = 66 %
24 day(s) = 80 %
28 day(s) = 80.5 %
Control substance : Benzoic acid, sodium salt
Kinetic : 4 day(s) = 54 %
14 day(s) = 80 %
Deg. product : no
Method : OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 evolution)"
Year : 2000
GLP : yes
Test substance :

Result : Mean cumulative production of carbon dioxide by mixtures containing 1,3-Butylene glycol was equivalent to 10% of the theoretical value after approximately three days of incubation, 60% after 12 days and 81% by the end of the test

on day 29. The biodegradation of sodium benzoate in the presence of the test substance was monitored in order to assess if there was any inhibitory effect on the activity of the microbial inoculum. No inhibitory effects were observed. The test substance is considered readily biodegradable.

Test condition : Activated sludge was obtained from a sewage treatment works that treats primarily domestic waste. It added to the test substance at a final suspended solids concentration of 30 mg/L. Duplicate test substance vessels, one reference substance vessel, and one vessel containing both test substance and reference substance were incubated for 29 days at a temperature between 21.3° C and 23.6° C. Carbon dioxide was collected from the aeration stream (30 to 70 ml/min.) determined and corrected against a blank vessel. Carbon dioxide was sampled on days 2, 4, 6, 8, 10, 12, 14, 19, 24, 28 and 29. The only protocol deviation was that the rate of air-flow through the two vessels on day 5 fell to a minimum of 20 ml/min, which is below the protocol recommended range of 30 to 100 ml/min. This is not considered to have affected the integrity of the study.
.

Test substance : 1,3-Butylene glycol 99.5 wt % min

Conclusion : The test substance is considered readily biodegradable.

Reliability : (1) valid without restriction

30.10.2001 (12)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other: Estimate
Species	:	other
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 9494 calculated
Method	:	other: calculated
Year	:	2002
GLP	:	
Test substance	:	

Method :

The fish LC50 value was estimated using the V0.99 ECOSAR Classes program found in EPIWIN version 3.05. The following equation for neutral organics was used for the calculation:

Log LC50 = -0.94 log Kow + 1.75

The LC50 is in millimoles per liter (mM/L); and the equation is based on the fish toxicity of known neutral organic compounds (N = 60 with the Coefficient of Determination (R2) = 0.942.)

The log Kow was estimated to be -0.29 using the KOWWIN (ver 1.66) program found in EPIWIN version 3.05.

This equation is considered appropriate for uncharged alcohols with log Kow vlaues less than 5.

Remark :

The ECOSAR prediction for green algae EC50 was found to be in accord with the experimental value. This supports the use of ECOSAR for 1,3-butanediol
Estimates using a reliable method are assigned a reliability of 2. In this case, since the estimated LD50 is high, and similar alcohols have fish LC50 in this same range the confidence that the LC50 is large (i.e above 100 mg/L) is high.

Conclusion : The 96 hour LC50 of 1,3-Butylene glycol for freshwater fish is estimated to be approximately 9,500 mg/L. This material is considered to present little hazard to fish.

Reliability : (2) valid with restrictions
06.07.2003 (9)

Type	:	semistatic
Species	:	Oryzias latipes (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	
LC50	:	> 100 measured/nominal
Limit test	:	yes
Analytical monitoring	:	yes
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1992
GLP	:	yes
Test substance	:	other TS

Method	:	OECD TG 203 (1992) was listed as the guideline followed. Groups of ten Medaka were placed to nominal concentration of 100 mg/l and dechlorinated tap water as control. The LC50 (96h) was over 100 mg/l. Measured concentrations at the start of exposure and after 48 h when test water was renewed were 85.6 and 99.9% of the nominal concentration, respectively.
Result	:	LC50 > 100 mg/L
Test substance	:	1,4-Butanediol CASNO 110-63-4, purity >98%
Reliability	:	(2) valid with restrictions Assigned 2 as original report not available for review

06.07.2003 (10)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	other
Species	:	other
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 8684 calculated
Method	:	other: calculated
Year	:	2002
GLP	:	
Test substance	:	

Method	:	The daphnia LC50 value was estimated using the V0.99 ECOSAR Classes program found in EPIWIN version 3.05. The following equation for neutral organics was used for the calculation: Log LC50 = 1.72 - 0.91 log Kow The LC50 is in millimoles per liter (mM/L); and the equation is based on the daphnia toxicity of known neutral organic compounds (N = 19 with the Coefficient of Determination (R2) = 0.992.) The log Kow was estimated to be -0.29 using the KOWWIN (ver 1.66) program found in EPIWIN version 3.05. This equation is considered appropriate for uncharged alcohols with log Kow values less than 5.
Remark	:	The ECOSAR prediction for green algae EC50 was found to be in accord with the experimental value. This supports the use of ECOSAR for 1,3-butanediol Estimates using a reliable method are assigned a reliability of 2. In this case, since the estimated ED50 is high, and similar alcohols have daphnia EC50s in this same range the confidence that the EC50 is large (i.e above 100 mg/L) is high.
Conclusion	:	The 48-hour LC50 of 1,3-Butylene glycol for daphnia is estimated to be approximately 8,700 mg/L. This material is considered to present little hazard to aquatic invertebrates.
Reliability	:	(2) valid with restrictions

06.07.2003 (9)

Type	:	semistatic
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	> 1000 measured/nominal
Limit Test	:	yes
Analytical monitoring	:	yes
Method	:	OECD Guide-line 202
Year	:	
GLP	:	yes
Test substance	:	other TS
Method	:	20 daphnids (4 replicates of 5 test organisms) were exposed to nominal concentration of 1000 mg/l. M4 medium was used for the test. Measured concentration after 48 h was grater than 80% of the nominal concentration.
Result	:	EC50 > 1000 mg/L
Test substance	:	1,4-Butanediol CASNO 110-63-4, purity >98%
Reliability	:	(2) valid with restrictions Assigned 2 as original report not available for review

06.07.2003 (10)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	> 1070 measured/nominal
EC50	:	> 1070 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2000
GLP	:	yes
Test substance	:	
Method	:	The study was conducted in accordance with EC Methods for Determination of Ecotoxicity Annex to Directive 92/69/EEC (O.J. No. L383A, 29.12.92) Part C, Method 3 "Algal Inhibition Test" and the OECD Guideline for Testing of Chemicals No. 201 "Alga, Growth Inhibition Test". CULTURE MEDIUM: Sterile algal nutrient medium as recommended in Official Journal No. L383A Part C.3 and OECD Procedure 201 (Appendix 1 PREPARATION OF TEST SUBSTANCE DILUTIONS: A concentrated, aqueous stock was prepared at a nominal concentration of 10 g/L by adding the test substance (1 g) to a volumetric flask (100 ml) and making up to volume with sterile culture medium. An aliquot (10 ml) of this stock was added to each vessel containing inoculated culture medium.

ANALYTICAL DETERMINATIONS:
The test concentration was measured using a GLC method of analysis. At the start of the definitive test, four samples (20 ml) were taken from additional flasks containing the freshly-prepared control and test medium; after 72 hours, the contents of the replicate flasks for each group were pooled and further samples were taken for analysis. Additional samples were also taken from flasks containing 1,3-Butylene glycol at 1000 mg/l but with no algal cells, in order to obtain information on the extent of adsorption/absorption of the test substance by the algal cells. On each occasion, two of the samples were analyzed immediately and the others were stored in a refrigerator in case further analysis was required.

TEST CONDITIONS
Test vessels (250 ml conical flasks), each containing algal medium (50 ml), were loosely stoppered with cotton wool, covered with aluminium foil which was secured by autoclave tape and sterilised by autoclaving. Following the addition of algal inoculum (40 ml) and the test substance (as a 10 ml aliquot of an aqueous stock), the initial cell density in each flask was approximately 1,000,000 cells/ml.Each flask was then loosely plugged with non-absorbent cotton wool. The cultures were incubated, without renewal of medium, for 72 hours under continuous illumination of approximately 9140 lux provided by 5 x 30 W "cool white" 1 meter fluorescent tubes. The temperature was maintained at 23 ± 2°C.

Samples were taken from control and test flasks at 24, 48 and 72 hours and the cell densities measured using a haemacytometer. The estimate of cell numbers in each sample was based on the mean of four or eight consecutive counts depending on the cell density of the cultures.

Remark : No significant deviations from the protocol occurred.

Result :

The intended level of 1,3-Butylene glycol in unfiltered samples of the test culture was adequately achieved and maintained. Mean measured concentrations ranged from 1.06 g/L at the start of the test to 1.08 g/L after 72 hours. The overall mean measured level of 1,3-Butylene glycol was 1.07 g/L.

After 72 hours, analysis of an unfiltered sample of medium containing 1,3-Butylene glycol which had been incubated without algal cells gave similar results to test medium incubated in the presence of algal cells; this indicates that the presence of algal cells had not affected the stability of 1,3-Butylene glycol under the test conditions.

Individual cell densities for each culture and the mean values are given in the table below.

Measured conc. (mg/L)	Replicate number	Cell Density (1000s) 24-hr	48-hr	72-hr
N.D.	R1	10.8	86.9	245
	R2	14.6	75.0	339
	R3	13.9	86.6	351
	R4	11.1	78.8	393
	R5	10.5	84.3	323
	R7	14.0	85.3	306
Mean		12.5	82.8	326
1070	R1	12.1	86.5	312
1070	R2	11.6	99.1	408
1070	R3	12.1	95.5	416
1070	R4	10.4	104	344
1070	R5	10.5	87.0	340
1070	R6	12.5	101	344
Mean		11.5	95.5	361

N.D = not detected, these were controls

Test substance : 1,3-Butylene glycol
CASNO 107-88-0
Purity 99.8%

Conclusion : 1,3-Butylene glycol was not inhibitory to the growth of Selenastrum capricornutum cultures when dissolved in algal nutrient medium at a mean measured level of 1070 mg/L.
The 72-hour median effect concentrations for inhibition of growth were not identified but must be greater than 1070 mg/L.
The no-observed effect concentration (NOEL) for inhibition of growth was > 1070 mg/l

Reliability : (1) valid without restriction
16.12.2002 (1)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 22800 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: no data
Year	:	1951
GLP	:	no
Test substance	:	no data
Method	:	Single-dose administration to non-fasted animals. Animals were observed for 14 days after dosing. Group size not specified in publication. Method may be provided in a references paper. LD50 determined by the method of Thompson using +- 1.96 standard deviations as the limits.
Result	:	The oral single-dose LD50 for non-fasted rats was determined to be 22.8 g/kg, with a range (plus or minus 1.96 standard deviations) of 21.8 to 23.9 g/kg.
Test substance	:	1,3-Butylene glycol (CASNO 107-88-0)
Reliability	:	(2) valid with restrictions Reliability 2, although few details were given the investigator's work is considered reliable.
Flag	:	Critical study for SIDS endpoint

06.11.2002 (47)

Type	:	LD50
Value	:	= 18610 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: no data
Year	:	1941
GLP	:	no data
Test substance	:	no data
Test substance	:	1,3-Butylene glycol (CASNO 107-88-0)
Reliability	:	(4) not assignable Considered 4 since taken from secondary literature

07.11.2002 (46)

Type	:	LD50
Value	:	= 12980 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	

Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: no data
Year	:	1956
GLP	:	no data
Test substance	:	no data

Test substance	:	1,3-Butylene glycol (CASNO 107-88-0)
Reliability	:	(4) not assignable Considered 4 since taken from secondary literature

07.11.2002 (54)

Type	:	LD50
Value	:	= 11500 mg/kg bw
Species	:	guinea pig
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: no data
Year	:	1941
GLP	:	no data
Test substance	:	no data

Test substance	:	1,3-Butylene glycol (CASNO 107-88-0)
Reliability	:	(4) not assignable Considered 4 since taken from secondary literature

07.11.2002 (48)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	other: Inhalation Hazard Test
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	8 hour(s)
Method	:	other: no data
Year	:	1951
GLP	:	no
Test substance	:	no data

Remark	:	Based on a vapor pressure of 0.08 hPa, the saturated vapor concentration is in the range of 60 ppm.
Result	:	No deaths from exposure to saturated vapor for 8 hours (concentration not specified).
Test substance	:	1,3-Butylene glycol (CASNO 107-88-0)
Reliability	:	(2) valid with restrictions Reliability 2, although few details were given the investigator's work is considered reliable.

06.11.2002 (47)

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	LD50
Value	:	= 10000 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other: no data
Year	:	1966
GLP	:	no data
Test substance	:	no data

Source : Hoechst Celanese NV Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.11.2001 (42)

Type	:	LD50
Value	:	= 11000 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other: no data
Year	:	1979
GLP	:	no data
Test substance	:	no data

Source : Hoechst Celanese NV Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.11.2001 (23)

Type	:	LD50
Value	:	= 20000 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	s.c.
Exposure time	:	
Method	:	other: no data

Year	:	1949
GLP	:	no data
Test substance	:	no data
Source	:	Hoechst Celanese NV Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.11.2001		(14)
Type	:	LD50
Value	:	= 9000 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	other: no data
Year	:	1980
GLP	:	no data
Test substance	:	no data
Source	:	Hoechst Celanese NV Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.11.2001		(25)

5.4 REPEATED DOSE TOXICITY

Type	:	Chronic
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	2 years
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	1.0, 3.0 10.0%
Control group	:	yes, concurrent no treatment
NOAEL	:	= 10 - 0 %
Method	:	other: no data
Year	:	1967
GLP	:	no data
Test substance	:	other TS: purity: 99.98%

Method :

Dosing was conducted by incorporating test material into food at 1, 3 or 10% by weight

Animals were weanling Sprague-Dawley rats

Dose group size was 30 animals of each sex

Control group size was 60 animals of each sex

Body weights were reported for animals at 0, 4, 20 and 52

weeks. Other body weights were not included in the publication.

Blood samples taken from representative animals in each group at six intervals during the study. Tests run were CBC, hematocrit and hemoglobin.

Pooled urine samples were taken from representative animals in each group at six intervals during the study. Tests run were specific gravity, pH, protein, sugar, acetone, urobilinogen and occult blood.

After one year, ten animals from each group were sacrificed and necropsied. Representative organ weights were recorded (data for liver, kidney, adrenal, thyroid and testes are given in the report from animals surviving for 2 years) and 17 organs were submitted for histopathologic evaluation. At the end of two years the same procedure was followed with all surviving animals

Remark : Feed consumption data not given in publication; however, as the body weight gains for all dosed groups were similar to controls, this is not considered a major deficiency.

Result :

Mortality, body weight gain, blood parameters, urine parameters, organ weights, incidence of neoplasm, and organ histopathology were unaffected by the two-year treatment
Mean Body Weights at 52 weeks were:
\\controls, 1%, 3% and 10%,
Males \\565g, 560g, 551g, 578g
Females \\347g, 320g, 347g, 370g

Reliability : (2) valid with restrictions
Study conducted prior to GLP implementation. Publication has adequate details for assessment of quality.

Flag : Critical study for SIDS endpoint

06.11.2002 (38)

Type : Chronic
Species : dog
Sex : male/female
Strain : Beagle
Route of admin. : oral feed
Exposure period : 2 years
Frequency of treatm. : daily
Post exposure period : none
Doses : 0.5, 1.0, 3.0%
Control group : yes, concurrent no treatment
NOAEL : = 3 - 0 %
Method : other: no data
Year : 1967
GLP : no data
Test substance : other TS: purity: 99.98%

Method :

Dosing was conducted by incorporating test material into food at 0.5, 1, or 3% by weight

Animals were 6-16 month old purebred beagles

Dose group size was 4 animals of each sex

Control group size was 4 animals of each sex

Body weights were reported for animals at 0, 4, 20 and 104 weeks. Other body weights were not included in the publication.

Blood samples taken from representative animals in each group at eight intervals during the study. Tests run were CBC, hematocrit, hemoglobin, sedimentation rate, BUN and bromosulphalein retention.

Pooled urine samples were taken from representative animals in each group at eight intervals during the study. Tests run were specific gravity, pH, protein, sugar, acetone, urobilinogen and occult blood.

After one year, two animals of each sex from each group were sacrificed and necropsied. Representative organ weights were recorded (data for liver, kidney, adrenal, thyroid and testes are given in the report from animals surviving for 2 years) and 19 organs were submitted for histopathologic evaluation.

Mortality, body weight gain, blood parameters, urine parameters, organ weights, incidence of neoplasm, and organ histopathology were unaffected by the two-year treatment

Result :

Mortality, body weight gain, blood parameters, urine parameters, organ weights, incidence of neoplasm, and organ histopathology were unaffected by the two-year treatment

Reliability : (2) valid with restrictions

Study conducted prior to GLP implementation. Publication has adequate details for assessment of quality

06.11.2002 (40)

Type : Sub-chronic
Species : dog
Sex : male/female
Strain : Beagle
Route of admin. : oral feed
Exposure period : 13-weeks
Frequency of treatm. : daily
Post exposure period :
Doses : 0, 3000, 6000, 9000 and 12000 mg/kg-day
Control group : yes, concurrent no treatment
NOAEL : = 6000 mg/kg
LOAEL : = 9000 mg/kg
Method :
Year : 1978
GLP : no data
Test substance :

Method : The test substance was thoroughly mixed into a basal diet at levels

providing an intake of 0, 3, 6, 9 or 12 g/kg body weight/ day. The diets were supplemented with an instant wheat product, glucose and soya bean oil in such a way that all diets were theoretically isocaloric. The diets were freshly prepared once a week and stored in closed containers at a temperature of 10-150C. The dogs were fed a restricted portion of food twice daily. The amount of food/kg body weight/day was either 50 or 40 g on different days, but was equal for the different dogs on one day.

The study was initiated with 20 male and 20 female purebred beagle dogs, about 7-8 weeks old. They were obtained from the colony maintained at the Central Institute for the Breeding of Laboratory Animals, CPB-TNO, Zeist, The Netherlands. The animals were divided into 5 groups (one control and 4 test groups) of four males and four females each, and individually housed in indoor kennels.

Conduct of the experiment:
Behavior and health of all dogs were checked daily.. Individual body weights were measured weekly. Individual food consumption was measured daily. Haematological investigations were carried out at the beginning and at weeks 2, 6 and 12 in all dogs. All blood samples were examined for: hemoglobin content, packed cell volume, methemoglobin content, erythrocyte fragility, erythrocytes count, leukocyte count, platelet count, differential white blood cell count, reticulocyte count and Heinz bodies.

Blood clinical chemistry parameters were SGPT, SAP, total serum protein, serum albumin, fasting blood glucose, blood urea-N, triglycerides, B-hydroxybutryric acid, acetoacetic acid. plasma free fatty acids and lactate. Urine analyses, including appearance, specific gravity, pH, sugar, protein, occult blood, ketones and microscopic examination of the sediment were conducted upon all dogs at the beginning and at week 6 and 12. A liver-function test (bromosulphophthalein method) was carried out upon all dogs of the control and highest dose group at week 13. A kidney-function test (phenolred excretion method) was conducted upon all dogs of the control and highest dose group at week 13.

After 13 weeks, all surviving dogs were anaesthetized by intravenous administration of Nembutal followed by exsanguinations. A thorough necropsy was performed on each animal immediately after death. The following organs were weighed: heart, kidneys, liver, spleen, lungs, testicles/ovaries, pituitary, thyroids, adrenals and brain. Samples of these organs together with a wide range of other organs and tissues were fixed. Detailed microscopic examination was done on all dogs. H and E stained paraffin sections of the organs weighed and also of the following organs and tissues were examined: spinal cord, sciatic nerve, salivary glands, skeletal muscle, thoracic aorta, skin, tonsils, bladder, esophagus, stomach, duodenum, jejunum, ileum, caecum, colon, pancreas, trachea, circumanal glands, eyes, epididymis, prostate, uterus, gall bladder, tongue and thymus.

Remark : Although the seizures were apparently dose related they may have been secondary to metabolic alterations (e.g. reduced blood glucose levels) affecting CNS function in this colony of dogs with a predisposition to idiopathic epilepsy.

Result : Reduction in body weight gain was observed at 9,000 and 12,000 mg/kg-day and was accompanied by organ weight, blood biochemistry, hematology, and behavioral changes. The treatment-related hematological changes were restricted to increases in platelet counts in the top two doses

and an increased level of methemoglobin at only the high dose level. Biochemistry changes consisted of an increase in SGPT at the two highest doses, increased SGOT in the top dose group at 6-weeks but not at 13 weeks, and a dose-related increase in free fatty acids that was statistically significant only at the high dose. Blood levels of free fatty acids, G-hydroxy butyric acid, acetoacetic acid and lactate increased with increasing feeding levels of BD. The excretion of phenol-red and bromosulphophthalein did not indicate impaired function of the liver or kidneys. Slight ketonuria was observed in dogs of the top-dose group at week 12. Small quantities of BD were recovered from feces of dogs fed 9 or 12 g BD/kg body weight/day.

Relative organ weights of liver, kidney, brain, adrenals and lung were increased and relative weights of thymus and spleen were decreased at the top dose. At 9,000 mg/kg-day liver and kidney weights were increased. There were no pathological findings correlating with this upon either gross or microscopic examination.

The most striking behavioral effect was epileptic-like seizures starting in the third week of the study in a high-dose animal. After the initial seizure the number of dogs with seizures and the frequency of seizures increased with time affecting both males and females of the two highest-dose groups. Idiopathic epilepsy is known to occur in the colony of dogs used in this study; however, the seizures were dose-related. The 6000 mg/kg level was a NOAEL.

Test substance : 1,3-Butylene glycol 99.5 wt % min
Reliability : (1) valid without restriction
Well documented study

12.11.2002 (52)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Bacterial reverse mutation assay
System of testing :
Test concentration : 0, 313, 625, 1250 and 5000 mcg/plate, for both + and - S9
Cycotoxic concentr. : Greater than 5000 mcg/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year :
GLP : no data
Test substance : other TS

Method : OECD 471 and OECD 472
Remark : Bacterial strains used were S. typhimurium TA100, TA98, TA1535, TA1537 and E coli WP2 uvrA.
S9 was produced from rat liver induced with phenobarbital and 5,6-benzoflavone.
Toxicity to bacteria was not observed at 5000 mcg/plate in all five strains with or without a S9 mix.
Result : Negative
Test substance : 1,4-Butanediol (Isomer of 1,3-butanediol, purity 98.0%)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
06.11.2002 (3)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Cytogenetic assay
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	13 weeks or longer
Doses	:	5, 10, 24%
Result	:	negative
Method	:	other: no data
Year	:	1981
GLP	:	no data
Test substance	:	
Method	:	This in vivo cytogenetics test utilized FIA, F2A and F3A animals from a concurrent multigenerational study. At least two rats per sex per group, continuously dosed with test substance at 0, 5, 10 or 24% by weight in the diet (semi-purified diet), were examined for cytogenetic analysis. Animals were sacrificed (presumabley at the terminal sacrifice (F1A at 77 weeks post gestational exposure, F2A at 11 weeks post gestational exposure and F3A at 9 weeks post gestational exposure) and bone marrow (femur) preparations were examined cytologically for treatment related aberrations in the chromosomal patterns. The selected rats were injected intraperitoneally with colchicine (1 mg/kg), 3-4 hours prior to sacrifice. Following dissection, the marrow was washed with 5 ml of Hank's balanced salts solution. The cells were centrifuged, washed repeatedly with fresh Hank's solution. The cells were then suspended in 6 ml of hypotonic fetal calf serum and incubated at 37 C for 20 minutes. The cells were fixed in a 3:1 mixture of methanol-glacial acetic acid at 4 C, overnight, before being coated on coverslips and stained with 2% aceto-orcein. The preparations were examined by phase-contrast microscopy at 900x magnification for aberrant chromosomes. One hundred to 250 metaphase cells were examined per group
Remark	:	at least 2 animals/sex/group from the F1A, F2A and F3A generations of a reproduction study were examined.
Result	:	The frequency of occurrence of abnormal cells was found to be within the normal range for the F1A, F2A and F3A animals in this multigenerational study. No specific abnormalities were consistently observed in any dosed group and no dose-related effects were noted.
Test substance	:	1,3-Butylene glycol (CASNO 107-88-0) obtained from the Celanese Chemical Corporation. Purity not specified
Reliability	:	(2) valid with restrictions

10.07.2003 (16)

Type	:	Dominant lethal assay
Species	:	rat
Sex	:	male

Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	13 weeks
Doses	:	5, 10, 24%
Result	:	
Method	:	other: no data
Year	:	1981
GLP	:	no data
Test substance	:	

Method :

This dominant lethal test utilized F1B male animals from a concurrent multigenerational study. Ten males per group were reared to maturity while being continuously dosed with test substance at 0, 5, 10 or 24% by weight in the diet (semi-purified diet). The sires and dams producing these males were dosed at the same levels throughout mating, gestation and lactation. Each male was housed individually in a mating cage and two virgin 100-day old untreated females were introduced and permitted to remain with a male for 7 days, this was repeated each week for eight consecutive weeks. After removal from the mating cage, each female was individually housed for an additional 7 days and then sacrificed for examination of the reproductive tract. The numbers of implant and/or resorption sites and viable and dead fetuses were recorded. These data were used to calculate the mutagenic index according to the method of Epstein and Shafner

Remark : Conducted as part of reproduction study; 10 mature F1B males per group were mated to virgin females each week for 8 consecutive weeks.

Study protocol was basically in accord with OECD 478. Slightly fewer males were treated and mated than recommended but the top dose level was higher than recommended, more total females were examined and the duration of dosing was longer than recommended. Overall, this appears to be a robust and well conducted study.

Result : All males in the dose groups sired litters. The percentage of pregnancies as well as the percentage of viable fetuses per implant site were not significantly different between treatment and control groups. The mutagenic index (resorptions as a percentage of implant sites) showed no trend with increasing dose of test substance in the diet.

Mutagenic Index

Dose	Average over 8 weeks
0%	5.5 (1101 viable fetuses)
5%	6.1 (962 viable fetuses)
10%	4.3 (1389 viable fetuses)
24%	3.2 (1269 viable fetuses)

Conclusion : Material is negative in this genotoxicity assay
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.11.2002 (18)

5.7 CARCINOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	2 years
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	1.0, 3.0, 10.0%
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	other TS: purity: 99.98%
Remark	:	30 animals/sex/dose group; 60 animals/sex/control group
Result	:	No increase in tumor incidence compared to the control.
Source	:	Hoechst Celanese NV Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

31.05.1995 (39)

5.8.1 TOXICITY TO FERTILITY

Type	:	other: five generation study
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	See Remarks below
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	Forr weeks before mating for F1a litter, 11 weeks before F1b
Female	:	Forr weeks before mating for F1a litter, 11 weeks before F1b
Duration of test	:	
No. of generation studies	:	5
Doses	:	5, 10, 24%
Control group	:	yes, concurrent no treatment
NOAEL parental	:	= 24 %
NOAEL F1 offspring	:	= 24 %
NOAEL F2 offspring	:	= 24 %
Method	:	other: no data
Year	:	1981
GLP	:	no data
Test substance	:	no data

Method : All generations: 25 male and 25 female animals/group. Test substance was substituted for equal ammounts by weight of corn starch and dextrose.

Five successive mating cycles were achieved with the F1A rats over a period of 77 weeks. The F2A litter was mated to produce the F3A and F3B litters, while the F2B, F2C, F2D and F2E litters were examined and sacrificed as part of the longevity phase of the study.

The mated F2A litters became the parents of the F3A and F3B litters. The F3A litter was used for the cytogenetic portion of the study and was mated to product the F4A and F4B litters, which are indicated by the chart in the original paper to be part of the cytogenetics study.

The pregnant dams (feom the F2A litters) producing the F3B litters were divided and 1/4 were allowed to give birth normally and 3/4 were used for the teratological examination on day 19 of gestation.

Statistical comparisons were made using the approximate chi-square test (as described by Bross, Fed Proc 34:2182-2185, 1975).

Reproductive indices were calculated for each series of litters.

For F1A rats, which survived at least 66 weeks, the gonads and pituitary glands were examined microscopically; however, the extend of this examination was not provided in the paper.

Result : Reproduction and lactation parameters were comparative to controls for four of five generations of dams and pups. The pregnancy rate of F1A rats decreased during five successive mating cycles. Excluding this group, the viability of F2 generation pups revealed no significant differences between litters or between control and test groups. No reason for the decrease in fertility index in the fifth generation was determined; however, controls were also affected but to a lesser degee.

Fertility Index: (percent)

	Generation				
	F2A	F2B	F2C	F2D	F2E
Control	72	44	64	60	40
5%	80	44	76	60	16
10%	92	64	68	40	20
24%	76	52	44	28	00

Mean Body Weight Pups at Birth: (grams)

	Generation				
	F2A	F2B	F2C	F2D	F2E
Control	10.0	10.0	10.9	10.4	11.1
5%	9.6	10.5	10.5	10.6	13.0
10%	9.3	10.6	10.0	10.5	11.0
24%	10.6	10.4	11.0	11.6	---

No significant treatment-related effects were noted on examination of testes, ovaries, or pituitary glands.

Test substance : 1,3-Butylene glycol (CASNO 107-88-0) obtained from Celanese Chemical Company, NY. Purity not specified.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

14.07.2003 (18)

Type	:	other: three generation study
Species	:	rat
Sex	:	male/female
Strain	:	no data
Route of admin.	:	oral feed
Exposure period	:	no data
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	20%
Control group	:	no data specified
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	no data

Result : No effect on fertility, litter size or number of live offspring, despite reduced weight gain in the parents of each generation.

06.11.2002 (8)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Long-Evans
Route of admin.	:	gavage
Exposure period	:	Day 6 to Day 15 gestation
Frequency of treatm.	:	daily
Duration of test	:	
Doses	:	706, 4236, 7060 mg/kg
Control group	:	yes, concurrent no treatment
NOAEL maternal tox.	:	= 7060 mg/kg bw
NOAEL teratogen.	:	= 7060 mg/kg bw
LOAEL Fetotoxicity	:	= 7060 mg/kg bw
NOAEL Fetotoxicity	:	= 4263 mg/kg bw
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	

Method :

Long-Evans rats (200-300 g), obtained from Blue Spruce Farms in Altamont, NY were mated to produce presumed-pregnant dams defined by the presence of sperm in the vaginal smear that was defined as day 0 of gestation. Presumed-pregnant dams were divided into four groups of 10 assigning animals to equalize bodyweights among groups.

Test material was administered daily by gavage, in water vehicle, from day 6 to day 15 of gestation, based on current bodyweights. The exposure levels were chosen as fractional doses (24, 14.4, and 2.4%) of the acute

LD50 value for the test substance. The exposure period was, the so-called critical period of organogenesis. Dose levels were 0, 706, 4236 or 7060 mg/kg-day. Animals were observed daily for mortality or for signs of intoxication (lethargy, ataxia, activity in response to a light cage tap). Food consumption was monitored by daily visual inspection of ground diet (Wayne Lab Blox) remaining in calibrated metal feed cups. All dams were overdosed with ether on day 20 of gestation, and fetuses were delivered by caesarean section. At necropsy on gestation day 20, total uterine weight, total litter weight, individual pup weights, crown-rump length, number of live pups, stillbirths and resorptions, implantation sites, sex distribution, and number of corpora lutea were recorded for each pregnancy.

All live pups were examined for gross malformations at birth. Soft tissue (internal) defects were evaluated by free-hand slicing and skeletal and cartilaginous variations were detected by alizarin red-S and alcian blue staining. Subjective fetal anomalies were judged as representing a marked deviation from normality according to standard criterion score sheets by blind observers. Live pups were classified according to contiguity with offspring of the same or opposite sex and analyses were conduced with reference to the treatment group and fetal subtype for bodyweight.

Remark : STATISTICAL METHOD: All data generated in the course of the study were entered, archived, and statistically analyzed on pc. Statistical analyses of the data were performed using an interactive, disc-based software package (Crunch Interactive software, version 83.1, Crunch Software, Inc.), using the litter as the experimental unit. Parametric analysis of variance and Newman-Keuls posthoc analyses were used to compare maternal bodyweights, uterine weights, litter weights, pup weights, crown-rump lengths, corpora lutes, implantations, percent of males per litter, intrauterine deaths per litter, malformed pups per litter, and pup bodyweights by contiguity classification on an absolute and relative (percent of control) basis. Contingency table analyses (Chisquare and Fisher exact test) were applied to litters bearing malformed pups. Linear regression analysis of butanediol dose against pup bodyweight was performed.

Result :

Reproductive Parameters

	Control	High	Mid	Low
Pregnant	10	8	9	8
Gestation weight gain (%)	50	54	47	50
Dam weight gain (%)	25	28	23	25
Total litter weight(g)	39	38	36	44
Avg pup weight (g)	3.5	3.1	3.3	3.5
Avg pup size (crown-rump length, cm)	3.5	3.5	3.5	3.6
Corpora lutea/dam	11.6	12.1	11.2	11.9
Implants/dam	11.8	14.5	12.4	12.4
Litter size	11.2	11.9	10.9	12.0
Percent males/litter	36.3	44.8	56.0	41.7
In utero deaths/dam	0.6	2.6	1.6	1.9
Malformed pups/dam	1.6	3.0	2.7	2.1
Litters with malformed	7	6	7	5

The investigators reported: Maternal exposure to high doses of 1,3-butancdiol, during organogeneeis was associated with a significant

decrease in offspring birthweights only at the highest (7060 mg/kg) dose. This birthweight depression selectively affected high-dose male offspring not contiguous in utero to a female sibling. Other pups were not significantly affected by 7060 mg/kg of butancdiol.

"These findings indicate that in utero levels of sex steroids modulate the expression of earlier fetal damage at parturition by inhibiting (testosterone) or enhancing (estradiol) cellular repair by a mechanism as yet undefined. From these data it is concluded that intrauterine position with respect to contiguous siblings is an important factor in the expression of developmental toxicity at parturition."
Not teratogenic; fetotoxicity was evidenced by a dose-dependent decrease in offspring birthweights. Maternal sedation noted at mid and high doses. No maternal mortality was observed. No maternal necropsy data was presented other than gestation weight gain, dam weight gain, coprea leuta, and total litter weights; none of these parameters was different from control values.

Test substance : 1,3-Butylene glycol (CASNO 107-88-0), Reagent Grade, 98%
Reliability : (2) valid with restrictions
Published article, good details
Flag : Critical study for SIDS endpoint
11.07.2003 (31)

Species : rat
Sex : female
Strain : Wistar
Route of admin. : oral feed
Exposure period : day 0 to day 19 of gestation
Frequency of treatm. : daily
Duration of test :
Doses : 5, 10, 24%
Control group : yes, concurrent no treatment
NOAEL maternal tox. : %
NOAEL teratogen. : = 24 %
NOAEL Fetotoxicity : = 5 %
Method : other: no data
Year :
GLP : no data
Test substance : no data

Remark : 14-15 animals/group
Result :

Incidence of fetal skeletal abnormalities in F3B generation rats

Dietary level(%)	0	5	10	24
Fetuses exam	124	103	120	103
Sternebrae				
Incomplete ossif'	31	31	48*	65*
Scrambled	1	0	0	0
Bipartite	1	1	0	3
Extra	1	0	0	0
Missing	10	3	13	31*
Ribs				
More then 13	4	4	1	1

Vertebra				
Incomplete ossif'	4	1	1	2
Scoliosis	1	0	0	0
Skull				
Incomplete closure	9	0	3	10
Hyoid bone				
Missing	2	0	0	2
Reduced	0	0	0	1

Maternal toxicity parameters were not reported for the developmental toxicity portion of the study. Examination of body-weight data reported for the other generations suggests that the high dose does not significantly affect body-weigh gain in non-pregnant females. High-dose males gained less body weight.

Other investigators have shown metabolic disturbances in rats fed levels of 1,3-butanediol in the range of the mid-dose level of this developmental toxicity study. For example, Rosmos et al. (Federation Proc 34: 2186, 1975) reported that rats fed 17-19% of their carbohydrate requirement as 1,3-butanediol has significantly decreased synthesis of free fatty acids in the liver and increased blood levels of beta-hydroxybutyrate (48%), acetoacetate (24%), plasma glucose (89%) and plasma triglycerides (65%). As these significant metabolic effects appear to occur at dose levels in the same range as the mid-dose of this developmental study and, as it is not known how this altered maternal metabolic profiles affects the conceptus, it is possible that the developmental delays (reduced ossification) are a direct result of the altered nutrient supply and not a direct effect of the test substance.

For the above reasons, and because only limited fetotoxicity occurred at these extraordinary high dose levels, this material is not considered a specific developmental toxin.

Resorption and implantation data for F3B generation rats

Diet Level	Number Preg			Implants #/dam	Resorp #/dam	Pup Wt (g)
	Female	# pups/liter				
		Viable	Non-V			
0	15	11.9	0	12.5	0.6	3.5
5	15	10.1	0	10.4	0.3	4.0
10	14	12.1	0	12.6	0.5	4.1
24	14	10.9	0	11.4	0.5	3-4

Conducted as part of reproduction study; no definitive dose-related teratological findings in either soft or skeletal tissue. Fetotoxicity(e.g., delayed ossification of sternebrae) noted at 10% and 24% doses.

Reliability : (2) valid with restrictions
Published article, good details

06.11.2002 (17)

(1) 1,3-Butylene glycol, Algal Growth Inhibition Assay. Huntingdon Life Sciences Ltd, Eye, Suffolk England. Report CSD030/994948 Issued 24 Feb 2000.

(2) APOWIN 1.90 program from Syracuse Research Corp, Syracuse NY

(3) As cited in the SIDS Initial Assessment Profile, CAS No 110-63-4, 1,4-Butanediol. Original source: Ministry of Health and Welfare, Japan "Toxicity Testing Reports of Environmental Chemicals" 5, 429-442 (1977)

(6) Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989; as cited in HSDB

(8) Dymaza H.A. & Adams P.K. (1969): Fedn Proc. Fedn Am. Socs exp. Biol. 28, p. 303.

(9) ECOSAR v0.99 program as found in EPIWIN 3.05, Syracuse Research Corp, Syracuse NY

(10) Environment Agency of Japan (1996) as cited in the OECD SIDS Document of 2000.

(11) EPIWIN 3.05, Syracuse Research Corp, Syracuse NY

(12) Final report: 1,3-Butylene glycol, Assessment of Ready Biodegradability - Modified Sturm Test. Study CSD 031/994835, Huntingdon Life Sciences Limited, 27 Jan 2000.

(14) Fischer, L. et al. (1949): Z. ges. exp. Med. 115, p. 22.

(16) Hess F.G. Jr et al. (1981): J. Appl. Toxicol. 1, p.202.

(17) Hess F.G. Jr. et al. (1961): J. Appl. Toxicol. 1, p. 202

(18) Hess F.G. Jr. et al. (1981): J. Appl. Toxicol. 1, p. 202.

(21) Hine, J. and Mookerjee, P.K. (1975): J. Org. Chem. 40, p. 292.

(22) Hoechst Cleanese Corpus Christi Technical Center Notebook No. 50991, page 7, May 23, 1995.

(23) Holman, N. W. Jr. et al. (1979): Toxic appl. Pharmac. 49, p. 385.

(24) Kirk-Othmer Encyclopedia of Chemical Technology, Third Edition, Vol II, John Wiley and Sons, New York, 1980, pp. 956 - 962.

(25) Kirsh, J. R. et al. (1980): Stroke 11, p. 506.

(27) Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 14th ed. New York, NY: John Wiley Co., 2001 p177

(28) Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993 185

(29) Lyman W, Reehl, W and Rosenblat, D. Handbook of Chemical Property Estimation Methods. American Chemical Society, Washingotn D.C. 1990, page 7-4

(30) Lyman, W.J. et al. (1990): Handbook of Chemical Property Estimation Methods, American Chemical Society, Washington, D.C., p 15-15 to 15-29.

(31) Mankes R.F. et al. Birthweight Depression in Male Rats Contiguous to Male Siblings in Utero Exposed to High Doses of 1,3-Butanediol During Organogenesis. J. Am. Coll. Toxicol. 5:189 (1986)

(34) Riddick, J.A., W.B. Bunger, Sakano T.K. Techniques of Chemistry 4th ed., Volume II. Organic Solvents. New York, NY: John Wiley and Sons., 1985. 268; as cited in HSDB

(38) Scala R.A. & Paynter O.E. (1967): Toxic. Appl. Pharmac. 10, p. 160

(39) Scala R.A. & Paynter O.E. (1967): Toxic. Appl. Pharmac. 10, p. 160.

(40) Scala R.A. & Paynter O.E. (1967): Toxic. Appl. Pharmac. 10, p.160.

(42) Sprince, H. et al. (1966): Life Sci. 5, p.2041.

(46) Symth H.F. Jr. et al. (1941): J. Ind. Hyg. Toxicol. 23, p. 259

(47) Symth H.F.Jr., CP Carpenter and CS Weil. Range-Finding Toxicity Data: List IV. Archs Industrial Hygiene 4: 119-122 (1951).

(48) Symth, H.F. Jr. et al (1941): J. Ind. Hyg. Toxicol. 23, p.259

(51) Ullman's Encyclopedia of Industrial Chemistry, Fifth Edition, Volume A4, VCH, New York, 1985, p. 461.

(52) Unpublished report of Subchronic Feeding Study with 1,3-Butanediol in Beagle Dogs. Report # R5485 CIVO-TNO. September 1978.

(54) Wenzel, D.G. & Koff G. Y. (1956): H, Am. Pharm. Ass. 45, p.669.

(55) WSKOW v1.40 program from Syracuse Research Corp, Syracuse NY