201-14953B1

I U C L I D

D a t a S e t

New Chemical	ID: 95-32-9
CAS No.	95-32-9
EINECS Name	benzothiazole, 2-(4-morpholinyldithio)-
EINECS No.	202-410-7
Molecular Formula	C11H12N2OS3
Molecular Weight	284.42
Structural Formula	c1ccc2)c2)s1)C3)C3

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Producer Related Part	
Company:	
Creation date:	29-SEP-2000
Substance Related Part	
Company:	
Creation date:	29-SEP-2000
Memo:	Rubber and Plastics Additives (RAPA) HPV Panel
Printing date:	09-OCT-2001
Revision date:	
Date of last Update:	09-OCT-2001
Number of Pages:	22
Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
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 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association) Rubber and Plastic Additives (RAPA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States
Phone: 703-741-5600

28-SEP-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

28-SEP-2001

Type: cooperating company
Name: Ciba Specialty Chemicals Corporation
Country: United States

28-SEP-2001

Type: cooperating company
Name: Crompton Corporation
Country: United States

28-SEP-2001

Type: cooperating company
Name: Flexsys America L.P.
Country: United States

28-SEP-2001

Type: cooperating company
Name: Noveon, Inc
Country: United States

28-SEP-2001

Type: cooperating company
Name: R.T. Vanderbilt Company, Inc.
Country: United States

28-SEP-2001

Type: cooperating company
Name: The Goodyear Tire & Rubber Company
Country: United States

28-SEP-2001

Type: cooperating company
Name: The Lubrizol Corporation
Country: United States

28-SEP-2001

Type: cooperating company
Name: UOP, LLC.
Country: United States

28-SEP-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information

Substance type: organic
Physical status: solid
Purity: 95 % w/w
Source: BFGoodrich Company
18-APR-2001

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms

2-(morpholinodithio)benzoliazole
18-APR-2001

2-benzothiazoyl morpholino disulfide
18-APR-2001

4-morpholinyl-2-benzothiazyl disulfide
18-APR-2001

Accelerator MF
18-APR-2001

Cure-Rite MBDS
18-APR-2001

Morfax
18-APR-2001

morpholino-2-benzothiazolyl disulfide
18-APR-2001

N-morpholinyl-2-benzothiazolyl disulfide
18-APR-2001

N-oxydiethyl-2-benzthiazolsulfenamid
18-APR-2001

Sulfenex MOB
18-APR-2001

Vulcuran 2
18-APR-2001

1.3 Impurities

CAS-No: 102-77-2
EINECS-No: 203-052-4
EINECS-Name: 2-(morpholinothio)benzothiazole
Contents: 1 % w/w
Source: BFGoodrich Company
18-APR-2001

CAS-No: 120-78-5
EINECS-No: 204-424-9
EINECS-Name: di(benzothiazol-2-yl) disulphide
Contents: .1 % w/w
Source: BFGoodrich Company
18-APR-2001

1.4 Additives

CAS-No: 8042-47-5
EINECS-No: 232-455-8
EINECS-Name: White mineral oil (petroleum)
Contents: 2 % w/w
18-APR-2001

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

```
Value:            173.1 degree C
Method:           other: MPBPWIN (v1.31)
  Year:           1999
   GLP:           no
Testsubstance:    other TS: molecular structure
Result:           Melting Point:  343.10 deg C (Adapted Joback Method)
                  Melting Point:  130.59 deg C (Gold and Ogle Method)
                  Mean Melt Pt :  236.85 deg C (Joback; Gold,Ogle Methods)
                    Selected MP:  173.09 deg C (Weighted Value)
Reliability:      (2)  valid with restrictions
                  Accepted calculation method
Flag:             Critical study for SIDS endpoint
28-SEP-2001                                                              (1)
```

2.2 Boiling Point

```
Value:            418.3 degree C
Method:           other: MPBPWIN v1.31 (Adapted Stein and Brown Method)
  Year:           1999
   GLP:           no
Testsubstance:    other TS: molecular structure
Reliability:      (2)  valid with restrictions
                  Accepted calculation method
Flag:             Critical study for SIDS endpoint
28-SEP-2001                                                              (1)
```

2.3 Density

-

2.3.1 Granulometry

-

2.4 Vapour Pressure

```
Value:            .000000116 hPa at 25 degree C
Method:           other (calculated): MPBPWIN v1.31
  Year:           1999
   GLP:           no
Testsubstance:    other TS: molecular structure
Result:           Vapor Pressure Estimations (25 deg C):
                  (Using BP: 418.31 deg C (estimated))
                  (Using MP: 173.09 deg C (estimated))
                  VP:  1.28E-008 mm Hg (Antoine Method)
                  VP:  8.7E-008 mm Hg (Modified Grain Method)
                  VP:  2.11E-007 mm Hg (Mackay Method)
                    Selected VP:  8.7E-008 mm Hg (Modified Grain Method)
Reliability:      (2)  valid with restrictions
                  Accepted calculation method
Flag:             Critical study for SIDS endpoint
```

28-SEP-2001 (1)

2.5 Partition Coefficient

log Pow: 1.59
Method: other (calculated): KOWWIN Program (v1.65)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
28-SEP-2001 (1)

2.6.1 Water Solubility

Value: 657.6 mg/l at 25 degree C
Method: other: (WSKOW v1.36)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Remark: Log Kow used by Water solubility estimates: 1.59

Equation Used to Make Water Sol estimate:
Log S (mol/L) = 0.796 - 0.854 log Kow - 0.00728 MW
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
28-SEP-2001 (1)

2.6.2 Surface Tension
-

2.7 Flash Point
-

2.8 Auto Flammability
-

2.9 Flammability
-

2.10 Explosive Properties
-

2.11 Oxidizing Properties
-

2.12 Additional Remarks
-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .0000000003449482 cm3/(molecule * sec)
Degradation: 50 % after .4 hour(s)
Method: other (calculated): AOP Program (v1.89)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
28-SEP-2001 (1)

3.1.2 Stability in Water

Type: abiotic
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air - water- soil - sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: EPIWIN Level III Fugacity Model
Year: 1999
Result:

	Distribution (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.000176	0.744	1000	2.94e-015
Water	36.6	900	1000	1.43e-016
Soil	63.3	900	1000	4.01e-015
Sediment	0.0926	3.6e+003	0	1.3e-016

Persistence Time: 879 hr
Reaction Time: 1.3e+003 hr

Advection Time: 2.73e+003 hr
Percent Reacted: 67.8
Percent Advected: 32.2

Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
09-OCT-2001 (1)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation

Species: other: calculation
Exposure period:
Concentration:
BCF: 3.37
Elimination:
Method: other: BCF Program (v2.13)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Result: Log Kow (estimated) : 1.59
Log Kow (experimental): not available from database
Log Kow used by BCF estimates: 1.59

Equation Used to Make BCF estimate:
Log BCF = 0.77 log Kow - 0.70

Estimated Log BCF = 0.528 (BCF = 3.369)
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
28-SEP-2001 (1)

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: other: calculated
Species: other: fish
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 512.09
Method: other: (calculated) ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
28-SEP-2001 (1)

Type: other: calculated
Species: other: fish
Exposure period: 14 day
Unit: mg/l Analytical monitoring: no
LC50: 869.073
Method: other: (calculated) ECOSAR v0.99e
Year: GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
28-SEP-2001 (1)

Type: other
Species:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

4.2 Acute Toxicity to Aquatic Invertebrates

Type: other: calculated
Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 533.392
Method: other: (calculated) ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
09-OCT-2001 (1)

Type: other: calculated
Species: Mysidopsis bahia (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50 : 197.9
Method: other: (calculated) ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
28-SEP-2001 (1)

Type:
Species:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

Type: other: calculated
Species: Daphnia magna (Crustacea)
Exposure period: 16 day
Unit: mg/l Analytical monitoring: no
EC50: 22.864
Method: other: (calculated) ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
28-SEP-2001 (1)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: other algae: green algae
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 325.584
Method: other: (calculated) ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Remark: Chronic value = 25.697 mg/l (96 hr)
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
28-SEP-2001 (1)

Species:
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

4.4 Toxicity to Microorganisms e.g. Bacteria
-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species: other: fish
Endpoint:
Exposure period: 30 day
Unit: mg/l Analytical monitoring: no
ChV : 61.751
Method: other: (calculated) ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
28-SEP-2001 (1)

4.5.2 Chronic Toxicity to Aquatic Invertebrates
-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:	other: calculated
Species:	Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint:	
Exposure period:	14 day
Unit:	other: mg/l
LC50:	2340.056
Method:	other: (calculated) ECOSAR v0.99e
Year:	1999 GLP: no
Test substance:	other TS: molecular structure
Reliability:	(2) valid with restrictions Accepted calculation method

28-SEP-2001 (1)

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: other
Species:
Strain:
Sex:
Number of
Animals:
Vehicle:
Value:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

5.1.2 Acute Inhalation Toxicity

-

5.1.3 Acute Dermal Toxicity

Type: other
Species:
Strain:
Sex:
Number of
Animals:
Vehicle:
Value:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

5.1.4 Acute Toxicity, other Routes

-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation
-

5.2.2 Eye Irritation
-

5.3 Sensitization
-

5.4 Repeated Dose Toxicity

Species: Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium, strains TA-1535, TA-1537, TA-98, TA-100
Concentration: 0.1,1.0,10,100,1000 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: GLP: no data
Test substance: other TS: CAS# 95-32-9, purity = 96.1%
Result: Cytotoxicity concentrations:
With metabolic activation = 100 ug/ plate
Without metabolic activation = 100-100 ug/ plate
(based on zero to low number revertants per plate)
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint

28-SEP-2001 (2)

Type: Mammalian cell gene mutation assay
System of testing: Clone I-13 of BALB 3T3 mouse cells
Concentration: 0.01, 0.1, 0.5, 1.0, 2.0 ug/ml
Cytotoxic Conc.: 26.7% survival at 3.91 ug/l; no survivors at 7.81 ug/l
Metabolic activation: without
Result: negative
Method: other: Litton Bionetics Assay Design No. 441
Year: GLP: yes
Test substance: other TS: Morfax
Remark: Cytotoxicity concentration:
80-20% survival over test range.
Precipitation concentration:
slight turbidity noted at 1.0 mg/ml stock solution, but not in lower concentrations obtained by serial dilution; none noted in test concentrations.
Reliability: (2) valid with restrictions
GLP guideline study
Flag: Critical study for SIDS endpoint
28-SEP-2001 (3)

5.6 Genetic Toxicity 'in Vivo'

Type:
Species: Sex:
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

5.7 Carcinogenicity

Species: other Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of
treatment:
Post. obs.
period:
Doses:
Result:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

5.8 Toxicity to Reproduction

Type: other
Species: Sex:
Strain:
Route of admin.:
Exposure Period:
Frequency of
treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

5.9 Developmental Toxicity/Teratogenicity

Species: Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of
treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: See IUCLID documents on CAS #149-30-4 and #120-78-5
09-OCT-2001

5.10 Other Relevant Information
-

5.11 Experience with Human Exposure
-

(1) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(2) The Goodyear Tire & Rubber Company, Laboratory report No. 79-76, Mutagenicity Evaluation of WTR No. 23e, January 25, 1980.

(3) Litton Bionetics, Inc. Project No 20992. January, 1981. submitted to The Goodyear Tire & Rubber Company.

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

103-34-4
4,4'-Dithiodimorpholine

201-14953B1

Molecular Formula: C8-H16-N2-S2O2
Molecular Weight: 236.35

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance: Organic
B. Physical State: White solid
C. Purity: 96-99% Typical for Commercial Products

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1.2 SYNONYMS

Sulfasan® DTDM
Sulfasan® R
Ekaland® DTDM
Vanax® A
Accicure® R
Naugex® SD-1
N,N'-Dithiodimorpholine
N,N'-Dithiomorpholine
DTDM

1.3 IMPURITIES

Morpholine (110-91-8) <0.5%

1.4 ADDITIVES

White Mineral Oil (8042-47-5) 0-2%

2. PHYSICAL-CHEMICAL DATA

*2.1 MELTING POINT

Value:	130°C
Decomposition:	No
Sublimation:	No
Method:	FF83.9-1 Initial and Final Melting Point of Organic Compounds 1996
GLP:	Yes
Remarks:	Instrumental - Capillary Tube Method. Typical range for initial to final melt point determinations is 126-130°C
Reference:	ASTM D-1519 / Flexsys Physical Methods of Analysis
Reliability:	(1) Valid without restriction

*2.2 BOILING POINT

Value:	334.98°C
Pressure:	1013 hPa
Decomposition:	No data
Method:	Estimation, Adapted Stein & Brown Method
GLP:	No
Remarks:	Estimation method based on molecular structure and measured melting point of 130°C and Log P 2.49
Reference:	EPIWIN/MPBPWIN v1.40

†2.3 DENSITY

Type:	Density
Value:	1.36
Temperature:	25°C
Method:	Density of solids by displacement, 1997
GLP:	Yes
Remarks:	Density of solids by displacement in kerosene
Reference:	FF97.8-1 Flexsys Standard Method 1997
Reliability:	(1) Valid without restriction

*2.4 VAPOUR PRESSURE

Value:	0.0000355 hPa
Temperature:	25°C
Method:	calculated; Modified Grain Method
GLP:	No
Remarks:	Calculation method based on molecular structure and measured melting point of 130°C and Log P of 2.49
Reference:	EPIWIN/MPBPWIN v1.40
Reliability:	(2) Valid with restrictions – modelling data

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

Log Pow:	2.49
Temperature:	25°C
Method:	measured HPLC Method for Log P, 1978
GLP:	No data
Test substance:	As prescribed by 1.1-1.4, purity: >96%
Remarks:	Octanol/water partition coefficient of the test compound was measured by preparing 1% and 0.1% solutions in 100 ml of n-octanol. A 50 ml aliquot of the octanol solution and 500 ml purified water were combined in a 1 liter glass bottle with a foil-lined cap and shaken in the dark for 48 hours. The mixture was allowed to stand quiescent for several days. The aqueous phase was centrifuged for 1 hour at 15,000 rpm and analyzed via HPLC. The n-octanol phase was also analyzed via HPLC. The partition coefficient, P, was calculated using the equation P = Co/Cw, where Co and Cw are the concentrations of the test compound in octanol and water, respectively. The Pow was 310 +/- 150, corresponding to a Log Pow between 2.20-2.66
Reference:	Monsanto ES-78-SS-20, December, 1978
Reliability:	(2) Valid with restrictions – lack of method detail

*2.6 WATER SOLUBILITY

A. Solubility

Value:	237 ppm
Temperature:	25°C
Description:	Of low solubility
Method:	Saturated Solution / HPLC Analysis, 1978

GLP:	No data
Test substance:	As prescribed by 1.1-1.4, purity: >96%
Remarks:	The aqueous solubility was determined by adding 1g of the test compound and 500ml purified water to a 1 liter glass bottle with an aluminium foil lined cap. The solution was mixed with a magnetic stirrer for several days to produce a saturated solution. Equilibration was performed in the dark to preclude photodegradation. Stirring was stopped one hour before sampling to permit phase (aqueous/solid) separation. The aqueous phase was centrifuged at 15,000 rpm for one hour to remove any suspended particles and then analyzed via HPLC. Duplicate runs were made after additional stirring to insure a saturated solution. From the HPLC analysis, it was apparent that the test compound was not stable in an air-equilibrated water solution. Degradation products were observed in the chromatogram. The reported solubility is the maximum concentration of the starting material (test compound) in the aqueous phase when a large excess of the test compound was equilibrated with water. In this experiment, the degradation products were not identified.
Reference:	Monsanto ES-78-SS-20, December, 1978
Reliability:	(2) Valid with restrictions – instability of test compound in water

Value:	92.9 mg/l
Temperature:	25°C
Description:	Of low solubility
Method:	Estimation; WSKOW v1.40
GLP:	No
Remarks:	Estimation method using molecular structure and measured melt point of 130°C and Log P of 2.49
Reference:	EPIWIN/WSKOW v1.40
Reliability:	(2) Valid with restrictions – modelling data

B. pH Value, pKa Value

pH Value:	Not applicable

2.7 FLASH POINT

Value:	154°C
Type:	Cleveland Open Cup
Method:	ASTM D 92-96
Reference:	Flexsys America Data, Test Method for Flash Points and Fire Points by Cleveland Open-cup Apparatus, ASTM D 92-96
Reliability:	(1) Valid without restrictions

2.11 OXIDISING PROPERTIES

†2.12 OXIDATION: REDUCTION POTENTIAL

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

B. Other data – Henry's Law Constant

Results:	3.03E-010 atm-m3/mole
Remarks:	Calculated at 25°C using molecular structure and measured melt point of 130°C and Log P of 2.49.
Reference:	EPIWIN/HENRYWIN v3.10
Reliability:	(2) Valid with restrictions – modelling data

3. ENVIRONMENTAL FATE AND PATHWAYS

*3.1.1 PHOTODEGRADATION

Type:	air
INDIRECT PHOTOLYSIS	
Sensitizer:	OH
Conc. of sens.	1560000 molecule/cm3
Rate constant:	.0000000001297621 cm3/(molecule-sec)
Degradation:	50 % after 0.029 days (20.556 minutes)
Method:	other (calculated): AOP Program (v1.89)
Year:	1999
GLP:	No
Test substance:	other TS: molecular structure and measured melting point of 130°C and Log P of 2.49
Reference:	EPIWIN/AopWin v1.90
Reliability:	(2) Valid with restrictions - Accepted calculation method

*3.1.2 STABILITY IN WATER

Type:	Abiotic (hydrolysis)
Half life:	Approximately 168 hours at pH 7.0 and 23 °C
Method:	Oxidative/Hydrolytic Stability via HPLC, 1978
GLP:	No data
Test substance:	As prescribed by 1.1-1.4, purity: >96%
Remarks:	The oxidative and/or hydrolytic stability of the test compound was determined by the following procedure: A borosilicate glass cylinder was filled with 1500 ml of purified water and adjusted to a 1 mg/l concentration of the test compound using 200:1 of a 7.5 mg/l acetone stock solution. The continuously stirred and aerated aqueous solution was then sampled as a function of time. Sample analysis was carried out via reverse phase high-performance liquid chromatography (HPLC) at a wavelength of 250 nm. Concentrations of the test compound were measured at 0, 1.5, 6.0, 24.0, 48.0, 72.0, 96.0 and 168.0 hours.

Exposure Time (hours)	Concentration (mg/l)
0	1.00
1.5	0.93
6.0	0.90
24.0	0.81
48.0	0.60
72.0	0.55
96.0	0.57
168.0	0.45

Reference:	Monsanto ES-78-SS-28 Environmental Sciences Labs 1978

Reliability: (1) Valid without restriction

*3.2 MONITORING DATA (ENVIRONMENTAL)

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

*3.3.1 TRANSPORT

Type: Adsorption
Media: Soil/Sediment
Method: SRC Structure estimation method based on molecular connectivity indices, 1992
Results: Koc = 19.64; Log Koc = 1.293
Remarks: Estimation based on molecular structure and measured melting point of 130°C and Log P of 2.49
Reference: EPIWIN/PCKOCWIN v1.66
Reliability: (2) Valid with restrictions – Modelling data

Type: Volatility
Media: Water
Method: Estimation Method, 1990
Results: Volatilization half-life from model river: 2.971E+006 hours
Volatilization half-life from model lake: 3.241E+007 hours
Remarks: Model river = 1 m deep flowing at 1 m/sec and wind velocity of 3 m/sec. Model lake = 1 m deep flowing at 0.05 m/sec and wind velocity of 0.5 m/sec.
Reference: Handbook of Chemical Property Estimation Methods, 1990
Reliability: (2) Valid with restrictions – Peer-reviewed published data from a generally accepted and validated estimation method

*3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Media: Air-biota-sediment-soil-water
Method: Fugacity level III
EPIWIN v3.10
Results:

	Mass Amount (%)	Half-life (hrs)	Emissions (kg/hr)
Air	0.00389	0.685	1000
Water	24.8	900	1000
Soil	75	900	1000
Sediment	0.175	3.6E+003	0

Remarks: Persistence time = 946 hours
Calculation based on molecular structure and measured boiling point of 230°C
Reference: EPISUITE/EPIWIN v3.10
Reliability: (2) Valid with restrictions – Modelling data

*3.5 BIODEGRADATION

Type: aerobic
Inoculum: adapted
Concentration of the chemical: 20.1 mg/l test substance

Medium:	sewage treatment
Degradation:	76% after 49 days
Results:	Biodegradable
Method:	Ultimate Biodegradation by CO2 Evolution, Thompson-Duthie-Sturm Procedure, 1973
GLP:	No data
Test substance:	As prescribed by 1.1-1.4, purity: >96%
Remarks:	A 9 liter bottle containing 50 ml of acclimated bacterial seed and 5500 ml of standard BOD water was prepared for the test material and a control. The bottles were connected to a source of CO2-free air and the effluent air passed through a set of aqueous barium hydroxide scrubbers. The evolved CO2 was trapped as barium carbonate and quantitated by titration of the remaining barium hydroxide with 0.1N HCl. CO2 values obtained for the control were subtracted from those obtained from the test material. The CO2 produced was compared to the theoretical yield based on the carbon composition and the weight of the test material. The test material had an unusually long induction or acclimation period of 21 days before significant CO2 evolution occurred.
Reference:	Monsanto ES-78-SS-28 Environmental Sciences Labs 1978
Reliability:	(1) Valid without restrictions

3.6 BIOACCUMULATION

Species:	Other
BCF:	29 (+/-8)
Method:	Neely et al., Environ. Sci. Technol. 8, 1113, 1974
GLP:	No
Remarks:	Calculated from measured octanol/water partition coefficient applying the equation of Neely, et al., for rainbow trout.
Reference:	Monsanto ES-78-SS-28 Environmental Sciences Labs 1978
Reliability:	(2) Valid with restrictions – accepted calculation method

4. ECOTOXICITY

*4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type of test:	static closed-system
Species:	Salmo gairdneri (Rainbow Trout)
Exposure period:	96 hours
Results:	LC_{50} (24h) = 4.1 mg/l LC_{50} (48h) = 2.7 mg/l LC_{50} (96h) = 1.8 mg/l NOEC = 1.0 mg/l LOEC = 1.4 mg/l
Analytical monitoring:	No
Method:	EPA Methods for Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA-660/3-75-900, 1975
GLP:	No data
Test substance:	As prescribed by 1.1-1.4, purity: >96%
Remarks:	The test material, in reagent-grade Acetone, was introduced into 15 liters of diluent water in all-glass vessels. Nominal test concentrations (duplicate) were 0, 1.0, 1.4, 1.8, 2.4, 3.2, 4.2 and

5.6 mg/l, plus a solvent control. To each test vessel, 10 rainbow trout, standard length 3.7 cm, were then added. The test fish were not fed 48 hours prior to testing, nor during exposure. No aeration was provided during the test, and temperature was maintained at 12°C. Dissolved oxygen ranged from 9.8 mg/l (92% saturation) to 5.2 mg/l (49% saturation) from beginning to end of exposure, respectively. pH values ranged from 7.5 initially, to 7.0 at the end of the test. Observations and mortality counts were made every 24 hours. Test concentrations and observed percentage mortality were converted to logarithms and probits, respectively, and these values were utilized in a least squares regression analysis. The LC50s and the 95% confidence intervals were calculated from the regression equation.

. Reference: Monsanto BN-76-260, EG&G Bionomics, 1976

Reliability: (2) Valid with restrictions – age of study, lack of method detail

Type of test: static
Closed system

Species: Lepomis machrochirus (Bluegill Sunfish)

Exposure period: 96 Hours

Results: LC_{50} (24h) = 3.2 mg/l
LC_{50} (48h) = 1.9 mg/l
LC_{50} (96h) = 1.6 mg/l
NOEC = 0.75 mg/l
LOEC = 1.0 mg/l

Analytical monitoring: No

Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA-660/3-75-900, 1975

GLP: No data

Test substance: As prescribed by 1.1-1.4, purity: >96%

Remarks: The test material, in reagent-grade Acetone, was introduced into 15 liters of diluent water in all-glass vessels. Nominal test concentrations (duplicate) were 0, 0.75, 1.0, 1.4, 1.8, 2.4, 3.2, 4.2 and 5.6 mg/l, plus a solvent control. To each test vessel, 10 bluegill, standard length 3.8 cm, were then added. The test fish were not fed 48 hours prior to testing, nor during exposure. No aeration was provided during the test, and temperature was maintained at 22°C. Dissolved oxygen ranged from 8.8 mg/l (100% saturation) to 0.3 mg/l (3% saturation) from beginning to end of exposure, respectively. The pH values ranged from 7.3 initially, to 6.7 at the end of the test. Observations and mortality counts were made every 24 hours. Test concentrations and observed percentage mortality were converted to logarithms and probits, respectively, and these values were utilized in a least squares regression analysis. The LC50s and the 95% confidence intervals were calculated from the regression equation.

Reference: Monsanto BN-76-260, EG&G Bionomics, 1976

Reliability: (2) Valid with restrictions – age of study, lack of method detail

Type of test: static
Closed-system

Species: Pimephales promelas (Fathead Minnows)

Exposure period: 96 Hours
Results: LC_{50} (24h) = 6.7 mg/l
LC_{50} (48h) = 4.5 mg/l
LC_{50} (96h) = 3.5 mg/l
NOEC = 1.0 mg/l
LOEC = 1.8 mg/l
Analytical monitoring: No
Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA-660/3-75-900, 1975
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: >96%.
Remarks: Test fish were obtained from Fattig Fish Hatchery in Brady, Nebraska. Test fish were held in culture tanks on a 16-hour daylight photoperiod and observed for at least 14 days prior to testing. A daily record of fish observations was maintained during the holding period, during which time the fish were fed a standard diet of commercial fish food until 48 hours prior to testing, when feeding was stopped. Test fish had a mean weight of 0.25 g and a mean standard length of 25.8 mm. The test was conducted in 5-gallon glass vessels containing 15liters of laboratory well water. The 0-hour measured control water parameters of this dilution water were dissolved oxygen 9.3 ppm, hardness (CaCO3) of 255 ppm and pH 8.2. The test vessels were kept in a water bath at 22°C.

Test fish were acclimated to the dilution water and test temperature, and held without food for 48 hours prior to testing. Nanograde Acetone was used to prepare the test solutions and as the solvent control. A 48-hour range-finding study preceded the definitive test. Test concentrations were 0, 1.0, 1.8, 3.2, 5.6 or 10.0 mg/l for the test compound. Fish were placed in the testing vessels within 20 minutes of the addition of the test material aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects. Dissolved oxygen values and pH ranges were monitored during the testing and remained within acceptable limits of >40-100% saturation for dissolved oxygen and pH value consistent with control. The ammonia concentration was below the toxic limit. Water hardness (CaCO3) was 255 ppm. As a quality check, test fish were challenged with Antimycin A. The estimated 96Hr LC50 and 95% confidence limits were within the 95% confidence limits reported in the literature, indicating that the fish were in good condition. These values were obtained by employing the statistical methods described by Litchfield and Wilcoxon (A Simplified Method for Evaluating Dose-Effect Experiments, 1949) or Stephan (methods for calculating an LC50, 1977).
Reference: Monsanto AB-80-0240, Analytical Bio-Chemistry Labs, 1980
Reliability: (1) Valid without restriction

Type of test: Dynamic (flow-through) – time independent
Open system
Species: Rainbow Trout
Exposure period: 168 hours (7 days)
Results: LC_{50} (24h) = >5.03 mg/l
LC_{50} (96h) = 3.68 mg/l

	LC_{50} (168h) = 3.68 mg/l NOEC = 2.70 mg/l LOEC = 5.03 mg/l
Analytical monitoring:	Yes
Method:	EPA Methods for Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA-660/3-75-900, 1975
GLP:	Yes
Test substance:	As prescribed by 1.1-1.4, purity: >96%
Remarks:	The test was performed under flow-through conditions using a Mount-Brungs diluter. It was conducted in duplicate 19L glass aquaria, with 10 fish per replicate. Flow rate was set to provide four tank volumes/day. Juvenile rainbow trout (mean length 6.09 cm, mean weight 1.94 g) were obtained from Mt. Lassen Trout Farm and maintained at SRI for at least two weeks prior to testing. Fish were fed frozen brine shrimp (5% of body weight) during the exposure period. Initial stock solutions were prepared every 48 hours by adding 2 grams of the test compound to 100 ml acetone. This concentration proved insufficient to produce appreciable mortality in a 96-hour period, so the concentration was doubled to 4g/100ml. The solution was metered into the diluter via syringe pump at a flow rate of 2ml/hour. A separate bottle was used to deliver a dilute acetone solution to maintain the concentration in the solvent control tanks at 90ul/l. Nominal test concentrations were 0, 0.25, 0.50, 1.00, 2.00, 4.00 mg/l plus the solvent control. Actual chemical concentrations were determined via HPLC. Measured concentrations of test compound were 0, 0.33, 0.73, 1.24, 2.70 and 5.03 mg/l. The test was terminated after seven days of exposure, as no deaths had occurred in the four previous days. Dissolved oxygen (DO), pH, temperature and chemical concentrations were monitored routinely, alternating between the replicates. Temperature was maintained at 13°C. DO measurements ranged from 5.8-10.2 mg/l and pH from 6.9-7.9. Hardness was 29 mg/l (CaCO3), alkalinity was 31 mg/l and acidity was <5.0. The LC50 values and 95% confidence limits were calculated using the binomial method and the probit method with Berkson's adjustment. Test results showed that the test compound exhibits high acute toxicity to rainbow trout within its solubility limits, but the pattern of mortality does not indicate cumulative toxicity.
Reference:	Monsanto SR-83X-063, SRI International, 1981
Reliability:	(1) Valid without restriction

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

*A. Daphnia

Type of test:	static Closed system
Species:	Daphnia magna
Exposure period:	48 Hours
Results:	EC_{50} (24h) = 13.0 mg/l EC_{50} (48h) = 4.5 mg/l

NOEC = 1.0 mg/l

Analytical monitoring: No

Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA 660/3-75009, 1975

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: >96%

Remarks: The Daphnia magna used in the test were cultured at the ABC facilities. Adult Daphnia were fed an algae and trout chow mixture daily until 24 hours prior to testing. The bioassay was conducted in 500 ml glass beakers containing 250 ml of ABC well water. During the test, dissolved oxygen concentration ranged from 8.6-7.5 mg/l, pH range was 7.7-8.0, hardness (CaCO3) was 220 mg/l, and alkalinity was 210 mg/l. Vessels were kept in a water bath at 19°C. The photoperiod was controlled to give 16 hours of daylight and 8 hours of darkness. An initial range-finding experiment was carried out to determine the exposure concentrations for the definitive test. Acetone was used as the solvent for the test solutions, and the experiment included both a control and a solvent control. Concentrations (in duplicate) of the test substance were 0, 1.0, 1.8, 5.6, 10 and 32 mg/l. Ten daphnia, first instar less than 18 hours old, were placed in each test chamber. Daphnia in all concentrations were observed once every 24 hours for mortality and abnormal effects. Water quality measurements were monitored throughout the testing and were considered adequate and equivalent to those measurements in the control chamber.

Statistical analysis of the concentration vs. effect data was calculated employing the techniques of Litchfield and Wilcoxon (1949).

Reference: Monsanto AB-78-356, Analytical Bio-Chemistry Labs, 1978

Reliability: (1) Valid without restriction

*4.3 TOXICITY TO AQUATIC PLANTS, e.g. algae

Species: Selenastrum capricornutum (Freshwater alga)

Endpoint: Biomass and Growth rate

Exposure period: 96 Hours

Results: EC_{50} (96h) = 29 ppm for a chlorophyll, 29 ppm for cell numbers

NOEC = 10 ppm

LOEC = 18 ppm

Analytical monitoring: No

Method: US EPA Algal Test Procedure: Bottle Test, 1971

Closed system

GLP: No data

Results: The test algae were obtained from the US EPA Environmental Research Laboratory in Corvallis, Oregon. Beginning cell numbers in the test flasks were 2.0 x 10(4) cells/ml. Cultures were incubated at 24°C under approximately 4,000 lux illumination. Triplicate cultures were employed for each of the test concentrations and the control. Test containers were 125ml flasks containing 50ml of test medium. Concentrations for the definitive test were based on the results of a 96-hr range-finding study. These concentrations were 0, 10, 18, 32, 56 and 100 ppm, plus a

solvent control (acetone). The measured pH values ranged from 7.8 to 8.1 during the course of the testing. There were no other water quality measurements besides temperature reported in this study. Statistical analysis involved converting each test concentration to a logarithm, and the corresponding percentage decrease of in vivo chlorophyll a or cell numbers was converted to a probit (Finny, 1971). The EC50s and 95% confidence limits were then calculated by linear regression. The toxicity of the test substance to algae was similar throughout the 96 hours of exposure. There was no significant difference between growth of the control and solvent control cultures after 96 hours of exposure by either measured parameter.

Test substance: As prescribed by 1.1-1.4, purity: >96%
Remarks: Both a chlorophyll and cell numbers measured to confirm results.
Reference: Monsanto BN-78-367, EG&G Bionomics, 1978
Reliability: (2) Valid with restrictions – no GLP statement

*5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

Type: LD_{50}
Species/strain: Rats, Sprague-Dawley Albino
Value: 5600 mg/kg bw
Sex: Male and female
# of Animals: 20
Vehicle: Corn Oil
Doses: 3890, 5010, 6310 or 7940 mg/kg bw
Recovery Period: 14 days
Method: Single Oral Dose, Younger Laboratories Protocol, 1973
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: >96%
Remarks: Four groups of male and female rats (5/sex/dose level) were fed a single oral dose of the test article as a 20% suspension in corn oil via oral gavage. Male rats had initial body weights of 210-240 grams: females had initial body weights of 230-235 grams. Clinical signs of toxicity included reduced activity and appetite for 3-5 days for survivors, and increasing weakness, collapse and death for decedents in 1-4 days. Gross autopsy findings on decedents were lung and liver hyperemia and acute gastrointestinal inflammation. Survivors were sacrificed after fourteen days. All viscera of survivors appeared normal. 95% confidence limits: 5320-5880 mg/kg.

Dose mg/kg	Mortalities-Male	Mortalities-Female	Combined
3980	0/2	0/3	0/5
5010	1/3	0/2	1/5
6310	1/2	2/3	3/5
7940	3/3	2/2	5/5

Reference: Monsanto Y-73-286, Younger Laboratories, 1974
Reliability: (2) Valid with restrictions – age of study, lack of method detail

Type:	LDL_0
Species/strain:	Rats
Value:	8-8.5 g/kg bw
Sex:	Male and female
# of Animals:	16
Vehicle:	Corn oil
Doses:	0.4 – 9.9 g/kg bw (16 animals, 16 dose levels)
Recovery Period:	12 days
Method:	Minimum Lethal Dose, Scientific Associates, 1951
GLP:	No data
Test substance:	As prescribed by 1.1-1.4, purity: >96%
Remarks:	The test article, in corn oil suspension, was introduced into the stomachs of healthy mature rats by means of a rubber catheter. Animals were weighed on Day 0 and Day 7. Beginning weights for males ranged from 0.24-0.33 kg; females ranged from 0.19-0.24 kg. Animals were observed daily for signs of toxicity and moribundity. Sixteen doses ranging from 0.4 g/kg to 9.9 g/kg were administered to one animal/dose level. No outward signs of toxicity were observed at feeding levels below 3.7 g/kg body weight. Above this level, the animals became listless and unsteady after 24 hours. This loss of muscular coordination was the most obvious outward sign of toxicity. There was an initial weight loss in rats dosed at 3.7-8.0 g/kg, but rats dosed with 0.4-2.5g/kg gained weight during the study. Mild diarrhea occurred in the rat dosed at 3.7 g/kg, and this effect was intensified in all higher-dose animals. Animals fed 8.5, 8.8, 9.1, 9.4 and 9.9 g/kg bw died on days 4, 3, 6, 3 and 4, respectively. Microscopic examination of the vital organs at autopsy of those animals that received a lethal dose showed no abnormalities.
Reference:	Monsanto M-29, Scientific Associates, 1951
Reliability:	(2) Valid with restrictions – age of study, lack of method detail

5.1.2 ACUTE INHALATION TOXICITY

Type:	LC_{50}
Species/strain:	Mice
Exposure time:	4 hours
Value:	1624 mg/m3
Method:	No data
GLP:	No data
Test substance:	As prescribed by 1.1-1.4, purity: commercial grade
Remarks:	None
Reference:	Datsenko, I.I. et al., 1988
Reliability:	(4) Not assignable – data from a secondary literature source

5.1.3 ACUTE DERMAL TOXICITY

Type:	LD_{50}
Species/strain:	Rabbits, New Zealand Albino
Value:	>5010 mg/kg bw
Sex:	Male/female
# of Animals:	4
Vehicle:	Corn Oil

Doses: 3160, 5010 or 7940 mg/kg bw
Exposure Time: 24 Hours
Recovery Period: 14 days
Method: Single Dermal Dose, Younger Laboratories Protocol, 1973
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: >96 %
Remarks: The test substance, as a 40.0% suspension in corn oil, was applied to the shaved skin of three groups of male and female rabbits for 24 hours as single dermal application at dose levels of 3160, 5010 or 7940 mg/kg/body weight. The males ranged in weight from 2.2-2.4 kg, and the females from 2.0-2.3 kg. The test material was held in place by means of an occlusive wrap of latex rubber and secured by bandaging and elastic tape. The occlusive wrap was removed after 24 hours and the excess material was wiped from the test animal. Clinical observations were made three times during the first eight hours after dosing, and twice daily thereafter until sacrifice on Day 14. Clinical signs of toxicity included reduced appetite and activity (three to five days in survivors), followed by increasing weakness, collapse and death (Day 2). Findings from the gross autopsy on decedents indicated hemorrhagic areas of the lungs, slight liver discoloration, enlarged gall bladder and gastrointestinal inflammation. Gross autopsy reports on survivors indicated that all viscera appeared normal.

Dose mg/kg	Mortalities-Male	Mortalities-Female	Combined
3160	---	0/1	0/1
5010	0/1	---	0/1
7940	0/1	1/1	1/2

Reference: Monsanto Y-73-286 Younger Laboratories, 1974
Reliability: (2) Valid with restrictions – age of study, lack of method detail

5.2.1 SKIN IRRITATION/CORROSION

Species/Strain: Rabbits, New Zealand Albino
Sex: Male and female
# of Animals: 6
Vehicle: None - undiluted
Value: 0.5/8.0
Results: Not Irritating
Classification: Non-Irritating
Method: Draize, J.H., Woodard, G., and Calvery, H.O., 1944
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: >96%
Remarks: 0.5 grams of the test substance, as a finely ground powder moistened with water, was applied to the shaved dorsal areas of six albino rabbits. The test material was applied to the skin under 1" square gauze patches and held in contact with the skin by means of an occlusive wrap of latex rubber secured by bandaging and elastic tape. The occlusive wrap and gauze patches were removed after 24 hours. Dermal irritation was scored by the Draize Method, and results were recorded 24, 48, 72 and 168 hours after topical

application. The Primary Irritation Index was calculated by averaging the mean scores at 24 and 72 hours. The Primary Irritation Index was found to be 0.5 on a scale of 0.0-8.0.

Reference: Monsanto Y-73-286 Younger Laboratories, 1974

Reliability: (2) Valid with restrictions – age of study, lack of method detail

Species/Strain: Humans

Sex: Male and female

# of Subjects: 10

Vehicle: None - undiluted

Results: Mildly Irritating

Classification: Mild Irritant

Method: Shelanski & Shelanski Occluded Patch Test, 1953

GLP: No data

Test substance: As prescribed by 1.1-1.4, purity: >96%

Remarks: Ten human volunteers (5 men, 5 women) were employed for this Primary Skin Irritation Study to determine if the test compound was irritating to human skin. Three areas, each 3 cm x 3 cm, were selected on the skin of the left arm of each individual. Each area was a discrete, with a space of at lease 2" separating it from the other areas. 10 mg of the test substance was applied to each area as a finely ground powder. The powder was covered with a lintine disc and secured to the arm by sealing around the edges with Blenderm tape. After two hours, the cover of one contact area was removed from each subject, the powder was lightly brushed away, and the site examined for reactions. After four hours, the second disk was removed and the skin examined. After six hours, the third disk was removed and the skin examined. All treatment sites were observed immediately after disk removal, and then again at 1, 4 and 24 hour intervals. One male subject exhibited slight erythema at 4 hours and marked erythema at 6 hours. One female subject exhibited slight erythema at 6 hours, and one female subject had marked erythema at 6 hours. All reactions disappeared in less than 24 hours. Based on the test results, the test compound is capable of eliciting a very mild primary irritation effect on human skin.

Reference: Monsanto SH-70-10, Food and Drug Research Laboratories, 1970

Reliability: (2) Valid with restrictions – age of study, lack of method detail

5.2.1 EYE IRRITATION/CORROSION

Species/strain: Rabbits, New Zealand Albino

Sex: Male and female

# of Animals: 6

Vehicle: None - undiluted

Value: 8.4/110.0

Results: Slightly irritating

Classification: Irritating

Exposure Time: 24 Hours

Method: Draize, J.H., Woodard, G., and Calvery, H.O., 1944

GLP: No data

Test substance: As prescribed in 1.1-1.4, purity: >96%

Remarks: 100.o mg of the test substance as a finely ground powder was applied to one eye of six albino rabbits. The other eye was not

treated and served as a control. The cornea, iris and conjuntivea were examined immediately after treatment, and then at intervals of 1 hour, and at 24, 48, 72 and 168 hours. The Draize Method was used for scoring eye irritation. Findings:
Immediate: slight discomfort
At 1 hour: moderate erythema, slight edema, copious discharge
At 24 hours: moderate to severe erythema, very slight edema, copious discharge containing whitish exudate
At 48 hours: gradual improvement
At 72 hours: gradual improvement
At 168 hours: all animals scored "0"
The average Draize score for 24, 48 and 72 hours was calculated for each animal and then averaged over the six animals. The average Draize score was 8.4 on a scale from 0-110.

Reference: Monsanto Y-73-286, Younger Laboratories, 1973
Reliability: (2) Valid with restrictions – age of study, lack of method detail

*5.3 SENSITIZATION

Type: Repeated Insult Patch Test
Species: Human
Number of subjects: 40 males (10 for each sample)
Dose: 20% w/v
Vehicle: Talc
Result: Irritating but not sensitizing or fatiguing
Classification: Primary Irritant
Not Sensitizing
Not Fatiguing
Method: Shelanski & Shelanski Repeated Insult Patch Test, 1953
Test substance: As prescribed by 1.1-1.4, 6 months old, purity >96%
As prescribed by 1.1-1.4, current production, purity >96%
Recrystallized, purity 99+%
Recrystallized and milled, purity 99+%
Remarks: Twenty-five mg aliquots of the test substance, as a 20% w/v mixture in talc, was spread evenly over a quartered lintine disc and affixed to the skin of 40 male volunteers. The disks were covered with polypropylene and secured with Blenderm tape. The patches remained in place for 24 hours, at which time the sites of contact were examined and visible skin changes graded and recorded. The contact sites were re-examined again 24 and 48 hours after removal of the patches. Fourteen days after the initial contact, the entire procedure was repeated, challenging the same contact sites in each volunteer. Talc was used as the diluent and control material throughout the test. The results indicated that the test material, in all cases, was capable of eliciting visible skin changes deemed characteristic of a primary skin irritant. It was not capable of eliciting visible skin changes deemed characteristic of a fatiguing agent or a skin sensitizer.
Reference: Monsanto SH-67-2, Industrial Biology Laboratories, 1967
Reliability: (2) Valid with restrictions – age of study, lack of method detail

*5.4 REPEATED DOSE TOXICITY

Species/strain: Rats, CD
Sex: Male/Female
# of Animals: 80
Route of Administration: Inhalation
Exposure period: 4 weeks
Frequency of treatment: 6 hours/day, 5 days/week (Total = 20 exposures)
Post exposure observation period: None
Dose: 0, 1.1, 9.9 or 29 mg/m3
Control group: Yes
Concurrent no treatment
NOEL: 9.9 mg/m3 (females)
1.1 mg/m3 (males)
LOEL: 29 mg/m3 (females)
9.9 mg/m3 (males, based on body weight depression)
Method: Other: International Research and Development Corporation Protocol, 1986
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity:>96%
Method: Four groups of young adult male and female rats (10/sex/dose) were exposed to zero, low, medium and high concentrations of the test article as a fine dust aerosol. Observations were made with respect to the incidence of mortality, reactions displayed and body weight effects. Hematologic and clinical chemistry studies and urinalyses were conducted on all test and control animals on the day following final exposure. All animals were subjected to a gross necropsy. A complete set of organs and tissues were removed from each animal and preserved. Histopathologic studies were conducted on selected tissues and organs from the control and high-concentration groups. Weights of selected organs were recorded and subjected to statistical analyses. Body weights hematological, biochemical and urinalysis parameters and absolute and relative organ weights were compared by analysis of variance (one-way classification), Bartlett's test for homogeneity of variances and the appropriate t-Test (for equal or unequal variances) as described by Steel and Torrie using Dunnett's multiple comparison tables to judge the significance of differences.
Results: All animals survived until terminal sacrifice. Clinical signs of toxicity were limited to the high exposure group and consisted of red discharge from the mouth and/or nose. Body weight depressions were seen in high-dose males and females, and to a lesser extent in mid-dose males. No evidence of treatment-related effects were observed in evaluations of ophthalmologic, serum biochemical, haematological, urinalysis, organ weight, macroscopic or microscopic parameters. This study was originally begun at exposure levels of 0, 20, 100 and 200 mg/m3. However, due to unexpected mortality at the two highest exposure groups, the study was terminated after two weeks and then restarted at the lower exposure levels. No lesions indicating a probable cause of death were found from a limited pathological examination on the 100 and 200 mg/m3 animals.
Reference: Monsanto IR-86-34, International Research & Development Corporation, 1986

Species/strain: Rats, Charles River CD
Sex: Female
# of Animals: 30
Route of Administration: Oral gavage
Exposure period: 10 days
Frequency of treatment: Daily
Post exposure observation period:
Dose: 0, 50, 100, 500, 1000 or 2000 mg/kg/day
Control group: Yes
Concurrent vehicle
NOEL: 100 mg/kg/day
LOEL: 500 mg/kg/day
Method: Other:
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: >96%
Results: In a preliminary range-finding study that preceded a developmental toxicity study, the test compound was administered to groups of five mated female rats at doses of 0, 50, 100, 500, 1000 or 2000 mg/kg/day for 10 days (day 6-15 of gestation). Mean body weights for the control group, 50, 100, 500, 1000 and 2000 mg/kg/day groups were 239, 233, 235, 236, 231 and 244 grams, respectively. The control group received the corn oil vehicle only, at a volume of 10 ml/kg, on a comparable regimen. The animals were observed twice daily for mortality and overt changes in appearance and behaviour. The presence and duration of clinical signs of toxicity were recorded once daily during the dosing period. Animals not surviving to the scheduled sacrifice were necropsied to determine cause of death. All surviving animals were sacrificed on gestation day 20. Individual body weights were recorded on gestation days 0, 6, 9, 12, 16 and 20. Individual food consumption was recorded for 24 hours on gestation days 0, 6, 9, 12 and 16. Immediately following sacrifice, the uterus and ovaries were exposed by an abdominal incision. The uterus was excised and weighed. The abdominal and thoracic cavities and organs were examined for grossly evident morphological changes. Survival was 100% in the control, 50 and 100 mg/kg/day groups. None of the animals in the 1000 and 2000 mg/kg/day survived to scheduled sacrifice. Mortalities occurred between gestation days 7-10 in the 1000 mg/kg/day animals, and between gestation days 7-9 in the 2000 mg/kg/day group. Some, but not all, of these animals had yellow staining on the anogenital haircoat or dried red matter around the nose and forelimb, but many had no visible abnormalities prior to death. At necropsy, gross lesions were present in only one animal. This 2000 mg/kg/day animal exhibited a hemorrhage in the abdominal soft tissue. In the 500 mg/kg/day group, one animal died on gestation day 11. Although the remaining animals in this group survived until sacrifice, there was an increased evidence of unkempt haircoat and respiratory difficulties. Other signs of toxicity noted were soft stools in some animals. Mean body weight gains were reduced relative to those of controls. In the 50 and 100 mg/kg/day groups, there were no meaningful differences between these animals and the controls. Mean body weight gains were comparable to those of controls. There were no clinical signs of

toxicity noted. All statistical analyses compared the treatment groups with the control group, with the levels of significance at $p<0.05$ and $p<0.01$. All means were accompanied by standard deviations. Bartlett's test for homogeneity of variance and the appropriate t-test (for equal or unequal variance) using Dunnett's multiple comparison table to determine the significance of differences.

Reference: Monsanto IR-86-407, International Research & Development Corporation, 1987

Reliability: (1) Valid without restriction

*5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

Type: Ames Bacterial Reverse Gene Mutation

System of testing: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA-100

Concentration: 0.1, 1.0, 10, 100 or 500 ug/plate

Metabolic activation: With and without

Results:

Cytotoxicity conc: With metabolic activation: 500 ug/plate
Without metabolic activation: 500 ug/plate

Genotoxic effects:

With metabolic activation: Negative
Without metabolic activation: Negative

Method: Ames Mutagenicity Plate Test (Overlay Method) 1975

GLP: No data

Test substance: As prescribed by 1.1-1.4, purity: >96 %

Remarks: The test compound was evaluated for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. The *Salmonella typhimurium* strains used for this experiment were obtained from Dr. Bruce Ames. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. The mutagenesis assay was carried out as the plate-incorporation test according to the Ames protocol. Chemicals used as positive controls for the non-activation assays were 10 ug/plate methylnitrosoguanidine (MNNG), 100 ug/plate 2-nitrofluorene (NF) and 10 ug/plate quinacrine mustard (QM). Positive control chemicals used for the activation assays were 100 ug/plate 2-anthramine (ANTH), 100 ug/plate 2-acetylaminofluorine (AAF) and 100 ug/plate 8-aminoquinoline (AMQ). Dimethylsulfoxide (DMSO) was used as the solvent and the solvent control. The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.

Reference: Monsanto BIO-76-231, Litton Bionetics, 1976

Reliability: (1) Valid without restriction

B. NON-BACTERIAL IN VITRO TEST

Type: Mammalian Cell Forward Gene Mutation Assay
System of testing: Mouse lymphoma cells L5178Y TK+/-
Concentration: 0.195 to 6.25 µg/ml without activation (triplicate)
0.78 to 30 µg/ml with activation (triplicate)
Metabolic activation: With and without
Results:
Cytotoxicity conc: With metabolic activation: 1.56 µg/ml
Without metabolic activation: 25 µg/ml
Precipitation conc: 5 mg/ml
Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative
Method: Other: Clive, D. and Spector, J.F.S. (1975) Mutation Res. 31, 17-29
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: >96%
Results: The test compound was dissolved in DMSO at 333 mg/ml for use in the preliminary cytotoxicity test. The compound was not completely soluble, but formed a fine suspension even at the lower stock concentrations (5 mg/ml) used for mutation experiments. Dilutions were performed with DMSO prior to the final 1:100 dilutions into growth medium to obtain an applied concentration range of 3333 ug/ml to 6.5 ug/ml. The activation system was the S9 fraction of rat liver homogenate and necessary cofactors (CORE). CORE consisted of NADP (sodium salt) and isocitric acid. Concentrations of 6.5 and 12.9 ug/ml were toxic and 25.8 ug/ml was completely lethal (without activation) to the mouse lymphoma cells within 24 hours of treatment. Therefore, the mutation assay was initiated with an applied concentration range of 50 to 0.0975 ug/ml. DMSO (1%) was used as the solvent control substance. Growth medium without the addition of solvent was used as a negative control. No genetic effects were attributed to the presence of the solvent. EMS (0.5 ul/ml) and DMN (0.3 ug/ml) were used as reference mutagens and induced mutation frequencies within the expected range. With and without activation, the mutant frequencies in the treated cultures were comparable to the background frequencies. The erratic effect of the compound on suspension growth and cloning efficiency (attributed to suspended material) caused the percent relative growth values to bear little relation to the applied concentrations. Nevertheless, even at the highly toxic doses of 1.56 ug/ml without activation (4.8% relative growth) and 25 ug/ml with activation (2.5% relative growth), the test compound did not induce a significant increase in mutant frequency.

Non-Activation Results

	Conc.	Mutant clones	Viable clones	Mutant frequency x10(-6)
Solvent Control	---	50.0	253.0	19.8
Negative Control	---	65.0	305.0	21.3
EMS	0.5 µl/ml	712.0	91.0	782.4
Test Cpd.	0.195	66.0	249.0	26.5
	0.390	77.0	261.0	29.5
	0.780	47.0	131.0	35.9
	1.560	18.0	49.0	36.7

3.130	53.0	273.0	19.4
6.250	[contaminated]	215.0	------

Activation with S-9 Results

	Conc.	Mutant clones	Viable clones	Mutant frequency x10(-6)
Solvent Control	---	81.0	258.0	31.4
Negative Control	---	95.0	272.0	34.9
DMN	0.3 µl/ml	354.0	59.0	600.0
Test Cpd.	2.5	88.0	210.0	41.9
	10.0	71.0	229.0	31.0
	20.0	58.0	172.0	33.7
	25.0	61.0	85.0	71.8
	30.0	76.0	121.0	62.8

Reference: Monsanto BO-78-238, Litton Bionetics, 1979
Reliability: (1) Valid without restriction

Type: Mitotic Recombination Assay
System of testing: Saccharomyces cerevisiae, D4
Concentration: 0.1, 1, 10, 100 and 500 micrograms/plate
Metabolic activation: With and without
Results:
Cytotoxicity conc: With metabolic activation: 500 ug/plate
Without metabolic activation: 100 ug/plate
Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative
Method: Ames Mutagenicity Plate Test (Overlay Method) 1975
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: >96%
Remarks: The test compound was evaluated for genetic activity in assays with and without the addition of mammalian metabolic activation preparations. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. The mutagenesis assay was carried out as the plate-incorporation test according to the Ames protocol. The chemical used as the positive control for the non-activation assay was methylnitrosoguanidine (MNNG) at 10 ug/plate. Positive control chemical used for the activation assay was DMNA at 100 micromoles/plate. Dimethylsulfoxide (DMSO) was used as the solvent and the solvent control. Statistical analysis included Bartlett's test for homogeneity of variance, and comparison of treatments with controls using within-levels pooled variance and a one-sided t-test. Grubbs' test was performed to determine if outliers were present.The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.
Reference: Monsanto BIO-76-231, Litton Bionetics, 1976
Reliability: (1) Valid without restriction

Type: *In vitro* Unscheduled DNA Synthesis (UDS)
System of testing: Primary rat hepatocyte cultures (Fischer-344 strain)
Concentration: 0.1 to 10 ug/ml (preliminary experiment)
1 to 10 ug/ml (replicate assay)
Metabolic activation: With and without
Results:
Cytotoxicity conc: Preliminary Assay: 50, 100, 250, 500 and 900 ug/ml
Replicate Assay: 50, 100 and 250 ug/ml
Precipitation conc: 900 ug/ml
Genotoxic effects: Negative
Method: Williams, G.M., Detection of Chemical Carcinogens by Unscheduled DNA Synthesis in Rat Liver Primary Cell Cultures, Cancer Research 37, pp. 1845-1851 (1977)
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 95%
Remarks: Acetone (1%) used as solvent and diluent. Primary rat liver cell cultures derived from the livers of two adult male rats weighing 241 and 293 grams (12 and 15 weeks old, respectively) were used for the preliminary and replicate experiments, respectively. Three controls were incorporated into each UDS assay: a positive control, a negative (solvent) control, and an untreated medium control. The positive control was 2-Acetylaminofluorene (2-AAF), the solvent control was acetone in the preliminary assay and in the replicate assay. The percentage of cells in repair was calculated as the percentage of cells with at least 5 net grains/nucleus. 150 cells were scored for each concentration reported for each experiment. All collection of data and pooling of slides were done via programs in the VAX 11/782 computer. Cytoxicity was observed at 50, 100, 250, 500 and 900 ug/ml in the preliminary experiment, and at 50, 100 and 250 ug/ml in the replicate experiment. UDS was measured at concentrations of the test compound between 0.1 and 10.0 ug/ml in the preliminary experiment, and between 1.0 and 10.0 ug/ml in the replicate experiment. The net grain counts were negative at each concentration of the test compound, in the solvent control and in the medium control, in contrast to the strong positive response produced by the positive control 2-AAF in both experiments (38.2 and 39.0 net grains/nucleus). These results indicate that the test compound is not a genotoxic agent under the conditions of the *in vitro* rat hepatocyte DNA repair assay.

Treatment	Conc.	NG	SE	Median	%IR
Control/medium	---	-10.2	0.6	-11.0	0
Control/solvent	1%	- 9.0	0.4	- 9.9	0
2-AAF ug/ml	3	39.0	5.6	38.0	96
Test Cpd. ug/ml	0.1	-9.1	0.9	-9.9	3
	0.5	-11.8	4.1	-12.5	2
	1.0	-10.3	2.6	-8.8	1
	5.0	-8.1	0.7	-7.7	0
	10.0	-12.1	2.6	-11.0	0
	50.0	----------toxic----------			
	100.0	----------toxic----------			

250.0 ----------toxic----------
-
500.0 ----------toxic----------
-
900.0 ----------toxic----------
-

Reference: Monsanto SR-86-139, SRI International, 1986
Reliability: (1) Valid without restriction

* 5.6 GENETIC TOXICITY IN VIVO

Type: Mammalian Bone Marrow Chromosomal Aberration Test
Species/strain: Rat, Fisher 344
Sex: Male and Female
Route of Administration: Oral gavage in corn oil vehicle
Exposure period: 6, 18 and 30 Hours
Doses: 2800 mg/kg bw
Results:
Effect on mitotic index or P/N ratio: No effect
Genotoxic effects: Negative
Method: In vivo Bone Marrow Cytogenetics Rat Metaphase Analysis 1981 OECD 475 Equivalent
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 96%
Remarks: The test compound was evaluated in a preliminary study at a dose of 2800 mg/kg bw using two young adult (55 days old) male and two female rats. Due to the pharmacotoxic signs observed at this dose, 2800 mg/kg was selected as an estimation of the maximum tolerated dose.
In the definitive test, 35 adult male and 35 adult female rats (5 male and 5 female rats/group) were dosed with the test article in a controlled study. No statistically significant differences in body weights were determined between the groups. Significance was evaluated in a one-way analysis of variance using the F distribution. At 6 hours after dosing, all animals exhibited abnormal gait, decreased body tone, piloerection, diarrhea and reddish-brown discoloration on forepaws and around the oral-nasal region. Four males and two females had an abnormal stance and arched backs. Five males and two females had decreased activity and three females had body drop. Males in this group lost an average of 1.2 grams while the females gained 0.6 grams average from the original fasted weights. In the 18-hour group, all rats exhibited diarrhea, decreased body tone, abnormal gait, abnormal stance, piloerection, arched back, and a brownish discoloration on forepaws and around the nasal-oral region. Three females and four males exhibited chromodacryorrhea and one male and two females had lacrimation. Both males and females lost an average of 5.2 grams from the original fasted weights. In the 30-hour group, all rats had an abnormal gait, abnormal stance, decreased body tone, piloerection, arched back and the brownish discoloration on forepaws and around the nasal-oral region. Males lost and average of 3.6 grams, while females gained and average

of 2.2 grams compared to original fasted body weights. These pharmacotoxic signs indicated that the test article was at or near the maximum tolerated dose. Animals from each group and dose level were sacrificed at 6, 18 and 30 hours after dosing. Control groups received either 10 ml/kg bw of vehicle control (corn oil), or 20 mg/kg bw of the positive control cyclophosphamide (CP). Two to three hours prior to sacrifice, each animal was given a single intraperitoneal dose of colchicine at 4 mg/kg bw to arrest dividing cells in metaphase. Bone marrow was sampled at 6, 24 and 48 hours after dosing with the vehicle or the test substance. A single sampling time of +24 hours was used for the positive control group. A total of 500 (if possible) well spread, intact metaphase cells were scored for the presence of chromosome aberration per experimental treatment point (50/animal) by two investigators (25 each/animal). Slides were scored for increases in the proportion of aberrant metaphases by Chi-square analysis and in the frequency of aberrations/cell by a one-way analysis of variance (ANOVA). No statistically significant increases in the proportion of aberrant cells or aberrations/cell were observed at the 6, 24 and 48 hour time points. No statistically significant differences from the vehicle controls were detected by this analysis in animals treated with the test compound. The positive control group (CP) yielded the expected large positive response, indicating the adequacy of the experimental test conditions for the detection of clastogens. The test compound was judged negative in its ability to induce structural chromosomal aberrations to the hemopoietic cells of the rat bone marrow under the experimental conditions of this assay.

Compound	Dose	Harvest time	# rats	# metaphazes analyzed	Aberrations/group
Corn Oil	10 ml/kg	6hr	10	500	2
Test Cpd.	2800 mg/kg	6hr	10	500	5
Corn Oil	10 ml/kg	18hr	10	500	2
Test Cpd.	2800 mg/kg	18hr	10	500	5
CP	20 mg/kg	18hr	10	460	1719
Corn Oil	10 mg/kg	30hr	10	500	2
Test Cpd.	2800 mg/kg	30hr	10	500	6

Reference: Monsanto PK-87-345, Pharmakon Research, 1988
Reliability: (1) Valid without restriction

*5.8 TOXICITY TO REPRODUCTION

*5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

Species/strain: Rat, Charles River COBS CD
Sex: Female
Route of Administration: Oral gavage
Duration of the test: Day 6-15 of gestation
Exposure period: 10 days

Frequency of treatment: Daily
Doses: 0, 50, 250 and 500 mg/kg/day
Control group: Yes
Concurrent vehicle
NOEL Maternal Toxicity: 50 mg/kg/day
NOEL teratogenicity: 500 mg/kg/day
Results: One hundred female rats, age 80-120 days old, were mated for this study. Pregnant rats were used to determine the teratogenic potential of the test substance. The above doses were administered orally by gavage as a single daily dose on days 6-15 of gestation at a constant volume of 10 ml/kg. The control group received the vehicle only (Mazola corn oil) on a comparable regimen at a volume of 10 ml/kg. Mean body weights for the control, 50, 250 and 500 mg/kg/day groups were 246, 237, 239 and 236 grams, respectively. Dams were observed daily for mortality and overt changes in appearance and behavior. Cesarean sections were performed on all dams on day 20 of gestation. The uterus was excised and weighed prior to removal of the fetuses. The number and location of viable and non-viable fetuses, early and late resorptions and the number of total implantations and corpora lutea were recorded. The abdominal and thoracic cavities and organs of the dams were examined for grossly evident morphological changes and the carcasses discarded. All fetuses were individually weighed and examined for external malformations and variations, including the palate and eyes. Each fetus was externally sexed and individually numbered and tagged for identification. Half of the fetuses were placed in Bouin's fixative for subsequent visceral examination by razor blade sectioning. The remaining fetuses were fixed in alcohol, macerated in potassium hydroxide, and dye-stained for subsequent skeletal anaylsis. All statistical analyses compared the treatment groups with the control group, with the levels of significance at $p<0.05$ and $p<0.01$. All means were accompanied by standard deviations. Male-to-female fetal sex ratios and the proportions of litters with malformations were compared using the Chi-square test criterion with Yates' correction for 2x2 contingency tables. The proportions of resorbed and dead fetuses and postimplantation losses were compared by the Mann-Whitney U-test to determine the significance of differences. Numbers of corpora lutea, total implantations and live fetuses and mean fetal body weights were compared by analysis of variance (one-way classification), Bartlett's test for homogeneity of variance and the appropriate t-test (for equal or unequal variance) using Dunnett's multiple comparison table to determine the significance of differences.

Maternal general toxicity: Survival was 100% at the 0, 50 and 250 mg/kg/day dosage levels. Four rats from the 500 mg/kg/day group died on study; one each on gestation days 9, 10, 11 and 15. Two of these animals had no apparent abnormalities prior to death while the other two had either brown staining on the nose and forelimbs or yellow anogential staining on the day of death. Clinical observations of yellow stained ventral or anogenital haircoat occurred in a dose-related pattern at 250 and 500 mg/kg/day. Additional observations noted solely in the two high-

dose groups included umkempt haircoat and respiratory rales. No test compound related post-mortem findings were evident in any dose group. On dam that had died had a small amount of fluid in the thoracic cavity, and one control dam had pus in the pericardial sac. Treatment at the 500 mg/kg/day level caused slightly depressed body weight change during the first and last intervals of treatment (gestation days 6-9 and 12-16). The resulting body weight gains were retarded over both the overall treatment and gestation periods (gestation days 6-15 and 0-20, respectively). No meaningful effects on body weights were evident at the lower dose levels. Mean and relative food consumption at the 500 mg/kg/day level exceeded the control group on the initial day of test compound administration (gestation day 6). All high-dose food intakes thereafter were lower than respective control group values. No abnormalities in food intake were evident at the 50 or 250 mg/kg/day dosage levels.

Pregnancy/litter data: A notable increase in mean postimplantation loss relative to concurrent and historical control values was present at the 500 mg/kg/day dosage level. The resulting mean viable fetuses was also reduced. Slight fetotoxicity was suggested in the high-dose group by a reduction in mean fetal body weights relative to the control group. High-dose values for corpora lutea, total implantations and fetal sex ratios were not remarkable. No toxicologically meaningful findings were evident at the 50 or 250 mg/kg/day dosage levels regarding any of the Cesarean section parameters evaluated. The mean postimplantation loss was significantly lower ($p<0.01$) in both treated groups than in the control group.

Foetal data: The test compound had no teratogenic effect on offspring at any dosage level. Although the number of malformed fetuses was slightly increased at the 500 mg/kg/day dosage level, the number of litters with malformations was not meaningfully different than the control group. No biologically meaningful differences were noted in any treated group regarding the mean numbers of fetuses and litters with developmental variations.

Method: Other: Wilson, J.G., Methods for Administering Agents and Detecting Malformations in Experimental Animals, Teratology – Principles and Techniques, 1965

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: >96%

Remarks: The test article did not produce a teratogenic response when administered orally by gavage to pregnant rats at a dose level of 500 mg/kg/day or less. The test compound was determined to be embryotoxic and fetotoxic at a dose level of 500 mg/kg/day, which was also associated with maternal toxicity.

Reference: Monsanto IR-86-408, International Research & Development Corporation, 1987

Reliability: (1) Valid without restriction

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

B. Toxicodynamics, toxicokinetics

*** 5.11 EXPERIENCE WITH HUMAN EXPOSURE**

.

6. REFERENCES

1. ASTM D-1519 / Flexsys Physical Methods of Analysis
2. EPIWIN/MPBPWIN v1.40
3. FF97.8-1 Flexsys Standard Method of Analysis – Density of Solids by Displacement, 1997
4. EPIWIN/MPBPWIN v1.40
5. Monsanto ES-78-SS-20, Water Solubility and Octanol/Water Partition Coefficient of Selected Rubber Chemicals, December 13, 1978
6. EPIWIN/WSKOW v1.40
7. Test Method for Flash Points and Fire Points by Cleveland Open-cup Apparatus, ASTM D92-96
8. EPIWIN/HENRYWIN v3.10
9. EPIWIN/AopWin v1.90
10. Monsanto ES-78-SS-28, Environmental Persistence Screening of Selected Rubber Chemicals, Environmental Sciences Labs, December 29, 1978
11. EPIWIN/PCKOCWIN v1.66
12. Handbook of Chemical Property Estimation Methods, 1990
13. EPISUITE/EPIWIN v3.10
14. Monsanto ES-78-SS-28 Environmental Sciences Labs 1978
15. Monsanto BN-76-260, Acute 96-Hour Toxicity of Sulfasan R to Rainbow Trout, EG&G Bionomics Aquatic Toxicology Laboratory, December, 1976
16. Monsanto BN-76-260, Acute 96-Hour Toxicity of Sulfasan R to Bluegill Sunfish, EG&G Bionomics Aquatic Yoxicology Laboratory, December, 1976
17. Monsanto AB-80-0240, Acute Toxicity of Sulfasan R to Fathead Minnows, Analytical Bio-Chemistry Labs, May 21, 1980
18. Monsanto SR-83X-063, Time-Independent Toxicity Study on Sulfasan R Using Rainbow Trout as the Test Organism, SRI International, September 8, 1981
19. Monsanto AB-78-356, Acute Toxicity of Sulfasan R to Daphnia magna, Analytical Bio-Chemistry Labs, September 30, 1978
20. Monsanto BN-78-367, Acute Toxicity of Sulfasan R to the Freshwater Alga Selenastrum capricornutum, EG&G Bionomics, September, 1978
21. Monsanto Y-73-286, Acute Oral Toxicity of Sulfasan R, Younger Laboratories, February 15, 1974
22. Monsanto M-29, Minimum Lethal Dose of Sulfasan R, Scientific Associates, March 9, 1951
23. Datsenko, I.I. et al., Toxicological Evaluation of N,N'-dithiomorpholine, Gig. Sanit. 53, 90-92, 1988
24. Monsanto Y-73-286, Acute Dermal Toxicity of Sulfasan R, Younger Laboratories, February 15, 1974
25. Monsanto Y-73-286, Primary Skin Irritation of Sulfasan R, Younger Laboratories, February 15, 1974
26. Monsanto SH-70-10, Primary Skin Irritation Study in Humans, Food and Drug Research Laboratories, July 8, 1970
27. Monsanto Y-73-286, Acute Eye Irritation of Sulfasan R, Younger Laboratories, February 15, 1974
28. Monsanto SH-67-2, 24 & 48 Hour Patch Test on Sulfasan R, Industrial Biology Laboratories, November 14, 1967

29. Monsanto IR-86-34, 4-Week Inhalation Study on Sulfasan R, International Research & Development Corporation, 1986
30. Monsanto IR-86-407, Range-Finding Developmental Toxicity Study in Rats, International Research & Development Corporation, march 24, 1987
31. Monsanto BIO-76-231, Mutagenicity Evaluation of Sulfasan R, Litton Bionetics, December 30, 1976
32. Monsanto BO-78-238, Mutagenicity Evaluation of Sulfasan R in the Mouse Lymphoma Forward Mutation Assay, Litton Bionetics, February, 1979
33. Monsanto BIO-76-231, Mutagenicity Evaluation of Sulfasan R, Litton Bionetics, December 30, 1976
34. Monsanto SR-86-139, Evaluation of the Potential of Sulfasan R to Induce Unscheduled DNA Synthesis in Primary Rat Hepatocyte Cultures, SRI International, September 15, 1986
35. Monsanto PK-87-345, In Vivo Bone Marrow Cytogenetics Rat Metaphase Analysis of Sulfasan R, Pharmakon Research, June 10, 1988
36. Monsanto IR-86-408, Developmental Toxicity Study in Rats with Sulfasan R, International Research & Development Corporation, October 16, 1987

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Data Set

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Existing Chemical	:	ID: 95-16-9
CAS No.	:	95-16-9
EINECS Name	:	benzothiazole
EC No.	:	202-396-2
Molecular Weight	:	135.2
Molecular Formula	:	C7H5NS

Producer related part

Company	:	Bayer Corporation
Creation date	:	03.06.2003

Substance related part

Company	:	Bayer Corporation
Creation date	:	03.06.2003
Status	:	
Memo	:	American Chemistry Council, Rubber and Plastic Additives Panel, Non-sponsored chemical – used for data purposes only
Printing date	:	19.06.2003
Revision date	:	
Date of last update	:	18.06.2003
Number of pages	:	47
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

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03.06.2003

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Cedex :
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Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type :
Name : Flexsys S.A.
Contact person :
Date :
Street : Woluwe Garden, Woluwedal 24
Town : B-1932 St.-Stevens-Woluwe
Country : Netherlands
Phone : +32 (2) 714 32 25
Telefax : +32 (2) 714 32 35
Telex :
Cedex :
Email :
Homepage :

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type :
Name : GENERAL QUIMICA, S.A.
Contact person :
Date :
Street : Km.4 Ctra. de Miranda a Puentelarra
Town : 01213 LANTARON COMUNION (ALAVA)
Country : Spain
Phone : 947-31 01 45

Telefax : 947-31 38 88
Telex : 39531
Cedex :
Email :
Homepage :

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

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 :
Smiles Code : c1ccc2ncsc2c1
Molecular formula : C7-H5-N-S
Molecular weight : 135.18
Petrol class :

03.06.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance
Substance type : organic
Physical status : liquid
Purity : 88 - 98 % v/v
Colour : Yellow to brown
Odour :

03.06.2003

Purity type :
Substance type : organic
Physical status : liquid
Purity : -
Colour :
Odour :

Source : Bayer AG Leverkusen
08.07.1994

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1-Thia-3-azaindene

Source : Flexsys S.A. St.-Stevens-Woluwe
Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.02.1999

Benzosulfonazole

Source : Flexsys S.A. St.-Stevens-Woluwe
Bayer Antwerpen N.V. Antwerpen
GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.02.1999

Benzothiazol

Source : Bayer AG Leverkusen
08.07.1994

Benzothiazole (6Cl, 8Cl, 9Cl)

Source : Flexsys S.A. St.-Stevens-Woluwe
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.02.1999

BT

03.06.2003

BTH

Source : Flexsys S.A. St.-Stevens-Woluwe
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.02.1999

Rubator BT

Source : GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
06.05.1998

Vangard® BT

Source : American Chemistry Council, Rubber and Plastic Additives (RAPA) Panel
03.06.2003

1.3 IMPURITIES

Purity :
CAS-No : 120-75-2
EC-No : 204-423-3
EINECS-Name : 2-methylbenzothiazole
Molecular formula :
Value : .5 - 5 % v/v

Source : American Chemistry Council, Rubber and Plastic Additives (RAPA) Panel
03.06.2003

Purity :
CAS-No : 62-53-3
EC-No : 200-539-3
EINECS-Name : aniline
Molecular formula :
Value : 0 - 4 % v/v

Source : American Chemistry Council, Rubber and Plastic Additives (RAPA) Panel
03.06.2003

Purity :
CAS-No : 108-88-3
EC-No : 203-625-9
EINECS-Name : toluene
Molecular formula :

Value : 0 - 1 % v/v

Source : American Chemistry Council, Rubber and Plastic Additives (RAPA) Panel
03.06.2003

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Non dispersive use

03.06.2003

Type of use : type
Category : Use in closed system

03.06.2003

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

03.06.2003

Type of use : use
Category : Intermediates

03.06.2003

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

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 : TSCA
Additional information :

03.06.2003

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 : 2 - °C
Decomposition : no, at - °C
Sublimation : no
Method : other: FF88.2-1, Determination of Crystallizing Point of Organic Compounds, 1998
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Flexsys Standard Method FF88.2-1, Determination of Crystallizing Point of Organic Compounds, January 09, 1988.
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
03.06.2003

Value : 2 - °C
Sublimation :
Method : other: Handbook value
Year :
GLP : no data
Test substance : other TS: benzothiazole (CAS# 95-16-9); purity not noted

Reliability : (2) valid with restrictions
Data from Handbook or collection of data
Flag : Critical study for SIDS endpoint
03.06.2003 (1)

2.2 BOILING POINT

Value : 231 - °C at 1013 hPa
Decomposition : no
Method : other: no data
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Measured boiling point for benzothiazole distillation from the Flexsys Standard Manufacturing Process Manual for MBT Solution.
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag : Critical study for SIDS endpoint
03.06.2003 (2)

Value : 231 - °C at
Decomposition :
Method : other: Handbook value
Year :
GLP : no data
Test substance : other TS: benzothiazole (CAS# 95-16-9); purity not noted

Reliability : (2) valid with restrictions
Data from Handbook or collection of data
Flag : Critical study for SIDS endpoint
03.06.2003 (1)

2.3 DENSITY

Type : density
Value : ca. 1.246 - at 22 °C

Method : other: FF97.4/ASTM D891-94, 1997
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Specific Gravity of Liquids by Hydrometers. Hydrometers must meet ASTM E100 specifications.
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
03.06.2003 (3)

Type : density
Value : 1.246 - at 20 °C
Method : other: Handbook value
Year :
GLP : no data
Test substance : other TS: benzothiazole (CAS# 95-16-9); purity not noted

Reliability : (2) valid with restrictions
Data from Handbook or collection of data
Flag : Critical study for SIDS endpoint
03.06.2003 (1)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : .01866 - hPa at 25 °C
Decomposition :
Method : other (measured)
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Vapor pressure for benzothiazole from the Flexsys Standard Manufacturing Process Manual for MBT Solution
Result : 3.866 hPa at 80°C
10.799 hPa at 100°C
89.326 hPa at 150°C
449.295 hPa at 200°C
1006.581 hPa at 230°C
Reliability : (1) valid without restriction
GLP study
Flag : Critical study for SIDS endpoint
04.06.2003 (2)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : 1.94 - at 25 °C
pH value : -
Method : other (measured): GC Method for Pow, 1978
Year :
GLP : no
Test substance :

Method : 1% and .01% solutions in 100 ml n-Octanol added to 500 ml water. Shaken for 48 hours, equilibration for several days.
Equilibration performed in the dark to preclude photodegradation. Analysis via GC to determine Pow; Pow = 88 +/- 4.

Remark : Good agreement with calculation method, SRC LogKow (KowWin) Program 1995.
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag : Critical study for SIDS endpoint
04.06.2003 (4)

Partition coefficient :
Log pow : 2.17 - at 25 °C
pH value : -
Method : other (calculated): EPIWIN/KOWWIN v1.66
Year :
GLP : no
Test substance : other TS: molecular structure of benzothiazole (CAS # 95-16-9)

Remark : Estimation method based on molecular structure fragments
Reliability : (2) valid with restrictions
Accepted calculation method
Flag : Critical study for SIDS endpoint
04.06.2003 (5)

Partition coefficient :
Log pow : 2 - at °C
pH value : -
Method : other (calculated): Leo, Hansch: Leo, A. CLOGP-3.63 (1991) Daylight, Chemical Information Systems Inc. Irvine, CA, USA
Year :
GLP :
Test substance :

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.05.1995 (6)

Partition coefficient :
Log pow : 2.01 - at °C
pH value : -
Method : other (measured)
Year :
GLP :
Test substance :

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
08.07.1994 (7)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : 3590 - 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: Saturated Solution / Solvent Extraction / GC Analysis, 1978
Year :
GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Method : The aqueous solubility was determined by adding 1g of the test compound and 500ml purified water to a 1 liter glass bottle with an aluminium foil lined cap. The solution was mixed with a magnetic stirrer for several days to produce a saturated solution. Equilibration was performed in the dark to preclude photodegradation. Stirring was stopped one hour before sampling to permit phase separation. The aqueous layer was extracted with methylene chloride and analyzed via gas chromatography.

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.

Flag : Critical study for SIDS endpoint

04.06.2003 (4)

Solubility in :
Value : ca. 3 - g/l at 20 °C
pH value : -
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

08.07.1994 (8)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : 115.6 °C
Type : open cup
Method : other: ASTM D 92, 1977
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (1) valid without restriction
Guideline study

04.06.2003 (9)

Value : ca. 107 °C
Type :
Method : other: DIN 51758
Year :
GLP :
Test substance :

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

08.07.1994 (8)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo	:	Henry's Law Constant
Method	:	ABC Protocol A-8301, Determination of Air-Water Henry's Law Constant, 1984, and Mackay, D. et al., Determination of Henry's Law Constants for Hydrophobic Pollutants, 1979 GLP Study.
Remark	:	The Henry's Law constant of the test substance in deionized water was determined as the mean of duplicate test systems to be 3.6 x 10-3 1-atm/mole with a standard deviation of 0.07 x 10-3.
Result	:	3.6 x 10-3 atm-m3/mole
Reliability	:	(1) valid without restriction GLP study

04.06.2003 (10)

3.1.1 PHOTODEGRADATION

Type : water
Light source : Sun light
Light spectrum : 250 - nm
Relative intensity : - based on intensity of sunlight
Conc. of substance : 1.018 mg/l at 26 °C
DIRECT PHOTOLYSIS
Halflife t1/2 : 110 - day(s)
Degradation : 100 - % after 170 day(s)
Quantum yield :
Deg. product :
Method : other (measured): Method similar to ASTM Draft Method No. 6, ASTM E35.24, Subcommittee, Aqueous Photolysis Task Group, 1980
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Both direct and sensitized photolysis rates were not significant, with half-lives of > 100 days observed, indicating that the test substance is very stable chemically in water. Samples were analyzed via direct aqueous injection into an HPLC equipped with a variable wavelength detector.
Result : Half life:
110 days in Milli-Q (purified) water
143 days in Mississippi River water
Degradation:
170 days in Milli-Q (purified) water
485 days in Mississippi River water
Test substance : purity: >94%
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
18.06.2003 (11)

Type : air
Light source :
Light spectrum : - nm
Relative intensity : - based on intensity of sunlight
INDIRECT PHOTOLYSIS
Sensitizer : OH
Conc. of sensitizer : 156000000 molecule/cm3
Rate constant : .000000000007 cm^3/(molecule*sec)
Degradation : 50 - % after 18.3 hour(s)
Deg. product :
Method : other (calculated): AOP Program v1.90, 2001
Year :
GLP : no
Test substance : other TS: molecular structure of benzothiazole (CAS# 95-16-9)

Accepted calculation method
Flag : Critical study for SIDS endpoint
18.06.2003 (12)

Type : air
Light source :
Light spectrum : - nm
Relative intensity : - based on intensity of sunlight
Deg. product :
Method : other (calculated): acc. to Atkinson: SRC-AOP for Microsoft Windows
Year :
GLP :

Test substance : other TS: molecular structure of benzothiazole (CAS# 95-16-9)

Remark : Sensitizer: OH
Conc. of Sensitizer: 0.5E6 OH/cm3
Rate Constant: 7.0E-12 cm3/molecule x sec
Half life time: 4.584 d

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
Accepted calculation method

04.06.2003 (13)

3.1.2 STABILITY IN WATER

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-sediment
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: EPIWIN v3.10
Year :

Remark : Calculations based on user input values of water solubility, vapor pressure, Henry LC, Log Kow, melt point and boiling point.

Result :

	Mass Amount (%)	Half-life (hrs)	Emissions (kg/hr)
Air	23.3	36.7	1000
Water	56.4	360	1000
Soil	20.1	360	1000
Sediment	0.16	1.44E+3	0

Persistence time estimated at 114 Hours

Reliability : (2) valid with restrictions
Accepted calculation method

Flag : Critical study for SIDS endpoint

04.06.2003 (12)

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: Estimation Method, 1990
Year :

Remark : Model river = 1 m deep flowing at 1 m/sec and wind velocity of 3 m/sec.
Model lake = 1 m deep flowing at 0.05 m/sec and wind velocity of 0.5 m/sec

Result : Volatilization half-life from model river: 1.376 hours
Volatilization half-life from model lake: 112.5 hours
Volatilization Constant from water: 3.6 x 10-3 atm-m3/mole

Reliability : (2) valid with restrictions

Accepted calculation method
Flag : Critical study for SIDS endpoint
04.06.2003 (14)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 20.4 mg/l related to Test substance
related to
Contact time :
Degradation : < 24 - (±) % after 36 day(s)
Result :
Deg. product :
Method : other: ASTM Proposed Standard Practice for the Determination of the Ultimate Biodegradability of Organic Chemicals, Draft No. 3, ASTM E35.24, Shake Flask CO2 Procedure, 1980
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : Triplicate flasks produced 0-24% theoretical CO2, suggesting that the microbial population was very sensitive to small changes in system parameters. Values in this range usually indicate that the test substance is resistant to biodegradation, that the test compound undergoes primary biodegradation and possibly partial mineralization to a more resistant metabolite, or that the test compound is mineralized to CO2, but at a very slow rate.
Test condition : Medium: soil, raw sewage and activated sludge mixed liquor
Test substance : purity: >94%
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
18.06.2003 (15)

Type : aerobic
Inoculum : other: sludge samplings from different sewage plants, rivers, bays and a lake
Concentration : 100 mg/l related to Test substance
related to
Contact time :
Degradation : 0 - (±) % after 28 day(s)
Result : under test conditions no biodegradation observed
Deg. product :
Method : other:
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : "Biodegradation test of chemical substance by microorganisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test I" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
Remark : related to BOD
sludge conc.: 30 mg/l

Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
04.06.2003 (16)

Type : aerobic
Inoculum : predominantly domestic sewage
Concentration : .8 mg/l related to
related to
Contact time :
Degradation : > 65 - (±) % after 21 day(s)
Result : inherently biodegradable
Deg. product :
Method : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year : 1984
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
04.06.2003 (17)

3.6 BOD5, COD OR BOD5/COD RATIO

Remark : ThOD: 2553 mg/g
COD: 2157 mg/g
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.08.1994 (17)

Remark : ThOD: 2553 mg/g
COD: 2157 mg/g
Source : Bayer AG Leverkusen
11.08.1994 (17)

3.7 BIOACCUMULATION

Species : Cyprinus carpio (Fish, fresh water)
Exposure period : 42 day(s) at °C
Concentration : .2 mg/l
BCF : 2.1 - 5.1
Elimination :
Method : other: MITI Bioaccumulation test of chemical substance in fish and shellfish, 1974. Corresponds to OECD 305C, Bioaccumulation: Degree of Bioconcentration in Fish, 1981
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : Conc. (mg/l) BCF
0.2 2.1-5.1
0.02 < 4.1-7.5
% lipid, average 4.0
Reliability : (1) valid without restriction
Guideline study
04.06.2003 (16)

Species	:	other
Exposure period	:	at °C
Concentration	:	
BCF	:	14 - 16
Elimination	:	
Method	:	other: Calculation, Neely, et. al., 1974
Year	:	
GLP	:	no
Test substance	:	
Remark	:	Calculation from measured octanol/water partition coefficient, Pow = 88.
Reliability	:	(2) valid with restrictions Accepted calculation method

04.06.2003 (4)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : flow through
Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 8.1 -
Limit test :
Analytical monitoring : yes
Method : other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, 1975
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The test was performed under continuous flow conditions using a Mount-Brungs diluter. It was conducted in 19-liter glass aquaria, with 10 fish/replicate. Flow rate was set to provide five tank volumes/day. Juvenile trout, obtained from Mt. Lassen Trout Farm, were maintained at SRI for at least two weeks prior to testing. Average fish length was 4.56 cm, and weight was 0.86 g. Fish were fed a daily ration (5% of body weight) of frozen brine shrimp. The stock solution was prepared by adding 50 grams of the test compound to 200 liters of diluent water and stirring for 48 hours. Nominal test concentrations were 0.0, 1.5, 3.1, 6.2, 12.5 and 25.0 mg/l. The test was terminated after 14 days of exposure.
The LC50 values and 95% confidence limits were calculated by using a computerized program that employed the binomial method and the probit test with Berkson's Adjustment.
Result : LC50 (24h) = >22.4 mg/l
LC50 (96h) = 8.1 mg/l
LC50 (336h) = 5.6 mg/l (14 days)
Test condition : Dissolved oxygen (DO), pH, temperature and chemical concentrations were measured routinely, alternating between the replicates. DO ranged from 9.4-10.8 mg/l, pH from 6.8 to 8.2, temperature between 13.0 and 14.0°C. Hardness, as CaCO3, was 28 mg/l, alkalinity was 29 mg/l, and acidity was <5.0 mg/l.
Test chemical concentrations were determined by an internal standard HPLC method. Measured concentrations of the test chemical were 0, 1.6, 4.4, 8.1, 14.9 and 22.9 mg/l.
Test substance : purity: 96%.
Conclusion : The mortality data indicate that the test compound has a fairly high acute toxicity to rainbow trout at levels quite a bit less than its solubility limits. In addition, the pattern of continuing mortality throughout the test period suggests that this compound is cumulatively toxic over longer exposure periods.
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
18.06.2003 (18)

Type : static
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : 18 -
LC50 : 47 -
Limit test :
Analytical monitoring : no
Method : other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1972).
Year :

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

Method : Test fish were obtained from Fattig Fish Hatchery in Brady, Nebraska. Test fish were held in culture tanks on a 16-hour daylight photoperiod and observed for at least 14 days prior to testing. A daily record of fish observations was maintained during the holding period, during which time the fish were fed a standard diet of commercial fish food until 48 hours prior to testing, when feeding was stopped.
Test fish had a mean weight of 0.15 g and a mean standard length of 21.7 mm. The test was conducted in 5-gallon glass vessels containing 15 liters of laboratory well water. Test fish were acclimated to the dilution water and test temperature, and held without food for 48 hours prior to testing. Nanograde Acetone was used to prepare the test solutions and as the solvent control. Test concentrations were 0, 10, 18, 32, 56 and 100 mg/l for the test compound.
Fish were placed in the testing vessels within 30 minutes of the addition of the test material aliquots. All groups were observed once every 24 hours for mortality and abnormal effects. As a quality check, test fish were challenged with Antimycin A.
The estimated 96Hr LC50 and 95% confidence limits were within the 95% confidence limits reported in the literature, indicating that the fish were in good condition. These values were obtained by employing the statistical methods described by Litchfield and Wilcoxon (A Simplified Method for Evaluating Dose-Effect Experiments, 1949) or Stephan (methods for calculating an LC50, 1977).

Result : LC50 (24h) = 47 mg/l
LC50 (48h) = 47 mg/l
LC50 (96h) = 47 mg/l
NOEC = 18 mg/l
LOEC = 32 mg/l

Test condition : The 0-hour measured control water parameters of this dilution water were dissolved oxygen 9.3 ppm, hardness ($CaCO_3$) of 255 ppm and pH 8.2. The test vessels were kept in a water bath at 22°C. Dissolved oxygen values and pH ranges were monitored during the testing and remained within acceptable limits of 40-100% saturation for dissolved oxygen and pH value consistent with control. The ammonia concentration was below the toxic limit. Water hardness ($CaCO_3$) was 255 ppm.

Test substance : purity: >94%

Reliability : (1) valid without restriction
GLP Guideline study

Flag : Critical study for SIDS endpoint

04.06.2003 (19)

Type : static
Species : Cyprinodon variegatus (Fish, estuary, marine)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : < 10 -
LC50 : 36 -
LOEC : 10 -
Limit test :
Analytical monitoring : no
Method : other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1972).
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Test fish were obtained from Multiaqua Culture System in Amagansett, New York. Test fish were held in culture tanks on a 16-hour daylight photoperiod and observed for at least 14 days prior to testing. A daily

record of fish observations was maintained during the holding period, during which time the fish were fed a mixed diet of brine shrimp nauplii and Tetramin® fish food daily until 48 hours prior to testing, when feeding was stopped. Test fish had a mean weight of 0.32 g and a mean standard length of 21 mm. The test was conducted in 5-gallon glass vessels containing 15 liters of reconstituted salt water and deionized water.
Test fish were acclimated to the dilution water and test temperature, and held without food for 48 hours prior to testing.
A 96-hour range-finding study preceded the definitive study. Test concentrations were 0, 10, 18, 32, 56 and 100 mg/l for the test compound. 1.5 ml of triethylene glycol was added to sample weights before mixing in the test chambers. Test concentrations were obtained by transferring appropriate weights of the test compound directly to the test chambers. Also included were a dilution water control and a solvent control. The solvent control received an aliquot of 1.5 ml of triethylene glycol. Fish were placed in the testing vessels within 30 minutes of the addition of the test material aliquots. All groups were observed once every 24 hours for mortality and abnormal effects.
Statistical analysis of the concentration vs. effect data was obtained by employing a computerized LC50 program developed by Stephan et al. This program calculated the LC50 statistic and its 95% confidence limits using the binomial, the moving average and the probit tests.

Result : LC50 (24h) = 70 mg/l
LC50 (48h) = 64 mg/l
LC50 (96h) = 36 mg/l
NOEC = <10 mg/l
LOEC = 10 mg/l

Test condition : The 0-hour measured control water parameters of this dilution water were dissolved oxygen 6.9 mg/l (corrected for salinity), salinity of 20 ppt, hardness (CaCO3) of 255-275 ppm and pH 8.1. The test vessels were kept in a water bath at 22°C.
Dissolved oxygen values and pH ranges were monitored during the testing and remained within acceptable limits of 95-75% saturation for dissolved oxygen and pH 8.1-7.6.

Test substance : purity: 99%

Reliability : (1) valid without restriction
GLP Guideline study

Flag : Critical study for SIDS endpoint

18.06.2003 (20)

Type : static
Species : Salmo gairdneri (Fish, estuary, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : 187 -
LC50 : 26 -
Limit test :
Analytical monitoring : no
Method : other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1972)
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : The test material, in reagent-grade acetone, was introduced into 15 liters of diluent water in all-glass vessels. Test concentrations were 0, 18, 24, 32, 42 or 56 mg/l for the test compound. Ten rainbow trout, standard length 3.7 cm, were added to each test vessel. The test fish were not fed for 48 hours prior to testing, nor during the exposure period. Observations and mortality counts were made every 24 hours during a 96-hour period following the initiation of exposure. Test concentrations and observed percentage mortality were converted to logarithms and probits, respectively, and these

values were utilized in a least squares regression analysis. The LC50 values and the 95% confidence intervals were calculated from the regression equation.

Result : LC50 (24h) = 35 mg/l
LC50 (48h) = 30 mg/l
LC50 (96h) = 26 mg/l
NOEC = 18 mg/l
LOEC = 24 mg/l

Test condition : No aeration was provided during the test. Temperature was maintained at 12°C. Dissolved oxygen content ranged from 9.9 mg/l (93% of saturation) at the beginning of the test, to 2.0 mg/l (19% of saturation) at the end of the exposure period. Beginning pH was 7.4; ending pH was 6.8. Water hardness (CaCO3) was 255 ppm.

Test substance : purity: >94%

Reliability : (1) valid without restriction
Guideline study

04.06.2003 (21)

Type : static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : 10 -
LC50 : 18 -
Limit test :
Analytical monitoring : no
Method : other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1972).
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : The test material, in reagent-grade acetone, was introduced into 15 liters of diluent water in all-glass vessels. Test concentrations were 0, 10, 14, 18, 24, 32, 42, 56 and 75 mg/l for the test compound. Ten bluegill, standard length 3.8 cm, were added to each test vessel. The test fish were not fed for 48 hours prior to testing, nor during the exposure period. Observations and mortality counts were made every 24 hours during a 96-hour period following the initiation of exposure. Test concentrations and observed percentage mortality were converted to logarithms and probits, respectively, and these values were utilized in a least squares regression analysis. The LC50 values and the 95% confidence intervals were calculated from the regression equation.

Result : LC50 (24h) = >56<75 mg/l
LC50 (48h) = 44 mg/l
LC50 (96h) = 18 mg/l
NOEC = 10 mg/l
LOEC = 14 mg/l

Test condition : No aeration was provided during the test. Temperature was maintained at 22°C. Dissolved oxygen content ranged from 9.1 mg/l (103% of saturation) at the beginning of the test, to 0.2 mg/l (2% of saturation) at the end of the exposure period. Beginning pH was 7.3; ending pH was 6.7. Water hardness (CaCO3) was 255 ppm.

Test substance : purity: >94%

Reliability : (1) valid without restriction
Guideline study

04.06.2003 (21)

Type : static
Species : Brachydanio rerio (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l

LC0 : 65.5 -
LC100 : 66 -
Limit test :
Analytical monitoring : no
Method : other: DIN 38 412, Teil 15: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, Fischtest (L 15) (Juni 1982)
Year : 1984
GLP : no
Test substance :

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
04.06.2003 (17)

Type : static
Species : Oryzias latipes (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : 87.2 -
Limit test :
Analytical monitoring : no data
Method : other: Japanese Industrial Standard (JIS K 0102-1986-71) "Testing methods for industrial waste water"
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Test substance : no data on purity
Reliability : (1) valid without restriction
Guideline study
04.06.2003 (16)

Type : flow through
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 64 -
Limit test :
Analytical monitoring : yes
Method :
Year : 1989
GLP :
Test substance : other TS: purity > 96 %

Remark : 96h-EC50: 60.7 mg/l
Analtyical monitoring: GLC
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
04.06.2003 (22)

Type :
Species : Oryzias latipes (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : 110 -
Method :
Year :
GLP : no
Test substance :

Remark : QSAR calculation
Source : Bayer Antwerpen N.V. Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
04.06.2003 (23)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : 5.6 -
EC50 : 20 -
Analytical monitoring : no
Method : other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA-660/3-75-009, 1975
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The Daphnia magna used in the test were cultured at the ABC facilities. The adult Daphnia were fed the algae Selenastrum capricornutum at least every three days prior to testing and supplemented with a suspension of trout chow. The bioassay was conducted in 500-ml glass beakers containing 250 ml of ABC well water.
An initial range-finding experiment was carried out to determine the exposure concentrations for the definitive test. Water was used as the solvent for the test solutions and as the control. Ten daphnia (first instar less than 18 hours old) were selected for each of the test concentrations (0, 1.0, 3.2, 5.6, 10, 32 and 56 mg/l) in duplicate. Daphnia in all concentrations were observed once every 24 hours for mortality and abnormal effects.
LC50 and 95% CI were calculated employing the technique of Litchfield and Wilcoxon.
Result : EC50 (24h) = 40 mg/l
EC50 (48h) = 20 mg/l
NOEC = 5.6 mg/l
Test condition : Water quality parameters were dissolved oxygen (DO) = 8.6 mg/l, pH = 7.7, hardness = 220 mg/l, and alkalinity = 210 mg/l. Vessels were kept at 19°C in a temperature- controlled area. Lighting was maintained at 50-70 foot-candles on a 16-hour daylight photoperiod.
DO levels and pH were monitored throughout the testing and were considered adequate and equivalent to those measurements in the control chamber. DO was >7.0 mg/l and pH was 7.9 at the end of the testing.
Test substance : purity: 96%.
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
18.06.2003 (24)

Type : static
Species : Mysidopsis bahia (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : 18 -
EC50 : 34 -
Analytical monitoring : no
Method : other: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA-660/3-75-009, 1975
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The mysid shrimp used in this study were obtained from Multi-Aqua Culture Systems in Amagansett, New York. The mysids received a diet of

approximately 1 liter of brine shrimp nauplii per day. The static bioassay was conducted in 400 ml glass vessels containing 300 ml of aged saltwater prepared by dissolving the appropriate amount of synthetic seawater salts in aged ABC well water.
The test mysids were fed approximately 2 ml of brine shrimp per vessel per day throughout the duration of the 96-hour test. A 96-hour range-finding study preceded the definitive study. Based on those results, five concentrations of the test compound (10, 18, 32, 56 and 100 mg/l), with ten mysids per concentration, were selected for the definitive bioassay. Also included were a dilution water control and a solvent control chamber. The mysids were added to the test chambers by random assignment within 30 minutes after addition of the test compound. All concentrations were observed once every 24 hours for mortality and abnormal effects.
LC50 and 95% CI were calculated employing a computerized program developed by Stephan et al. using the binomial, the moving average and the probit tests.

Result : LC50 (24h) = 40 mg/l
LC50 (48h) = 34 mg/l
LC50 (96h) = 28 mg/l
NOEC = 18 mg/l
LOEC = 32 mg/l

Test condition : The saltwater used for culture and testing was prepared to yield a salinity of between 23-28 o/oo and a pH of 8.1-8.3. The 0-hour measured control water parameters of this dilution water were dissolved oxygen (DO) of 7.0 mg/l, salinity 27 o/oo and pH 8.3. Test vessels were kept in a water bath at 25° C.
Dissolved oxygen levels corrected for salinity and temperature, salinity and pH were monitored throughout the testing and were considered adequate and equivalent to those measurements in the control chamber. DO ranged from 5.6-7.0 mg/l (84-104% saturation @ 25°C), salinity ranged from 27-28, and pH from 8.2-8.3.

Test substance : purity: 99%.

Reliability : (1) valid without restriction
GLP Guideline study

05.06.2003 (25)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : growth rate
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : 10 -
EC50 : 67 -
Limit test :
Analytical monitoring : no
Method : other: US EPA Phytotoxicity Method - Algal Assay Procedure: Bottle Test (1971)
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : The test algae were obtained from the US EPA Environmental Research Laboratory in Corvallis, Oregon. Beginning cell numbers in the test flasks were 2.0 x 10(4) cells/ml. Cultures were incubated at 24°C under approximately 4,000 lux illumination. Triplicate cultures were employed for each of the test concentrations and the control. Test containers were 125ml flasks containing 50ml of test medium. Concentrations for the definitive test were based on the results of a 96-hr range-finding study. These concentrations were 0, 6, 10, 32, 56 and 100 mg/ml. Test concentrations were dissolved in reagent-grade acetone. The solvent control was 0.05 ml acetone in water.

Statistical analysis involved converting each test concentration to a logarithm, and the corresponding percentage decrease of in vivo chlorophyll a or cell numbers was converted to a probit (Finny, 1971). The EC50s and 95% confidence limits were then calculated by linear regression. Student's t-test was used to determine whether growth of the solvent control differed from that of the culture medium control. Differences were considered significant at the 95% confidence level.

Result : Decrease in Chlorophyll a:
EC50 (24.h) = >100 mg/l
EC50 (48.h) = >100 mg/l
EC50 (72.h) = 73 mg/l
EC50 (96.h) = 67 mg/l
NOEC = 10 mg/l

Test condition : pH values during the test ranged from 7.8 (0-hour) to 8.1 (96-hour)
Test substance : purity: 99%.
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
18.06.2003 (26)

Species : Selenastrum capricornutum (Algae)
Endpoint : biomass
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : 10 -
EC50 : 64 -
Limit test :
Analytical monitoring : no
Method : other: US EPA Phytotoxicity Method - Algal Assay Procedure: Bottle Test (1971)
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : The test algae were obtained from the US EPA Environmental Research Laboratory in Corvallis, Oregon. Beginning cell numbers in the test flasks were 2.0 x 10(4) cells/ml. Cultures were incubated at 24°C under approximately 4,000 lux illumination. Triplicate cultures were employed for each of the test concentrations and the control. Test containers were 125ml flasks containing 50ml of test medium. Concentrations for the definitive test were based on the results of a 96-hr range-finding study. These concentrations were 0, 6, 10, 32, 56 and 100 mg/ml. Test concentrations were dissolved in reagent-grade acetone. The solvent control was 0.05 ml acetone in water.
Statistical analysis involved converting each test concentration to a logarithm, and the corresponding percentage decrease of in vivo chlorophyll a or cell numbers was converted to a probit (Finny, 1971). The EC50s and 95% confidence limits were then calculated by linear regression. Student's t-test was used to determine whether growth of the solvent control differed from that of the culture medium control. Differences were considered significant at the 95% confidence level.

Test condition : pH values during the test ranged from 7.8 (0-hour) to 8.1 (96-hour)
Test substance : purity: 99%.
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
05.06.2003 (26)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : activated sludge

Exposure period : 3 hour(s)
Unit : mg/l
EC50 : 635 -
EC05 : 216 -
Analytical monitoring : no
Method : ISO 8192 "Test for inhibition of oxygen consumption by activated sludge"
Year : 1990
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
lack of method detail
05.06.2003 (17)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 30 minute(s)
Unit : mg/l
LC0 : 250 -
Analytical monitoring : no
Method : other: Bewetung toxischer Wasserinhaltsstoffe aus ihrer Inhibitorwirkung auf die Substratoxydation von Pseudomonas Stamm Berlin mit Hilfe polarographischer Sauerstoffmessungen. Robra, K.H.: gwf wasser/abwasser 117(2), 80-86 (1976)
Year : 1984
GLP : no
Test substance : no data

Remark : Study completed in 1984
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
data from secondary literature source
05.06.2003 (17)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 18 hour(s)
Unit : mg/l
LC0 : 50 -
Analytical monitoring : no
Method :
Year : 1990
GLP : no
Test substance :

Remark : Method:
Grenzwerte der Schadwirkung wassergefaehrdender Stoffe gegen Bakterien (Pseudomonas putida) und Gruenalgen (Scenedesmus quadricauda) im Zellvermehrungshemmtest. Bringmann, G.; Kuehn, R.: Z. f. Wasser-und Abwasser-Forschung 10 (3/4), 87-98 (1977)
Study completed in 1990
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
data from secondary literature source
05.06.2003 (17)

Type : aquatic

Species	:	Tetrahymena pyriformis (Protozoa)
Exposure period	:	24 hour(s)
Unit	:	mg/l
EC50	:	160 -
Analytical monitoring	:	no data
Method	:	other: static at 30 degrees C
Year	:	
GLP	:	no data
Test substance	:	other TS: analytical grade

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
07.10.1994 (27)

Type	:	
Species	:	activated sludge
Exposure period	:	3 hour(s)
Unit	:	mg/l
EC50	:	650 -
Method	:	OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year	:	
GLP	:	
Test substance	:	

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.08.1994 (23)

Type	:	
Species	:	activated sludge
Exposure period	:	3 hour(s)
Unit	:	mg/l
EC50	:	650 -
Method	:	OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year	:	
GLP	:	
Test substance	:	

Source : Bayer AG Leverkusen
17.08.1994 (23)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : 380 - mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 20
Vehicle : other: undiluted
Doses : 251, 316, 398 or 501 mg/kg bw
Method : other: Single Oral Dose, Younger Laboratories Protocol, 1976
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Four groups of male and female rats (5 animals/dose level) were fed a single oral dose of the undiluted test article via oral gavage. Male rats had initial body weights of 225-255 grams: females had initial body weights of 235-260 grams. Dosages were 251, 316, 398 and 501 mg/kg body weight.

Result : Clinical signs of toxicity included reduced activity and appetite (one to two days in survivors) followed by increasing weakness, collapse and death for decedents within several hours to two days, with most deaths occurring within one day. Gross autopsy findings on decedents were lung and liver hyperemia and gastrointestinal inflammation. Survivors were sacrificed after fourteen days. All viscera of survivors appeared normal.
LD50 = 380 mg/kg bw 95% confidence limits: 340-420 mg/kg.

Dose mg/kg	Mortalities		
	Male	Female	Combined
251	0/3	0/2	0/5
316	1/2	0/3	1/5
398	1/3	2/2	3/5
501	2/2	3/3	5/5

Test substance : purity: >96 %
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag : Critical study for SIDS endpoint
18.06.2003 (28)

Type : LD50
Value : 492 - mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 20
Vehicle : other: Corn Oil (10% solution)
Doses : 398, 501, 631 or 794 mg/kg bw
Method : other: Oral LD50 by Single Oral Dose, Younger Laboratories Protocol, 1963
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Four groups of male and female rats (5 animals /dose level) were fed a single oral dose of the test article as a 10% solution in corn oil via stomach tube. Male rats had initial body weights of 225-265 grams: females had initial body weights of 210-240 grams. After the approximate Minimum Lethal Dose was determined, rats were fed in increasing doses at

increments of 0.1 fractional log intervals at four levels designed to blanket the toxicity range. This supplied data for the calculation of the LD50, which was done according to a modification of the method of E.J. de Beer. Dosages were 398, 501, 631 and 794 mg/kg body weight. Observations were made for toxic signs and the viscera of the animals that died were examined macroscopically.

Result : Survival time was overnight to four days, with most deaths occurring in three to four days. Clinical signs of toxicity included tremors, diarrhea, increasing weakness, collapse and coma from 24 to 72 hours duration. At autopsy, findings of macroscopic examination were tissue edema, with liver and renal hyperemia.

Dose mg/kg	Mortalities		
	Male	Female	Combined
398	0/2	1/3	1/5
501	1/2	2/3	3/5
631	2/3	1/2	3/5
794	3/3	2/2	5/5

Test substance : purity: >96 %
Reliability : (2) valid with restrictions
age of study, lack of method detail
Flag : Critical study for SIDS endpoint
18.06.2003 (29)

Type : LD50
Value : = 479 - mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year : 1986
GLP : yes
Test substance : other TS

Remark : value = 493.3 mg/kg (m), 465.6 mg/kg (f)
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : purity: 99 %
27.07.1994 (30)

Type : LD50
Value : = 257 - mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year : 1982
GLP : no
Test substance : no data

Remark : value = 0.206 ml/kg; density: 1.246 g/l; male rat
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.07.1994 (31)

Type : LD50

Value : = 177 - mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year : 1982
GLP : no
Test substance : no data

Remark : value = 0.142 ml/kg; density: 1.246 g/l; female rat
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.07.1994 (32)

Type : LD50
Value : -
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year :
GLP : no data
Test substance : no data

Remark : dependent on the number of animals in each dose group LD50 values from 180 (1 rat/dose) to 375 mg/kg (5 rats/dose) were calculated
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.07.1994 (33)

Type : LD50
Value : = 900 - mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other
Year :
GLP : no data
Test substance : no data

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.07.1994 (34)

Type : other
Value : -
Species : cat
Strain :
Sex :
Number of animals : 2
Vehicle : other: undiluted
Doses : 25 mg/kg bw

Method : other
Year : 1985
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : 2 cats, 25 mg/kg with gavage: slightly elevated MetHb concentration (up to ca. 10 % after 3 hours), no effect after 7 hours; up to 100 % of the erythrocytes with Heinz bodies
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : purity: ca. 98 %
Reliability : (4) not assignable
18.06.2003 (35)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC50
Value : ca. 5 - mg/l
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : OECD Guide-line 403 "Acute Inhalation Toxicity"
Year : 1992
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : the following analytical concentrations were tested: 0.377 mg/l (vapour); 2.36 mg/l (aerosol) and 6.154 mg/l (aerosol) (analytical aerosol concentration)
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : purity: 97.4 %
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
16.06.2003 (36)

Type : LC50
Value : > 1400 - mg/m3
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals : 4
Vehicle :
Doses :
Exposure time : 6 hour(s)
Method : other: A.T.S., 08/1973
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Four male rats (weight 150 grams each) were placed in a glass dessicator, 250 mm diameter, and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 100ml of the test compound contained in a 250ml tall form gas washing bottle with fritted disc. Vapors from the bottle passed into a one liter bottle to remove droplets, and then on into the chamber. Air flow through the sample was 4

liters/minute as measured by a calibrated rotameter. This air flow was sufficient to violently agitate the liquid. No supplementary air was introduced, as the above supply was ample for the animals' oxygen requirements. Air temperature was 77°F, and test chamber humidity was 54%. The volume of sample remaining after 6 hours was 98ml, indicating 2% vaporization.

Result : All animals survived the six hour exposure and the ten day observation period. Initial exposure produced signs of irritation (occasional pawing at nose, some ocular and nasal discharge during the first 5-10 minutes) and slight weakness. This improved after three to four hours, and at no time were the animals in danger of collapse. Breathing was nearly normal when the animals were removed from the test chamber. Inflammation of the nasal mucosa disappeared within two to three days. No respiratory complications were noted during the ten-day observation period.

Test substance : purity: >96%

Reliability : (1) valid without restriction
Guideline study

Flag : Critical study for SIDS endpoint

16.06.2003 (37)

Type : LC50
Value : -
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals : 6
Vehicle :
Doses :
Exposure time : 6 hour(s)
Method : other: A.T.S., 08/1973
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Six male rats in a 35 liter (volume) test chamber were exposed to a stream of ambient air (air temperature 27°C, air flow rate of 4.0 l/min, chamber humidity of 80%) flowing over a reservoir containing 128.6 grams of the test material for 6 hours. At the conclusion of the test, the contents of the sample reservoir still weighed 128.6 grams, indicating that the test material was not volatile under test conditions.

Result : LC50 = Not determined - No vaporization of test material
The test animals exhibited no signs of toxicity. Following a 14-day observation period, all animals were sacrificed. All viscera appeared normal.

Test substance : purity: >96%

16.06.2003 (38)

Type : other: LC
Value : > 1.5 - mg/l
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time : 6 hour(s)
Method : other: no data
Year :
GLP : no data
Test substance : no data

Source : Bayer Antwerpen N.V. Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
data from secondary literature source
16.06.2003 (39)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : 933 - 1231 mg/kg bw
Species : rat
Strain :
Sex : male/female
Number of animals :
Vehicle : other: undiluted
Doses :
Method : other: Directive 84/449EEC, B.3.
Year : 1992
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : LD50: 1231 mg/kg (male), 933 mg/kg (female)
NOEL = 500 mg/kg
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : purity: 97.4 %
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
18.06.2003 (40)

Type : LD50
Value : 400 - mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 20
Vehicle : other: undiluted
Doses : 316, 398, 501, 631 or 794 mg/kg bw
Method : other: Younger Laboratories Protocol B.1.30, Acute Dermal Toxicity by Single Dermal Application, 06/28/1984
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The undiluted test substance was applied to the intact dorsal skin of male and female rabbits (2/sex/dose level) for a period of 24 hours, followed by a 14 day observation period. Initial weights for males in this study were 2.1-2.3 kg, and 2.2-2.3 kg for females. weighed. Dosages were 316, 398, 501, 631 or 794 mg/kg bw. Remaining test material was wiped from the exposed sites after 24 hours.
Result : LD50 = 500 mg/kg bw (males) C.I. = 355-700 mg/kg bw
LD50 = 400 mg/kg bw (females) C.I. = 310-520 mg/kg bw
LD50 = 400 mg/kg bw (combined) C.I. = 300-535 mg/kg bw

Clinical signs of toxicity included lethargy lasting up to two days, weakness and collapse. Deaths occurred in all but the lowest dose levels at 1-2 days after exposure. Necropsy findings included hemorrhagic areas of the lungs, liver, kidney and spleen discoloration, gall bladder enlargement and gastrointestinal inflammation. Surviving animals had no visible signs of pathology at necropsy, and all had gained weight.

Dose mg/kg	Mortalities Male	Female	Combined
316	0/2	0/2	0/4
398	1/2	1/2	2/4
501	1/2	2/2	3/4
631	1/2	2/2	3/4
794	2/2	2/2	4/4

Test substance : "Nitro composite" approximately 94%
Reliability : (1) valid without restriction
Comparable to Guideline study
Flag : Critical study for SIDS endpoint
18.06.2003 (41)

Type : LD50
Value : 126 - 200 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 5
Vehicle : other: undiluted
Doses : 79.4, 126, 200, 398 or 501 mg/kg bw
Method : other: LD50 by Single Dermal Dose, Younger Laboratories Protocol, 1975
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : The undiluted test substance was applied to the shaved skin of male and female rabbits (1 animal/dose level) for a period of 24 hours, followed by a 14 day recovery period. Males in this study weighed 1.8-1.9 kg, and females weighed 1.9 kg. Dosages were 79.4, 126, 200, 398 or 501 mg/kg bw. The test material was held in place by means of an occlusive wrap of latex rubber and secured by bandaging and elastic tape. The occlusive wrap was removed after 24 hours and the excess material was wiped from the test animal.
Result : Clinical signs of toxicity were reduced appetite and activity -two to three days in survivors - followed by increasing weakness, collapse and death. Deaths occurred in 2-5 days. Gross autopsy findings on decedents included hemorrhagic areas of the lungs, liver, and spleen, kidney discoloration, enlarged gall bladed, and gastrointestinal inflammation. Survivors were sacrificed following the recovery period. All viscera appeared normal in these animals.

Dose mg/kg	Mortalities Male	Female	Combined
79.4	0/1	---	0/1
126.0	---	0/1	0/1
200.0	1/1	---	1/1
398.0	---	1/1	1/1
501.0	1/1	---	1/1

Test substance : purity: 96%.
Reliability : (2) valid with restrictions
age of study, lack of method detail
16.06.2003 (42)

Type : LDLo
Value : > 631 - mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 6
Vehicle : other: undiluted
Doses : 251, 398, 631, 1000, 1580 or 2510 mg/kg bw

Method : other: Minimum Lethal Dose by Skin Absorption, Younger Laboratories Protocol, 1963
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : The undiluted test substance was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of albino male and female rabbits. The treated areas were covered with plastic strips and the animals placed in wooden stocks for periods of up to 24 hours, after which time the test material was wiped away and the animals were placed into individual cages. Observations were made for toxic symptoms and the viscera of the animals that died on test were examined macroscopically.
Result : Clinical signs of toxicity were dyspnea, salivation, followed by weakness within two to four hours at the three highest dose levels. Survival times at the three highest doses were 8-24 hours. Animals given the three lower doses survived, and either gained or maintained weight. At autopsy, the only finding noted was pulmonary congestion.
Test substance : purity: 96%.
Reliability : (2) valid with restrictions
age of study, lack of method detail

16.06.2003 (43)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50
Value : ca. 100 - 200 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Route of admin. : i.p.
Exposure time :
Method : other: no data
Year :
GLP : no data
Test substance : no data

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

28.07.1994 (44)

Type : LD50
Value : = 95 - mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Route of admin. : i.v.
Exposure time :
Method : other: no data
Year :
GLP : no data
Test substance : no data

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

28.07.1994 (45)

Type : LDLo
Value : -
Species : other
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Route of admin. : other
Exposure time :
Method : other: no data
Year :
GLP : no data
Test substance : no data

Remark : cat, i.v. 100 mg/kg; rat, i.v. 200-300 mg/kg;
rat, i.p. 1000 mg/kg; rat, oral 3000 mg/kg
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

27.07.1994 (46)

Type : LD50
Value : = 310 - mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Route of admin. : other: no data
Exposure time :
Method : other: no data
Year :
GLP : no data
Test substance : no data

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

27.07.1994 (47)

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle :
PDII : .6
Result : slightly irritating
Classification : not irritating
Method : other: F.H.S.A./Draize, J.H., Woodard, G., and Calvery, H.O., 1944
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : 0.5ml of the undiluted test substance was applied to the shaved dorsal areas of six albino rabbits. The test material was applied to the skin under 1" square gauze patches and held in contact with the skin by means of an occlusive wrap of latex rubber secured by bandaging and elastic tape. The

occlusive wrap and gauze patches were removed after 24 hours. Dermal irritation was scored by the Draize Method, and results were recorded 24, 48, 72 and 168 hours after topical application. The Primary Irritation Index was calculated by averaging the mean scores at 24 and 72 hours and found to be 0.6 on a scale of 0.0-8.0.

Result : A slight defatting effect was noted - skin flaked off in seven to ten days. There was no injury in depth.
Test substance : purity: >96%
Reliability : (2) valid with restrictions
age of study, lack of method detail

18.06.2003 (48)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 3
Vehicle :
PDII : 3
Result : moderately irritating
Classification : irritating
Method : other: F.H.S.A./Draize, J.H., Woodard, G., and Calvery, H.O., 1944
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : The undiluted test substance was applied to the clipped, intact skin of three albino rabbits and removed after 24 hours. The application was covered with plastic strips to retard evaporation and avoid contamination. Observations were made at 1 hour, and then again at 24, 48, 72 and 120 hours. Dermal irritation was scored by the Draize Method.
Result : Redness developed within minutes. After one hour, there was a well-defined to moderate erythema with slight edema for an average score of 3.0 (out of 8.0) Edema disappeared in two animals in 24 hours, and inflammation reduced to slight redness in all animals within 72 hours. All animals scored "0" within 5 days.
Test substance : purity: >96%
Reliability : (2) valid with restrictions
age of study, lack of method detail, scoring at 1 hour instead of 24-72 hours

18.06.2003 (49)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result : not irritating
Classification :
Method : OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year : 1983
GLP : no
Test substance : no data

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

18.06.2003 (50)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : 24 hour(s)
Comment : not rinsed
Number of animals : 6
Vehicle :
Result : slightly irritating
Classification : not irritating
Method : other: F.H.S.A./Draize, J.H., Woodard, G., and Calvery, H.O., 1944
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : 0.1ml of the undiluted test compound was applied to one eye of six albino rabbits. The other eye was not treated and served as a control. The cornea, iris and conjuntivea were examined immediately after treatment, and then at intervals of 10 minutes, 1 hour, and then at 24, 48, 72, 120 and 168 hours. The Draize Method was used for scoring eye irritation.

Result :

Exposure time	Mean score (X/110)
1 hour	15.0
24 hours	23.5
48 hours	12.5
72 hours	4.8
120 hours	0.0
168 hours	0.0

Test substance : purity: 96%.
Reliability : (2) valid with restrictions
age of study, lack of method detail

18.06.2003 (51)

Species : rabbit
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : irritating
Classification :
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1983
GLP : no
Test substance : no data

Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

18.06.2003 (52)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex : male/female
Strain :
Route of admin. : oral feed
Exposure period : 6 months
Frequency of treatm. : daily

Post exposure period : no data
Doses :
Control group : yes, concurrent vehicle
Method : other: no data
Year :
GLP : no
Test substance : no data

Remark : In a limited study, benzothiazole and similar compounds were administered to rats for six months in a dietary admixture. No evidence of carcinogenic activity was noted. No other data was presented.
Reliability : (3) invalid
Documentation insufficient for assessment
16.06.2003 (53)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Bacterial reverse mutation assay
System of testing : Salmonella typhimurium TA-98, TA-100, TA-1535, TA-1537, TA-1538
Test concentration : 0.001, 0.01, 0.10, 1.00 or 5.00 ul/plate (duplicate)
Cycotoxic concentr. : With and without metabolic activation: 5.00 ul/plate
Metabolic activation : with and without
Result : negative
Method : other: Ames Plate Test (Overlay method) 1975
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The test compound was evaluated for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. The Salmonella typhimurium strains used for this experiment were obtained from Dr. Bruce Ames. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. The mutagenesis assay was carried out as the plate-incorporation test according to the Ames protocol. Chemicals used as positive controls for the non-activation assays were 10 ug/plate Methylnitrosoguanidine (MNNG), 100 ug/plate 2-nitrofluorene (NF) or 10 ug/plate Quinacrine mustard (QM). Positive controls used for the activation assays were 100 ug/plate 2-anthramine (ANTH), 100 ug/plate 2-Acetylaminofluorene (AAF) or 100 ug/plate 8-Aminoquinoline (AMQ). Dimethylsulfoxide (DMSO, 2.5%/plate) was used as the solvent and the solvent control. Statistical analysis was performed on plate incorporation assay results after transforming revertant/plate values as Log10 (revertants/plate). Analysis included Bartlett's test for homogeneity of variance, and comparison of treatments with controls using within-levels pooled variance and a one-sided t-test. Grubbs' test was performed to determine if outliers were present.
Result : The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.
Positive control treatments produced the expected large increases in the frequency of histidine revertants.
Test substance : purity: >98%
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
16.06.2003 (54)

Type : Gene mutation in Saccharomyces cerevisiae
System of testing : Saccharomyces cerevisiae, D4
Test concentration : 0.001, 0.01, 0.10, 1.00 or 5.00 ul/plate (duplicate)

Cycotoxic concentr. : With and without metabolic activation: 5.00 ul/plate
Metabolic activation : with and without
Result : negative
Method : other: Ames Mutagenicity Plate Test (Overlay Method) 1975
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The test compound was evaluated for genetic activity with and without the addition of mammalian metabolic activation preparations. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. The mutagenesis assay was carried out as the plate-incorporation test according to the Ames protocol. The chemical used as the positive control for the non-activation assay was methylnitrosoguanidine (MNNG) at 10 ug/plate. The positive control chemical used for the activation assay was DMNA at 100 micromoles/plate. Dimethylsulfoxide (DMSO, 2.5%/plate) was used as the solvent and the solvent control. Statistical analysis included Bartlett's test for homogeneity of variance, and comparison of treatments with controls using within-levels pooled variance and a one-sided t-test. Grubbs' test was performed to determine if outliers were present.
Result : The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.
Test substance : purity: >98%
Reliability : (1) valid without restriction
GLP Guideline study

18.06.2003 (54)

Type : Ames test
System of testing : S. typhimurium TA 98, TA 100, TA 1535, TA 1537
Test concentration : up to 5000 ug/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: see remark
Year : 1991
GLP : yes
Test substance : other TS

Remark : method: as described by Ames, B.N. et al., Proc. nat. Acad. Sci. (USA) 70, 2281-2285 (1973); Ames, B.N. et al., Mutat. Res. 31, 347-364 (1975) and Maron, D.M. & Ames, B.N., Mutat. Res. 113, 173-215 (1983)
No deviations from protocol noted.
Source : Bayer Antwerpen N.V. Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : purity: 97.4 %
Reliability : (1) valid without restriction
GLP Guideline study

18.06.2003 (55)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

Endpoint	:	Neurotoxicity
Study descr. in chapter	:	
Reference	:	
Type	:	
Species	:	other: Cyprinodon variegates (Sheepshead Minnows)
Sex	:	
Strain	:	
Route of admin.	:	
No. of animals	:	
Vehicle	:	
Exposure period	:	
Frequency of treatm.	:	
Doses	:	3.75, 7.5, 15, 30 and 60 mg/l
Control group	:	
Observation period	:	
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The neurotoxic potential of benzothiazole was investigated following in vivo and in vitro exposure of sheepshead minnows at the above doses. Following exposure, the test fish were evaluated for survival, growth and histological alterations
Remark	:	Benzothiazole cytotoxicity to primary cultures of brain cells from sheepshead minnow and tilapia (Oreochromis niloticus) and two epithelial cell lines was evaluated using a tetrazolium salt assay (MTT) at one and four days. The in vitro results indicated that primary cultures of brain cells are less sensitive to benzothiazole than epithelial cell lines. Significant cytotoxicity to the epithelial cell lines was noted at the two highest concentrations tested (30 mg/l and 60 mg/l).
Result	:	Fish mortality occurred after five days of exposure to the highest dose level of 60 mg/l. The LC50 value was determined to be 41.9 mg/l. Significant decreases in larval growth were noted at all test concentrations. Histologically, gills had cellular alterations but the central nervous system lacked severe cellular damage
Conclusion	:	Histologically and cytotoxicologically, the results indicated that benzothiazole is a gill toxicant but not a neurotoxicant.
Reliability	:	(4) not assignable Secondary literature

18.06.2003 (56)

5.10 EXPOSURE EXPERIENCE

Remark	:	Upon the flexor surface of the left wrist of 43 subjects (5f/38m) approx. 25 mg/kg were placed; 17 subjects with positive reactions (no further information)
Source	:	Bayer Antwerpen N.V. Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	other TS

27.07.1994 (46)

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

9. References

(1) CRC Handbook of Chemistry and Physics. 80th edition (1999-2000) David R. Lide, ed. CRC Press, New York. p3-80, No. 2861.

(2) Flexsys MBT Solution Process, Physical Constants Data on Benzothiazole, March, 1996

(3) Flexsys Standard Method FF97.4/ASTM D891-94, Specific Gravity of Liquids by Hydrometers, April 14, 1997

(4) Monsanto ES-78-SS-20, Water Solubility and Octanol/Water Partition Coefficients of Selected Rubber Chemicals, MIC Environmental Sciences, December, 1978.

(5) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(6) Calculation Bayer AG, WV-UWS

(7) THOR database Pomona 89, MedChemSoftware 1989, Daylight, Chemical Information Systems, Claremont, CA 91711, USA

(8) Safety Data Sheet Bayer AG

(9) American Society for Testing and Materials (ASTM), Test Method for Flash Points and Fire Points of Liquids by Cleveland Open Cup, 1977

(10) Monsanto ABC 32287, Determination of Henry's Law Constant in Infinitely Dilute Aqueous Solution for Benzothiazole, Analytical Bio-Chemistry Laboratories, December 20, 1985

(11) Monsanto MO-92-9058/ES-80-SS-43, Aqueous Photolysis Screening of Selected Rubber Chemicals, MIC Environmental Sciences, December 29, 1980

(12) Meylan W. and Howard P. (2001) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(13) Calculation Bayer AG, WV-UWS/Produktsicherheit 1995

(14) Handbook of Chemical Property Estimation Methods, 1990

(15) Monsanto ES-80-SS-42, Biodegradation Screening of Selected Rubber Chemicals, MIC Environmental Sciences, 1980

(16) MITI/CITI, Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL, Japan. Compiled under the Supervision of Chemical Products Safety Division, Basic Industries Bureau MITI, Edited by CITI, October, 1992

(17) Bayer AG data

(18) Monsanto SR-80-1803057, Time Independent Toxicity Study on Benzothiazole Using Rainbow Trout, SRI International, September 8, 1981

(19) Monsanto AB-80-1803035-A1, Acute Toxicity of Benzothiazole to Fathead Minnows, Analytical Bio-Chemistry Laboratories, June 23, 1980

(20) Monsanto AB-32316, Acute Toxicity of Benzothiazole to Sheepshead Minnow, Analytical Bio-Chemistry Laboratories, March 11, 1985

(21) Monsanto BN-76-167, Acute (96-hour) Toxicity of Benzothiazole to Rainbow Trout, EG&G Bionomics, December, 1976

(22) Geiger, D.L. et al., Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas) Vol. V, Center for Lake Superior Environmental Studies, University of Wisconsin-Superior, WI, ISBN 0-9614968-5-1 (1990)

(23) Yoshioka, Y. et al., Ecotox. Environ. Saf. 12 (3), 206-212 (1986)

(24) Monsanto AB-78-1384318-3a, Acute Toxicity of Benzothiazole to Daphnia magna, Analytical Bio-Chemistry Laboratories, September 30, 1978

(25) Monsanto AB-85-32317, Acute Toxicity of Benzothiazole to Mysid Shrimp, Analytical Bio-Chemistry Laboratories, February 5, 1985

(26) Monsanto BN-78-1384318, Acute Toxicity of Benzothiazole to the Freshwater Alga Selenastrum capricornutum, EG&G Bionomics, September, 1978

(27) Yoshioka, Y. et al., The Science of the Total Environment 43, 149-157 (1985)

(28) Monsanto Y-76-332, Acute Oral Toxicity of Benzothiazole, Younger Laboratories, October 15, 1976.

(29) Monsanto Y-64-1, Toxicological Investigation of Benzothiazole - Oral LD50, Younger Laboratories, January 22, 1964.

(30) Mayhew, D.A. et al., American Biogenics Corporation, AD-A172-647 September 1986

(31) Loeser, E., Untersuchungen zur akuten oralen Toxizitaet an maennlichen Ratten, July 27, 1982

(32) Loeser, E., Untersuchungen zur akuten oralen Toxizitaet an weiblichen Ratten, July 29, 1982

(33) Lorke, D., Arch. Toxicol. 54, 275-287 (1983)

(34) Moran, E.J. & Easterday, O.D., Drug Chem. Toxicol. 3, 249-258 (1980)

(35) Schmidt, W.M. & Loeser, E., Untersuchungen zur akuten oralen Toxizitaet an der Katze, December 20, 1985

(36) Bayer AG data, Report No. 21675, September 16, 1992

(37) Monsanto Y-64-1, Inhalation of Benzothiazole Vapors by Rats, Younger Laboratories, January 22, 1964

(38) Monsanto Y-76-332, Acute Inhalation Toxicity of Benzothiazole, Younger Laboratories, October 15, 1973

(39) United States EPA, Office of Pesticides and Toxic Substances. 8EHQ-1190-0987S, cited in RTECS April 1994

(40) Bayer AG data, Report No. 20998, January 21, 1992

(41) Monsanto YO-84-039, Acute Dermal Toxicity Study with Benzothiazole, Younger Laboratories, October 16, 1984

(42) Monsanto Y-76-332, Acute Dermal Toxicity of Benzothiazole, Younger Laboratories, October 15, 1976.

(43) Monsanto Y-64-1, The Minimum Lethal Dose of Benzothiazole by Skin Absorption in Rabbits, Younger Laboratories, January 22, 1964

(44) Doull, J. et al., AD277-689, 1-124 (1962)

(45) Domino, E.F. et al., J. Pharm. Exp. Ther. 105, 486-497 (1952)

(46) Bogert, M.T. & Husted, H.G., J. Pharm. Exp. Ther. 45, 189-207 (1932)

(47) Anonymous, Khimiko Farmatsevticheskii Zhurnal 9 (12), 11 (1975), cited in RTECS April 1994

(48) Monsanto Y-76-332, Primary Skin Irritation of Benzothiazole, Younger Laboratories, October 15, 1976

(49) Monsanto Y-64-1, Skin Irritation (Rabbits) with Benzothiazole, Younger Laboratories, January 22, 1964

(50) Suberg, H., Untersuchungen auf primaere Reiz-/Aetzwirkung an der Kaninchenhaut, January 3, 1983

(51) Monsanto Y-76-332, Acute Eye Irritation of Benzothiazole, Younger Laboratories, October 15, 1976

(52) Suberg, H., Untersuchungen auf Schleimhautreizwirkung am Kaninchenauge, January 3, 1983

(53) Brown, E.V., Carcinogenic Activity of Analogues of p-Dimethylaminoazobenzene, Acta Unis Int. Contra Cancrum 19, 551-553, 1963

(54) Monsanto BIO-76-175, Mutagenicity Evaluation of Benzothiazole, Litton Bionetics, November 24, 1976

(55) Bayer AG data, Report No. 20847, November 26, 1991

(56) Evans, J.J., Shoemaker, C.A., Klesius, P.H., Maryland Department of Natural Resources, Fisheries Services, Oxford Laboratory, Oxford, MD., The In vivo and In vitro effects of Benzothiazole on Sheepshead Minnows, Marine Environmental Research 50 (1-5) 257-261, Jul-Dec, 2000

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT

102-77-2
2-(Morpholinothio)benzothiazole

201-14953B1

Molecular Formula: C11-H12-N2-O-S2
Molecular Weight: 252.3

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance: Organic
B. Physical State: Off-white to tan solid
C. Purity: 95-99% Typical for Commercial Products

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1.2 SYNONYMS

Santocure® MBS
Santocure® MOR
Cure-Rite® OBTS
Delac® MOR
Vulkacit® MOZ
AMAX®
MOR
MBS
OBTS

1.3 IMPURITIES

Morpholine (110-91-8) <0.4%
2-Mercaptobenzothiazole (149-30-4) <1%
Mercaptobenzothiazole Disulfide (120-78-5) <1%
Benzothiazole (95-16-9) <0.4%

2. PHYSICAL-CHEMICAL DATA

*2.1 MELTING POINT

Value:	82-88°C
Decomposition:	No
Sublimation:	No
Method:	ASTM D-1519/FF83.9-1
GLP:	Yes
Remarks:	Capillary Melt Point determination
Reference:	ASTM D-1519/Flexsys Standard Methods of Analysis, 1983
Reliability:	(1) Valid without restriction

Value:	81.9-84.79°C
Decomposition:	No
Sublimation:	No
Method:	Differential Scanning Calorimeter (DSC)
GLP:	Yes
Remarks:	Onset at 81.9°C. Final melt at 84.79°C
Reference:	Flexsys Analytical Research Report 2003.012, 2003
Reliability:	(1) Valid without restriction

Value:	216.1°C (Decomposition Temperature)
Pressure:	1 Atm
Decomposition:	Yes
Method:	Differential Scanning Calorimeter (DSC)
GLP:	Yes
Remarks:	Decomposition begins at 216.1°C, complete at 219.37°C Conditions were 5°C/minute under nitrogen
Reference:	Flexsys Analytical Research Report 2003.012, 2003
Reliability:	(1) Valid without restriction

†2.3 DENSITY (relative density)

Type:	Density
Value:	1.4
Temperature:	20 °C
Method:	FF97.8-1 Density of Solids
GLP:	Yes
Remarks:	Density of solids by displacement
Reference:	FF97.8-1 Flexsys Standard Methods of Analysis, 1997
Reliability:	(1) Valid without restriction

***2.4 VAPOUR PRESSURE**

Value:	0.000002013 hPa
Temperature:	25 °C
Method:	calculated – Antoine Method MPBPWIN v1.40.
GLP:	No
Remarks:	Calculated using MP = 82°C
Reference:	EPIWIN/MPBPWIN v1.40
Reliability:	(2) Valid with restrictions – modelling data

Value:	0.0000023 hPa
Temperature:	20 °C
Method:	calculated
GLP:	No
Remarks:	None
Reference:	Bayer AG Data

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

Log Pow:	1.025
Temperature:	25 °C
Method:	calculated KOWWIN v1.40
GLP:	No
Remarks:	Calculated using MP = 82°C and solubility of 0.039 mg/l
Reference:	EPIWIN/KOWWIN v1.40
Reliability:	(2) Valid with restrictions – modelling data

Log Pow:	3.49
Temperature:	25 °C

Method:	Measured HPLC Method for Pow
GLP:	No
Remarks:	1% and .01% solutions in 100 ml n-Octanol added to500 ml water. Shaken for 48 hours, equilibration for several days. Equilibration performed in the dark to preclude photodegradation. Analysis via HPLC to determine Pow; Pow = 3100 +/- 1400
Reference:	Monsanto ES-78-SS-20, 1978
Reliability:	(2) Valid with restrictions – lack of method detail

*2.6 WATER SOLUBILITY

A. Solubility

Value:	0.039 mg/l (Degradation noted)
Temperature:	25 °C
Description:	Of very low solubility
Method:	HPLC of saturated water solution
GLP:	No
Remarks:	1g of test chemical added to 500ml water. Stirred in the dark for several days. Analysis via HPLC. One or more degradation products observed in the chromatogram. Results indicate the maximum amount of test compound in aqueous phase when a large excess is equilibrated with water.
Reference:	Monsanto ES-78-SS-20, 1978
Reliability:	(2) Valid with restrictions – unstable compound under test Conditions

Value:	24.01 mg/l
Temperature:	25 °C
Description:	Of very low solubility
Method:	Estimation, WSKOW v1.40
GLP:	No
Remarks:	EPIWIN estimation based on a Log Kow of 3.49
Reference:	EPIWIN/WSKOW v.140
Reliability:	(2) Valid with restrictions – modelling data

2.7 FLASH POINT

Value:	177°C
Type:	Cleveland Open Cup
Method:	ASTM D 92-96
Reference:	Flexsys America Data
Reliability:	(1) Valid without restrictions

Value:	188°C
Type:	Open Cup
Method:	DIN 51584
Reference:	Bayer AG data
Reliability:	(1) Valid without restrictions

2.11 OXIDISING PROPERTIES

†2.12 OXIDATION: REDUCTION POTENTIAL

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

B. Other data – Henry's Law Constant

Results: 7.551E-008 atm-m3/mole
Remarks: Calculated at 25°C
Reference: EPIWIN/HENRYWIN v3.10
Reliability: (2) Valid with restrictions – modelling data

3. ENVIRONMENTAL FATE AND PATHWAYS

*3.1.1 PHOTODEGRADATION

Type: Air
Indirect Photolysis:
Type of sensitizer: OH
Concentration of sensitizer: 156000 molecule/m3
Rate constant (radical): 0.0000000001199482 cm^3/molecule*sec
Degradation: 50% after 1.070 hours
Method: calculated
AOP Program v1.89, 1999
GLP: No
Test substance: Other (calculated)
Reference: AopWin v1.89
Reliability: (2) Valid with restrictions – accepted calculation method

Type: Water
Light source: Sunlight
Spectrum of substance: 300 nm
Concentration of Substance: 1.006 mg/l
Temperature: 26 °C
Direct photolysis:
Half life: 1 hour
Degradation: 97 % after 4 hours
Method: measured
Method similar to ASTM Draft Method No. 6, ASTM E35.24 Subcommittee, Aqueous Photolysis Task Group, 1980
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: 96%
Remarks: Dark control recovery was 97% at 4 hours. Test substance values at 0, 1, 2, 3 and 4 hours were 100%, 45%, 15% and 3%, respectively, for light exposed conditions.
Reference: Monsanto MO-92-9058/ES-80-SS-43, 1980

*3.1.2 STABILITY IN WATER

Type: Abiotic (hydrolysis)
Degradation: 24% at pH 7 at 20 °C after 25 hours
100% at pH 7 at 20°C after 7 days

Method: Phase I Hydrolysis Screening Study
H. Suffet, et. al., Hydrolysis Protocols – Effects of Water On the Environmental Fate of Chemicals, 1980
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 96%
Remarks: The experiment was run under dark conditions. Detection of hydrolysis products was performed by HPLC and GC/MS.
Hydrolysis products:
Benzothiazole (95-16-9), 64%
2-Mercaptobenzothiazole (149-30-4), 21%
Unknown, proposed comp. C11-H14-S2-N2-O2, 15%
Morpholine (110-91-8), % not determined
Reference: Monsanto AB-84-131, Analytical Bio-Chemistry Labs, 1984
Reliability: (1) Valid without restriction

*3.2 MONITORING DATA (ENVIRONMENTAL)

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

*3.3.1 TRANSPORT

Type: Volatility
Media: Water
Method: Estimation Method, 1990
Results: Volatilization half-life from model river: 1.71E+008 hours
Volatilization half-life from model lake: 1.865E+009 hours
Volatilization Constant from water: 5.44E-012 atm-m3/mole
Remarks: Model river = 1 m deep flowing at 1 m/sec and wind velocity of 3 m/sec.
Model lake = 1 m deep flowing at 0.05 m/sec and wind velocity of 0.5 m/sec.
Reference: Handbook of Chemical Property Estimation Methods, 1990
Reliability: (2) Valid with restrictions – modelling data

*3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Media: Air-biota-sediment-soil-water
Method: Fugacity level III
EPIWIN v3.10
Results:

	Mass Amount (%)	Half-life (hrs)	Emissions (kg/hr)
Air	7.5e-005	2.14	1000
Water	20.3	900.00	1000
Soil	78.8	900.00	1000
Sediment	0.944	3.6e+003	0

Persistence time estimated at 1.03e+003 Hours

Remarks: Calculations based on user input values of water solubility of 24.01 mg/l, Log Kow of 3.49, and melting point of 82°C
Reference: EPISUITE/EPIWIN v3.10
Reliability: (2) Valid with restrictions – modelling data

*3.5 BIODEGRADATION

Type: aerobic
Inoculum: predominately domestic sewage
Concentration of the chemical: 100 mg/l related to COD (Chemical Oxygen Demand)
Degradation: 0% after 28 days
Results: under test condition no biodegradation observed
Method: Directive 84/449/EEC, C.7, Biotic Degradation – Modified MITI
GLP: No
Test substance: As prescribed by 1,1-1.4, purity: >93%
Remarks: Meets national standards method
Reference: Bayer AG data
Reliability: (1) Valid without restriction

3.6 BOD5, COD or BOD5/COD Ratio

ThOD: 1880 mg/g
Reference: Bayer AG data

3.7 BIOACCUMULATION

Species: Other
BCF: 100 (+/-30)
Method: Calculation, Neely, et. al., 1974
GLP: No data
Remarks: Calculation from measured octanol/water partition coefficient Pow = 3100 (+/- 1400)
Reference: Monsanto ES-78-SS-20, 1978
Reliability: (2) Valid with restrictions – acceptable calculation method

Species: Other
BCF: 97.12
Method: BCFWIN v2.14
GLP: No
Remarks: Calculation using measured Log Pow = 3.49. Excellent Agreement with calculated BCF of 100 (above)
Reference: EPIWIN/BCFWIN v2.14
Reliability: (2) Valid with restrictions – modelling data

4. ECOTOXICITY

*4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type of test: static
closed-system
Species: Pimephales promelas (Fathead Minnow)
Exposure period: 96 hours
Results: LC_{50} (24h) = 4.0 mg/l
LC_{50} (48h) = 4.0 mg/l
LC_{50} (96h) = 3.5 mg/l
NOEC = 1.0 mg/l
LOEC = Not Determined

Analytical monitoring: No
Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1972).
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 96%
Remarks: Test fish were obtained from Fattig Fish Hatchery in Brady, Nebraska. Test fish were held in culture tanks on a 16-hour daylight photoperiod and observed for at least 14 days prior to testing. A daily record of fish observations was maintained during the holding period, during which time the fish were fed a standard diet of commercial fish food until 48 hours prior to testing, when feeding was stopped. Test fish had a mean weight of 0.25 g and a mean standard length of 25.8 mm. The test was conducted in 5-gallon glass vessels containing 15liters of laboratory well water. The 0-hour measured control water parameters of this dilution water were dissolved oxygen 9.3 ppm, hardness (CaCO3) of 255 ppm and pH 8.2. The test vessels were kept in a water bath at 22°C.

Test fish were acclimated to the dilution water and test temperature, and held without food for 48 hours prior to testing. Nanograde Acetone was used to prepare the test solutions and as the solvent control. A 48-hour range-finding study preceded the definitive test. Test concentrations were 0, 1.0, 1.8, 3.2, 5.6 or 10.0 mg/l for the test compound. Fish were placed in the testing vessels within 20 minutes of the addition of the test material aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects. Dissolved oxygen values and pH ranges were monitored during the testing and remained within acceptable limits of 40-100% saturation for dissolved oxygen and pH value consistent with control. The ammonia concentration was below the toxic limit. Water hardness (CaCO3) was 255 ppm. As a quality check, test fish were challenged with Antimycin A. The estimated 96Hr LC50 and 95% confidence limits were within the 95% confidence limits reported in the literature, indicating that the fish were in good condition. These values were obtained by employing the statistical methods described by Litchfield and Wilcoxon (A Simplified Method for Evaluating Dose-Effect Experiments, 1949) or Stephan (methods for calculating an LC50, 1977).
Reference: Monsanto AB-80-0240, Analytical Bio-Chemistry Labs, 1980
Reliability: (1) Valid without restriction

Type of test: static
closed-system
Species: Lepomis macrochirus (fish, fresh water)
Exposure period: 96 hours
Results: LC_{50} (96h) = 11.5 mg/l
Analytical monitoring: Yes
Method: Other: Standard Methods for the Examination of Water and Wastewater, 13th ed., American Public Health Association, 1971
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: >93%
Remarks: Test fish (1-3" in length) were obtained from a state licensed commercial fish hatchery and were retained for at least 10 days

before use. The dilution water was natural pond water with a hardness expressed as 44 ppm CaCO3. A saturated aqueous extract (SAE) was made by allowing the test material to sit in distilled water after vigorous shaking for at least 24 hours. The SAE was filtered and then tested. All tests were conducted at room temperature (22°C), pH 6.5-8.5, and all dissolved oxygen levels remained above 4 mg/l at all times during the tests.

Reference: Uniroyal Chemical Unpublished Report, 1972

Reliability: (1) Valid without restriction – meets National standards method (AFNOR/DIN)

Type of test: static
closed-system

Species: Lepomis macrochirus (Bluegill Sunfish)

Exposure period: 96 hours

Results: LC_{50} (24h) = >7.5 mg/l
LC_{50} (48h) = 6.0mg/l
LC_{50} (96h) = 4.4 mg/l
NOEC = 3.7 mg/l
LOEC = 4.2 mg/l

Analytical monitoring: No

Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1972).

GLP: No data

Test substance: As prescribed by 1.1-1.4, purity: 96%.

Remarks: The test material, in reagent-grade acetone, was introduced into 15 liters of diluent water in all-glass vessels. Test concentrations ranged from 3.7-10.0 mg/l for the test compound. Ten bluegill, standard length 3.8 cm, were added to each test vessel. The test fish were not fed for 48 hours prior to testing, nor during the exposure period. No aeration was provided during the test. Temperature was maintained at 22°C. Dissolved oxygen content ranged from 8.8 mg/l (100% of saturation) at the beginning of the test, to 0.7 mg/l (8% of saturation) at the end of the exposure period. Beginning pH was 7.5; ending pH was 6.7. Water hardness (CaCO3) was 255 ppm. Observations and mortality counts were made every 24 hours during a 96-hour period following the initiation of exposure. Test concentrations and observed percentage mortality were converted to logarithms and probits, respectively, and these values were utilized in a least squares regression analysis. The LC50 values and the 95% confidence intervals were calculated from the regression equation.

Reference: Monsanto BN-76-172, EG&G Bionomics, 1976

Reliability: (1) Valid without restriction

Type of test: static
closed-system

Species: Brachydanio rerio (fish, fresh water)

Exposure period: 96 hours

Results: LC_{0} (96h) = 1 mg/l
$LC100_{50}$ (96h) = 5 mg/l

Analytical monitoring: No

Method: No data, 1989
GLP: No
Test substance: As prescribed by 1.1-1.4, purity: no data
Remarks: The test substance was given in water and stirred for 24 hours using a magnetic stirrer. At all test concentrations, undissolved particles remained in the medium.
Reference: Bayer AG data

Type of test: static
closed-system
Species: Oncorhynchus mykiss (Rainbow Trout)
Exposure period: 96 hours
Results: LC_{50} (24h) = 5.3 mg/l
LC_{50} (48h) = 1.4 mg/l
LC_{50} (96h) = 1.3 mg/l
NOEC = 1.0 mg/l
LOEC = 1.4 mg/l
Analytical monitoring: No
Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates
and Amphibians (1972)
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: 96%.
Remarks: The test material, in reagent-grade acetone, was introduced into 15 liters of diluent water in all-glass vessels. Test concentrations ranged from 1.0 to 10.0 mg/l for the test compound. Ten rainbow trout, standard length 2.7 cm, were added to each test vessel. The test fish were not fed for 48 hours prior to testing, nor during the exposure period. No aeration was provided during the test. Temperature was maintained at 12°C. Dissolved oxygen content ranged from 9.8 mg/l (92% of saturation) at the beginning of the test, to 2.5 mg/l (23% of saturation) at the end of the exposure period. Beginning pH was 7.7; ending pH was 6.8. Water hardness (CaCO3) was 255 ppm. Observations and mortality counts were made every 24 hours during a 96-hour period following the initiation of exposure. Test concentrations and observed percentage mortality were converted to logarithms and probits, respectively, and these values were utilized in a least squares regression analysis. The LC50 values and the 95% confidence intervals were calculated from the regression equation.
Reference: Monsanto BN-76-172, EG&G Bionomics, 1976
Reliability: (1) Valid without restriction

Type of test: flow-through
open-system
Species: Oncorhynchus mykiss (Rainbow Trout)
Exposure period: 144 hours
Results: LC_{50} (24h) = 0.46 mg/l
LC_{50} (96h) = 0.31 mg/l
LC_{50} (144h) = 0.31 mg/l
Analytical monitoring: Yes
Method: EPA Methods for Acute Toxicity Tests with Fish,

Macroinvertebrates and Amphibians, 1975

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 96%.

Remarks: The test was performed under continuous flow conditions using a Mount-Brungs diluter. It was conducted in 19-liter glass aquaria, with 10 fish/replicate. Flow rate was set to provide 4 tank volumes/day. Juvenile trout, obtained from Mt.Lassen Trout Farm, were maintained at SRI for at least two weeks prior to testing. Average fish length was 6.65 cm, and weight was 2.48 g. Fish were fed a daily ration (5% of body weight) of frozen brine shrimp. The stock solution of the test compound was prepared by mixing the test compound in Acetone at a concentration of 40g/l. the stock solution was metered into the diluter with a syringe pump set at 3 ml/min. The test solution was freshly made every 48 hours. A separate bottle was used to deliver a dilute Acetone solution to maintain the concentration in the solvent control tanks at 150 ul/l. Nominal test concentrations were 0.00, 0.12, 0.25, 0.50, 1.00, 2.00 mg/l plus the solvent control. The test was terminated after 6 days of exposure, as no deaths had occurred for two consecutive days. Dissolved oxygen (DO), pH, temperature and chemical concentrations were measured routinely, alternating between the replicates. DO ranged from 8.6 to 11.8 mg/l, pH from 7.7 to 8.9, temperature between 12.0 and 13.0°C. Hardness, as CaCO3, was 27 mg/l, alkalinity was 24 mg/l, and acidity was <5.0 mg/l. Test chemical concentrations were determined by an internal standard HPLC method. Measured concentrations of the test chemical were less than the nominal concentrations, indicating that degradation was taking place. The test substance exhibited a high acute toxicity to rainbow trout under the test conditions.

Reference: Monsanto SR-80-66, SRI International, 1981

Reliability: (1) valid without restriction

Type of test: static

Species: Oncorhynchus kisutch (fish, fresh water, marine)

Exposure period: 24 hours

Results: LC_{50} (24h) = >10 mg/l

Analytical monitoring: No

Method: No data

GLP: No

Test substance: As prescribed by 1.1-1.4, purity: No data

Remarks: The compound was tested at 10 mg/l. Length of test fish was 5-10 cm. Loss of equilibrium occurred in 7-10 hours.

Reference: MacPhee and Ruelle, U. of Idaho, 1969

Reliability: (4) Not assignable – data from a secondary literature source

Type of test: static

Species: Oncorhynchus tschawytscha (fish, fresh water, marine)

Exposure period: 24 hours

Results: LC_{50} (24h) = >10 mg/l

Analytical monitoring: No

Method: No data

GLP: No

Test substance:	As prescribed by 1.1-1.4, purity: No data
Remarks:	The compound was tested at 10 mg/l. Length of test fish was 5-10 cm
Reference:	MacPhee and Ruelle, U. of Idaho, 1969
Reliability:	(4) Not assignable – data from a secondary literature source

Type of test:	static closed-system
Species:	Ptychochelius oregonensis (fish, fresh water)
Exposure period:	24 hours
Results:	LC_{50} (24h) = >10 mg/l
Analytical monitoring:	No
Method:	No data
GLP:	No
Test substance:	As prescribed by 1.1-1.4, purity: No data
Remarks:	The compound was tested at 10 mg/l. Length of test fish was 5-10 cm
Reference:	MacPhee and Ruelle, U. of Idaho, 1969
Reliability:	(4) Not assignable – data from a secondary literature source

Type of test:	static
Species:	Brachydanio rerio (fish, fresh water)
Exposure period:	96 hours
Results:	LC_0 at dilution 1:8 LC_{100} at dilution 1:2
Analytical monitoring:	No
Method:	No data, 1988
GLP:	No
Test substance:	As prescribed by 1.1-1.4, purity: No data
Remarks:	The test compound was eluted in the concentration of 1g/l for two hours, filtered, and then the filtrate was tested. DOC of the filtrate was 11 mg/l.
Reference:	Bayer AG data

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

*A. Daphnia

Type of test:	static closed-system
Species:	Daphnia magna (crustacean)
Exposure period:	48 hours
Results:	EC_{50} (24h) = 6.8 mg/l EC_{50} (48h) = 4.0 mg/l NOEC = 1.0 mg/l
Analytical monitoring:	No
Method:	EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, 1975
GLP:	No
Test substance:	As prescribed by 1.1-1.4, purity: 96%.
Remarks:	The Daphnia magna used in the test were cultured at the ABC facilities. The adult Daphnia were fed the algae Selenastrum

capricornutum at least every three days prior to testing and supplemented with a suspension of trout chow. The bioassay was conducted in 500-ml glass beakers containing 250 ml of ABC well water. Water quality parameters were DO = 8.7 mg/l, pH = 7.7, hardness = 220 mg/l, and alkalinity = 210 mg/l. Vessels were kept at 19°C in a temperature- controlled area. Lighting was maintained at 50-70 foot-candles on a 16-hour daylight photoperiod. An initial range-finding experiment was carried out to determine the exposure concentrations for the definitive test. Acetone was used as the solvent for the test solutions, and the experiment included both a control and a solvent control. Ten daphnia (first instar less than 18 hours old) were selected for each of the five test concentrations (1.0 – 10.0 mg/l) in duplicate. Daphnia in all concentrations were observed once every 24 hours for mortality and abnormal effects. Dissolved oxygen levels and pH were monitored throughout the testing and were considered adequate and equivalent to those measurements in the control chamber. Do was 7.8 mg/l and pH was 8.0 at the end of the testing. LC50 and 95% CI were calculated employing the technique of Litchfield and Wilcoxon.

Reference: Monsanto AB-78-355, Analytical Bio-Chemistry Labs, 1978

Reliability: (1) Valid without restriction

Type of test: static
closed-system

Species: Paratanytareum parthenogenetica (Midge)

Exposure period: 48 hours

Results: EC_{50} (24h) = 8.6 mg/l
EC_{50} (48h) = 5.3 mg/l
NOEC = 1.8 mg/l

Analytical monitoring: No

Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1972), and Methods of Conducting Acute Toxicity Tests with Midge (Paratanytarsus parthenogenetica (1980)

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 99%

Remarks: Test midge for this study were cultured at the ABC facilities. The adult midge were fed a suspension of trout chow and alfalfa daily until 24 hours prior to testing. The test was carried out using 3rd and 4th instar larvae, 8-10 days old. The static bioassay was conducted in 250-ml glass beakers containing 200-ml of ABC well water. The 0-hour measured control water parameters of this dilution water were dissolved oxygen 9.2 mg/l, hardness (CaCO3) of 255 ppm and pH 7.8. The test vessels were kept in a water bath at 20°C. The photoperiod was controlled to give 16 hours of daylight and 8 hours of darkness. An initial range finding experiment preceded the definitive bioassay. Nanograde Acetone was used to prepare the test solutions, which ranged from 1.0 to 18 mg/l, and as the solvent control. Tests were run in duplicate. All concentrations were observed once every 24 hours for mortality and abnormal effects. Dissolved oxygen content ranged from 9.2 to 8.7 mg/l and pH ranged from 8.3 to 7.8 during the

testing. Water quality parameters of temperature, dissolved oxygen content and pH were measured at the termination of the test and were within acceptable limits. The LC50 values were calculated via a computerized program performing the following statistical tests: binomial, moving average and probit tests.

Reference: Monsanto AB-81-357, Analytical Bio-Chemistry Labs, 1981

Reliability: (1) Valid without restriction

*4.3 TOXICITY TO AQUATIC PLANTS, e.g. algae

Endpoint: Biomass and Growth rate

Exposure period: 96 hours

Results: Chlorophyll a. EC_{50} (96.h) = 2 mg/l
Cell Count EC50 (96.h) = 2 mg/l
NOEC = 0.6 mg/l
LOEC = Not Determined

Analytical monitoring: No

Method: US EPA Phytotoxicity Method - Algal Assay Procedure: Bottle Test (1971)
closed-system

GLP: No data

Test substance: As prescribed by 1.1-1.4, purity: 96%

Remarks: The test algae were obtained from the US EPA Environmental Research Laboratory in Corvallis, Oregon. Beginning cell numbers in the test flasks were 2.0 x 10(4) cells/ml. Cultures were incubated at 24°C under approximately 4,000 lux illumination. Triplicate cultures were employed for each of the test concentrations and the control. Test containers were 125ml flasks containing 50ml of test medium. Concentrations for the definitive test were based on the results of a 96-hr range-finding study. These concentrations were 0, 0.6, 1, 3, 6 or 10 mg/ml.. Test concentrations were dissolved in reagent-grade acetone. The solvent control was 0.05 ml acetone in water. There were no water quality measurements reported in this study. The toxicity of the test compound appeared to reach a maximum after 28 hours of exposure. Statistical analysis involved converting each test concentration to a logarithm, and the corresponding percentage decrease of in vivo chlorophyll a or cell numbers was converted to a probit (Finny, 1971). The EC50s and 95% confidence limits were then calculated by linear regression.

Reference: Monsanto BN-73-363, EG&G Bionomics 1973

Reliability: (2) Valid with restrictions – no water quality data

*4.4 TOXICITY TO MICROORGANISMS, e.g. Bacteria

Type: Aquatic

Species: Activated Sludge

Exposure period: 3 hours

Unit: ug/ml

Analytical monitoring: No

EC_{50}: >10,000 ug/ml

Method: ISO 8192, Test for Inhibition of Oxygen Consumption by Activated Sludge, 1988

Test substance: As prescribed by 1.1-1.4, Purity not stated

GLP: No
Remarks: Direct weight
Reference: Bayer AG data
Reliability: (1) Valid without restriction – meets National standard method

5. TOXICITY

*5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

Type: LD_{50}
Species/strain: Rat, Sprague-Dawley
Sex: Male and female
Nunber of animals: 16
Vehicle: Corn oil
Value: 12,560 mg/kg bw
Method: Other: Industrial Bio-Test laboratories, Inc. Protocol, 1974
GLP: No
Test substance: As prescribed by 1.1-1.4, purity: 90-94%
Remarks: Initial screen was conducted to determine general level of toxicity. Two rats/sex/dose were administered the test material by gavage. The rats were then housed individually and observed for 14 days. Initial and final body weights, mortalities and reactions were recorded. A necropsy examination was conducted on all animals. The acute oral median lethal dose was calculated using the techniques of Weil, CS (1952), Thompson, WR (1947), and Thompson, WR and Weil, CS (1952)
Results: Adverse reactions observed at:
4556 mg/kg: hyporeactivity and ruffed fur
6834 mg/kg: as above, plus salivation and labored breathing
10250 mg/kg: as above, plus muscular weakness, prostration and diuresis.

Dose ug/kg	Mortality rate	% Mortality
4566	0 of 4	0
6834	0 of 4	0
10205	1 of 4	25
15380	3 of 4	75

Reference: BF Goodrich AN-3546, Industrial Bio-Test Labs, 1974
Reliability: (2) Valid with restrictions – meets generally accepted scientific standards, well-documented, and acceptable for assessment

Type: LD_{50}
Species/strain: Rat, Wistar
Sex: Male and female
Nunber of animals: 20
Vehicle: Propylene Glycol
Value: >10,000 mg/kg bw
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: not stated
Method: The test material was given as a 33% (w/v) suspension in Propylene glycol to groups of 10 male and 10 female rats in a

single dose of 30 ml/kg bw [10 g test substance/kg bw]. The animals received feed and water ad libitum during the fourteen day observation period. The rats were observed daily for signs of intoxication and mortality. All animals were necropsied. No deaths occurred during the observation period. Microscopic examination did not reveal any treatment-related alterations.

Reference: de Groot, A.P., CIVO-TNO, 1976

Reliability: (2) Valid with restrictions – meets generally accepted scientific standards, well-documented and acceptable for assessment

Type: LD_{50}
Species/strain: Rats, Sprague-Dawley Albino
Value: >7940 mg/kg bw
Sex: Male and female
# of Animals: 15
Vehicle: Corn Oil
Doses: 5010, 6310 or 7940 mg/kg bw
Method: Single Oral Dose Protocol, Younger Labs, 1973
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: 96 %
Remarks: The test material was administered to three groups of male and female rats (5 animals/dose level) as a 25.0% suspension in corn oil. Male rats had initial average body weights of 210-235 grams: females had initial average body weights of 215-220 grams. Clinical signs of toxicity included reduced appetite and activity (one to three days in survivors), followed by increasing weakness, collapse and death. There were no deaths in males at any dose level, and only one in females on Day 2 at the highest dose level. Surviving animals were sacrificed on Day 7. Gross autopsy findings on the decedent were hemorrhagic lungs and liver, and acute gastrointestinal inflammation. Findings on survivors were that all viscera appeared normal.

Dose mg/kg	Mortalities-Male	Mortalities-Female	Combined
5010	0/2	0/3	0/5
6310	0/3	0/2	0/5
7940	0/2	1/3	1/5

Reference: Monsanto Y-73-194, Younger Laboratories, 1973
Reliability: (2) Valid with restrictions – age of study, lack of method detail

5.1.2 ACUTE INHALATION TOXICITY

Type: LC_{50}
Species/strain: Rat
Sex: Male
Number of animals: 10
Vehicle: None - undiluted test article
Exposure time: 1 hour
Value: >151 mg/l
Method: Other, technique specified in Federal Register, 08/12/1961
GLP: No
Test substance: As prescribed by 1.1-1.4, purity: Not noted
Remarks: The test substance was ground in a blender and filtered through a 40-mesh screen to produce a fine dust. During the one-hour exposure, animals generally exhibited excessive preening and

masticatory movements, excessive salivation, and occasional periods of excited activity. Two rats died on the 4th or 10th day post-exposure. No other mortalities occurred. Signs of toxicity prior to mortalities were depression, depressed righting and placement reflexes, ataxia (1 animal, 10th day psot-exposure), and diarrhea stains of 2 days duration (1 animal – 10th day post-exposure). Surviving rats exhibited normal appearance and behavior throughout the 14-day observation period.

Reference: BF Goodrich T-99, Top Hill Research, 1969

Reliability: (1) Valid without restriction

Type: LC_{50}

Species/strain: Rat

Sex: Male and female

Number of animals: 20

Vehicle: None – undiluted powder

Exposure time: 4 hours

Value: >0.09 mg/l

Method: Other – Industrial Bio-Test Laboratory Protocol, 1974

GLP: No

Test substance: As prescribed by 1.1-1.4

Method: Ten albino rats were exposed to the dust of the test material for four hours in a 70-liter chamber. The concentration was determined by sampling the test atmosphere in the animals' breathing zone and collection on a glass fiber filter. The average filter concentration was 0.09 mg/l of air. The 10 exposed animals and 10 untreated control animals were observed for 14 days.

Results: There were no deaths during exposure or the observation period. All rats in both treated and control groups gained weight during the study. There were no gross pathologic findings attributable to inhalation of the test material. Gross pathologic changes in test and untreated control animals were essentially the same.

Reference: IBT #663-04730

Reliability: (2) Valid with restrictions- Meets generally accepted scientific Standards, well-documented and acceptable for assessment

5.1.3 ACUTE DERMAL TOXICITY

Type: LD_{50}

Species/strain: Rabbit, New Zealand White

Sex: Male and female

Number of animals: 4

Vehicle: None

Value: >3000 mg/kg bw

Method: Other: - Industrial Bio-Test Laboratories Protocol, 1974

GLP: No

Test substance: As prescribed by 1.1-1.4

Method: Young adult New Zealand albino rabbits were acclimated and examined prior to testing. Twenty four hours prior to testing, the backs of the animals (approximately 30% total body surface) were shaved free of hair. The test material was applied as received to abraded, pre-moistened skin. The test material was applied at the highest reasonable dosage and the test site was covered with

plastic sheeting. After 24 hours, the plastic sheeting and the test material were removed. The animals were examined for local skin reactions, behavioral abnormalities and mortality for 14 days. A necropsy was conducted on all animals.

Results: No animals died during the study.

Reference: BF Goodrich AN-3546, Industrial Bio-Test Labs, 1974

Reliability: (2) Valid with restrictions- Meets generally accepted scientific standards, well-documented and acceptable for assessment

Type: LD_{50}

Species/strain: Rabbits, New Zealand Albino

Value: >5010 mg/kg bw

Sex: Male and female

# of Animals: 4

Vehicle: Corn Oil

Doses: 3160, 5010 or 7940 mg/kg bw

Exposure Time: 24 Hours

Method: Other – Younger Laboratories Protocol, 1973

Test substance: As prescribed by 1.1-1.4, purity 96%

Method: The test substance, as a 40.0% suspension in corn oil, was applied to the shaved skin of three groups of male and female rabbits for 24 hours as single dermal application at dose levels of 3160, 5010 or 7940 mg/kg/body weight. Body weights of males were 2.3-2.4 kg, and females, 1.8-2.3 kg. The test material was held in place by means of an occlusive wrap of latex rubber and secured by bandaging and elastic tape. The occlusive wrap was removed after 24 hours and the excess material was wiped from the test animal. Clinical observations were made three times during the first eight hours after dosing, and twice daily thereafter until sacrifice.

Results: Clinical signs of toxicity included reduced appetite and activity for one to three days. There were no mortalities. All animals were sacrificed on Day 14.

Dose mg/kg	Mortalities-Male	Mortalities-Female	Combined
3160	----	0/1	0/1
5010	0/1	---	0/1
7940	0/1	0/1	0/2

Reference: Monsanto Y-73-194, Younger Laboratories, 1973

Reliability: (2) Valid with restrictions – age of study, lack of method detail

5.2.1 SKIN IRRITATION/CORROSION

Species/Strain: Rabbits

Concentration: 0.5 g undiluted

Number of animals:

PDII: 0.8

Results: Slightly Irritating

Classification: Not a Primary Skin Irritant

Method: Draize, J.H., Woodard, G., and Calvery, H.O., 1944

GLP: No data

Test substance: As prescribed by 1.1-1.4

Results: A dose of 0.5g of the undiluted test article was applied to the intact and abraded skin of albino rabbits and occluded for 24 hours.

Sample tested	Primary Irritation Score
OBTS 1-A	0.1
OBTS 1-B	0.2
OBTS 1-C	0.1
OBTS 1-D	0.8

Reference: BF Goodrich AN-3546, Industrial Bio-Test Labs, 1974
Reliability: (2) Valid with restrictions- Meets generally accepted scientific Standards, well-documented and acceptable for assessment

Species/Strain: Rabbits, New Zealand Albino
Concentration: 0.5 g undiluted
Number of animals: 6
PDII: 0.6
Results: Slightly Irritating
Classification: Not a Primary Skin Irritant
Method: Draize, J.H., Woodard, G., and Calvery, H.O., 1944
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: >96%
Remarks: 0.5 grams of the test substance, as a finely ground powder moistened with water, was applied to the shaved dorsal areas of six albino rabbits. The test material was applied to the skin under 1" square gauze patches and held in contact with the skin by means of an occlusive wrap of latex rubber secured by bandaging and elastic tape. The occlusive wrap and gauze patches were removed after 24 hours. Dermal irritation was scored by the Draize Method, and results were recorded 24, 48, 72 and 168 hours after topical application. The Primary Irritation Index was calculated by averaging the mean scores at 24 and 72 hours.
Reference: Monsanto Y-73-191 Younger Laboratories, 1973
Reliability: (2) Valid with restrictions – age of study, lack of method detail

5.2.2 EYE IRRITATION/CORROSION

Species/strain: Rabbits, New Zealand Albino
Concentration: 100 mg undiluted
Exposure time: 24 hours
Number of animals: 6
Results: Slightly Irritating
Classification: Irritating
Method: Draize, J.H., Woodard, G., and Calvery, H.O., 1944
GLP: No data
Test substance: As prescribed in 1.1-1.4, purity: 96%
Remarks: 100 mg of the test substance, as a finely ground powder, was applied to one eye of six albino rabbits. The other eye was not treated and served as a control. The cornea, iris and conjuntivea were examined immediately after treatment, and then at intervals of 10 minutes, 1 hour, and then at 24, 48, 72 and 168 hours.
The Draize Method was used for scoring eye irritation.

Exposure time	Mean score (X/110)
24 hours	12.0
48 hours	5.0

	72 hours	1.0
	168 hours	0.0

Reference: Monsanto Y-73-191 Younger Laboratories, 1973
Reliability: (2) Valid with restrictions – age of study, lack of method detail

Species/strain: Rabbits, New Zealand Albino
Concentration: 100 mg undiluted
Exposure time: 24
Number of animals: 24
Results: Moderately Irritating
Classification: Irritating
Method: Draize, J.H., Woodard, G., and Calvery, H.O., 1944
GLP: No data
Test substance: As prescribed in 1.1-1.4, purity: not noted
Remarks: Not rinsed
Reference: BF Goodrich AN-3546, Industrial Bio-Test Labs, 1974
Reliability: (2) Valid with restrictions- Meets generally accepted scientific standards, well-documented and acceptable for assessment

*5.3 SENSITIZATION

Type: Patch test
Species: Human
Number of animals: 49
Dose: 75% active
Vehicle: Petrolatum
Result: Positive, 24/49
Classification: Sensitizer
Method: Shelanski & Shelanski Repeated Insult Patch Test, 1953
Test substance: As prescribed by 1.1-1.4, purity 96%
Remarks: The test substance, as a 75% preparation in petrolatum, was applied to the skin of 49 human volunteers. 24 of the 49 exhibited a sensitization reaction. No evidence of primary irritation observed.
Reference: Monsanto SH-82-8, Product Investigations, Inc. 1982
Reliability: (1) Valid without restriction

Type: Patch test
Species: Human
Number of animals: 30 and 21
Dose: 10% w/w or 1% w/w
Vehicle: Petrolatum
Result: Positive (23/30 @ 10%, 3/21 @ 1%)
Classification: Sensitizer
Method: Shelanski & Shelanski Insult Patch Test, 1953
Test substance: As prescribed by 1.1-1.4, purity 96%
Remarks: Induction phase was 4 days/week for three weeks, followed by a one week rest period. Challenge phase was 4 days/week on a naïve site for two consecutive weeks.
Reference: Monsanto SH-86-255, Product Investigations, Inc. 1986
Reliability: (1) Valid without restriction

Type: Patch test
Species: Human

Number of animals:	30 and 21
Dose:	10% w/w or 1% w/w
Vehicle:	Petrolatum
Result:	Positive (23/30 @ 10%, 3/21 @ 1%)
Classification:	Sensitizer
Method:	Shelanski & Shelanski Repeated Insult Patch Test, 1953
Test substance:	As prescribed by 1.1-1.4, purity 96%
Remarks:	Induction phase was 4 days/week for three weeks, followed by a one week rest period. Challenge phase was 4 days/week on a naïve site for two consecutive weeks.
Reference:	Monsanto SH-86-255, Product Investigations, Inc. 1986
Reliability:	(1) Valid without restriction

Type:	Patch test
Species:	Human
Number of animals:	20
Dose:	10% w/w
Vehicle:	Petrolatum
Result:	Negative
Classification:	Not sensitizing (1/20)
Method:	Shelanski & Shelanski Repeated Insult Patch Test, 1953
Test substance:	Other TS: recrystallized, purity = 99=%
Remarks:	The test substance, highly purified via recrysatallization, was tested for potential to induce a sensitization response. Induction phase was 4 days/week for three weeks, followed by a one week rest period. Challenge phase was 4 days/week on a naïve site for two consecutive weeks. Only one volunteer reacted to the purified material
Reference:	Monsanto SH-86-255, Product Investigations, Inc. 1986
Reliability:	(1) Valid without restriction

Type:	In vitro Lymphocyte Transformation Assay
Species:	Human
Result:	Positive for oxidized impurities
Classification:	Sensitizer
Method:	Nowell, P.C., 1960
Test substance:	As prescribed by 1.1-1.4, purity 96% Other TS: 2-mercaptobenzothiazole Other TS: Morpholine Other TS: Santocure MOR sulfoxide (oxidized impurity) Other TS: Santocure MOR sulphone (oxidized impurity)
Remarks:	The test substance, along with four known impurities in the commercial-grade product, was tested on human lymphocytes obtained from the blood of seven previously sensitized volunteers (two males and five females who gave 4+ or greater reactions in the Shelanski Repeat Insult Patch Test) to see if DNA synthesis/stimulation would result. The test showed that the oxidized impurities are primarily responsible for the sensitization response.
Reference:	Monsanto ML-87-68, 1987

*5.4 REPEATED DOSE TOXICITY

Species/strain: Rats, Charles River CD
Sex: Male/Female
Number of animals: 50
Route of Administration: Oral feed
Exposure period: 4 weeks
Frequency of treatment: Daily
Post exposure observation period: None
Dose: 0, 100, 200, 500 or 1000 mg/kg bw
Control group: Yes
Concurrent no treatment
NOEL: 200 mg/kg
LOEL: 500 mg/kg
Method: Other – Hazleton Laboratories Europe Protocol, 1979
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity 97.3%
Method: The purpose of this range-finding study was to determine an appropriate dosage for a teratology study, to determine the stability of the test article on rat feed, and to determine the palatability of the test article/rat feed mixtures. Four groups of rats (5/sex/dose level) were fed diets containing the test substance for four consecutive weeks. A similar group of five males and five females served as controls, receiving only the basic powdered diet. The diet samples were analyzed via HPLC to determine actual dose levels and stability of the test material on the rat feed. Animals were observed twice daily during the first week of the study for signs of toxicity, and then at daily intervals thereafter. Body weight, food and water consumption were recorded weekly. No blood or urine analyses were conducted. All animals were subjected to a necropsy. Major organs and tissues were examined for gross lesions. Organ weights were recorded for adrenals, brain, heart, liver, spleen, kidneys, gonads, lungs and thyroids.
Results: All animals survived until terminal sacrifice. There were no changes in the animals' condition that could be related to treatment. Male rats at the two highest dose levels gained weight more slowly than controls from the first week of treatment. By the end of the study, the weight difference was approximately 12%. The livers of several high-dose males were found to be enlarged. Mean lever weights were also higher in this group. The mean relative kidney weight was higher in high-dose males than those of control animals.
Reference: Monsanto HL-79-031, Hazleton Laboratories, 1979
Reliability: (2) Valid with restrictions- Meets generally accepted scientific standards, well-documented and acceptable for assessment

Species/strain: Rabbits, New Zealand White
Sex: Male/Female
Number of animals: 80
Route of Administration: Dermal
Exposure period: 21 days [1x/day for 6 hours, 5 days/week]
Frequency of treatment: Daily
Post exposure observation period: None

Dose:	0, 125, 500 or 2000 mg/kg bw
Control group:	Yes Concurrent vehicle (0.9% physiological saline)
NOEL:	2000 mg/kg
LOEL:	Not determined
Method:	Other: International Research and Development Corporation Protocol, 1979
GLP:	Yes
Test substance:	As prescribed by 1.1-1.4, purity: 96.2%
Method:	The test substance was administered to three groups of 10 male and 10 female rabbits (young adults, 2.0-3.5 kg bw), half with intact skin and half with abraded skin, five days/week for three consecutive weeks. An identical control group was treated with saline. Criteria evaluated for treatment effect included mortality, pharmacotoxic signs, body weights, dermal irritation, hematological and clinical biochemical determinations, organ weights, and macroscopic and selected microscopic evaluation of tissues. Rabbits were observed twice daily for mortality, once daily for pharmacotoxic signs and evidence of dermal irritation. Body weights were obtained and recorded during the pretest period and 1x/week thereafter. Once during the pretest period and on Day 21 of the study, laboratory tests were conducted on five rabbits/sex/group.
Results:	One death (not considered to be treatment-related) occurred in each of the three test article groups, and one control animal was sacrificed in extremis. All remaining animals survived until terminal sacrifice. No test article-related signs were noted for any animal in the test groups during the study period. A number of incidental and spontaneous pharmacotoxic signs were noted for a few rabbits in all groups (nasal discharge, eye discharge, soft stool, possible anorexia). No statistically significant differences were seen in group mean body weights. A few rabbits in the test groups exhibited very slight to slight erythema, edema and desquamation. In the control group, a few rabbits exhibited very slight desquamation and red raised areas on the shaven backs. Although some differences were seen between control and treated rabbits in the hematological studies (slight decreases in hematocrit, hemoglobin and total erythrocytes in high-dose females, slightly lower LDH and higher cholesterol values in high-dose males), these differences were not considered to be related to treatment with the test article. Both the control and groups, and the males and females presented similar changes. The main lesions on the skin from the application site of control and experimental animals were hyperkeratosis and infiltration of inflammatory cells in the dermis. Body weights (Week 3), hematological, biochemical and urinalysis parameters (Day 20), and absolute and relative organ weights (terminal sacrifice) were compared by analysis of variance (one-way classification), Bartlett's test for homogeneity of variances and the appropriate t-Test (for equal or unequal variances) as described by Steel and Torrie using Dunnett's multiple comparison tables to judge the significance of differences.
Reference:	Monsanto IR-79-264, International Research & Development Corp., 1981

Reliability: (1) Valid without restriction

Species/strain: Rat, Sprague-Dawley
Sex: Male/Female
Number of animals: 40
Route of Administration: Inhalation
Exposure period: 4 weeks
Frequency of treatment: 6 hours/day, 5 days/week
Post exposure observation period: None
Dose: 0, 4.4, 9.8 or 10.2 mg/m3
Control group: Yes
Concurrent no treatment
NOEL: 9.8 mg/m3
LOEL: 10.2 mg/m3
Method: Other: International Research and Development Corporation Protocol, 1979
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 96.2%
Method: Four groups of young adult male and female rats (5/sex/dose) were exposed to zero, low, medium and high concentrations of the test article as a fine dust. Observations were made with respect to the incidence of mortality, reactions displayed and body weight effects. Hematologic and clinical chemistry studies and urinalyses were conducted on all test and control animals on the day following final exposure. All animals were subjected to a gross necropsy. A complete set of organs and tissues were removed from each animal and preserved. Histopathologic studies were conducted on selected tissues and organs from the control and high-concentration groups. Weights of selected organs were recorded and subjected to statistical analyses. Body weights hematological, biochemical and urinalysis parameters and absolute and relative organ weights were compared by analysis of variance (one-way classification), Bartlett's test for homogeneity of variances and the appropriate t-Test (for equal or unequal variances) as described by Steel and Torrie using Dunnett's multiple comparison tables to judge the significance of differences.
Results: All animals survived until terminal sacrifice. Exposure to the test article caused slight irritation in exposed animals. Slight body weight reductions and reductions in lung weights were observed in male rats in the high-concentration group. Histopathologic examination revealed no alterations in the tissues of the high-dose males or females as compared to controls. Slight depressions in blood glucose and elevations in SGOT values were noted in rats at all exposure levels, but these findings were not associated with the presence of any tissue lesions.
Reference: Monsanto IR-78-96, International Research & Development Corp., 1979
Reliability: (1) Valid without restriction

Species/strain: Rat, Charles River CD
Sex: Male/Female
Route of Administration: Dietary

Exposure period: 2 years
Frequency of treatment: Daily
Post-exposure observation: None
Doses: 0, 5, 50 or 400 mg/kg/day (50/sex/dose)
Control group: Yes, concurrent no treatment
Results: The test compound was fed at the above doses to groups of 200 male and 200 female rats (50/sex/dose) over a two-year period, beginning when the males were 28 days old and the females 29 days old. The diet samples were analyzed via HPLC to determine actual dose levels and stability of the test material on the rat feed. Animals were observed twice daily during the first week of the study for signs of toxicity, and then at daily intervals thereafter. All animals were subjected to a necropsy. Major organs and tissues were examined for gross lesions. Organ weights were recorded for adrenals, brain, heart, liver, spleen, kidneys, gonads, lungs and thyroids. Body weight, food consumption, behavior, hematology, blood chemistry and urinalysis results were recorded throughout the study. Complete gross necropsies were conducted on all animals found dead, on all animals sacrificed in extremis, and on all remaining animals at 24 months.
Method: Other – Hazleton Laboratories Europe Protocol, 1979
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity 96%
Remarks: The test substance was evaluated for chronic toxicity in a two-year chronic feeding study in male and female rats. The animals were exposed to concentrations of the test material in the diet equivalent to 0, 5, 50 or 400 mg/kg/day. There were no deaths that were attributed to exposure to the test material during the course of this study. Both males and females in the 50 and 400 mg dose groups exhibited statistically significant reductions in both body weight gain and food consumption as compared to control animals. Dose-related increases in kidney and liver weights were also observed in these to dose levels. Histopathologic examination of the tissues and organs taken from animals of the control group and the high- and mid-dose groups at sacrifice revealed no treatment-related lesions. Under the conditions of this test, no evidence of chronic toxicity was found.
Reference: Monsanto HL-79-39, Hazelton Laboratories, 1979
Reliability: (1) Valid without restriction

*5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

Type: Ames Bacterial Reverse Gene Mutation
System of testing: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA-100
Concentration: 0.1, 1.0, 10, 100 or 500 ug/plate
Metabolic activation: With and without
Results:
Cytotoxicity conc: With metabolic activation: 500 ug/plate
Without metabolic activation: 500 ug/plate
Genotoxic effects:
With metabolic activation: Negative

Without metabolic activation: Negative

Method: Ames Mutagenicity Plate Test (Overlay Method) 1975

GLP: No data

Test substance: As prescribed by 1.1-1.4, purity: 97 %

Remarks: The test compound was evaluated for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. The *Salmonella typhimurium* strains used for this experiment were obtained from Dr. Bruce Ames. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. The mutagenesis assay was carried out as the plate-incorporation test according to the Ames protocol. Chemicals used as positive controls for the non-activation assays were methylnitrosoguanidine (MNNG), 2-nitrofluorene (NF) and quinacrine mustard (QM). Positive control chemicals used for the activation assays were 2-anthramine (ANTH), 2-acetylaminofluorine (AAF) and 8-aminoquinoline (AMQ). Dimethylsulfoxide (DMSO) was used as the solvent and the solvent control. The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.

Reference: Monsanto BIO-76-180, Litton Bionetics, November 1976

Reliability: (1) Valid without restriction

Type: Ames Bacterial Reverse Gene Mutation

System of testing: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA-100

Concentration: 1, 10, 100, 500, 1000, 2500 ug/plate (duplicate)

Metabolic activation: With and without

Results:

Cytotoxicity conc: With metabolic activation: 1000 ug/plate
Without metabolic activation: 500 ug/plate

Precipitation conc: No data

Genotoxic effects:

With metabolic activation: Negative
Without metabolic activation: Negative

Method: Ames Mutagenicity Plate Test (Overlay Method) 1975

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 95-97% (2 commercial grades)
Other: Recrystallized 4x, purity 99+%

Remarks: The test compound was evaluated for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. The *Salmonella typhimurium* strains used for this experiment were obtained from Dr. Bruce Ames. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. The mutagenesis assay was carried out as the plate-incorporation test according to the Ames protocol. Chemicals used as positive controls for the non-activation assays were 1 ug/plate sodium azide, 10 ug/plate 2-nitrofluorene (NF) or 50 ug/plate 9-aminoacridine (9AA). Positive control used for

the activation assays was 2.5 ug/plate 2-anthramine (ANTH). Dimethylsulfoxide (DMSO) was used as the solvent and the solvent control. Positive control treatments produced the expected large increases in the frequency of histidine revertants. The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.

Reference: Litton Bionetics for CMA final report, 1981

Reliability: (1) Valid without restriction

Type: Bacterial Reverse Gene Mutation

System of testing: *Salmonella typhimurium* TA-1535, TA-1537, TA-1538, TA-98, TA-100 and *Escherichia coli* WP_2 $uvrA^-$

Concentration: 0.5 µg to 5,000 µg/plate (duplicate)

Metabolic activation: With and without

Results:

Cytotoxicity conc: 1,000 µg/plate and above

Genotoxic effects:

With metabolic activation: Negative

Without metabolic activation: Negative

Method: OECD Guideline 471, Genetic Toxicology: Salmonella typhimurium Reverse Mutation Assay, 1979

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 90-95%

Remarks: The test compound was evaluated for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. The methods are described in Hinderer et al., 1983 as follows:

"*Salmonella typhymurium* strains TA-1535, TA-1537, TA-1538, TA-98 and TA-100 were obtained from Dr. Bruce Ames. All indicator strains were kept at 4ºC on minimal medium plates supplemented with a trace of biotin and an excess of histadine (Ames, 1980). In addition, the plates with the plasmid-carrying *Salmonella* strains (TA-98 and TA-100) were supplemented with 26µg/ml of ampicillin to ensure stable maintenance of the plasmid pKM101. "

"The bacterial strains were cultured at 37ºC in Oxid Media #2 (nutrient broth), and Vogel Bonner Medium E with 2% glucose was used as the selective medium (Vogel and Bonner, 1956). The overlay agar was prepared according to the method of Ames et al (1975). S-9 liver homogenates, which were prepared from Aroclor 1254-induced and noninduced adult Sprague-Dawley male rats as described by Ames et al (1975, were prepared from Binetics Laboratory Products, Litton Bionetics, Inc. An S-9 mix was prepared by adding the following ingredients per milliliter of mix: 4 µmoles NADP (sodium salt), 5 µmoles D-glucose-6-phosphate, 8 µmoles $MgCL_2$, 33 µmoles KCL, 100 µmoles sodium phosphate buffer (pH 7.4), and 100 µl of rat liver S-9 fraction."

"All tests were based on the methods of Ames et al (1975). Test compounds were dissolved in dimethylsulfoxide (DMSO). Solvent and positive controls were used as listed in Table II." (Table II is summarized as follows: Positive controls for the non-activation assays were 1 ug/plate sodium azide for TA-1535 and TA-100, 50 ug/plate 9-aminoacridine for TA-1537, 10 µg 2-nitrofluorene for TA-1538 and TA-98. The positive control used for the activation assays was 2.5 ug/plate 2-anthramine.) "The highest dose was established as one which produced some toxicity."

"Criteria which were used to determine whether a chemical was mutagenic were: 1) an increase in revertants in strains TA-1535, TA-1537, TA-1538 of three times the solvent control; 2) an increase in revertants in strains TA-98 and TA-100 of twice the solvent control; 3) reproducibility; and 4) a dose-related response, and a consistent pattern of response between strains derived from the same parental strain ----."

"The *E. coli* strain WP_2 $uvrA^-$ was obtained from Dr. M.H.L. Green, MRC Cell Mutation Unit, University of Sussex, England. The indicator strain was kept at 4ºC on standard methods agar plates or minimal medium plates supplemented with an excess triptophan. Laboratory cultures were grown at 37ºC in Oxoid #2 (nutrient broth). Vogel Bonner medium E (Vogel and Bonner, 1956) with 2% glucose was used as the selective medium. The overlay agar was prepared according to the method of Green and Murie. (1976). The S-9 activation system was prepared as described for the *Salmonella* plate assay. The procedures were based on a modification of the methods described by Ames et al (1975)."

DMSO was also used as the solvent to dissolve the test material. For the nonactivation test 10 µg of methylnitrosoguanidine was the positive control. For the activation test 2.5 µg of 2-(2-furyl)-3-(5-nitro-2-furyl)-acrylamide was the positive control.

"A chemical was considered mutagenic if there was a dose-related response over a minimum of three test concentrations."

The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.

Note: A GLP- signed quality assurance statement was provided.

Reference: Hinderer et al., Environmental Mutagenesis, 1983
Reliability: (1) Valid without restrictions. Meets generally accepted scientific method and is described in sufficient detail

Type: Ames Bacterial Reverse Gene Mutation
System of testing: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA-100

Concentration: 0.1 to 1000 ug/plate (duplicate)
Metabolic activation: With and without
Results:
Cytotoxicity conc: >= 100 ug/plate
Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative
Method: OECD Guideline 471, Genetic Toxicology: Salmonella typhimurium Reverse Mutation Assay, 1979
GLP: Yes
Test substance: > 99%
Remarks: The standard Ames protocol was followed, with one exception. Instead of duplicate plates for the positive controls in trial #1, one of the plates contained twice the standard dose.
The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.
Reference: Kurtz and Riddle, 1981 Unpublished
Reliability: (1) Valid without restrictions. Meets generally accepted scientific method and is described in sufficient detail

Type: DNA Repair Test
System of testing: Escherichia coli W3110 (pol A+) and W3078 (pol A-)
Concentration: 0.5 – 2500 ug/plate (triplicate)
Metabolic activation: With and Without
Results:
Cytotoxicity conc: With metabolic activation: Not determined (>2500 ug/plate)
Without metabolic activation: Not determined (>2500 ug.plate)
Precipitation conc: No data
Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative
Method: Rosencranz and Leifer, Determining the DNA-modifying activity of chemicals using DNA-polymerase-deficient E. coli, 1980
Ames Mutagenicity Plate Test (Overlay Method) 1975
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 95-97% (2 commercial grades)
Other: Recrystallized 4x, purity 99+%
Remarks: The E. coli strains used were obtained from Dr. H. Rosenkranz, Columbia University, NY. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. Positive control chemicals were Methylmethane sulfonate (10ul/plate, nonactivation) and Dimethylnitrosamine (100 ul/plate, activation). The solvent used, DMSO, was also the negative control. The survival index was obtained by dividing the % survival of the pol A- culture by the % survival of the pol A+ culture. A survival index below 0.85 indicated a DNA-modifying effect. The positive controls exhibited the expected reductions of the survival index. The test material exhibited some slight reductions in the survival index in this test, but this was not considered significant due to the lack of dose response

phenomena. Overall, te treatment did not induce preferential killing of the DNA repair deficient pol A- strain, indicating that the test compound was not genotoxic under test conditions.

Reference: Litton Bionetics for CMA final report, 1981

Reliability: (1) Valid without restriction

B. NON-BACTERIAL IN VITRO TEST

Type: Mammalian Cell Forward Gene Mutation Assay

System of testing: Mouse lymphoma cells L5178Y TK+/-

Concentration: 0.156, 0.625, 2.5, 7.5, 15.0 µg/ml without activation (triplicate)
2.5, 10, 20, 40, 50 µg/ml with activation (triplicate)

Metabolic activation: With and without

Results:

Cytotoxicity conc: With metabolic activation: 40 µg/ml
Without metabolic activation: 15 µg/ml

Precipitation conc: None – soluble at all conc. in Acetone

Genotoxic effects:

With metabolic activation: Positive
Without metabolic activation: Negative

Method: Other: Clive, D. and Spector, J.F.S. (1975)
Mutation Res. 31, 17-29

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 95-97% (2 commercial grades)
Other: Recrystallized 4x, purity 99+%

Results: The test substance was dissolved in acetone at 5 g/l. Stocks were prepared and serially diluted in acetone. The stocks were then diluted 1:100 into tubes of culture media containing the cells to initiate the treatments. The test compound appeared to be soluble in acetone over the entire range of concentrations selected. Concentrations greater than 40 µg/ml proved to be highly cytotoxic in the presence of a rat liver S-9 preparation activation system, and cytotoxic at 15 ug/ml without activation. Acetone (1%) was used as the solvent control substance. Growth medium without the addition of solvent was used as a negative control. No genetic effects were attributed to the presence of the solvent. EMS (0.5 ul/ml) and DMN (0.3 ug/ml) were used as reference mutagens and induced mutation frequencies within the expected range. The test material induced significant increases in the TK locus in L5178Y mouse lymphoma cells only in the presence of S9 activation. The test material induced positive responses at two highly toxic treatments (40 and 50 ug/ml, percent relative growths 17% and 10.9%, respectively). In the absence of microsomal activation, moderately toxic concentrations up to 7.5 ug/ml were not mutagenic. Therefore, the test compound was considered to be active only in the presence of activation in this assay.

Non-Activation Results

	Conc.	Mutant clones	Viable clones	Mutant frequency x10(-6)
Solvent Control	---	44.0	252.0	17.5
Negative Control	---	49.0	289.0	17.0
EMS	0.5 µl/ml	321.0	126.0	254.8
Test Cpd.	0.156	47.0	307.0	15.3
	0.625	36.0	220.0	16.4
	2.5	24.0	189.0	12.7

	7.5	24.0	194.0	12.4
	15.0	7.7	112.0	39.3

Activation with S-9 Results

	Conc.	Mutant clones	Viable clones	Mutant frequency x10(-6)
Solvent Control	---	32.0	240.0	13.3
Negative Control	---	48.0	223.0	21.5
DMN	0.3 µl/ml	39.0	15.0	260.0
Test Cpd.	2.5	38.0	154.0	24.7
	10.0	52.0	139.0	37.4
	20.0	57.0	210.0	27.1
	40.0	71.0	110.0	64.5
	50.0	65.0	122.0	53.3

Reference: Litton Bionetics for CMA final report, 1981
Reliability: (1) Valid without restriction

Type: Mammalian Cell Forward Gene Mutation Assay
System of testing: Mouse lymphoma cells L5178Y TK+/-
Concentration: 0.78, 1.56, 3.13, 6.25, 12.5 µg/ml without activation (duplicate)
1.56, 3.13, 6.25, 12.5, 25.0 µg/ml with activation (duplicate)
Metabolic activation: With and without
Results:
Cytotoxicity conc: With metabolic activation: 50 µg/ml
Without metabolic activation: >12.5 µg/ml
Precipitation conc: 300 ug/ml (in DMSO)
Genotoxic effects:
With metabolic activation: Weak Positive
Without metabolic activation: Negative
Method: Other: Clive, D. and Spector, J.F.S. (1975)
Mutation Res. 31, 17-29
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 96%
Results: The test substance was dissolved in DMSO at 25 mg/ml. Stocks were prepared and serially diluted in DMSO. The stocks were then diluted 1:100 into tubes of culture media containing the cells to initiate the treatments. A preliminary cytotoxicity experiment preceded the mouse lymphoma assay. Concentrations greater than 50 µg/ml proved to be highly cytotoxic in the presence of a rat liver S-9 preparation activation system, and cytotoxic above 12.5 ug/ml without activation. DMSO (1%) was used as the solvent control substance. Growth medium without the addition of solvent was used as a negative control. No genetic effects were attributed to the presence of the solvent. EMS (0.5 ul/ml) and DMN (0.3 ug/ml) were used as reference mutagens and induced mutation frequencies within the expected range. The test material induced a slight, but significant, increase in the TK locus in L5178Y mouse lymphoma cells only in the presence of S9 activation, and only at the highest dose tested. In the absence of microsomal activation, moderatley toxic concentrations up to 12.5 ug/ml were not mutagenic. Therefore, the test compound was considered to be weakly active only in the presence of activation in this assay.

Non-Activation Results

	Conc.	Mutant clones	Viable clones	Mutant frequency x10(-6)
Solvent Control	---	73	238	30.7
Negative Control	---	69	254	27.2
EMS	0.5 µl/ml	549	111	494.6
Test Cpd.	0.78	90	202	44.6
	1.56	89	232	38.4
	3.13	127	225	56.4
	6.25	78	196	39.8
	12.5	69	167	41.3

Activation with S-9 Results

	Conc.	Mutant clones	Viable clones	Mutant frequency x10(-6)
Solvent Control	---	143	181	79.0
Negative Control	---	155	274	56.6
DMN	0.3 µl/ml	49	9	544.4
Test Cpd.	1.56	146	289	50.5
	3.13	190	252	75.4
	6.25	172	256	67.2
	12.50	152	317	47.9
	25.00	242	130	186.2

Reference: Monsanto BO-78-223, Litton Bionetics, 1979
Reliability: (1) Valid without restriction

Type: Mammalian Cell Transformation Assay
System of testing: BALB/3T3 cells
Concentration: 30.0 ug/ml – 0.75 ug/ml
Metabolic activation: Without
Results:
Cytotoxicity conc: 31.3 ug/ml
Precipitation conc: >0.25 mg/ml
Genotoxic effects: Negative
Method: Kakunaga , T., A Quantitative System for Assay of Malignant Transformation by Chemical Carcinogens using a Clone Derived from BALB/3T3, 1973
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 95-97% (2 commercial grades)
Other: Recrystallized 4x, purity 99+%
Remarks: The I(13) BALB/3T3 mouse cell clones for this study were obtained from Dr. Kakunaga of the National Cancer Institute. Further subclones, selected for low spontaneous frequencies of foci formation, were used for the assay. DMSO was used for the solvent and the solvent (negative) control. A known carcinogen, 3-methylcholanthrene (MCA, 5 ug/ml) was used as the positive control. A preliminary cytotoxicity test determined the concentrations selected for the transformation assay (30 ug/ml – 0.75 ug/ml, corresponding to a survival range of 20-90%). Under the conditions of this assay, the test substance did not induce a significant increase in transformed foci over the applied concentration range.
Reference: Litton Bionetics for CMA final report, 1981
Reliability: (1) Valid without restriction

Type: Mammalian Cell Cytogenics Assay – Sister Chromatid Exchange
System of testing: CHO Cells, clone K1-BH4
Concentration: 1, 5, 10, 20, or 40 ug/ml without metabolic activation (duplicate)
5, 10, 15, 30 or 60 ug/ml with metabolic activation (duplicate)
Metabolic activation: With and without
Results:
Cytotoxicity conc: With metabolic activation: 100 ug/ml
Without metabolic activation: 50 ug/ml
Precipitation conc: None
Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative
Method: A quantative assay of mutation induction at the HG/PRT locus in Chinese hamster ovary cells, Mutation Research 45: 91-101
O'Neil et al., 1977; OECD 479
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 95-97% (2 commercial grades)
Other: Recrystallized 4x, purity 99+%
Remarks: The Chinese hamster ovary cells used for this cytogenetics assay were acquired from the Oak Ridge National Laboratories, TN. An Aroclor 1254-induced rat liver homogenate preparation (S-9) was the activation system. The solvent used for concentration solutions and for the solvent control was DMSO. The positive control for the assay with S9 was Dimethylnitrosamine (DMN) at 100 mg/ml of medium. The positive control for the assay without S9 was Ethyllmethanesulfonate (EMS) at 200 ug/ml of medium. In a preliminary cytotoxicity assay, the relative cell survival decreased from 74% at 30 ug/ml to 43% at 50 ug/ml in non-activated cultures, and from 80% at 10 ug/ml to 23% at 100 ug/ml in activated cultures. Test cells were treated for 5 hours, washed 3 times, and then incubated for 19 hours. The mutant frequency was calculated by correcting the total number of mutant clones by the cloning efficiency of the cells at the time of mutant selection. Dose-response analyses were performed on the transformed mutant frequency data by the one-way analysis of variance method (Snee and Irr, 1981). A statistically significant (t-test, $p<=0.05$) but less than 2-fold increase in SCE frequency was observed at 20 and 40 ug/ml in the non-activated tests, and at 30 and 60 ug/ml in the activated tests. However, dose response was not observed in any experiment. Therefore, the results were interpreted as non-mutagenic under the conditions of this assay.
Reference: Pharmakon Research International for CMA, 1984
Reliability: (1) Valid without restriction

Type: Mammalian Cell Cytogenics Assay – Sister Chromatid Exchange
System of testing: CHO Cells, clone K1-BH4
Concentration: 5 to 75 ug/ml without metabolic activation (duplicate)
5 to 100 ug/ml with metabolic activation (duplicate)
Metabolic activation: With and without
Results:

Cytotoxicity conc: With metabolic activation: No data
Without metabolic activation: No data
Precipitation conc: None
Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative
Method: A quantative assay of mutation induction at the HG/PRT locus in Chinese hamster ovary cells, Mutation Research 45: 91-101
O'Neil et al., 1977; OECD 479
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 95-97% (2 commercial grades)
Other: Recrystallized 4x, purity 99+%
Remarks: The Chinese hamster ovary cells used for this cytogenetics assay were acquired from the Oak Ridge National Laboratories, TN. An Aroclor 1254-induced rat liver homogenate preparation (S-9) was the activation system. The solvent used for concentration solutions and for the solvent control was Acetone. The positive control for the assay with S9 was Dimethylnitrosamine (DMN) at 100 mg/ml of medium. The positive control for the assay without S9 was Ethyllmethanesulfonate (EMS) at 200 ug/ml of medium. Test cells were treated for 5 hours, washed 3 times, and then incubated for 19 hours. The mutant frequency was calculated by correcting the total number of mutant clones by the cloning efficiency of the cells at the time of mutant selection. Dose-response analyses were performed on the transformed mutant frequency data by the one-way analysis of variance method (Snee and Irr, 1981). A statistically significant (t-test, p<=0.05) but less than 2-fold increase in SCE frequency was observed at 50 and 75 ug/ml in the non-activated tests, and at all doses except 5 ug/ml in the activated tests. The effect was dose-related in the presence of activation. The relative cell survival was observed to range from 65-82% in non-activated cultures and from 66-82% in activated cultures during the experiment. Due to the lack of two-fold doubling, the results were interpreted as non-mutagenic under the conditions of this assay.
Reference: Pharmakon Research International for CMA, 1984
Reliability: (1) Valid without restriction

Type: Mammalian Cell Cytogenics Assay – Sister Chromatid Exchange
System of testing: CHO Cells, clone K1-BH4
Concentration: 5, 20, 40, 60, 80 ug/ml without metabolic activation (duplicate)
10, 40, 80, 120, 240 ug/ml with metabolic activation (duplicate)
Metabolic activation: With and without
Results:
Cytotoxicity conc: With metabolic activation: 150 ug/ml
Without metabolic activation: 50 ug/ml
Precipitation conc: None
Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative
Method: A quantative assay of mutation induction at the HG/PRT locus in Chinese hamster ovary cells, Mutation Research 45: 91-101

O'Neil et al., 1977; OECD 479

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 95-97%

Remarks: The Chinese hamster ovary cells used for this cytogenetics assay were acquired from the Oak Ridge National Laboratories, TN. An Aroclor 1254-induced rat liver homogenate preparation (S-9) was the activation system. The solvent used for concentration solutions and for the solvent control was Acetone. The positive control for the assay with S9 was Dimethylnitrosamine (DMN) at 100 mg/ml of medium. The positive control for the assay without S9 was Ethyllmethanesulfonate (EMS) at 200 ug/ml of medium. Test cells were treated for 5 hours, washed 3 times, and then incubated for 19 hours. The mutant frequency was calculated by correcting the total number of mutant clones by the cloning efficiency of the cells at the time of mutant selection. Dose-response analyses were performed on the transformed mutant frequency data by the one-way analysis of variance method (Snee and Irr, 1981). A statistically significant (t-test, $p<0.05$) increase in mutant frequency was not observed at any dose level in the presence or absence of activation.

Reference: Pharmakon Research International for CMA, 1984

Reliability: (1) Valid without restriction

Type: Mammalian Cell Cytogenics Assay – Sister Chromatid Exchange

System of testing: CHO cells

Concentration: 0.625, 1.25, 2.5, 5, 7.5 and 10 ug/ml (duplicate)

Metabolic activation: With and without

Results:

Cytotoxicity conc: With metabolic activation: None
Without metabolic activation: None

Precipitation conc: None

Genotoxic effects:

With metabolic activation: Negative
Without metabolic activation: Negative

Method: A quantative assay of mutation induction at the HG/PRT locus in Chinese hamster ovary cells, Mutation Research 45: 91-101
O'Neil et al., 1977

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 95-97%

Remarks: Based on a preliminary toxicity screen, both activated and non-activated cultures were treated with doses of the test article ranging from 0.625–10 ug/ml. An Aroclor 1254-induced rat liver homogenate preparation (S-9) was the activation system. The solvent used for concentration dilutions and for the solvent control was Acetone. The positive control for the assay with S9 was 0.00025 M Cyclophosphamide. The positive control for the assay without S9 was Triethylenemelamine at 0.75 ug/ml of medium. Test cells were treated for 2 hours, washed 3 times, and then incubated for 17 hours. Colcemid was added for the last three hours of incubation. Fifty cells per treatment were analyzed for chromosomal aberrations. The mutant frequency was calculated by correcting the total number of mutant clones

by the cloning efficiency of the cells at the time of mutant selection. Dose-response analyses were performed on the transformed mutant frequency data by the one-way analysis of variance method (Snee and Irr, 1981). The positive controls produced the expected large increases in the frequency of chromosomal aberrations. A statistically significant (t-test, $p<0.05$) increase in mutant frequency was not observed at any dose level of the test substance in the presence or absence of activation.

Reference: Litton Bionetics/BF Goodrich, 1979

Reliability: (1) Valid without restriction

* 5.6 GENETIC TOXICITY IN VIVO

Type: Dominant Lethal Assay

Species/strain: Rat, Sprague-Dawley

Sex: Male

Route of Administration: Gavage

Exposure period: 56 days

Doses: 0, 125, 250 or 500 mg/kg bw/day

Results:

Effect on mitotic index or P/N ratio: Negative

Genotoxic effects: Negative

Method: Other: Food and Drug Research Labs Protocol, 1980

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 90-95%

Remarks: The test substance was evaluated for genotoxicity in the dominant lethal test in groups of 10 male rats treated by gavage at the above dose levels. Following treatment, each male rat was housed with two virgin female rats/week for two weeks. The females were sacrificed thirteen days after mating for determination of dominant lethal effects. The treatment had no adverse effects with respect to clinical signs, mortality rate, body weight gain, or organ weights of adult male rats. The treatment also had no effect on pregnancy, early fetal death, implantation, or preimplantation losses in the females. Positive control treatment with a single intraperitoneal injection of 0.25 mg/kg bw Triethylenemelamine produced the expected dominant lethal effects. Under the conditions of this assay, the test compound results were negative, indicating that the compound was not mutagenic to the germ cells of male rats.

Reference: BF Goodrich/Food and Drug Research Laboratories, 1980

Reliability: (1) Valid without restriction

Type: Modified Dominant Lethal Assay

Species/strain: Rat

Sex: Male and female

Route of Administration: Gavage

Exposure period: 2 days prior to mating for both males and females

Doses: 200 mg/kg bw/day

Results:

Effect on mitotic index or P/N ratio: No data
Genotoxic effects:

Method: Other, 1980
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: 96%
Remarks: The test substance was evaluated in a modified dominant lethal assay in which 200 mg/kg was administered to both male and female rats two days prior to mating. In increase in total embryonic mortality, reduced fetal body weights, and a delay in the onset of conception was reported.
Reference: Aleksandrov, S.E. Byull. Eksp. Biol. Med., 1982
Reliability: (4) Not assignable - data from a secondary literature source

5.7 CARCINOGENICITY

Species/strain: Mice, B6C3F1 and B6AKF1
Sex: Male/Female
Route of Administration: Oral gavage on days 7-28, oral feed for remainder
Or Single subcutaneous injection on Day 28
Exposure period: 79 weeks
Frequency of treatment: Daily for feed study, once for injection study
Post-exposure observation: 78 weeks for injection, none for intubation/feed
Doses: Gavage = 215 mg/kg bw
Feed = 90 mg/kg/day
Injection = 1000 mg/kg
Control group: Yes
Other: Positive Control
Results: In a National Cancer Institute study, 18 virgin male and 18 virgin female mice from two hybrid strains were dosed with the test substance. Two types of studies were run simultaneously. One group of 36 mice received a single subcutaneous injection administered in the nape of the neck at the 28th day of age, with no exposure to the test substance thereafter. The second group of 26 mice received a daily oral gavage dose of the test article administered from the 7th to 28th days of age, and then daily in their feed mix thereafter. All compounds administered orally as positive controls were carcinogenic, while only two of the positive controls (urethane, ethyleneimine) administered subcutaneously had carcinogenic activity. There were no findings of carcinogenic effects attributed to the test substance in either 79-week study.
Method: Litton Bionetics Research Labs Protocol, 1968
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity 96%
Remarks: Study was undertaken to determine the carcinogenic potential of 130 chemicals that had been used in the formulations of insecticides, herbicides and fungicides.
Reference: Litton Bionetics/NCI Report # PB223-159 (1968)
Reliability: (2) Valid with restrictions - Intubation/feed part of this study followed generally accepted parameters for a 1968 carcinogenicity assessment, but not all test parameters comply with current guidelines. No GLP data. The reliance on a single

subcutaneous injection as adequate for the other portion of this study is questionable.

Species/strain: Rat, Charles River CD
Sex: Male/Female
Route of Administration: Dietary
Exposure period: 2 years
Frequency of treatment: Daily for
Post-exposure observation: None
Doses: 0, 5, 50 or 400 mg/kg/day (50/sex/dose)
Control group: Yes, concurrent no treatment
Results: The test compound was fed at the above doses to groups of 200 male and 200 female rats over a two-year period, beginning when the males were 28 days old and the females 29 days old. The diet samples were analyzed via HPLC to determine actual dose levels and stability of the test material on the rat feed. Animals were observed twice daily during the first week of the study for signs of toxicity, and then at daily intervals thereafter. Body weight, food and water consumption were recorded weekly. All animals were subjected to a necropsy. Major organs and tissues were examined for gross lesions. Organ weights were recorded for adrenals, brain, heart, liver, spleen, kidneys, gonads, lungs and thyroids. Body weight, food consumption, behavior, hematology, blood chemistry and urinalysis results were recorded throughout the study. Complete gross necropsies were conducted on all animals found dead, on all animals sacrificed in extremis, and on all remaining animals at 24 months.
Method: Other – Hazleton Laboratories Europe Protocol, 1979
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity 96%
Remarks: The test substance was evaluated for oncogenicity in a two-year chronic feeding study in male and female rats. 200 animals (50/sex/dose) were exposed to concentrations of the test material in the diet equivalent to 0, 5, 50 or 400 mg/kg/day. There were no deaths that were attributed to exposure to the test material during the course of this study. Both males and females in the 50 and 400 mg/kg dose groups exhibited statistically significant reductions in both body weight gain and food consumption as compared to control animals. Dose-related increases in kidney and liver weights were also observed in these to dose levels. Histopathologic examination of the tissues and organs taken from animals of the control group and the high- and mid-dose groups at sacrifice revealed no treatment-related lesions. Microscopic examinations of any suspect neoplasms were conducted on all sacrificed animals and any animal that died during the study. No differences were noted between test and control rats as to the organ system involved, type or classification of neoplasms. The spectrum of neoplasms observed compared favorably to the historical data at this laboratory for rats of this age and strain. Under the conditions of this test, no evidence of oncogenicity was found.
Reference: Monsanto HL-79-39, Hazelton Laboratories, 1979
Reliability: (1) Valid without restriction

*5.8 TOXICITY TO REPRODUCTION

Type: Fertility
Species/strain: Rats
Sex: Male
Route of Administration: Gavage
Exposure period: 56 days
Frequency of treatment: Daily, 7 days/week
Post exposure observation period: 2 weeks
Doses: 0, 125, 250 or 500 mg/kg/day
Control group: Yes, Concurrent vehicle
Results: The test substance was evaluated for genotoxicity in the dominant lethal test in groups of 10 male rats treated by gavage at the above dose levels. Following treatment, each male rat was housed with two virgin female rats/week for two weeks. The females were sacrificed thirteen days after mating for determination of dominant lethal effects. The treatment had no adverse effects with respect to clinical signs, mortality rate, body weight gain, or organ weights of adult male rats. The treatment also had no effect on pregnancy, early fetal death, implantation, or preimplantation losses in the females. Positive control treatment with a single intraperitoneal injection of 0.25 mg/kg bw Triethylenemelamine produced the expected dominant lethal effects. Under the conditions of this assay, the test compound results were negative, indicating that the compound was not mutagenic to the germ cells of male rats.

No evidence of reduced fertility was observed. Treated animals had similar conception rates to those of controls. Mean body weight and mean body weight gain did not reveal any statistically significant effect in any of the dose groups. Tissue-to-body weight ratios were normal, with the exception of an increase in the stomach/body weight ratio in the 125 and 250 mg/kg dose groups. No abnormalities were noted in selected animals during gross pathological examination.
Method: Green et al. (1974) Toxicol. Appl. Pharmacol 39:549-552; Russel and Matter (1980) Mutat. Res. 75:279-302.
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: >95%
Remarks: None
Reference: Hinderer, et al., Tox. Appl. Pharm., 1982
Reliability: (1) Valid without restriction

Type: Fertility
Species/strain: Rats
Sex: Male and female
Route of Administration: Gavage
Exposure period: 3 days
Frequency of treatment: 1st and 3rd days of estrus (female); twice at intervals of 3 days
Post exposure observation period: Until 19th day of pregnancy
Premating exposure period: No data
Duration of the test: No data
Doses: 0 or 200 mg/kg bw

Control group: Yes, Concurrent vehicle
Results: There were no visible signs of poisoning in the parent animals. Changes in the estrous cycle were noted, as well as delays in conception in treated females. Decreased fetal weights were observed. There was in increase in total embryonic mortality, but postimplantation embryonic mortality was within the normal range.
Method: No data
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: >95%
Remarks: Embryonic mortality study
Reference: Aleksandrov, S.E., Byull. Eksp. Biol. Med., 1982
Reliability: (4) Not assignable - data from a secondary literature source

*5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

Species/strain: Rat, Charles River COBS CD
Sex: Female
Route of Administration: Oral gavage
Duration of the test: Day 6-15 of gestation
Exposure period: 10 days
Frequency of treatment: Daily
Doses: 0, 100, 300 or 1000 mg/kg/day
Control group: Yes
Concurrent vehicle
NOEL Maternal Toxicity: 100 mg/kg/day
NOEL teratogenicity: 1000 mg/kg/day
Results: One hundred female rats, age 80-120 days old, were mated for this study. Pregnant rats were used to determine the teratogenic potential of the test substance. The above doses were administered orally by gavage as a single daily dose on days 6-15 of gestation at a constant volume of 10 ml/kg. The control group received the vehicle only (Mazola corn oil) on a comparable regimen at a volume of 10 ml/kg. Dams were observed daily for mortality and overt changes in apperance and behavior. Cesarean sections were performed on all dams on day 20 of gestation. The uterus was excised and weighed prior to removal of the fetuses. The number and location of viable and non-viable fetuses, early and late resorptions and the number of total implantations and corpora lutea were recorded. The abdominal and thoracic cavities and organs of the dams were examined for grossly evident morphological changes and the carcasses discarded. All fetuses were individually weighed and examined for external malformations and variations, including the palate and eyes. Each fetus was externally sexed and individually numbered and tagged for identification. Half of the fetuses were placed in Bouin's fixative for subsequent visceral examination by razor blade sectioning. The remaining fetuses were fixed in alcohol, macerated in potassium hydroxide, and dye-stained for subsequent skeletal anaylsis.
<u>Maternal general toxicity:</u> One death occurred in the high-dosage group on gestation day 14, but this was attributed to a gavage error. All other animals survived until terminal sacrifice. A dose-related increase in matting and staining of the anogenital hair coat

was noted in the 300 and 1000 mg/kg/day treatment groups, and by decreases in mean maternal body weight gain as well. There was also a slight increase in hair loss.
Pregnancy/litter data: No biologically meaningful or statistically significant differences were observed in the mean numbers of corporea lutea, total implantations, viable fetuses, early or late resorptions, postimplantation loss, mean fetal body weights, or mean fetal sex distribution in the treated groups when compared to the control group.
Foetal data: There were no biologically meaningful or statistically significant differences in the number of litters with malformations in the treated groups when compared to the control group. No biologically meaningful differences in the number of fetuses or litters with developmental or genetic variations were observed in the treated groups when compared to the control group.

Method: Other: Wilson, J.G., Embryological Considerations in Teratology, Teratology – Principles and Techniques, 1965
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: >96%
Remarks: The test article did not produce a teratogenic response when administered orally by gavage to pregnant rats at a dose level of 1000 mg/kg/day or less.
Reference: Monsanto IR-78-102, International R & D Corp., 1981
Reliability: (1) Valid without restriction

Species/strain: Rat
Sex: Female
Route of Administration: Gavage
Duration of the test: Until 11th day of pregnancy
Exposure period: 2 days
Frequency of treatment: 4th and 11th day of pregnancy
Doses: 200 mg/kg bw
Control group: Yes
NOEL Maternal Toxicity: Not determined
NOEL teratogenicity : Not determined
Results: The object of this investigation was to study the level of embryonic mortality.
Maternal general toxicity: No visible signs of poisoning were noted.
Pregnancy/litter data: Increased incidence of total, preimplantation and postimplantation lethality
Foetal data: Slight decreased in fetal weights.
Method: No data
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: >96%
Remarks: None
Reference: Aleksandrov, S.E., Byull. Eksp. Biol. Med., 1982
Reliability: (4) Not assignable - data from a secondary literature source

Species/strain: Rat, Wistar
Sex: Female
Route of Administration: Oral feed

Duration of the test:
Exposure period: Day 0 of gestastion – Day 21 postparturition
Frequency of treatment: Daily
Doses: 0, 3.9 or 81 mg/mg/day
Control group: Yes, Concurrent no treatment
NOEL Maternal Toxicity: 81 mg/kg/day
NOEL teratogenicity: 81 mg/kg/day
Results:

Maternal general toxicity: No toxic effects noted
Pregnancy/litter data: Slight increase in the stillborn litter number
Foetal data: No harmful effects on the fetuses with respect to external, skeletal or visceral anomalies. The postnatal development of the offspring was normal.

Method: No data
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity >95%
Remarks: None
Reference: Morita, et al., 1981
Reliability: (4) Not assignable - data from a secondary literature source

Species/strain: Rat, Wistar
Sex: Female
Route of Administration: Oral feed
Duration of the test: 21 days
Exposure period: Day 0 – Day 21 of gestation
Frequency of treatment: Daily
Doses: 0, 13 or 270 mg/kg
Control group: Yes, Concurrent no treatment
NOEL Maternal Toxicity: 270 mg/kg
NOEL teratogenicity: 270 mg/kg
Results:

Maternal general toxicity: No toxic effects noted
Pregnancy/litter data: No toxic effects noted
Foetal data: No harmful effects on the fetuses with respect to external, skeletal or visceral anomalies. The postnatal development of the offspring was normal.

Method: No data
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity >95%
Remarks: None
Reference: Morita, et al., 1981
Reliability: (4) Not assignable - data from a secondary literature source

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

Type: Biochemical or cellular interactions
Results: The reactions of representative amino acids Lysine, Cysteine and Glyzine with the test compound were examined. New compounds were confirmed between the test compound and all three amino acids. No reaction was observed with morpholine. The new

compounds were examined spectroscopically. The conjugation between the test compound and Cysteine was postulated as a reaction of the test compound's disulfide bond and the –SH and –NH2 groups of the amino acid moieties.

Reference: Wang and Tabor, Contact Dermatitis, 1988

Reliability: (4) Not assignable - data from a secondary literature source

B. Toxicodynamics, toxicokinetics

Type: Metabolism/Metabolites

Results: The metabolic fate of the test article in rats was studied using tracer techniques. The compound, given orally to rats, was rapidly excreted in the urine and feces. Five urinary metabolites, (2-mercaptobenzothiazole, its three conjugates mercapturate, glucuronide and sulfate, and 2-mercaptobenzothiazole disulfide) were confirmed. 2-mercaptobenzothiazole disulfide was also found as a fecal metabolite. The test compound was partially transformed in the stomach to 2-mercaptobenzothiazole disulfide, which was predominately excreted into the feces. In the liver, the test compound was mainly transformed to 2-mercaptobenzothiazole and its conjugates. The S-glucuronide and S-sulfate conjugates were predominately excreted into the bile.

Reference: Fukuoka, et al., Archives of Toxicology, 1995

Reliability: (4) Not assignable - data from a secondary literature source

* 5.11 EXPERIENCE WITH HUMAN EXPOSURE

6. REFERENCES

1. ASTM D-1519/Flexsys Standard Methods of Analysis, 1983
2. Flexsys Analytical Research Report 2003.012, 2003
3. Flexsys Analytical Research Report 2003.012, 2003
4. FF97.8-1 Flexsys Standard Methods of Analysis, 1997
5. EPIWIN/MPBPWIN v1.40
6. Bayer AG Data
7. EPIWIN/KOWWIN v1.40
8. Monsanto ES-78-SS-20, Water Solubility and Octanol/Water Partition Coefficient of Selected Rubber Chemicals, Monsanto Environmental Health Laboratories, 1978
9. EPIWIN/WSKOW v.140
10. ASTM D 92-96, Flash Point and Fire Point by Cleveland Open Cup
11. DIN 51584, Bayer AG data
12. EPIWIN/HENRYWIN v3.10
13. AOP Program v1.89, 1999
14. Monsanto MO-92-9058/ES-80-SS-43, 1980
15. Monsanto AB-84-131, Phase I Hydrolysis Screening Study of Santocure MOR, Analytical Bio-Chemistry Labs, 1984
16. Handbook of Chemical Property Estimation Methods, 1990
17. EPISUITE/EPIWIN v3.10
18. Bayer AG data - Biotic Degradation – Modified MITI Test
19. Bayer AG data, ThOD Determination
20. Monsanto ES-78-SS-20, Water Solubility and Octanol/Water Partition Coefficient of Selected Rubber Chemicals, Monsanto Environmental Health Laboratories, 1978

21. EPIWIN/BCFWIN v2.14
22. Monsanto AB-80-0240, Acute Toxicity of Santocure MOR to Fathead Minnows, Analytical Bio-Chemistry Labs, 1980
23. Uniroyal Chemical Unpublished Report, Acute Toxicity in Bluegill Sunfish, 1972
24. Monsanto BN-76-172, Acute Toxicity of Santocure MOR to Bluegill Sunfish, EG&G Bionomics, 1976
25. Bayer AG data, Acute Toxicity in Freshwater Fish, 1989
26. Monsanto BN-76-172, Acute Toxicity of Santocure MOR to Rainbow Trout, EG&G Bionomics, 1976
27. Monsanto SR-80-66, A Time-Independent Study of Acute Toxicity of Santocure MOR to Rainbow Trout, SRI International, 1981
28. MacPhee and Ruelle, U. of Idaho, Acute Fish Toxicity, 1969
29. Bayer AG data, Acute Fish Toxicity
30. Monsanto AB-78-355, Acute Toxicity of Santocure MOR to Daphnia magna, Analytical Bio-Chemistry Labs, 1978
31. Monsanto AB-81-357, Acute Toxicity of Sanotcure MOR to Midge, Analytical Bio-Chemistry Labs, 1981
32. Monsanto BN-73-363, Acute Toxicity of Santocure MOR to Freshwater Algae, EG&G Bionomics 1973
33. Bayer AG data, Activated Sludge Inhibition Test, 1988
34. BF Goodrich AN-3546, IBT# 601-04729, Industrial Bio-Test Labs, 1974
35. de Groot, A.P., CIVO-TNO, Short Report, March 18, 1976
36. Monsanto Y-73-194, Acute Oral LD50 of Santocure MOR, Younger Laboratories, 1973
37. BF Goodrich T-99, Top Hill Research, 1969
38. IBT Study #663-04730, 1974
39. BF Goodrich AN-3546, Industrial Bio-Test Labs, 1974
40. Monsanto Y-73-194, Acute Dermal LD50 of Santocure MOR, Younger Laboratories, 1973
41. BF Goodrich AN-3546, Industrial Bio-Test Labs, 1974
42. Monsanto Y-73-191, Acute Skin Irritation of Santocure MOR, Younger Laboratories, 1973
43. Monsanto Y-73-191, Acute Eye Irritation of Santocure MOR, Younger Laboratories, 1973
44. BF Goodrich AN-3546, Industrial Bio-Test Labs, 1974
45. Monsanto SH-82-8, Skin Sensitization Studies, Product Investigations, Inc. 1982
46. Monsanto SH-86-255, Skin Sensitization Studies, Product Investigations, Inc. 1986
47. Monsanto ML-87-68, In vitro Lymphocyte Transformation Assay, Santocure MOR and Oxidized Forms of S-MOR,1987
48. Monsanto HL-79-031, Preliminary Range-Finding Study on Santocure MOR, Hazleton Laboratories, 1979
49. Monsanto IR-79-264, 21-Day Dermal Toxicity Study on Santocure MOR, International Research & Development Corp., 1981
50. Monsanto IR-78-96, 4-week Inhalation Study on Santocure MOR, International Research & Development Corp., 1979
51. Monsanto HL-79-39, 2-year Feeding Study on Santocure MOR, Hazelton Laboratories, 1979
52. Monsanto BIO-76-180, Ames Mutagenicity Study of Saantocure MOR, Litton Bionetics, November 1976
53. Litton Bionetics for CMA final report, December, 1981
54. Hinderer, R.K. et al., Environmental Mutagenesis 5, 193-215, 1983
55. Litton Bionetics for CMA final report, December, 1981
56. Litton Bionetics for CMA final report, December, 1981
57. Monsanto BO-78-223, Mouse Lymphoma Assay of Santocure MOR, Litton Bionetics, 1979
58. Litton Bionetics for CMA final report, BALB/3T3 Assay, December, 1981
59. Pharmakon Research International for CMA, Report # PH 314-CMA-001-83 and PH 314-CMA-002-83, Microfiche # 0308, Doc. ID FYI-AX-0484-0308IN, February 03, 1984
60. Litton Bionetics/BF Goodrich, 1979
61. BF Goodrich/Food and Drug Research Laboratories, 1980

62. Aleksandrov, S.E. Byull. Eksp. Biol. Med. 93, 107-109, 1982
63. Litton Bionetics/NCI Report # PB223-159 (1968)
64. Monsanto HL-79-39, Hazelton Laboratories, 1979
65. Hinderer, R.K. et al., Tox. Appl. Pharm. 62, 335-341, 1982
66. Aleksandrov, S.E., Byull. Eksp. Biol. Med. 93, 87-88, 1982
67. Monsanto IR-78-102, A Teratology Study on Santocure MOR in Rats, International Research and Development Laboratories, 1981
68. Aleksandrov, S.E., Byull. Eksp. Biol. Med., 1982
69. Morita, S.H. et al., Annual Report, Osaka City Institute of Public Health Environ. Science 43, 90-97, 1981
70. Wang, X. and Tabor, W., Contact Dermatitis 19, 16-21, 1988
71. Fukuoka, et al., Archives of Toxicology 70(1), 1-9, 1995

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I U C L I D

D a t a S e t

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Existing Chemical	ID: 110-91-8
CAS No.	110-91-8
EINECS Name	morpholine
EC No.	203-815-1
TSCA Name	Morpholine
Molecular Formula	C4H9NO

Producer Related Part
Company: EUROPEAN COMMISSION - European Chemicals Bureau
Creation date: 10-FEB-2000

Substance Related Part
Company: EUROPEAN COMMISSION - European Chemicals Bureau
Creation date: 10-FEB-2000

Printing date:	21-NOV-2002
Revision date:	10-FEB-2000
Date of last Update:	10-FEB-2000

Number of Pages: 114

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

Name: ANCHOR CHEMICAL(UK)LTD
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Country: United Kingdom
Phone: O61-223-2461
Telefax: 061-223-5488

Name: BASF AG
Street: Karl-Bosch-Str
Town: 67056 Ludwigshafen
Country: Germany

Name: EIGENMANN & VERONELLI S.P.A.
Street: DELLA MOSA 6
Town: 20017 RHO (MI)
Country: Italy
Phone: 02/935391
Telefax: 02/93539361

Name: Huels AG
Street: Postfach
Town: D-45764 Marl
Country: Germany

Name: Texaco Ltd/Huntsman Corporation Ltd
Street: 195 Knightsbridge
Town: SW7 1RU London
Country: United Kingdom
Phone: ++4471 581 5500
Telefax: ++44 71 581 9163

1.0.2 Location of Production Site, Importer or Formulator

-

1.0.3 Identity of Recipients

-

1.0.4 Details on Category/Template
-

1.1.0 Substance Identification
-

1.1.1 General Substance Information

Substance type: organic
Physical status: liquid

1.1.2 Spectra
-

1.2 Synonyms and Tradenames

1-oxa-4-azacyclohexane

Source: Texaco Ltd/Huntsman Corporation Ltd London

1-Oxa-4-azacyclohexane

Source: BASF AG Ludwigshafen

2H-1,4-Oxazine, tetrahydro-

Source: BASF AG Ludwigshafen

4H-1,4-Oxazine, tetrahydro-

Source: BASF AG Ludwigshafen

BASF 238

Source: BASF AG Ludwigshafen

Diethylene imidoxide

Source: Texaco Ltd/Huntsman Corporation Ltd London
BASF AG Ludwigshafen

Diethylene oximide

Source: BASF AG Ludwigshafen

Diethyleneimide oxide

Source: Texaco Ltd/Huntsman Corporation Ltd London

diethyleneoximide

Source: Texaco Ltd/Huntsman Corporation Ltd London

Diethylenimide oxide

Source: BASF AG Ludwigshafen

Drewamine

Source: BASF AG Ludwigshafen

Morpholin

Source: BASF AG Ludwigshafen

Morpholine (8CI, 9CI)

Source: BASF AG Ludwigshafen

p-Isoxazine, tetrahydro-

Source: BASF AG Ludwigshafen

Tetrahydro-1,4-isoxazine

Source: Texaco Ltd/Huntsman Corporation Ltd London

Tetrahydro-1,4-oxazine

Source: Texaco Ltd/Huntsman Corporation Ltd London
BASF AG Ludwigshafen

tetrahydro-1,4-oxazine

Source: Huels AG Marl

Tetrahydro-2H-1,4-oxazine

Source: BASF AG Ludwigshafen

Tetrahydro-p-isoxazine

Source: Texaco Ltd/Huntsman Corporation Ltd London

Tetrahydro-p-oxazine

Source: BASF AG Ludwigshafen

1.3 Impurities
-

1.4 Additives
-

1.5 Total Quantity

Quantity: 10000 - 50000

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: (C) corrosive
(E) For substances ascribed Nota E the risk phrases R20, R22

to R28 and all combinations of these risk phrases shall be preceded by the word 'also'. E.g. R23 'also' toxic by inhalation
Specific limits: yes
R-Phrases: (10) Flammable
(20/21/22) Harmful by inhalation, in contact with skin and if swallowed
(34) Causes burns
S-Phrases: (1/2) Keep locked up and out of reach of children
(23) Do not breathe ...
(36) Wear suitable protective clothing
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

1.6.2 Classification

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

Classified: as in Directive 67/548/EEC
Class of danger: corrosive

R-Phrases: (34) Causes burns

Classified: as in Directive 67/548/EEC
R-Phrases: (10) Flammable

1.6.3 Packaging
-

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use resulting in inclusion into or onto matrix

Type: industrial
Category: Agricultural industry

Type: industrial
Category: Chemical industry: used in synthesis

Type: industrial
Category: Fuel industry

Type: industrial
Category: other

Type: use
Category: Cleaning/washing agents and disinfectants

Type: use
Category: Corrosive inhibitors

Type: use
Category: Intermediates

Type: use

Category: Lubricants and additives

Type: use
Category: pH-regulating agents

Type: use
Category: Pharmaceuticals

Type: use
Category: Solvents

Type: use
Category: Viscosity adjustors

Type: use
Category: Vulcanizing agents

Type: use
Category: other

1.7.1 Detailed Use Pattern
-

1.7.2 Methods of Manufacture
-

1.8 Regulatory Measures
-

1.8.1 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value: 70 mg/m3

Source: Texaco Ltd/Huntsman Corporation Ltd London
(1)

Type of limit: MAK (DE)
Limit value: 20 ml/m3
Short term exposure
Limit value: 40 ml/m3

Schedule: 5 minute(s)
Frequency: 8 times

Source: BASF AG Ludwigshafen

(2)

Type of limit: MAK (DE)
Limit value: 70 mg/m3

Remark: Die Reaktion mit nitrosierenden Agentien kann zur Bildung der kanzerogenen N-Nitrosoverbindungen fuehren. hautresorptiv
Source: BASF AG Ludwigshafen

(2)

Type of limit: MAK (DE)
Limit value: 70 mg/m3

Remark: Die Reaktion mit nitrosierenden Agentien kann zur Bildung der kanzerogenen N-Nitrosoverbindungen fuehren. hautresorptiv
Source: BASF AG Ludwigshafen

(2)

Type of limit: MAK (DE)
Limit value: 20 ml/m3
Short term exposure
Limit value: 20 ml/m3

Country: Germany
Source: Huels AG Marl

Type of limit: MAK (DE)
Limit value: 70 mg/m3
Short term exposure
Limit value: 70 mg/m3

Country: Germany
Source: Huels AG Marl

Type of limit: OES (UK)
Limit value: 70 mg/m3
Short term exposure
Limit value: 105 mg/m3

Source: Texaco Ltd/Huntsman Corporation Ltd London

(3)

Type of limit: TLV (US)
Limit value: 71 mg/m3
Short term exposure
Limit value: 107 mg/m3

Source: Texaco Ltd/Huntsman Corporation Ltd London
(4)

Type of limit: TLV (US)
Limit value: 71 mg/m3

Remark: Wert bezieht sich auf Haut.
Source: BASF AG Ludwigshafen
(5)

Type of limit: TLV (US)

Remark: Limit value: 20 ppm
Wert bezieht sich auf Haut.
Source: BASF AG Ludwigshafen
(5)

Type of limit: other
Limit value: 70 mg/m3
Short term exposure
Limit value: 105 mg/m3

Remark: French VME (Longer term) and VLE (short term) values respectively.
Source: Texaco Ltd/Huntsman Corporation Ltd London
(6)

Type of limit: other
Limit value: 70 mg/m3
Short term exposure
Limit value: 105 mg/m3

Remark: Swedish exposure limits, "level" limit and "short term limit" respectively.
Source: Texaco Ltd/Huntsman Corporation Ltd London
(7)

Remark: Tests carried out by Texaco at UK manufacturing site 1979-1989. Method US NIOSH Method S-150, detection limit of test = 1 mg/m3 (3mg/m3 for 1979 tests). Tests measured Morpholine in air exposure by personal and static monitoring covering different job roles and sites throughout the plant. Overall results were the following for 1979-1989:

	No. Air samples	No. Workers	Avge sample time/shift mins	avge air vol/sample litres	Mor conc Mg/m3 Range	Avge
Personal samples	75	65	268	26	<1-40	<3
Static samples	109		386	30	<1-22	<1

Avge and maximum figures well below HSE TWA of 70 mg/m3

Values determined in 1993 for personal and static monitoring by plant safety personnel over several months did not detect morpholine at the detection limit of 0.06 ppm for personal monitoring.
Texaco Huntsman MSDS requires Gloves, Protective clothing and eye face protection for workers coming into contact with morpholine via production/storage/distribution process

Source: Texaco Ltd/Huntsman Corporation Ltd London

(8)

1.8.2 Acceptable Residues Levels

-

1.8.3 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 2 (water polluting)

Source: BASF AG Ludwigshafen

Classified by: KBwS (DE)
Class of danger: 2 (water polluting)

Source: BASF AG Ludwigshafen

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 2 (water polluting)

Country: Germany
Remark: No. 158 in catalogue
Source: Huels AG Marl

(9)

1.8.4 Major Accident Hazards

Legislation: Stoerfallverordnung (DE)
Substance listed: no

Source: BASF AG Ludwigshafen

(10)

Legislation: Stoerfallverordnung (DE)
Substance listed: yes

Country: Germany
Remark: Anhang IV Kat. 7: Entzuendliche Fluessigkeiten
Source: Huels AG Marl

(9)

1.8.5 Air Pollution

Classified by: other: BASF
Labelled by: other: BASF
Number: 3.1.7 (organic substances)
Class of danger: II

Remark: Der Stoff wurde als endgueltig eingestuft dem VCI gemeldet.
Source: BASF AG Ludwigshafen

Classified by: other: VCI
Labelled by: other: VCI
Number: 3.1.7 (organic substances)
Class of danger: II

Country: Germany
Source: Huels AG Marl

(9)

1.8.6 Listings e.g. Chemical Inventories
-

1.9.1 Degradation/Transformation Products
-

1.9.2 Components
-

1.10 Source of Exposure

Remark: EMISSION DATA

Checks at 59 possible site emission points for Morpholine as VOC were carried out in 1993, areas covered included storage tanks, loading areas and pipework. At an apparatus detection limit of 2 ppm No morpholine was detected. NB The plant is currently introducing a periodic program of VOC emission tests for Morpholine

Ref Texaco 1993
Morpholine is manufactured by Texaco/ Huntsman at One Site in Europe (Wales, UK) The basic process involves the following:

1. Reaction of Diethylene Glycol (CAS 111-46-6) and Ammonia at high temperature and pressure in a Hydrogen atmosphere over a nickel catalyst

2. Separation of gas/liquid phases

3. Distillation of liquid phase to isolate and purify morpholine, which is then piped into bulk storage tanks

Due to the process requirements it is considered to be a closed process. Plant control procedures are in place to minimise potential process loss and environmental/health exposure, see also IH monitoring data for plant in section 1.8.

Plant Manufactures avge 30 tonnes per day on an average 200 morpholine production days/year, production is a continous process during production campaigns.
PLANT POTENTIAL ENVIRONMENTAL EXPOSURE and CONTROLS

The site possesses a bunded wall spill containment system consisting of an on site drainage system, running into a sump, from where material transfers via switchable valve to either;

(i) a covered strong effluent tank capacity 265 tonnes.
or
(ii) weak effluent tank capacity 2500 tonnes.

During Morpholine manufacture under normal conditions

any waste material from sampling/ temporary minor leaks from any defective equipment runs into the weak effluent tank.
Concentration organics < 0.4% in weak effluent system.
Morpholine concentration of tank contents approx 0.25%.
CODs of weak effluent (< 5000 ppm) determined weekly
BODs determined monthly
pH determined daily
Weak effluents are discharged to land by spray heads

Certain key points are bunded direct to the strong effluent system. Under normal circumstances Morpholine does not reach this system. As indicated above system is switchable in case of emergency. Contents of strong effluent system, from waste manufacturing streams (organics approx 5%) are incinerated.
Summarised from approved UK HMIP application, see ref below

Source: Texaco Ltd/Huntsman Corporation Ltd London

(11)

1.11 Additional Remarks

Remark: From manufacturing plant in Llanelli, Wales.
an avge maximum of 1 truck per day would leave the plant for destinations in and outside the EC, product is normally transported in bulk.
Product can be disposed of by incineration at an approved site at a temperature of greater than 1200 Deg C. No heavy metals are expected in significant quantities.
By careful addition under controlled conditions (normally neutralised) to adapted waste water treatment plants containing activated sludge, rapid biodegradation is expected to occur. No adverse effects are expected on the degradative activity of the bacteria at the product levels expected as a maximum under any normal foreseen conditions within treatment plants
The following transport classifications apply to Morpholine;

UN No: 2054
ADR/RID: 3,31(c)
HI Kemler No 30
CEFIC TREMCARD No 30G35/697
ICAO/IATA Class 3
Not clqssed as a marine pollutant
UK HAZCHEM 2P

Source: Texaco Ltd/Huntsman Corporation Ltd London

1.12 Last Literature Search
-

1.13 Reviews
-

2.1 Melting Point

Value: = -5 degree C

Source: BASF AG Ludwigshafen
(12)

2.2 Boiling Point

Value: = 128 - 130 degree C

Source: BASF AG Ludwigshafen
(12)

2.3 Density

Type: density
Value: = 1 g/cm? at 20 degree C

Source: BASF AG Ludwigshafen
(12)

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: = 10 hPa at 20 degree C

Source: BASF AG Ludwigshafen
(12)

Value: = 62.3 hPa at 60 degree C

Source: BASF AG Ludwigshafen
(12)

2.5 Partition Coefficient

log Pow: = -2.55 at 25 degree C

Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"

Remark: Messwert gilt fuer pH 7.
Fuer pH 10,2 wurde der log Pow = -0.84 gemessen (es liegt ein proteolytisches Gleichgewicht vor).

Source: BASF AG Ludwigshafen

(13)

log Pow: = -1.08

Method: other (calculated): Leo, Hansch

Source: BASF AG Ludwigshafen

(14)

log Pow: = -.826

Method: other (calculated): Inkrementenmethode von Rekker mit Computerprogramm der Firma CompuDrug Ltd.

Source: BASF AG Ludwigshafen

(15)

2.6.1 Solubility in different media

Value: at 20 degree C
pH value: 10.6
Conc.: 5 g/l at 20 degree C
Descr.: miscible

Source: BASF AG Ludwigshafen

(12)

2.6.2 Surface Tension

-

2.7 Flash Point

Value: = 32 degree C

Method: other: DIN 51 755

Source: BASF AG Ludwigshafen

(12)

2.8 Auto Flammability

Value: = 275 degree C

Method: other: DIN 51 794

Source: BASF AG Ludwigshafen

(12)

2.9 Flammability
-

2.10 Explosive Properties

Result: other: Explosionsgrenzen in Luft: 1.4 - 13.1 Vol. %

Source: BASF AG Ludwigshafen

(12)

2.11 Oxidizing Properties
-

2.12 Dissociation Constant
-

2.13 Viscosity
-

2.14 Additional Remarks

Remark: Gefaehrliche Reaktionen: Exotherme Reaktion mit Saeuren.
Source: BASF AG Ludwigshafen

(12)

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm?

Remark: Die Geschwindigkeitskonstante fuer den Abbau von Morpholin in der Atmosphaere durch OH-Radikale wurde bislang nicht gemessen. Nach Atkinson laesst sich die OH-Geschwindigkeitskonstante berechnen (298 K), wobei die azide >NH-Gruppierung den mit Abstand groessten Beitrag zur k(OH)-Geschwindigkeitskonstante leistet: k(OH) = 9.5*10^-11 (Bereich: 1.9 *10^-11 bis 47.5*10^-11). Der angegebene Bereich basiert auf einem Unsicherheitsfaktor von 5. Dieser wurde zugrundegelegt, da fuer N-enthaltende Kohlenwasserstoffe nur eine extrem schmale Datenbasis existiert. Bei einer angenommenen troposphaerischen OH-Radikal-Konzentration von 500000 Molekuelen/cm^3 liegt die Halbwertszeit bei t1/2 = < 1 Tag.
Source: BASF AG Ludwigshafen

(16)

Type: other: Atmosphaere / Hydrosphaere

Remark: Da Morpholin im UV-Spektrum >260 nm keine Absorption aufweist, ist ein direkter photochemischer Abbau weder in der Atmosphaere noch in der Hydrosphaere zu erwarten.
Source: BASF AG Ludwigshafen

(16)

3.1.2 Stability in Water

Method: other

Remark: Morpholin unterliegt bei hoeheren Temperaturen (>400 Grad C) in Wasserdampf einer thermischen Zersetzung. Es ist anzunehmen, dass der Stoff unter freilandrelevanten Bedingungen stabil ist.

Source: BASF AG Ludwigshafen

(17)

3.1.3 Stability in Soil

Method: other

Remark: Nur unter der Annahme, dass die Sorbenten im trockenen Zustand vorliegen, ist aufgrund der Polaritaet des Stoffes mit einer nennenswerten Bindung an Boeden bzw. Sedimenten zu rechnen. Bei der im Regelfall im humiden Klima erfolgenden Befeuchtung der Austauscher wuerde dann eine rasche Desorption eintreten, wobei insgesamt keine Geoakkumulation zu erwarten ist.

Source: BASF AG Ludwigshafen

(18)

3.2.1 Monitoring Data (Environment)

Medium: air

Remark: Nach Angaben der BG Chemie (1990) wurden im Zeitraum von 1980 bis 1990 bei der Untersuchung der Arbeitsplatzatmosphaere von 15 Betrieben der chemischen, der kunststoffverarbeitenden und der Gummiindustrie ein Orientierungswert von 70 mg/m^3 in keinem Fall ueberschritten (35 Messdaten). 90% der Messwerte wiesen eine Konzentration von <0.26 mg/m^3 auf.

Source: BASF AG Ludwigshafen

(19)

Medium: air

Remark: Im Rahmen einer NIOSH-Studie fanden Taft & Stroman (1979) bei 7 personen- und 5 ortsbezogenen Messungen in einer Reifenfabrik nur in einer Probe Morpholin. Bei einer Erfassungsgrenze von 1.1 mg/m^3 (gaschromatographisch bestimmt, keine weiteren Angaben zur Methode) ermittelten die Autoren in der Atemzone eines Arbeiters eine Konzentration von 1.4 mg/m^3 Morpholin.

Source: BASF AG Ludwigshafen

(20)

Medium: air

Remark: Fajen et al. bestimmten den Gehalt von Morpholin in einer Reifenfabrik in Ohio (USA) zu 0.23 +/- 0.11 mg/m^3 und in der zugehoerigen chemischen Fabrik (Herstellung von Vulkanisationsbeschleunigern) zu 0.042 +/- 0.005 mg/m^3.

Source: BASF AG Ludwigshafen

(21)

Medium: surface water

Remark: Seit Mitte 1990 wird Morpholin routinemaessig vom Landesamt fuer Wasser und Abfall NRW erfasst. Die Bestimmung erfolgt mittels gaschromatographischer Analyse eines Dichlormethan-Extraktes. Bei diesem Verfahren liegt die Bestimmungsgrenze fuer Morpholin bei etwa 5 ug/l. Von Mitte Juni bis Ende August 1990 wurde Morpholin weder im Rhein (Messstellen Bad Honnef, km 640, Duesseldorf, km 732 und Kleve-Bimmen, km 865) noch an den Messstellen des LWA an den Nebenfluessen Ruhr, Sieg, Lippe, Wupper und Erft nachgewiesen.

Source: BASF AG Ludwigshafen

(22)

Medium: biota

Remark: Das Vorkommen von Morpholin in der Biosphaere, insbesondere in Nahrungs- und Genussmitteln, ist von besonderer Bedeutung, da zahlreiche Hinweise in der Literatur vorliegen, dass der Stoff auch unter Bedingungen, wie sie im menschlichen Organismus vorliegen, nitrosiert werden kann.

Source: BASF AG Ludwigshafen

(23)

Medium: biota

Remark: Singer & Lijinsky fanden in Fischen (Forelle, Flussbarsch, Lachs aus US-amerikanischen Fluessen) Morpholinkonzentrationen zwischen </= 0.7 (Flussbarsch) und 6.0 mg/kg (Forelle) (Nachweisgrenze 0.3 mg/kg). Es handelt sich hierbei jedoch um Einzelergebnisse. Lediglich eine Forelle wurde untersucht, die Messwerte der uebrigen Fischarten sind Mittelwerte einer nicht genannten Zahl von Proben.

Source: BASF AG Ludwigshafen

(24)

Medium: food

Remark: Durch Behandlung von Obst mit morpholinhaltigen Konservierungsmitteln, Dampfbehandlung von Lebensmitteln waehrend der Verarbeitung und Verwendung von morpholin-haltigem Verpackungspapier kann es zu einer Kontamination von Lebensmitteln kommen.

Source: BASF AG Ludwigshafen

(25)

Medium: food

Remark: Ohnishi et al. stellten an Schalen handelsueblicher Zitrusfruechte Morpholinkonzentrationen bis zu 71.1 mg/kg fest. Im Fruchtfleisch war der Gehalt mit < 0.2 mg/kg (Nachweisgrenze) bis 0.7 mg/kg wesentlich geringer. Marmeladen aus ganzen Zitrusfruechten wiesen Konzentrationen von 0.3 bis 0.7 mg/kg auf. Der Morpholingehalt der zur Herstellung der Marmeladen verwendeten Zitrusfruechte ist nicht bekannt.

Source: BASF AG Ludwigshafen

(26)

Medium: food

Remark: Durch Waschen der Fruechte unter Verwendung von Haushaltsspuelmitteln laesst sich der Morpholingehalt nur zu etwa einem Viertel reduzieren. 20-minuetiges Kochen dagegen ent-

fernt 2/3 bis 3/4 des Stoffes aus der Schale. Die Substanz laesst sich dann quantitativ im Wasch- oder Kochwasser nachweisen.
Source: BASF AG Ludwigshafen

(26)

Medium: food

Remark: Hoffmann et al. fanden in verpackten Lebensmitteln zwischen 0.005 und 0.077 mg/kg Morpholin.
Source: BASF AG Ludwigshafen

(27)

Medium: other

Remark: Die Kontamination von verpackten Lebensmitteln laesst sich mit der Verwendung von Morpholin bei der Herstellung von Papier und Pappe erklaeren. Hotchkiss & Vecchio fanden in 12 Lebensmittelverpackungen aus Papier bzw. Pappkarton im Durchschnitt 0.38 mg/kg Morpholin (0.098 bis 0.842 mg/kg).
Source: BASF AG Ludwigshafen

(28)

Medium: food

Remark: Angaben ergeben sich aus dem Durchschnitt mehrerer Proben; genaue Anzahl nicht angegeben; Bezugsgroesse ausser bei Kaffee: Frischgewicht.
Morpholingehalt ausgewaehlter Lebensmittelproben:
Thunfisch (in Dosen): </= 0.6 mg/kg; Seebarsch (gefroren): 9.0 mg/kg; Schinken (baked ham): 0.5 mg/kg; Frankfurter Wuerstchen: 0.4 mg/kg; Trockenmilch: 0.2 mg/kg; Kaffee (Mischproben aus zwei Marken; Bezugsgroesse: Trockengewicht): 1.2 mg/kg; Dosenbier: 0.4 mg/kg; Flaschenbier: </= 0.2 mg/kg; Wein: </= 0.7 mg/kg.
Source: BASF AG Ludwigshafen

(24)

Medium: food

Remark: Bezugsgroesse: Frischgewicht
Schinken (baked ham), 5 Proben: 0.2 mg Morpholin/kg
Source: BASF AG Ludwigshafen

(29)

Medium: food

Remark: Morpholingehalte von Milchprodukten / ihren Verpackungen (Angaben in mg/kg)
Butter: 0.058/0.22; Schmelzkaese: 0.077/0.68;

Joghurt: 0.038/3.06; Huettenkaese: 0.044/17.2;
Kaese, halbweich (BRD): 0.009/0.026; Gouda: 0.035/0.035.

Source: BASF AG Ludwigshafen

(30)

Medium: other: tobacco

Remark: Brunnemann et al. fanden in fuenf US-amerikanischen Schnupftabakwaren 1.5-4.0 mg/kg Morpholin (Trockengewicht), in fuenf schwedischen Produkten 0.2-2.5 mg/kg (Nachweisgrenze 0.002 mg/kg). Die Autoren nehmen an, dass ein Teil des Morpholins aus dem gewachsten Verpackungskarton in den Tabak diffundiert. Der Morpholingehalt der US-amerikanischen Tabaksdosen lag zwischen 0.17 und 4.74 mg/kg, der der schwedischen zwischen 0.46 und 4.83 mg/kg. Morpholin kann aber auch bei der Tabakverarbeitung durch kuenstliche Zusatzstoffe (nicht spezifiziert) in den Tabak gelangen.

Source: BASF AG Ludwigshafen

(31)

Medium: other: tobacco

Remark: Singer & Lijinsky fanden Morpholin in Zigarettentabak in einer Konzentration von 0.3 mg/kg. Im Rauchkondensat von Zigaretten konnten die Autoren einen Morpholingehalt von < 5 mg/kg nachweisen, entsprechend einer Menge von 0.08 ug/Zigarette.

Source: BASF AG Ludwigshafen

(24)

Medium: other

Remark: In der Bundesrepublik Deutschland ist Morpholin gemaess Kosmetik-Verordnung seit 1985 als Zusatz zu Kosmetika verboten (BGB 1., 1989). Nach Angaben des Chemischen Landesuntersuchungsamtes NRW (1990) konnte Morpholin in Koerperpflegemitteln weder 1988 noch 1989 nachgewiesen werden.

Source: BASF AG Ludwigshafen

(32) (33)

Medium: air

Remark: Im Rahmen einer NIOSH-Studie fanden Taft & Stroman (1979) bei 7 personen- und 5 ortsbezogenen Messungen in einer Reifenfabrik nur in einer Probe Morpholin. Bei einer Erfassungsgrenze von 1.1 mg/m^3 (gaschromatographisch bestimmt, keine weiteren Angaben zur Methode) ermittelten

die Autoren in der Atemzone eines Arbeiters eine Konzentration von 1.4 mg/m^3 Morpholin.
Source: BASF AG Ludwigshafen

(20)

Medium: air

Remark: Fajen et al. bestimmten den Gehalt von Morpholin in einer Reifenfabrik in Ohio (USA) zu 0.23 +/- 0.11 mg/m^3 und in der zugehoerigen chemischen Fabrik (Herstellung von Vulkanisationsbeschleunigern) zu 0.042 +/- 0.005 mg/m^3.
Source: BASF AG Ludwigshafen

(21)

Medium: biota

Remark: Singer & Lijinsky fanden in Fischen (Forelle, Flussbarsch, Lachs aus US-amerikanischen Fluessen) Morpholinkonzentrationen zwischen </= 0.7 (Flussbarsch) und 6.0 mg/kg (Forelle) (Nachweisgrenze 0.3 mg/kg). Es handelt sich hierbei jedoch um Einzelergebnisse. Lediglich eine Forelle wurde untersucht, die Messwerte der uebrigen Fischarten sind Mittelwerte einer nicht genannten Zahl von Proben.
Source: BASF AG Ludwigshafen

(24)

Medium: food

Remark: Ohnishi et al. stellten an Schalen handelsueblicher Zitrusfruechte Morpholinkonzentrationen bis zu 71.1 mg/kg fest. Im Fruchtfleisch war der Gehalt mit < 0.2 mg/kg (Nachweisgrenze) bis 0.7 mg/kg wesentlich geringer. Marmeladen aus ganzen Zitrusfruechten wiesen Konzentrationen von 0.3 bis 0.7 mg/kg auf. Der Morpholingehalt der zur Herstellung der Marmeladen verwendeten Zitrusfruechte ist nicht bekannt.
Source: BASF AG Ludwigshafen

(26)

Medium: food

Remark: Durch Waschen der Fruechte unter Verwendung von Haushalts-spuelmitteln laesst sich der Morpholingehalt nur zu etwa einem Viertel reduzieren. 20-minuetiges Kochen dagegen entfernt 2/3 bis 3/4 des Stoffes aus der Schale. Die Substanz laesst sich dann quantitativ im Wasch- oder Kochwasser nachweisen.
Source: BASF AG Ludwigshafen

(26)

Medium: food

Remark: Hoffmann et al. fanden in verpackten Lebensmitteln zwischen 0.005 und 0.077 mg/kg Morpholin.
Source: BASF AG Ludwigshafen

(27)

Medium: food

Remark: Angaben ergeben sich aus dem Durchschnitt mehrerer Proben; genaue Anzahl nicht angegeben; Bezugsgroesse ausser bei Kaffee: Frischgewicht.
Morpholingehalt ausgewaehlter Lebensmittelproben:
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Source: BASF AG Ludwigshafen

(24)

Medium: food

Remark: Bezugsgroesse: Frischgewicht
Schinken (baked ham), 5 Proben: 0.2 mg Morpholin/kg
Source: BASF AG Ludwigshafen

(29)

Medium: food

Remark: Morpholingehalte von Milchprodukten / ihren Verpackungen (Angaben in mg/kg)
Butter: 0.058/0.22; Schmelzkaese: 0.077/0.68;
Joghurt: 0.038/3.06; Huettenkaese: 0.044/17.2;
Kaese, halbweich (BRD): 0.009/0.026; Gouda: 0.035/0.035.
Source: BASF AG Ludwigshafen

(30)

Medium: other: tobacco

Remark: Singer & Lijinsky fanden Morpholin in Zigarettentabak in einer Konzentration von 0.3 mg/kg. Im Rauchkondensat von Zigaretten konnten die Autoren einen Morpholingehalt von < 5 mg/kg nachweisen, entsprechend einer Menge von 0.08 ug/Zigarette.
Source: BASF AG Ludwigshafen

(24)

Medium: other

Remark: In der Bundesrepublik Deutschland ist Morpholin gemaess Kosmetik-Verordnung seit 1985 als Zusatz zu Kosmetika verboten (BGB 1., 1989). Nach Angaben des Chemischen Landesuntersuchungsamtes NRW (1990) konnte Morpholin in Koerperpflegemitteln weder 1988 noch 1989 nachgewiesen werden.
Source: BASF AG Ludwigshafen

(32) (33)

3.2.2 Field Studies
-

3.3.1 Transport between Environmental Compartments

Type: volatility
Media: water - air

Remark: Die Fluechtigkeit von Morpholin steigt mit zunehmender Konzentration. Nach der Einstufung von Smith et al. gehoert Morpholin zu den mittelfluechtigen Substanzen.
Source: BASF AG Ludwigshafen

(34)

Type: volatility
Media: water - air

Remark: Nach Messungen von Donath et al. ist der Verteilungskoeffizient k, d.h. das Verhaeltnis der in der Dampfphase vorhandenen Menge des Stoffes zu der in der waessrigen Phase vorhandenen Menge konzentrationsabhaengig.
Extrapoliert man den im Temperaturbereich von 50-130 Grad C fuer Morpholinkonzentrationen von 10-15 mg/l experimentell ermittelten Verteilungskoeffizienten aus der Messkurve graphisch auf Raumtemperatur (20 Grad C), so erhaelt man einen Wert von ca. 0.02 entsprechend einer Henry-Konstante von 49 Pa*m^3/mol.
Source: BASF AG Ludwigshafen

(35)

Type: volatility
Media: water - air

Remark: Nach Messungen von Donath et al. ist der Verteilungskoeffizient k, d.h. das Verhaeltnis der in der Dampfphase vorhandenen Menge des Stoffes zu der in der waessrigen Phase vorhandenen Menge konzentrationsabhaengig.
Extrapoliert man den im Temperaturbereich von 50-130 Grad C fuer Morpholinkonzentrationen von 10-15 mg/l experimentell ermittelten Verteilungskoeffizienten aus der Messkurve graphisch auf Raumtemperatur (20 Grad C), so erhaelt man einen Wert von ca. 0.02 entsprechend einer Henry-Konstante von 49 Pa*m^3/mol.
Source: BASF AG Ludwigshafen

(35)

3.3.2 Distribution

Media: water - air

Remark: Toogood & Hobson berechneten fuer den TLV (MAK-Wert) von 70 mg/m^3 (entspricht 1.75 mg/mol) eine Konzentration in Wasser von 36900 mg/l (entspricht 663.7 mg/mol) bei 25 Grad

C bzw. 10500 mg/l (=188.8 mg/mol) bei 40 Grad C, d.h. bei Gleichgewichtsverteilung ist die Konzentration in Wasser 380 bzw. 108 mal so gross wie in der Luft.
Source: BASF AG Ludwigshafen

(36)

3.4 Mode of Degradation in Actual Use

Remark: Soweit Morpholin unter trockenen Bedingungen freigesetzt wird, ist ein rascher Abbau durch OH-Radikale (t1/2 < 1 d) zu erwarten.
Source: BASF AG Ludwigshafen

(16)

Remark: Morpholin ist aerob durch adaptierte Mikroorganismen potentiell biologisch abbaubar und wird als potentiell mineralisierbar eingestuft, wobei ein Befund auf eine leichte Abbaubarkeit hinweist.
In adaptierten Industrieklaeranlagen ist ein Abbau moeglich, in der Praxis jedoch bisher wegen analytischen Schwierig-

keiten nicht nachgewiesen.
Das in die Geosphaere eingetragene bzw. dort durch Abbau von Morpholinderivaten freigesetzte Morpholin duerfte aufgrund seiner hydrophilen Eigenschaften letztendlich in die Hydrosphaere gelangen, welches das ueberwiegende Zielkompartiment fuer Morpholin darstellt.

Source: BASF AG Ludwigshafen

(37)

Remark: Morpholin ist aerob durch adaptierte Mikroorganismen potentiell biologisch abbaubar und wird als potentiell mineralisierbar eingestuft, wobei ein Befund auf eine leichte Abbaubarkeit hinweist.
In adaptierten Industrieklaeranlagen ist ein Abbau moeglich, in der Praxis jedoch bisher wegen analytischen Schwierigkeiten nicht nachgewiesen.
Das in die Geosphaere eingetragene bzw. dort durch Abbau von Morpholinderivaten freigesetzte Morpholin duerfte aufgrund seiner hydrophilen Eigenschaften letztendlich in die Hydrosphaere gelangen, welches das ueberwiegende Zielkompartiment fuer Morpholin darstellt.

Source: BASF AG Ludwigshafen

(37)

3.5 Biodegradation

Type: aerobic
Inoculum: other bacteria: BASF-Klaeranlagenablauf (adaptiertes Inokulum)
Concentration: 19 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 91 % after 21 day(s)

Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: 1990
GLP: no

Remark: lag-Phase =14 Tage / Abbauphase = 7 Tage
Source: BASF AG Ludwigshafen

(38)

Type: aerobic
Inoculum: other bacteria: kommunaler Klaeranlagenablauf (Laborklaeranlage)
Concentration: 20 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 93 % after 25 day(s)

Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: 1990

GLP: no

Remark: lag-Phase = 15 Tage; Abbauphase = 10 Tage.
Morpholin ist biologisch leicht abbaubar.
Source: BASF AG Ludwigshafen

(39)

Type: aerobic
Inoculum: other bacteria: kommunaler Klaeranlagenablauf (Laborklaeranlage)
Concentration: 20 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 93 % after 25 day(s)

Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: 1990

GLP: no

Remark: lag-Phase = 15 Tage; Abbauphase kleiner 10 Tage
Morpholin ist biologisch leicht abbaubar.
Source: BASF AG Ludwigshafen

(39)

Type: aerobic
Inoculum: other bacteria: BASF-Belebtschlamm
Concentration: 400.1 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 97 % after 21 day(s)
7 day(s) = 17 %
10 day(s) = 76 %
14 day(s) = 93 %

Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 1990
GLP: no

Remark: lag-Phase = 3-7 Tage; Substanz ist gut eliminierbar.
Source: BASF AG Ludwigshafen

(40)

Type: aerobic
Inoculum: other bacteria: Belebtschlamm, kommunal
Concentration: 400.3 mg/l related to DOC (Dissolved Organic Carbon)

Degradation: = 98 % after 31 day(s)
14 day(s) = 3 %
21 day(s) = 18 %

Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 1990
GLP: no

Remark: lag-Phase = 21 Tage; Substanz ist gut eliminierbar.
Source: BASF AG Ludwigshafen

(40)

Type: aerobic
Inoculum: other bacteria: Abwasser, adaptiert
Degradation: < 1 % after 10 day(s)

Method: other: BSB-Test; (BSB des THSB)

Remark: Testkonzentration 60-1000 ppm
Source: BASF AG Ludwigshafen

(41)

Type: aerobic
Inoculum: other bacteria: adaptiertes Inokulum
Degradation: < 1 % after 5 day(s)

Method: other: BSB-Test; (BSB des THSB)

Remark: Ausserdem: BSB5 des THSB =1% (Inokulum nicht bekannt).
BSB5 des THSB =0% (mit adaptiertem Inokulum).
Source: BASF AG Ludwigshafen

(42)

Type: aerobic
Inoculum: other: activated sludge (different sources), river water (different locations)
Concentration: 174 mg/l related to Test substance

Method: other: Die Away Test

Remark: All activated sludges and nearly all river water contamined morpholine degrading microorganisms. They were therefore capable of morpholine degradation, because of the slow

growth rate of morpholine degraders, die away test had a long lag-phase.
Source: BASF AG Ludwigshafen

(43)

Type: aerobic
Concentration: 40 mg/l related to Test substance
Degradation: = 65 % after 20 hour(s)

Method: other: Die-Away-Test

Remark: In a die-away test the kinetics of morpholine biodegradation in this treatment plant could be determined. 20 hours after adding 40 mg/l of morpholine 65% of the morpholine was degraded. After 25 hours less than 10% of the added morpholine was still present. The maximum degradation rate of morpholine was about 3 mg / g MLSS * h. The degradation occurred without any lag period and the maximum degradation rate was reached after 18 hours.
Source: BASF AG Ludwigshafen

(44)

Type: aerobic
Inoculum: other: activated sludge, municipal
Concentration: 40 mg/l related to Test substance
Degradation: = 65 % after 20 hour(s)

Method: other: Kontinuierliche Laborklaeranlage

Remark: In a die-away test the kinetics of morpholine biodegradation in this treatment plant could be determined. 20 hours after adding 40 mg/l of morpholine 65% of the morpholine was degraded. After 25 hours less than 10% of the added morpholine was still present. The maximum degradation rate of morpholine was about 3 mg / g MLSS * h. The degradation occurred without any lag period and the maximum degradation rate was reached after 18 hours.
Source: BASF AG Ludwigshafen

(44)

Type: aerobic
Inoculum: activated sludge, adapted
Concentration: 5 mg/l related to Test substance
Degradation: > 80 %

Method: other: Kontinuierliche Laborklaeranlage mit kommunalem Abwasser
GLP: no

Remark: A laboratory-scale wastewater treatment plant was operated with municipal wastewater which was supplemented with 4.5 to 5.0 mg/l morpholine. The treatment plant could eliminate ammonia by nitrification to an extent greater than 99%. The TOC degradation ranged between 80 and 94%. The time taken for the sludge to adapt to morpholine was 10 to 12 days. The adapted sludge of this treatment plant was able to degrade morpholine over a test period of one month to more than 90% as determined by gas chromatography.
Source: BASF AG Ludwigshafen

(44)

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Degradation: = 0 % after 14 day(s)

Method: other: MITI-Test (BOD of THOD)

Source: BASF AG Ludwigshafen
Test condition: Concentration of sludge: 30 mg/l

(45)

Type: aerobic
Inoculum: other: Belebtschlamm (30 mg/l bezogen auf Trockensubstanz)
Concentration: 100 mg/l related to Test substance
Degradation: = 0 % after 14 day(s)

Method: other: MITI-Test (BSB des ThSB)

Source: BASF AG Ludwigshafen
Test condition: Concentration of sludge: 30 mg/l

(45)

Type: aerobic
Inoculum: other bacteria: Abwasser, adaptiert
Degradation: < 1 % after 10 day(s)

Method: other: Modified BSB10-Test; (BSB des THSB)
Year: 1953
GLP: no

Remark: Testkonzentration 60-1000 ppm
Source: BASF AG Ludwigshafen

(41)

Type: aerobic
Inoculum: aerobic microorganisms
Concentration: 100 mg/l related to Test substance
Degradation: < 1 % after 14 day(s)

Method: other: Respirometrischer Test (Sapromat); (BSB des THSB)

Remark: BSB des THSB =0%.
Source: BASF AG Ludwigshafen

(46)

Type: aerobic
Inoculum: other bacteria: adapted treatment plant sludge bacteria
Concentration: 100 mg/l related to Test substance
Degradation: < 1 % after 14 day(s)

Method: other: Respirometrischer Test (Sapromat); (BSB des THSB)

Remark: BSB des THSB =0%.
Source: BASF AG Ludwigshafen

(46)

Type: aerobic
Inoculum: other bacteria: river mud bacteria
Concentration: 100 mg/l related to Test substance
Degradation: < 1 % after 14 day(s)

Method: other: Respirometrischer Test (Sapromat); (BSB des THSB)

Remark: BSB des THSB =0%.
Source: BASF AG Ludwigshafen

(47)

Type: aerobic
Inoculum: other bacteria: treatment plant sludge bacteria
Concentration: 100 mg/l related to Test substance
Degradation: < 1 % after 14 day(s)

Method: other: Respirometrischer Test (Sapromat); (BSB des THSB)

Remark: BSB des THSB =0%.
Source: BASF AG Ludwigshafen

(46)

Type: aerobic
Inoculum: activated sludge, adapted
Degradation: > 80 %

Remark: A laboratory-scale wastewater treatment plant was operated with municipal wastewater which was supplemented with 4.5 to 5.0 mg/l morpholine. The treatment plant could eliminate ammonia by nitrification to an extent greater than 99%. The TOC degradation ranged between 80 and 94%. The time taken for the sludge to adapt to morpholine was 10 to 12 days. The adapted sludge of this treatment plant was able to degrade morpholine over a test period of one month to more than 90% as determined by gas chromatography.
Source: BASF AG Ludwigshafen

(44)

Concentration: 35 mg/l related to Test substance

Remark: In a shock loading experiment it could be shown that 3 hours after addition of morpholine (35 mg/l) a morpholine concentration of 28 mg/l could be found in the effluent. The morpholine concentration in the aeration vessel and the effluent started to decrease after 9 hours due to wash out and biodegradation processes.
It is obvious that the decrease in morpholine is mainly due to wash out. Biodegradation processes also occur, but are not the prominent mechanism of elimination.
Source: BASF AG Ludwigshafen

(44)

3.6 BOD5, COD or BOD5/COD Ratio

Method: other
Year:
Method:
Remark: no data are available
Source: BASF AG Ludwigshafen

3.7 Bioaccumulation

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 42 day(s) at 25 degree C
Concentration: 5 mg/l
BCF: < .3 - .65

Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"

Source: BASF AG Ludwigshafen

(45)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 42 day(s) at 25 degree C
Concentration: .5 mg/l
BCF: < 2.8

Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"

Source: BASF AG Ludwigshafen

(45)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 42 day(s) at 25 degree C
Concentration: 5 mg/l
BCF: < .3 - .65

Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"

Source: BASF AG Ludwigshafen

(45)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 42 day(s) at 25 degree C
Concentration: .5 mg/l
BCF: < 2.8

Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"

Source: BASF AG Ludwigshafen

(45)

Method: other

Remark: Der log Pow von -2.55 bei pH 7 laesst kein Bioakkumulations-potential erwarten.

Source: BASF AG Ludwigshafen

(48)

3.8 Additional Remarks

-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: other: oral (force-fed)
Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 46 hour(s)
Unit: Analytical monitoring: no

Method: other: nach Loeb, H.A. und Kelly, W.H.: Fish and Game Journal 7 (2), 160
Year: 1960
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Dosierungen waren 131, 148 und 157 mg/kg; Ergebnis: "no effect" nach 46 Stunden
Source: BASF AG Ludwigshafen

(49)

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: > 1000

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

Remark: Wasserhaerte: 250 mg CaCO3/l
Source: BASF AG Ludwigshafen

(50)

Type: static
Species: Gambusia affinis (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 320
LC100: = 560

Method: other: nach American Public Health Association, Standard Methods for the examination of water and wastewater, 12th ed., New York
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Marines aquatisches Testsystem
Source: BASF AG Ludwigshafen

(51)

Type: static
Species: Gambusia affinis (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 320
LC100: = 560

Method: other: nach American Public Health Association, Standard Methods for theexamination of water and wastewater, 12th ed., New York
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Marines aquatisches Testsystem
Source: BASF AG Ludwigshafen

(51)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 350

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

Remark: Wasserhaerte: 55 mg CaCO3/l
Source: BASF AG Ludwigshafen

(52)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 100
LC50: = 240
LC100: = 301

Method: other: statischer Fischtest nach Mann, Deutsche Einheitsverfahren zur Wasser-, Abwasser- und Schlamm-Untersuchung, Teil L15, In: Vom Wasser 46, 291-195
Year: 1976
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Wasserhaerte: 220-320 mg CaCO3/l
Source: BASF AG Ludwigshafen

(53)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 250
LC50: = 285
LC100: = 340

Method: other: statischer Fischtest nach Mann, Deutsche Einheitsverfahren zur Wasser-, Abwasser- und Schlamm-Untersuchung, Teil L15, In: Vom Wasser 46, 291-195
Year: 1976
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Wasserhaerte: 220-320 mg CaCO3/l
Source: BASF AG Ludwigshafen

(53)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 100
LC50: = 240
LC100: = 301

Method: other: statischer Fischtest nach Mann, Deutsche Einheitsverfahren zurWasser-, Abwasser- und Schlamm-Untersuchung, Teil L15, In: Vom Wasser 46,291-195
Year: 1976
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Wasserhaerte: 220-320 mg CaCO3/l
Source: BASF AG Ludwigshafen

(54) (53)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 250
LC50: = 285
LC100: = 340

Method: other: statischer Fischtest nach Mann, Deutsche Einheitsverfahren zurWasser-, Abwasser- und Schlamm-Untersuchung, Teil L15, In: Vom Wasser 46,291-195
Year: 1976
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Wasserhaerte: 220-320 mg CaCO3/l
Source: BASF AG Ludwigshafen

(53)

Type: static
Species: Menidia beryllina (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 400

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

Remark: Marines aquatisches Testsystem
Source: BASF AG Ludwigshafen

(52)

Type: static
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 180

Method: other: nach IRSA, Quaderni dell'Istituto di Ricerca sulle Acque, 11, Consiglio Nazionale delle Richerche, Roma
Year: 1973

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

Remark: Verwendet wurde weiches Wasser (20 mg CaCO3/l)
Source: BASF AG Ludwigshafen

(55)

Type: static
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 380

Method: other: nach IRSA, Quaderni dell'Istituto di Ricerca sulle Acque, 11, Consiglio Nazionale delle Richerche, Roma
Year: 1973

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

Remark: Verwendet wurde hartes Wasser (320 mg CaCO3/l)
Source: BASF AG Ludwigshafen

(55)

Type: static
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 180

Method: other: nach IRSA, Quaderni dell'Istituto di Ricerca sulle Acque, 11,Consiglio Nazionale delle Richerche, Roma
Year: 1973
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Verwendet wurde weiches Wasser (20 mg CaCO3/l)
Source: BASF AG Ludwigshafen

(55)

Type: static
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no

LC50: = 380

Method: other: nach IRSA, Quaderni dell'Istituto di Ricerca sulle Acque, 11,Consiglio Nazionale delle Richerche, Roma
Year: 1973
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Verwendet wurde hartes Wasser (320 mg CaCO3/l)
Source: BASF AG Ludwigshafen

(55)

Type: static
Species: other: Chelon engeli
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 100
LC100: = 320

Method: other: nach American Public Health Association, Standard Methods for the examination of water and wastewater, 12th ed., New York
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Marines aquatisches Testsystem
Source: BASF AG Ludwigshafen

(51)

Type: static
Species: other: Chelon engeli
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 100
LC100: = 320

Method: other: nach American Public Health Association, Standard Methods for theexamination of water and wastewater, 12th ed., New York
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Marines aquatisches Testsystem
Source: BASF AG Ludwigshafen

(51)

Type: static
Species: other: Tilapia sp.
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: > 1000

Method: other: nach American Public Health Association, Standard Methods for the examination of water and wastewater, 12th ed., New York
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Marines aquatisches Testsystem
Source: BASF AG Ludwigshafen

(51)

Type: static
Species: other: Tilapia sp.
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: > 1000

Method: other: nach American Public Health Association, Standard Methods for theexamination of water and wastewater, 12th ed., New York
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Marines aquatisches Testsystem
Source: BASF AG Ludwigshafen

(51)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
IC50 : = 119

Method: other: AFNOR-Test; (Immobilisation)

Source: BASF AG Ludwigshafen

(46)

Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = 16
EC50: = 100
EC100: = 500

Method: other: Schwimmfaehigkeitshemmtest

Source: BASF AG Ludwigshafen

(56)

Species: other aquatic arthropod: Daphnia magna Straus
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = 68
EC50: = 101
EC100: = 260

Method: other: Daphnien-Kurzzeittest, DIN 38412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse

Source: BASF AG Ludwigshafen

(57)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Chlorella vulgaris (Algae)
Unit: mg/l Analytical monitoring:
LOEC: = 5 - 100

Method: other: Wachstumshemmtest; (Flaeche unter Wachstumskurve); Testzeit: 24-120 h

Remark: Testergebnis in Abhaengigkeit vom Naehrmedium
Source: BASF AG Ludwigshafen

(58)

Species: Scenedesmus quadricauda (Algae)
Exposure period: 8 day(s)
Unit: mg/l Analytical monitoring:
TGK : = 4.1

Method: other: Zellvermehrungshemmtest

Source: BASF AG Ludwigshafen

(59) (60)

Species: Scenedesmus subspicatus (Algae)
Unit: mg/l Analytical monitoring:
LOEC: = 5 - 50

Method: other: Wachstumshemmtest; (Flaeche unter Wachstumskurve);
Testzeit: 24-120 h

Remark: Testergebnis in Abhaengigkeit vom Naehrmedium
Source: BASF AG Ludwigshafen

(61)

Species: Selenastrum capricornutum (Algae)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = 10
EC50: = 28

Method: other: Wachstumshemmtest

Remark: EC100(96h)=80 mg/l.
Source: BASF AG Ludwigshafen

(46)

Species: Selenastrum capricornutum (Algae)
Unit: mg/l Analytical monitoring:
LOEC: = 50 - 100

Method: other: Wachstumshemmtest; (Flaeche unter Wachstumskurve);
Testzeit: 24-120 h

Remark: Testergebnis in Abhaengigkeit vom Naehrmedium
Source: BASF AG Ludwigshafen

(61)

Species: Selenastrum capricornutum (Algae)
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring:

NOEC: = 80

Method: other: Wachstumshemmtest; (Flaeche unter der Wachstumskurve)

Source: BASF AG Ludwigshafen

(62)

Species: other algae: Planktonalgen
Endpoint: other: photosynthetische Sauerstoffproduktion
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC10: = 33
EC50: = 68

Method: other: Assimilationstest

Remark: graphische Auswertung (Wahrscheinlichkeitsnetz); Nominalkonzentration
Source: BASF AG Ludwigshafen

(63)

4.4 Toxicity to Microorganisms e.g. Bacteria

Species: Microcystis aeruginosa (Bacteria)
Exposure period: 192 hour(s)
Unit: mg/l Analytical monitoring:
TGK : = 1.7

Method: other: Zellvermehrungshemmtest

Source: BASF AG Ludwigshafen

(59)

Species: Photobacterium phosphoreum (Bacteria)
Exposure period: 30 minute(s)
Unit: mg/l Analytical monitoring:
EC50: = 57.6

Method: other: Microtox-Test
GLP: no

Remark: Einheit: mg/l entsprechend ppm

Source: BASF AG Ludwigshafen

(64)

Species: Pseudomonas fluorescens (Bacteria)
Exposure period: 16 hour(s)
Unit: mg/l Analytical monitoring:
TGK : = 310

Method: other: Vereinfachte Modifikation des DEV L8 (1960); Messung der beginnenden Hemmung der Glucose-Assimilation; turbidometrische Zellzahlbestimmung

Source: BASF AG Ludwigshafen

(65)

Species: Pseudomonas putida (Bacteria)
Exposure period: 16 hour(s)
Unit: mg/l Analytical monitoring:
TGK : = 310

Method: other: Zellvermehrungshemmtest

Source: BASF AG Ludwigshafen

(60)

Species: Pseudomonas sp. (Bacteria)
Unit: mg/l Analytical monitoring:
EC10: > 8700

Method: other: Wachstumshemmtest; pH=7; 31 Grad C; Succinat-Mineralsalzmedium; optimale Wachstumsbedingungen

Remark: 8700 mg/l beeinflussen das Wachstum nicht.
Source: BASF AG Ludwigshafen

(66)

Species: other bacteria: BASF-Belebtschlamm
Exposure period: 30 minute(s)
Unit: mg/l Analytical monitoring:
EC10: > 1000

Method: ISO 8192 "Test for inhibition of oxygen consumption by activated sludge"
Year: 1990
GLP: no

Remark: Keine Wirkung auf die Atmungsaktivitaet von Belebtschlamm bis 1000 mg/l.
Source: BASF AG Ludwigshafen
(67)

Species: other bacteria: BASF-Belebtschlamm oder komm.Belebtschlamm/Laborklaeranlage
Exposure period: 30 minute(s)
Unit: mg/l Analytical monitoring:
EC10: > 1000

Method: other: Test for Inhibition of Oxygen Consumption by Activated Sludge, ISO 8192
Year: 1990
GLP: no

Remark: Keine Wirkung auf die Atmungsaktivitaet von Belebtschlamm bis 1000 mg/l.
Source: BASF AG Ludwigshafen
(67)

Species: other bacteria: Bakterienmischpopulation
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC10: = 54
EC50: = 290

Method: other: Zehrungstest (Sauerstoffzehrung)

Remark: graphische Auswertung (Wahrscheinlichkeitsnetz); Nominalkonzentration
Source: BASF AG Ludwigshafen
(63)

Species: other bacteria: Mycobacterium aurum
Unit: mg/l Analytical monitoring:
EC10: > 5000

Remark: Keine Hemmung der Stoffwechselaktivitaet bis 5000 mg/l.
Source: BASF AG Ludwigshafen
(68)

Species: other bacteria: activated sludge, adapted and not adapted
Exposure period: 30 minute(s)
Unit: mg/l Analytical monitoring:
EC20 : > 1000

Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"

Source: BASF AG Ludwigshafen
Test condition: pH 7

(44)

Species: other bacteria: activated sludge, not adapted
Unit: mg/l Analytical monitoring:
EC20 : ca. 1000

Remark: The dehydrogenase activity of activated sludge was determined by measuring the reduction of resazurin to resorufin.
Source: BASF AG Ludwigshafen
Test condition: pH 6.0 to 7.5

(44)

Species: other bacteria: specially adapted culture of nitrifying bacteria
Unit: mg/l Analytical monitoring:
EC0: = 2 - 50
EC5 : = 100

Remark: Nitrification activity
Source: BASF AG Ludwigshafen
Test condition: pH 7.2

(44)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish
-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: other

Remark: no data are available
Source: BASF AG Ludwigshafen

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants

Species: Lactuca sativa (Dicotyledon)
Endpoint: other: germination
Expos. period: 3 day(s)
Unit: mg/l
EC50: ca. 383

Remark: Bei Keimungstests an der Salatpflanze Lactuca sativa wurden die Samen 3 Tage lang in verschlossenen Plastikbehaeltern bei 30 Grad C auf Agar gehalten. Morpholin hemmte die Keimung mit einer EC50 von 4.4 +/- 0.9 mol/m^3 (ca.383 mg/l).
Source: BASF AG Ludwigshafen

(69)

4.6.3 Toxicity to Soil Dwelling Organisms

Type: other

Remark: no data are available
Source: BASF AG Ludwigshafen

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring

Remark: no data are available
Source: BASF AG Ludwigshafen

4.8 Biotransformation and Kinetics

Type: other

Remark: no data are available
Source: BASF AG Ludwigshafen

4.9 Additional Remarks

Remark: Die unterschiedlichen Abbauergebnisse duerften hauptsaechlich auf die verschieden adaptierten Inokula zurueckzufuehren sein. Morpholin ist als potentiell biologisch abbaubar und mineralisierbar einzustufen.
Source: BASF AG Ludwigshafen
(17)

Remark: Kramer et al. untersuchten die akute Toxizitaet von Morpholin auf Stechmueckenlarven (Aedes aegyptii). Die Tests wurden in Glasbechern mit 50 ml Testloesung durchgefuehrt.
Der LC50-Wert (4 h) betrug 1000 mg/l.
Source: BASF AG Ludwigshafen
(70)

Remark: Kramer et al. untersuchten die akute Toxizitaet von Morpholin auf Stechmueckenlarven (Aedes aegyptii). Die Tests wurden in Glasbechern mit 50 ml Testloesung durchgefuehrt.
Der LC50-Wert (4 h) betrug 1000 mg/l.
Source: BASF AG Ludwigshafen
(70)

5.0 Toxicokinetics, Metabolism and Distribution
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Value: = 1600 mg/kg bw

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

Remark: Appliziert als Verduennung mit 4 Teilen Wasser
Source: BASF AG Ludwigshafen
(71)

Type: LD50
Species: rat
Value: = 1050 mg/kg bw

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

Source: BASF AG Ludwigshafen
(72)

Type: LD50
Species: rat
Value: ca. 1913 mg/kg bw

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Applikationsform: 4- u. 20%ige waessrige Loesung.
Die Originalangabe lautet: LD50 ca. 1900 ul/kg
Source: BASF AG Ludwigshafen

(73)

Type: LD50
Species: rat
Value: = 1050 mg/kg bw

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

Source: BASF AG Ludwigshafen

(74)

Type: LD50
Species: rat
Value: 1420 - 1440 mg/kg bw

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

Source: BASF AG Ludwigshafen

(75)

Type: LD50
Species: rat
Value: 1610 - 1630 mg/kg bw

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

Source: BASF AG Ludwigshafen

(76)

Type: LD50
Species: rat

Value: = 1050 mg/kg bw

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

Source: BASF AG Ludwigshafen

(74)

Type: LD50
Species: rat
Value: = 1450 mg/kg bw

Method: other
GLP: no data
Test substance: other TS

Source: BASF AG Ludwigshafen

(77)

Type: LD100
Species: rat
Value: = 100 mg/kg bw

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

Remark: Appliziert in unverduennter Form
Source: BASF AG Ludwigshafen

(71)

Type: other
Species: rat
Value: = 1000 mg/kg bw

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

Remark: Kein Exitus bei dieser Dosierung.
Source: BASF AG Ludwigshafen

(78)

Type: LD50
Species: mouse
Value: = 525 mg/kg bw

Method: other: no data
GLP: no data

Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen

(79)

Type: LD50
Species: mouse
Value: = 525 mg/kg bw

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

Source: BASF AG Ludwigshafen

(80)

Type: LD50
Species: guinea pig
Value: = 900 mg/kg bw

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

Remark: Appliziert in einer Verduennung mit 4 Teilen Wasser
Source: BASF AG Ludwigshafen

(71)

Type: LD50
Species: guinea pig
Value: = 595 mg/kg bw

Method: other
GLP: no data
Test substance: other TS

Remark: The compound was applied undiluted, spectra of values 423-846 mg/kg bw, authors quoted a LD50 of 595 mg/kg bw.
Source: BASF AG Ludwigshafen
Test substance: Morpholine no further data

(81)

Type: LD100
Species: guinea pig
Value: = 100 mg/kg bw

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

Remark: Appliziert in unverduennter Form
Source: BASF AG Ludwigshafen

(71)

Type: LD50
Species: mammal
Value: = 1220 mg/kg bw

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

Source: BASF AG Ludwigshafen

(82)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Exposure time: unspecified
Value: = 7.8 - 8.2 mg/l

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

Remark: 7.8 mg/l fuer weibliche, 8.2 mg/l fuer maennliche Tiere
Source: BASF AG Ludwigshafen

(83)

Type: other
Species: rat
Exposure time: 6 hour(s)
Value: = 18.1 mg/l

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

Remark: Letalitaet bei 9 von 10 eingesetzten Tieren.
Source: BASF AG Ludwigshafen

(84)

Type: other
Species: rat
Exposure time: 8 hour(s)
Value: = 31 mg/l

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

Remark: Letalitaet bei 1 von 6 eingesetzten Tieren.
Source: BASF AG Ludwigshafen

(85)

Type: other
Species: rat
Exposure time: 4 hour(s)
Value: = 24 mg/l

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

Remark: Kein Exitus bei 6 eingesetzten Tieren
Source: BASF AG Ludwigshafen

(85)

Type: other
Species: rat
Exposure time: 4 hour(s)
Value: = 260 mg/l

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

Remark: Kein Exitus.
Source: BASF AG Ludwigshafen

(86)

Type: other
Species: rat

Exposure time: 8 hour(s)
Value: = 43.4 mg/l

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

Remark: Die 8stuendige Exposition gegenueber einer Atmosphaere mit einer Substanzkonzentration von 12000 ppm = 43.4 mg/l fuehrte nicht zur Mortalitaet (keine Angaben zu Tierzahl und Geschlecht).
Source: BASF AG Ludwigshafen

(71)

Type: other
Species: rat
Exposure time: 1 hour(s)
Value: = 22 mg/l

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

Remark: Kein Exitus.
Source: BASF AG Ludwigshafen

(87)

Type: other
Species: rat
Exposure time: 8 hour(s)
Value: = 28.9 mg/l

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

Remark: Die 8stuendige Exposition gegenueber einer Atmosphaere mit einer Substanzkonzentration von 8000 ppm = 28.9 mg/l fuehrte bei keinem von 6 Tieren zur Mortalitaet innerhalb der Beobachtungszeit von 14 Tagen.

Source: BASF AG Ludwigshafen

(72)

Type: other
Species: rat
Exposure time: 8 hour(s)
Value: = 43.4 mg/l

Method: other
GLP: no

Test substance: as prescribed by 1.1 - 1.4

Remark: Die 8stuendige Exposition gegenueber einer Atmosphaere mit einer Substanzkonzentration von 12000 ppm = 43.4 mg/l fuehrte nicht zur Mortalitaet (keine Angaben zu Tierzahl und Geschlecht).
Source: BASF AG Ludwigshafen

(71)

Type: other
Species: rat
Exposure time: 8 hour(s)
Value: = 28.9 mg/l

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

Remark: Die 8stuendige Exposition gegenueber einer Atmosphaere mit einer Substanzkonzentration von 8000 ppm = 28.9 mg/l fuehrte bei keinem von 6 Tieren zur Mortalitaet innerhalb der Beobachtungszeit von 14 Tagen.
Source: BASF AG Ludwigshafen

(88) (72)

Type: other: IRT
Species: rat
Exposure time: 8 hour(s)
Value: = 65.2 mg/l

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

Remark: Die 8stuendige Exposition gegenueber einer bei Raumtemperatur gesaettigten Atmosphaere (18000 ppm = 65.2 mg/l) fuehrte nicht zur Mortalitaet (keine Angaben zu Tierzahl und Geschlecht).
Source: BASF AG Ludwigshafen

(71)

Type: other: IRT
Species: rat
Exposure time: 5.5 hour(s)

Method: other: BASF-Test

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

Remark: Keine Mortalitaet nach 1 Stunde Exposition in einer bei 20 Grad Celsius angereicherten bzw. gesaettigten Atmosphaere.
Letalitaet nach laengerer Exposition:
2/6 Tiere nach 3 Stunden Exposition
6/6 Tiere nach 5.5 Stunden Exposition
Source: BASF AG Ludwigshafen

(73)

Type: other: IRT
Species: rat
Exposure time: 1 hour(s)

Method: other: Smyth Jr., H.F. und Carpenter, C.P.: J. Ind. Hyg. Toxicol. 26, 269 (1944); 30, 63 (1948); 31, 60 (1949 und A.M.A. Arch. Ind. Hyg. 4, 119
Year: 1951
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Die 1stuendige Exposition gegenueber einer bei Raumtemperatur gesaettigten Atmosphaere fuehrte nicht zur Mortalitaet
Source: BASF AG Ludwigshafen

(72)

Type: other: IRT
Species: rat
Exposure time: 4 hour(s)

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

Remark: Die Exposition in einer gesaettigten Atmosphaere fuehrte bei 4 von 6 Tieren zur Mortalitaet.
Source: BASF AG Ludwigshafen

(89)

Type: other: IRT
Species: rat
Exposure time: 1 hour(s)

Method: other: Smyth Jr., H.F. und Carpenter, C.P.: J. Ind. Hyg. Toxicol. 26,269 (1944); 30, 63 (1948); 31, 60 (1949 und A.M.A. Arch. Ind. Hyg. 4, 119
Year: 1951
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Die 1stuendige Exposition gegenueber einer bei Raumtemperatur gesaettigten Atmosphaere fuehrte nicht zur

Mortalitaet
Source: BASF AG Ludwigshafen

(72)

Type: other: IRT
Species: rat
Exposure time: 4 hour(s)

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

Remark: Die Exposition in einer gesaettigten Atmosphaere fuehrte bei 4 von 6 Tieren zur Mortalitaet.
Source: BASF AG Ludwigshafen

(89)

Type: LC50
Species: mouse
Exposure time: unspecified
Value: = 5.2 - 6.9 mg/l

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

Remark: 5.2 mg/l fuer maennliche, 6.9 mg/l fuer weibliche Tiere
Source: BASF AG Ludwigshafen

(83)

Type: LC50
Species: mouse
Exposure time: unspecified
Value: = 4.9 mg/l

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

Source: BASF AG Ludwigshafen

(90)

Type: LC50
Species: mouse
Exposure time: 2 hour(s)
Value: = 1.32 mg/l

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

Source: BASF AG Ludwigshafen
(91)

Type: LC50
Species: mammal
Exposure time: unspecified
Value: 12 mg/l

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

Source: BASF AG Ludwigshafen
(92)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Value: = 500 mg/kg bw

Method: other: nach Draize, J.H. et al.: J. Pharmacol. and Exper. Therap. 82, 377
Year: 1944
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: 24 Stunden exponiert, Exitus innerhalb 14 Tagen.
Source: BASF AG Ludwigshafen
(72)

Type: LD50
Species: rabbit
Value: = 1210 mg/kg bw

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

Source: BASF AG Ludwigshafen

Type: LD50
Species: rabbit
Value: 310 - 810 mg/kg bw

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

Source: BASF AG Ludwigshafen

(94)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Route of admin.: i.p.
Value: ca. 403 mg/kg bw

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Applikationsform: 4- u. 20%ige waessrige Loesung.
Die Originalangabe lautet: LD50 ca. 400 ul/kg
Source: BASF AG Ludwigshafen

(73)

Type: LD50
Species: mouse
Route of admin.: i.p.
Value: = 413 mg/kg bw

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

Source: BASF AG Ludwigshafen

(95)

Type: LD50
Species: mouse
Route of admin.: i.p.
Value: = 1350 mg/kg bw

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

Source: BASF AG Ludwigshafen

(96)

Type: LD100
Species: rat
Route of admin.: i.p.
Value: = 400 mg/kg bw

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

Source: BASF AG Ludwigshafen

(97)

Type: other
Species: rat
Route of admin.: i.p.
Value: = 100 mg/kg bw

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

Remark: Letalitaet bei 1 von 4 eingesetzten Tieren.
Source: BASF AG Ludwigshafen

(97)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Result: corrosive

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

Remark: Verwendet wurden 900 mg/kg unverduenntes Morpholin. 2 von 7 eingesetzten Tieren verstarben. Mit Schwefelsaeure auf pH 7

neutralisiertes Morpholin fuehrte zu keinen Hautschaeden, so dass die kutanen Wirkungen des Morpholins auf seine starke Basizitaet zurueckgefuehrt wurden.

Source: BASF AG Ludwigshafen

(98)

Species: rabbit
Result: corrosive

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

Source: BASF AG Ludwigshafen

(72)

Species: rabbit
Result: corrosive

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen

(73)

Species: rabbit
Result: irritating

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

Remark: Es wurden waessrige Loesungen von 2, 20, 40 und 60 % Morpholin eingesetzt. Die Beurteilung der behandelten Hautareale (je 10 cm2) geschah nach 0.5, 24, 48 sowie 72 Stunden. Kriterien waren Hautroetung und Oedematisierung. 2 % Morpholinloesung fuehrte nach 72 Stunden zur Hautreizung, die 40 und 60 %ige Loesung riefen gleich starke Hautroetung hervor (keine weiteren Angaben).

Source: BASF AG Ludwigshafen

(99)

Species: rabbit
Result: corrosive

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

Remark: Arbeit bezieht sich auf die Versuche von Shea (1939) und Smyth et al. (1954).
Source: BASF AG Ludwigshafen
(100) (101)

Species: rabbit
Result: corrosive

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

Remark: Verwendet wurden 900 mg/kg unverduenntes Morpholin. 2 von 7 eingesetzten Tieren verstarben. Mit Schwefelsaeure auf pH 7 neutralisiertes Morpholin fuehrte zu keinen Hautschaeden, so dass die kutanen Wirkungen des Morpholins auf seine starke Basizitaet zurueckgefuehrt wurden.
Source: BASF AG Ludwigshafen
(98)

Species: rabbit
Result: corrosive

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

Source: BASF AG Ludwigshafen
(72)

Species: rabbit
Result: corrosive
EC classificat.: corrosive (causes burns)

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen
(73)

Species: rabbit
Result: irritating

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

Remark: Es wurden waessrige Loesungen von 2, 20, 40 und 60 %

Morpholin eingesetzt. Die Beurteilung der behandelten Hautareale (je 10 cm2) geschah nach 0.5, 24, 48 sowie 72 Stunden. Kriterien waren Hautroetung und Oedematisierung. 2 % Morpholinloesung fuehrte nach 72 Stunden zur Hautreizung, die 40 und 60 %ige Loesung riefen gleich starke Hautroetung hervor (keine weiteren Angaben).

Source: BASF AG Ludwigshafen

(99)

Species: rabbit
Result: corrosive

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

Remark: Arbeit bezieht sich auf die Versuche von Shea (1939) und Smyth et al. (1954).

Source: BASF AG Ludwigshafen

(100) (101)

Species: guinea pig

Method: other
GLP: no data
Test substance: other TS: lipophile Salbe bzw. hydrophiles Gel mit je 10% Morpholin

Remark: Getestet wurde Morpholin bei lokaler Applikation von je 0.3 g lipophiler Salbe bzw. hydrophilen Gels mit je 10 % Morpholin an 15 Meerschweinchen waehrend 14 Tagen. Ziel der Versuche war der Nachweis einer antimykotischen Wirkung von Morpholin, das in dieser Konzentration die Mykose (Trichophyton) heilte; auch die pilzbedingten Hautveraenderungen (Roetung, Infiltrate, Blaeschen, Erosion,Kruste und Schuppen) bildeten sich zurueck.

Source: BASF AG Ludwigshafen

(102)

Species: guinea pig

Method: other: Patch-Test
GLP: no data
Test substance: other TS: 10% Morpholin in Vaseline

Remark: Patch-Test an 2 Tieren. 100 mg einer 10 %igen Morpholinloesung in Vasiline fuehrten 1, 24 und 48 Stunden nach 24-stuendiger okklusiver Applikation zu keiner Hautreizung.
Source: BASF AG Ludwigshafen

(103)

5.2.2 Eye Irritation

Species: rabbit
Result: irritating

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen

(73)

Species: rabbit
Result: irritating

Method: other: nach Carpenter, C.P. und Smyth Jr., H.F.: Am. J. Ophth. 29, 1363
Year: 1946
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen

(72)

Species: rabbit
Result: irritating
EC classificat.: risk of serious damage to eyes

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen

(73)

5.3 Sensitization

Type: Buehler Test
Species: guinea pig
Result: not sensitizing

Method: other
GLP: no data
Test substance: other TS: 2% Morpholin in Vaseline

Remark: Es wurden 10 Tiere eingesetzt. Morpholin (2% in Vaseline) erwies sich als nicht hautsensibilisierend.
Source: BASF AG Ludwigshafen

(103)

Type: other
Species: other: in vitro Assay

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

Remark: In einem in-vitro Ansatz wurde untersucht, ob Morpholin als Hapten mit Aminosaeuren reagiert und dadurch eine sensibilisierende Wirkung entfalten kann. Weder mit Lysin noch mit Cystein oder Glycin trat eine Reaktion auf.
Source: BASF AG Ludwigshafen

(104)

5.4 Repeated Dose Toxicity

Species: rat Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: 4 Tage
Frequency of treatment: 4 Stunden taeglich
Post exposure period: keine Angaben
Doses: 7.2 mg/l
Control Group: no data specified

Method: other: no data
GLP: no data

Test substance: as prescribed by 1.1 - 1.4

Result: Kein Exitus
Source: BASF AG Ludwigshafen

(105)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 9 Tage
Frequency of treatment: 6 Stunden taeglich
Post exposure period: keine Angaben
Doses: 0.36; 1.81; 3.62; 18.1 mg/l (109; 500; 1000; 5000 ppm)
Control Group: yes

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: 0.36 mg/l: Gewichtsabnahme bei weiblichen Tieren
1.81 mg/l: Reizung von Nase und Augen, Gewichtsabnahme; Verringerung der Milz/Gehirn-Gewichtsquotienten; Tod von 2/20
3.62 und
18.1 mg/l: Tod von 10/10
Source: BASF AG Ludwigshafen

(84)

Species: rat Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: 5 Tage
Frequency of treatment: 34 Stunden (gesamt)
Post exposure period: keine Angaben
Doses: 65.2 mg/l (18000 ppm, gesaettigte Atmosphaere)
Control Group: no data specified

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

Result: Leberverfettung und Nekrosen in Leber und Nierentubuli
Source: BASF AG Ludwigshafen

(71)

Species: rat Sex: male
Strain: no data
Route of administration: inhalation
Exposure period: 8 Tage
Frequency of treatment: 4 Stunden taeglich
Post exposure period: keine Angaben
Doses: 0.08 mg/l
Control Group: yes

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

Result: Hypersekretion der Thyreoidea, groessere Akkumulation von J-131 in der Thyreoidea
Source: BASF AG Ludwigshafen

(106)

Species: rat Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: 30 Tage
Frequency of treatment: 4 Stunden taeglich, 5 Tage pro Woche
Post exposure period: keine Angaben
Doses: 1.63 mg/l
Control Group: no data specified

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

Result: Verringerte Gewichtszunahme; Residualvolumen und totale Lungenkapazitaet erhoeht
Source: BASF AG Ludwigshafen

(105)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: inhalation

Exposure period: 13 Wochen
Frequency of treatment: 6 Stunden taeglich, 5 Tage pro Woche
Post exposure period: keine
Doses: 0.09; 0.36; 0.9 mg/l (25; 100; 250 ppm)
Control Group: yes, concurrent no treatment

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: Pro Gruppe wurden 20 m und 20 w Tiere eingesetzt.
0.09 mg/l: Keine signifikanten Veraenderungen von Koerpergewicht, klinisch-chemischen und haematologischen Parametern und Organgewichten; keine Laesionen in der Nase
0.36 mg/l: Bei 2/40 fokale Nekrosen in der Nasenhoehle
0.9 mg/l: Entzuendung um Nase und Mund; nach 7 Wochen bei 8 Tieren fokale Metaplasie und Nekrosen in der Nasenmuschel; nach 13 Wochen Intensivierung des Befundes; Pneumonie
Source: BASF AG Ludwigshafen

(107) (108)

Species: rat Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: 15 Wochen
Frequency of treatment: 6 Stunden taeglich, 5 Tage pro Woche
Post exposure period: keine Angaben
Doses: 1.09 mg/l
Control Group: no data specified

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

Result: 20 Tiere. Signifikanter Anstieg der Succinatdehydrogenase-aktivitaet im Rueckenmark; keine signifikante Aenderung der Enzymaktivitaet im Muskel; von Expositionsdauer abhaengiger Anstieg der Morpholinkonzentration im Gehirn
Source: BASF AG Ludwigshafen

(109)

Species: rat Sex: male
Strain: no data
Route of administration: inhalation
Exposure period: 16 Wochen
Frequency of treatment: 34 Stunden waehrend 5 Tagen (0.008 mg/l); 4 Stunden taeglich, 5 Tage pro Woche (0.07 mg/l)
Post exposure period: keine Angaben
Doses: 0.008; 0.07 mg/l
Control Group: yes

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

Result: 0.008 mg/l: Reversible Veraenderungen in Leber, Niere, Lunge, Milz, Blutbild, Myokard
0.07 mg/l: Veraenderungen in Blutbild, Leber, Niere, Lunge, Milz, Myokard
Source: BASF AG Ludwigshafen

(110)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 104 Wochen
Frequency of treatment: 6 Stunden taeglich, 5 Tage pro Woche
Post exposure period: keine
Doses: 0.036, 0.18 und 0.54 mg/l (10, 50 und 150 ppm)
Control Group: yes, concurrent no treatment

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: 0.036 und 0.18 mg/l: Vereinzelt lokale Entzuendungen um Augen und Nase
0.54 mg/l: Lokale Entzuendungen um Augen, Nase; Keratokonjunktivitis; Fokale Plattenepithel-Metaplasien, Nekrosen und Infiltration neutrophiler Granulocyten in der vorderen Nasenhoehle. Die Befunde werden von den Autoren als Folge lokaler Reizwirkungen interpretiert.
Source: BASF AG Ludwigshafen

(111) (112) (113)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 9 Tage
Frequency of treatment: 6 Stunden taeglich
Post exposure period: keine Angaben
Doses: 0.36; 1.81; 3.62; 18.1 mg/l (109; 500; 1000; 5000 ppm)
Control Group: yes

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: 0.36 mg/l: Gewichtsabnahme bei weiblichen Tieren
1.81 mg/l: Reizung von Nase und Augen, Gewichtsabnahme; Verringerung der Milz/Gehirn-Gewichtsquotienten; Tod von 2/20
3.62 und
18.1 mg/l: Tod von 10/10
Source: BASF AG Ludwigshafen

(84)

Species: rat Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: 15 Wochen
Frequency of treatment: 6 Stunden taeglich, 5 Tage pro Woche
Post exposure period: keine Angaben
Doses: 1.09 mg/l
Control Group: no data specified

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

Result: 20 Tiere. Signifikanter Anstieg der Succinatdehydrogenase-aktivitaet im Rueckenmark; keine signifikante Aenderung der Enzymaktivitaet im Muskel; von Expositionsdauer abhaengiger Anstieg der Morpholinkonzentration im Gehirn
Source: BASF AG Ludwigshafen

(114)

Species: rat Sex: male
Strain: no data
Route of administration: inhalation
Exposure period: 16 Wochen
Frequency of treatment: 34 Stunden waehrend 5 Tagen (0.008 mg/l); 4 Stunden taeglich, 5 Tage proWoche (0.07 mg/l)
Post exposure period: keine Angaben
Doses: 0.008; 0.07 mg/l
Control Group: yes

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

Result: 0.008 mg/l: Reversible Veraenderungen in Leber, Niere, Lunge, Milz, Blutbild, Myokard
0.07 mg/l: Veraenderungen in Blutbild, Leber, Niere, Lunge, Milz, Myokard
Source: BASF AG Ludwigshafen
(110)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 104 Wochen
Frequency of treatment: 6 Stunden taeglich, 5 Tage pro Woche
Post exposure period: keine
Doses: 0.036, 0.18 und 0.54 mg/l (10, 50 und 150 ppm)
Control Group: yes, concurrent no treatment

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: 0.036 und 0.18 mg/l: Vereinzelt lokale Entzuendungen um Augen und Nase
0.54 mg/l: Lokale Entzuendungen um Augen, Nase; Keratokonjunktivitis; Fokale Plattenepithel-Metaplasien, Nekrosen und Infiltration neutrophiler Granulocyten in der vorderen Nasenhoehle. Die Befunde werden von den Autoren als Folge lokaler Reizwirkungen interpretiert.
Source: BASF AG Ludwigshafen
(111) (112) (113) (115)

Species: rat Sex: no data
Strain: no data
Route of administration: gavage
Exposure period: 30 Tage
Frequency of treatment: taeglich
Post exposure period: keine Angaben
Doses: 160; 320; 800 mg/kg/d
Control Group: yes

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

Result: 160 mg/kg: Beginnende Schaedigung von Leber, Niere und Magenschleimhaeuten; Tod von 8/20
320 mg/kg: Schaedigung von Leber, Niere, Magen; Tod von 8/20
800 mg/kg: Gewichtsabnahme, Lethargie, starke Schaedigung von Leber, Niere, Magen; nach 20 d Tod von 19/20
Source: BASF AG Ludwigshafen

(71)

Species: rat Sex: no data
Strain: no data
Route of administration: oral unspecified
Exposure period: 56 Tage
Frequency of treatment: taeglich
Post exposure period: keine Angaben
Doses: 500 mg/kg/d
Control Group: no data specified

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

Result: Tiere nach 270 Tagen getoetet, maessige Leberverfettung
Source: BASF AG Ludwigshafen

(116)

Species: mouse Sex: male/female
Strain: no data
Route of administration: drinking water
Exposure period: 91 Tage
Frequency of treatment: kontinuierlich im Trinkwasser
Post exposure period: keine Angaben
Doses: 70; 140; 200; 400; 700 mg/kg/d Morpholin (0.15; 0.3; 0.6; 1.25; 2.5 % Morpholin-Fettsaeuresalz im Trinkwasser)
Control Group: no data specified

Method: other: no data
GLP: no data
Test substance: other TS: Morpholin-Fettsaeuresalz

Result: 70 und 140 mg/kg: Keine signifikanten Veraenderungen
200 mg/kg: m: Anstieg des spezifischen Gewichtes des Urins; w: Anstieg des Blutharnstoffs
400 mg/kg: Anstieg des spezifischen Gewichts des Urins und des Blutharnstoffs
700 mg/kg: Verringerte Gewichtszunahme; Anstieg des spezifischen Gewichtes des Urins und des Blutharnstoffs; vergroessertes relatives Nierengewicht mit Schwellung proximaler Tubuli

Pro Gruppe und Gewicht wurden 10 Tiere eingesetzt
Source: BASF AG Ludwigshafen

(117)

Species: mouse Sex: male/female
Strain: no data
Route of administration: drinking water
Exposure period: 672 Tage

Frequency of treatment: kontinuierlich im Trinkwasser
Post exposure period: keine Angaben
Doses: 50-140; 70-170; 280-500; 210-570 mg/kg/d Morpholin (0.25; 0.25; 1; 1 % Morpholin-Fettsaeuresalz im Trinkwasser)
Control Group: no data specified

Method: other: no data
GLP: no data
Test substance: other TS: Morpholin-Fettsaeuresalz

Result: 50-140 mg/kg m: Keine signifikanten Veraenderungen
70-170 mg/kg w: Verringerte Gewichtszunahmen
280-500 mg/kg m: Verringerte Gewichtszunahme, Blutharnstoff erhoeht, Hyperplasie im Vormagenepithel
210-570 mg/kg w: Verringerte Gewichtszunahme

Pro Gruppe wurden 50 Tiere eingesetzt
Source: BASF AG Ludwigshafen

(117)

Species: mouse Sex: male/female
Strain: no data
Route of administration: drinking water
Exposure period: 91 Tage
Frequency of treatment: kontinuierlich im Trinkwasser
Post exposure period: keine Angaben
Doses: 70; 140; 200; 400; 700 mg/kg/d Morpholin (0.15; 0.3; 0.6; 1.25; 2.5 %Morpholin-Fettsaeuresalz im Trinkwasser)
Control Group: no data specified

Method: other: no data
GLP: no data
Test substance: other TS: Morpholin-Fettsaeuresalz

Result: 70 und 140 mg/kg: Keine signifikanten Veraenderungen
200 mg/kg: m: Anstieg des spezifischen Gewichtes des Urins; w: Anstieg des Blutharnstoffs
400 mg/kg: Anstieg des spezifischen Gewichts des Urins und des Blutharnstoffs
700 mg/kg: Verringerte Gewichtszunahme; Anstieg des spezifischen Gewichtes des Urins und des Blutharnstoffs; vergroessertes relatives Nierengewicht mit Schwellung proximaler Tubuli

Pro Gruppe und Gewicht wurden 10 Tiere eingesetzt
Source: BASF AG Ludwigshafen

(117)

Species: mouse Sex: male/female
Strain: no data
Route of administration: drinking water
Exposure period: 672 Tage
Frequency of treatment: kontinuierlich im Trinkwasser
Post exposure period: keine Angaben
Doses: 50-140(m); 70-170(w); 280-500(m); 210-570(w) mg/kg/d
Morpholin (0.25; 0.25; 1; 1 %Morpholin-Fettsaeuresalz im Trinkwasser)
Control Group: no data specified

Method: other: no data
GLP: no data
Test substance: other TS: Morpholin-Fettsaeuresalz

Result: 50-140 mg/kg m: Keine signifikanten Veraenderungen
70-170 mg/kg w: Verringerte Gewichtszunahmen
280-500 mg/kg m: Verringerte Gewichtszunahme, Blutharnstoff erhoeht, Hyperplasie im Vormagenepithel
210-570 mg/kg w: Verringerte Gewichtszunahme

Pro Gruppe wurden 50 Tiere eingesetzt
Source: BASF AG Ludwigshafen

(117)

Species: rabbit Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: 33 Tage
Frequency of treatment: 6 Stunden taeglich, 5 Tage pro Woche
Post exposure period: keine Angaben
Doses: 0.9 mg/l
Control Group: no data specified

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

Result: Gesteigerte Enzymgehalte in Bronchiallavage
Source: BASF AG Ludwigshafen

(118)

Species: guinea pig Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: 16 Wochen
Frequency of treatment: 4 Stunden taeglich, 5 Tage pro Woche
Post exposure period: keine Angaben
Doses: 0.008; 0.07 mg/l

Control Group: yes

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

Result: 0.008 mg/l: Lymphknoten der Milz geschwollen
0.07 mg/l: Geschwollene Alveolen, Atrophie der Lymphgefaesse in Lunge und Milz; Steigerung des Hb und der Erythrozytenzahl, Abnahme der Leukozyten
Source: BASF AG Ludwigshafen

(119)

Species: guinea pig Sex: no data
Strain: no data
Route of administration: dermal
Exposure period: 13 Tage
Frequency of treatment: taeglich
Post exposure period: keine
Doses: 900 mg/kg/d
Control Group: no data specified

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

Result: Die unverduennte Testsubstanz wurde auf die rasierte Haut appliziert und mit Gaze abgedeckt. Die insgesamt 7 eingesetzten Tiere verloren an Koerpergewicht. Die Haut an der Applikationsstelle war nekrotisch und oedematoes; die darunterliegenden Organe zeigten Blutstauungen. Keines der Tiere ueberlebte 13. Applikationen. Die Lebern zeigten

Zunahmen der interstitiellen Zellen und waren z.T. zirrhotisch und zeigten Fettdegeneration. Bei den Nieren waren sowohl tubulaere Nekrosen, haemorrhagische Zonen und exzessive Sekretion in die Tubuli, als auch Blutstauungen und Schwellungen festzustellen.
Die 30taegige Applikation von neutralisiertem Morpholin (neutralisiert mit Schwefelsaeure) bei 3 Tieren fuehrte in keinem Fall zur Mortalitaet bzw. zu makroskopischen und mikroskopischen Organveraenderungen. Lediglich die Haut an den Applikationsstellen war angeschwollen, jedoch nicht nekrotisch.

Source: BASF AG Ludwigshafen

(71)

Species: guinea pig Sex: no data
Strain: no data
Route of administration: oral unspecified
Exposure period: 30 Tage
Frequency of treatment: taeglich
Post exposure period: keine Angaben
Doses: 90; 180; 450 mg/kg
Control Group: no data specified

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

Result: 90 mg/kg: Tod von 3/20; leichte Veraenderung von Leber, Niere
180 mg/kg: Tod von 12/20; Schaedigung von Leber, Niere, Magen
450 mg/kg: Fettleber, Tod von 16/20; starke Schaedigung von Leber Niere, Magen

Source: BASF AG Ludwigshafen

(71)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA 98, 100, 1535, 1537
Concentration: 109 bis 10900 ug/Platte
Metabolic activation: with and without
Result: negative

Method: other: nach Ames et al. und Yahagi et al.
Year: 1975
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen

(120)

Type: Ames test
System of testing: Salmonella typhimurium TA98, 1535, 1537
Concentration: 15.8, 50, 158, 500, 1580, 5000, 10000 und 50000 ug/Platte
Metabolic activation: with and without
Result: negative

Method: other: nach Ames, B.N. et al.: Mutation Research 31, 347-364
Year: 1975
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen

(121)

Type: Ames test
System of testing: Salmonella typhimurium TA 100
Concentration: 50000 ug/Platte
Metabolic activation: with and without
Result: positive

Method: other: nach Ames, B.N. et al.: Mutation Research 31, 347-364
Year: 1975
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Steigerung der Mutantenzahl: f < 2
Source: BASF AG Ludwigshafen

(121)

Type: Ames test
System of testing: Escherichia coli WP2 uvrA
Concentration: 50000 ug/Platte
Metabolic activation: with and without
Result: positive

Method: other: nach Ames, B.N. et al.: Mutation Research 31, 347-364
Year: 1975
GLP: no

Test substance: as prescribed by 1.1 - 1.4

Remark: Negativ ohne S9-Mix, positiv mit S9-Mix; Steigerung der Mutantenzahl: f = 2
Source: BASF AG Ludwigshafen

(121)

Type: DNA damage and repair assay
System of testing: Rattenhepatozyten, Primaerkultur
Concentration: 0.1 - 100 ug/ml
Metabolic activation: without
Result: negative

Method: other: nach Williams, G.M.: The detection of chemical mutagens ..., In: F.J. de Serres und A. Hollaender, Chemical Mutagens, Vol. VI, Plenum, New York, Seite 61-79
Year: 1980
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Keine Induktion einer DNA-Reparatur
Source: BASF AG Ludwigshafen

(122)

Type: Mouse lymphoma assay
System of testing: Maus-Lymphomzellen TK +/-
Concentration: 0.5, 0.625, 0.75, 1 und 1.25 ul/ml
Metabolic activation: with and without
Result: ambiguous

Method: other: nach Clive, D. und Spector, J.F.S.: Mutation Research 31, 17-29
Year: 1975
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte geringe Steigerungen der Mutationsfrequenz am TK Lokus in L5178Y Mauslymphomzellen imuntersuchten Dosisbereich ohne metabolische Aktivierung. DieTestsubstanz zeigte hohe zytotoxische Wirkung; die Erhoehungder Mutationsfrequenz war mit metabolischer Aktivierung im Grenzbereich der Detektierbarkeit (Faktor 2.5).
Die Autoren bewerteten die Testsubstanz als sehr schwach aktiv im untersuchten Testsystem.
Source: BASF AG Ludwigshafen

(123) (124)

Type: other: Zelltransformation

System of testing: Balb/3T3 Zellen
Concentration: 0.001, 0.025, 0.1, 0.2 und 0.3 ul/ml
Metabolic activation: without
Result: positive

Method: other: nach Kakunaga, T.: Int. J. Cancer 12, 463-473
Year: 1973
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte im untersuchten Konzentrationsbereich signifikante Erhoehungen der Frequenz transformierter Foci. Der untersuchte Konzentrationsbereich entsprach im Zytotoxizitaetstest einer Ueberlebensrate zwischen 78 und 52%.
Source: BASF AG Ludwigshafen

(123) (125)

Type: other: Zelltransformation
System of testing: Balb/3T3 Zellen
Concentration: 0.000122, 0.00195, 0.0156, 0.125 und 0.250 ul/ml
Metabolic activation: without
Result: positive

Method: other: nach Kakunaga, T.: Int. J. Cancer 12, 463-473
Year: 1973
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte in den Konzentrationen von 0.125 und 0.25 ul/ml signifikante Erhoehungen der Frequenz transformierter Foci. Die Konzentrationen von 0.0156 und 0.00195 ul/ml zeigten nur schwach transformierende Aktivitaeten ausserhalb der statistischen Signifikanz. Der untersuchte Konzentrationsbereich entsprach im Zytotoxizitaetstest einer Ueberlebensrate zwischen 71 und 55%.
Source: BASF AG Ludwigshafen

(126)

Type: other: Zelltransformation
System of testing: Balb/3T3 Zellen
Concentration: 15 - 1400 nl/ml (ohne Aktivierung) bzw. 17.5 - 700 nl/ml (mit Aktivierung)
Metabolic activation: with and without
Result: negative

Method: other: nach Kakunaga, T.: Int. J. Cancer 12, 463-473
Year: 1973
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte im untersuchten Konzentrationsbereich keine signifikante Erhoehungen der Frequenz transformierter Foci. Der untersuchte Konzentrationsbereich entsprach im Zytotoxizitaetstest einer Ueberlebensrate zwischen 20 und 100%.
Source: BASF AG Ludwigshafen

(127)

Type: Sister chromatid exchange assay
System of testing: CHO-Zellen
Concentration: 0.16, 0.8, 4, 20 und 100 nl/ml
Metabolic activation: with and without
Result: positive

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte im untersuchten Konzentrationsbereich signifikante Erhoehungen der SCE-Frequenz.
Source: BASF AG Ludwigshafen

(128)

Type: Sister chromatid exchange assay
System of testing: CHO-Zellen
Concentration: 3.13, 6.25, 12.5, 25, 50 und 100 nl/ml
Metabolic activation: with and without
Result: negative

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte im untersuchten Konzentrationsbereich nur teilweise signifikante Erhoehungender SCE-Frequenz ohne Dosis-Wirkungsbeziehungen. Die Autoren bewerteten die Ergebnisse als "unbedeutende" Erhoehung der SCE-Frequenz.
Source: BASF AG Ludwigshafen

(129)

Type: Ames test
System of testing: Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100, TA100NR3
Concentration: 10 - 5000 ug/Platte
Metabolic activation: with and without
Result: negative

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

Source: BASF AG Ludwigshafen

(130)

Type: Ames test
System of testing: Salmonella typhimurium (keine weiteren Angaben)
Concentration: keine Angaben
Metabolic activation: no data
Result: negative

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

Source: BASF AG Ludwigshafen

(131)

Type: DNA damage and repair assay
System of testing: Rattenhepatozyten, Primaerkultur
Concentration: 0.1 - 100 ug/ml
Metabolic activation: without
Result: negative

Method: other: nach Williams, G.M.: The detection of chemical mutagens ..., In:F.J. de Serres und A. Hollaender, Chemical Mutagens, Vol. VI, Plenum, NewYork, Seite 61-79
Year: 1980
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Keine Induktion einer DNA-Reparatur
Source: BASF AG Ludwigshafen

(122)

Type: Mouse lymphoma assay
System of testing: Maus-Lymphomzellen TK +/-
Concentration: 0.5, 0.625, 0.75, 1 und 1.25 ul/ml
Metabolic activation: with and without
Result: ambiguous

Method: other: nach Clive, D. und Spector, J.F.S.: Mutation Research 31, 17-29
Year: 1975
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte geringe Steigerungen der Mutationsfrequenz am TK Lokus in L5178Y Mauslymphomzellen imuntersuchten Dosisbereich ohne metabolische Aktivierung. DieTestsubstanz zeigte hohe zytotoxische Wirkung; die Erhoehungder Mutationsfrequenz war mit metabolischer Aktivierung im Grenzbereich der Detektierbarkeit (Faktor 2.5).
Die Autoren bewerteten die Testsubstanz als sehr schwach aktiv im untersuchten Testsystem.
Source: BASF AG Ludwigshafen

(123) (124) (132)

Type: other: Zelltransformation
System of testing: Balb/3T3 Zellen
Concentration: 0.001, 0.025, 0.1, 0.2 und 0.3 ul/ml
Metabolic activation: without
Result: positive

Method: other: nach Kakunaga, T.: Int. J. Cancer 12, 463-473
Year: 1973
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte im untersuchten Konzentrationsbereich signifikante Erhoehungen der Frequenz transformierter Foci. Der untersuchte Konzentrationsbereich entsprach im Zytotoxizitaetstest einer Ueberlebensrate zwischen 78 und 52%.
Source: BASF AG Ludwigshafen

(123) (125) (132)

Type: other: Zelltransformation
System of testing: Balb/3T3 Zellen
Concentration: 0.000122, 0.00195, 0.0156, 0.125 und 0.250 ul/ml
Metabolic activation: without
Result: positive

Method: other: nach Kakunaga, T.: Int. J. Cancer 12, 463-473
Year: 1973
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte in den Konzentrationen von 0.125 und 0.25 ul/ml signifikante Erhoehungen der Frequenz

transformierter Foci. Die Konzentrationen von 0.0156 und 0.00195 ul/ml zeigten nur schwach transformierende Aktivitaeten ausserhalb der statistischen Signifikanz. Der untersuchte Konzentrationsbereich entsprach im Zytotoxizitaetstest einer Ueberlebensrate zwischen 71 und 55%.
Source: BASF AG Ludwigshafen

(126)

Type: other: Zelltransformation
System of testing: Balb/3T3 Zellen
Concentration: 15 - 1400 nl/ml (ohne Aktivierung) bzw. 17.5 - 700 nl/ml (mit Aktivierung)
Metabolic activation: with and without
Result: negative

Method: other: nach Kakunaga, T.: Int. J. Cancer 12, 463-473
Year: 1973
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte im untersuchten Konzentrationsbereich keine signifikante Erhoehungen der Frequenz transformierter Foci. Der untersuchte Konzentrationsbereich entsprach im Zytotoxizitaetstest einer Ueberlebensrate zwischen 20 und 100%.

Source: BASF AG Ludwigshafen

(127)

Type: Sister chromatid exchange assay
System of testing: CHO-Zellen
Concentration: 0.16, 0.8, 4, 20 und 100 nl/ml
Metabolic activation: with and without
Result: positive

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte im untersuchten Konzentrationsbereich signifikante Erhoehungen der SCE-Frequenz.

Source: BASF AG Ludwigshafen

(128) (132)

Type: Sister chromatid exchange assay
System of testing: CHO-Zellen
Concentration: 3.13, 6.25, 12.5, 25, 50 und 100 nl/ml
Metabolic activation: with and without
Result: negative

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Die Testsubstanz induzierte im untersuchten Konzentrationsbereich nur teilweise signifikante Erhoehungender SCE-Frequenz ohne Dosis-Wirkungsbeziehungen. Die Autoren bewerteten die Ergebnisse als "unbedeutende" Erhoehung der SCE-Frequenz.
Source: BASF AG Ludwigshafen

(129) (132)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535 and TA 1537
Concentration: 20 to 5 000 µg/plate
Metabolic activation: with and without
Result: negative

Method: other: according to Ames
GLP: no data
Test substance: other TS

Source: BASF AG Ludwigshafen

Test substance: Morpholine was obtained from Tokyo Kasei with a purity of 95%.

(133)

Type: Ames test
System of testing: Escherichia coli WP2uvrA
Concentration: 20 to 5 000 µg/plate
Metabolic activation: with and without
Result: negative

Method: other: according to Ames
GLP: no data
Test substance: other TS

Source: BASF AG Ludwigshafen
Test substance: Morpholine was obtained from Tokyo Kasei with a purity of 98%.

(133)

Type: Ames test
System of testing: Salmonella typhimurium TA 1535
Concentration: 100 to 400 µl urine of treated mice (combined treatment with morpholine (250 mg/kg bw) and sodium nitrate (up to 2000 mg/kg bw))
Metabolic activation: with and without
Result: ambiguous

GLP: no data
Test substance: other TS

Result: Urine of 333, 666 and 2000 mg/kg bw sodium nitrate treated mice and urine of combined treated mice (333 and 666 mg nitrite/ 250 mg/kg bw morpholine, and urine of combined treated mice (333 and 2000 mg/kg bw nitrate/250 mg morpholine/and 15 and 30 mg/kg bw ascorbic acid) had no mutagenic activity.

Only a combined treatment of 2000 mg/kg bw nitrate and 250 mg/kg bw morpholine showed mutagenicity of this urine.
Source: BASF AG Ludwigshafen
Test substance: Morpholine, no further data

(134)

Type: Ames test
System of testing: Salmonella typhimurium TA 100 and TA 98
Concentration: no data
Metabolic activation: with and without

Result: negative

Method: other: according to Ames
GLP: no data
Test substance: other TS

Source: BASF AG Ludwigshafen
Test substance: Morpholine no further data

(135)

Type: DNA damage and repair assay
System of testing: rat hepatocytes
Concentration: up to 1% solution
Metabolic activation: without
Result: negative

Method: other: according to Williams
GLP: no data
Test substance: other TS

Source: BASF AG Ludwigshafen
Test substance: Identitiy Compound No. 4236-48-10

(136)

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
Species: hamster Sex: female
Strain: no data
Route of admin.: gavage
Exposure period: 11. oder 12. Tag der Traechtigkeit
Doses: 500 mg/kg

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

Result: In den Embryozellen in Kultur traten weder Chromosomenaberrationen, Micronucleus-Bildung noch 8-Azaguanin- oder Quabain-resistente Mutationen auf.
Source: BASF AG Ludwigshafen

(137)

Type: Cytogenetic assay
Species: rat Sex: male
Strain: no data
Route of admin.: inhalation

Exposure period: 4 Monate
Doses: 0.008 oder 0.07 mg/l

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

Result: In Knochenmarkszellen wird vom Autor ein Anstieg von Chromosomenaberrationen beschrieben. Dieser Befund kann wegen der unzureichenden Versuchsdokumentation nicht bewertet werden.
Source: BASF AG Ludwigshafen

(119)

Type: other: Host Mediated Assay
Species: mouse Sex: no data
Strain: NMRI
Route of admin.: unspecified
Exposure period: keine Angaben
Doses: 126 - 253 mg/kg

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

Remark: Die Originalangabe zur Dosis lautet: 1450 - 2900 umol/kg; die Ergebnisse liegen lediglich in tabellarischer Form vor.
Result: negativ;
Teststamm: Salmonella typhimurium TA1950
Source: BASF AG Ludwigshafen

(138)

Type: other: Host Mediated Assay
Species: mouse Sex: no data
Strain: CD-1
Route of admin.: unspecified
Exposure period: keine Angaben
Doses: 4 mg/kg

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

Remark: die Ergebnisse liegen lediglich in tabellarischer Form vor
Result: negativ;
Teststamm: Salmonella typhimurium TA1530
Source: BASF AG Ludwigshafen

(139)

Type: other: Host Mediated Assay

Species: mouse Sex: female
Strain: CD-1
Route of admin.: i.v.
Exposure period: keine Angaben
Doses: keine Angaben

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

Result: negativ;
Teststamm: Salmonella typhimurium TA1530
Source: BASF AG Ludwigshafen

(140)

5.7 Carcinogenicity

Species: rat Sex: no data
Strain: Fischer 344/DuCrj
Route of administration: drinking water
Exposure period: 2 Jahre
Frequency of treatment: kontinuierlich im Trinkwasser
Post exposure period: keine Angaben
Doses: 0.3; 0.6 % im Trinkwassser; ca. 200; 400 mg/kg/d
Control Group: no data specified

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

Result: Die Studie wird zur Zeit in Japan durchgefuehrt. Die Ergebnisse dieser Arbeit sind noch nicht publiziert.
Source: BASF AG Ludwigshafen

(141)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of administration: drinking water
Exposure period: 96 Wochen
Frequency of treatment: kontinuierlich im Trinkwasser
Post exposure period: 8 Wochen
Doses: 0.25; 1 % Morpholinoelsaeuresalz im Trinkwasser (entspr. 0.06; 0.24 % Morpholin im Trinkwasser); ca. 75; 300 mg/kg/d
Control Group: yes

Method: other: no data
GLP: no

Test substance: other TS: Morpholinoelsaeuresalz

Result: Eingesetzt wurden 50 m und 50 w Tiere je Gruppe. Die Ueberlebensrate wurde nicht beeinflusst. Das Koerpergewicht wurde bei den maennlichen Tieren in der hohen Dosierung und bei den weiblichen Tieren in beiden Dosierungen signifikant reduziert. Lediglich bei den maennlichen Tieren der 1 % - Gruppe war die Inzidenz von Hyperplasien im Vormagenepithel im Vergleich mit den Kontrollen signifikant erhoeht.
Source: BASF AG Ludwigshafen

(142)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of administration: drinking water
Exposure period: 96 Wochen
Frequency of treatment: kontinuierlich im Trinkwasser
Post exposure period: 8 Wochen
Doses: 0.25; 1 % Morpholinoelsaeuresalz im Trinkwasser (entspr. 0.06; 0.24 %Morpholin im Trinkwasser); ca. 75; 300 mg/kg/d
Control Group: yes

Method: other: no data
GLP: no
Test substance: other TS: Morpholinoelsaeuresalz

Result: Eingesetzt wurden 50 m und 50 w Tiere je Gruppe. Die Ueberlebensrate wurde nicht beeinflusst. Das Koerpergewicht wurde bei den maennlichen Tieren in der hohen Dosierung und bei den weiblichen Tieren in beiden Dosierungen signifikant reduziert. Lediglich bei den maennlichen Tieren der 1 % - Gruppe war die Inzidenz von Hyperplasien im Vormagenepithel im Vergleich mit den Kontrollen signifikant erhoeht.
Source: BASF AG Ludwigshafen

(143)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 104 Wochen; 10 Tiere pro Geschlecht und Gruppe 53 Wochen
Frequency of treatment: 6 Stunden taeglich, 5 Tage/Woche
Post exposure period: keine
Doses: 0.036; 0.181; 0.543 mg/l (10; 50; 150 ppm)

Control Group: yes, concurrent no treatment

Method: other
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Es wurden folgende Gewebe und Organe von Kontroll- und Versuchstieren der hoechsten Dosisgruppe histologisch untersucht:
Nasenhoehlen, Herz, Lunge, Bronchien, Trachea, Pharynx, Thyroidea, Lymphknoten, Speicheldruese, Oesophagus, Aorta, Thymus, Milz, Leber, Pankreas, Nieren, Nebennieren, Hoden oder Ovarien, Prostata oder Uterus, Harnblase, Magen, Duenn-und Dickdarm, Skelettmuskel, Milchdruesen, Gehirn, Hypophyse, Rueckenmark, Ischiasnerv, Knochen und Knochenmark, Augen und Harder'sche Druesen. Zusaetzlich wurden Augen- und Nasenhoehlenschnitte von Ratten aus der niedrigen und der mittleren Dosisgruppe untersucht.
Result: Insgesamt wurden 560 Tiere in 4 Gruppen mit je 70 m und w Ratten eingesetzt. Es wurde kein behandlungsbedingter Anstieg der Tumorinzidenz festgestellt.
Source: BASF AG Ludwigshafen

(144) (112) (113)

Species: rat Sex: no data
Strain: SIV 50
Route of administration: oral feed
Exposure period: 56 Tage
Frequency of treatment: kontinuierlich im Futter
Post exposure period: Toetung der Tiere nach 270 Tagen
Doses: 500 mg/kg KG pro Tag (aus dem Futterverbrauch geschaetzt);(0.5 % im Futter)
Control Group: no data specified

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

Result: Es wurden 8 Tiere eingesetzt. Es wurden keine Tumoren gefunden.
Source: BASF AG Ludwigshafen

(145)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: oral feed

Exposure period: Mehrgenerationen-Langzeitversuche (125 Wochen)
Frequency of treatment: kontinuierlich im Futter
Post exposure period: keine
Doses: 1000 mg/kg im Futter, ca. 66.7 mg/kg/d
Control Group: yes, concurrent no treatment

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

Result: Vom Tag der Konzeption wurden Muttertiere mit 0 oder 1000 mg/kg Diaet gefuettert. Die F1 und die F2 Generation wurden ebenso bis zum Versuchsende gefuettert. Die Tiere nahmen nach einer Dosisabschaetzung aus dem Futterverbrauch als Jungtiere 10 mg und als alte Tiere 20 mg Morpholin/d auf. Die mittlere Ueberlebenszeit betrug fuer die behandelten Ratten 117 Wochen (Kontrollen: 109 Wochen). Fuer die Studie wurden Nachkommen bei Ratten von F1 und F2 untersucht, die Ueberlebenden wurden in der 125. Woche getoetet. Neben Karzinomen in der Leber und Angiosarkomen in der Lunge traten bei 104 Ratten 2 maligne Gliome auf (statistisch nicht signifikant). Nitrosaminbildung wird von den Autoren nicht ausgeschlossen.
Source: BASF AG Ludwigshafen

(146)

Species: rat Sex: no data
Strain: SIV 50
Route of administration: oral feed
Exposure period: 56 Tage
Frequency of treatment: kontinuierlich im Futter
Post exposure period: Toetung der Tiere nach 270 Tagen
Doses: 500 mg/kg KG pro Tag (aus dem Futterverbrauch geschaetzt);(0.5 % imFutter)
Control Group: no data specified

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

Result: Es wurden 8 Tiere eingesetzt. Es wurden keine Tumoren gefunden.
Source: BASF AG Ludwigshafen

(145)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: oral feed
Exposure period: Mehrgenerationen-Langzeitversuche (125 Wochen)
Frequency of treatment: kontinuierlich im Futter
Post exposure period: keine
Doses: 1000 mg/kg im Futter, ca. 66.7 mg/kg/d
Control Group: yes, concurrent no treatment

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

Result: Vom Tag der Konzeption wurden Muttertiere mit 0 oder 1000 mg/kg Diaet gefuettert. Die F1 und die F2 Generation wurden ebenso bis zum Versuchsende gefuettert. Die Tiere nahmen nach einer Dosisabschaetzung aus dem Futterverbrauch als Jungtiere 10 mg und als alte Tiere 20 mg Morpholin/d auf. Die mittlere Ueberlebenszeit betrug fuer die behandelten Ratten 117 Wochen (Kontrollen: 109 Wochen). Fuer die Studie wurden Nachkommen bei Ratten von F1 und F2 untersucht, die Ueberlebenden wurden in der 125. Woche getoetet. Die alleinige Gabe von Morpholin induzierte nicht signifikant Tumore. Bei 2 Ratten traten maligne Gliome auf (statistisch nicht signifikant). Bei gleichzeitiger Nitritgabe wurde ein Anstieg der Tumorinzidenz festgestellt.
Source: BASF AG Ludwigshafen

(146)

Species: mouse Sex: no data
Strain: NMRI
Route of administration: oral feed
Exposure period: 48 Tage
Frequency of treatment: kontinuierlich im Futter
Post exposure period: Sektion der Tiere 1 Jahr nach Exposition
Doses: 300; 750 mg/kg KG/Tag (geschaetzt); (0.2; 0.5 % im Futter)
Control Group: no data specified

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

Result: Es wurden 9 (0.2 %) bzw. 11 (0.5 %) Tiere eingesetzt. Bei 0.2 % traten keine Tumoren auf. Bei 0.5 % fuehrte eine Exposition von 18 Tagen bei 4 von 11 Maeusen zu Lungenadenomen. Da die Tierzahlen im Versuch sehr gering waren und keine historischen Kontrolldaten gegeben wurden, ist die Aussagekraft der Studie gering.
Source: BASF AG Ludwigshafen

(145)

Species: mouse Sex: male/female
Strain: Swiss
Route of administration: oral feed
Exposure period: 28 Wochen
Frequency of treatment: kontinuierlich im Futter
Post exposure period: 12 Wochen
Doses: 900 mg/kg KG pro Tag (geschaetzt); (6330 mg/kg Futter)
Control Group: yes, concurrent no treatment

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

Result: Eingesetzt wurden 20 m und 20 w Tiere. Verglichen mit den Kontrollen (80 m und 80 w Tiere) wurde keine behandlungsbedingte Steigerung der Tumorrate in der Lunge gefunden. Wegen der kurzen Versuchsdauer ist die Studie wenig aussagekraeftig.
Source: BASF AG Ludwigshafen

(147)

Species: hamster Sex: male/female
Strain: other: Goldhamster
Route of administration: oral feed
Exposure period: Mehrgenerationen-Langzeitversuche (125 Wochen)
Frequency of treatment: kontinuierlich im Futter
Post exposure period: keine
Doses: 1000 mg/kg Futter
Control Group: yes, concurrent no treatment

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

Result: Vom Tag der Konzeption wurden Muttertiere mit 0 oder 1000 mg/kg Diaet gefuettert. Die F1 und die F2 Generation wurden ebenso bis zum Versuchsende gefuettert. Die Tiere nahmen nach einer Dosisabschaetzung aus dem Futterverbrauch als Jungtiere 10 mg und als alte Tiere 20 mg Morpholin/d auf. Estraten neue Lebertumoren auf. Wegen der geringen Versuchstierzahl ist die Aussagekraft der Ergebnisse eingeschraenkt. Die Autoren schliessen nicht aus, dass die Tumorbildung durch Nitrosierung des Morpholins in der Diaet hervorgerufen worden sein kann, obwohl weder Nitrit noch N-Nitrosomorpholin in der Diaet nachgewiesen werden konnte.
Source: BASF AG Ludwigshafen

(148)

Species: hamster Sex: male/female
Strain: other: Goldhamster
Route of administration: oral feed
Exposure period: Mehrgenerationen-Langzeitversuche (125 Wochen)
Frequency of treatment: kontinuierlich im Futter
Post exposure period: keine
Doses: 1000 mg/kg Futter
Control Group: yes, concurrent no treatment

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

Result: Vom Tag der Konzeption wurden Muttertiere mit 0 oder 1000 mg/kg Diaet gefuettert. Die F1 und die F2 Generation wurden ebenso bis zum Versuchsende gefuettert. Die Tiere nahmen nach einer Dosisabschaetzung aus dem Futterverbrauch als Jungtiere 10 mg und als alte Tiere 20 mg Morpholin/d auf. Es traten keine Lebertumoren auf. Wegen der geringen Versuchstierzahl ist die Aussagekraft der Ergebnisse eingeschraenkt.
Source: BASF AG Ludwigshafen

(148)

5.8.1 Toxicity to Fertility
-

5.8.2 Developmental Toxicity/Teratogenicity
-

5.8.3 Toxicity to Reproduction, Other Studies
-

5.9 Specific Investigations
-

5.10 Exposure Experience

Remark: Im Selbstversuch tratzen bei Exposition gegenueber 43 g/m3

Morpholin ueber 1.5 Minuten Reizungen der Augen, Nase und des Mundes und Hustenreiz auf. Pipettieren der konzentrierten Loesung fuehrte zu Entzuendung und Roetung des Rachen. Die unverduennte Loesung fuehrte zur Zerstoerungdes Epi- und Hypochondriums ueber dem Nagel und einem starken brennenden Schmerz. Noch die Verduennung (1:40) wurde als unangenehm empfunden.

Source: BASF AG Ludwigshafen

(149)

Remark: Die Expsoition gegenueber 16 mg/m3 Morpholin ueber 1 Minute wurde als unangehm empfunden.

Source: BASF AG Ludwigshafen

(150)

Remark: Bericht ueber Schleirsehen bei Chemiearbeiter beim Umgang mit Morpholin.

Source: BASF AG Ludwigshafen

(151)

Remark: Patch-Tests an 320 Probanden mit zwei kosmetischen Produkten, die 1 % Morpholin enthielten, ergaben bei 6 Probanden eine unspezifische Reizung. Untersuchungen bei der
Anwendung von kosmetischen Produkten, die 1 % Morpholin enthielten, ergaben sich bei Augenkontakt leichte Reizungen.

Source: BASF AG Ludwigshafen

(152)

Remark: Lymphozytenuntersuchungen bei 24 Beschaeftigten, die gegenueber Morpholinkonzentrationen in der Luft von 0.54 -0.9e mg/m3, bei Spitzenwerten von 0.74 -2.14 mg/m3 exponiert waren, zeigten 2.08 % Chromosomenbrueche gegenueber 1.61 % in der Kontrollgruppe.

Source: BASF AG Ludwigshafen

(153)

Remark: Die Geruchsschwelle fuer Morpholin wird in der Luft mit 0.01
ppm angegeben.

Source: BASF AG Ludwigshafen

(154)

Remark: Die Expsoition gegenueber 16 mg/m3 Morpholin ueber 1 Minute wurde als unangehm empfunden.
Source: BASF AG Ludwigshafen

(150)

Remark: Bericht ueber Schleirsehen bei Chemiearbeiter beim Umgang mit Morpholin.
Source: BASF AG Ludwigshafen

(151)

Remark: Patch-Tests an 320 Probanden mit zwei kosmetischen Produkten, die 1 % Morpholin enthielten, ergaben bei 6 Probanden eine unspezifische Reizung. Untersuchungen bei der
Anwendung von kosmetischen Produkten, die 1 % Morpholin enthielten, ergaben sich bei Augenkontakt leichte Reizungen.
Source: BASF AG Ludwigshafen

(152)

Remark: Lymphozytenuntersuchungen bei 24 Beschaeftigten, die gegenueber Morpholinkonzentrationen in der Luft von 0.54 -0.9e mg/m3, bei Spitzenwerten von 0.74 -2.14 mg/m3 exponiert waren, zeigten 2.08 % Chromosomenbrueche gegenueber 1.61 % in der Kontrollgruppe.
Source: BASF AG Ludwigshafen

(153)

Remark: Die Geruchsschwelle fuer Morpholin wird in der Luft mit 0.01
ppm angegeben.
Source: BASF AG Ludwigshafen

(154)

5.11 Additional Remarks

Type: Distribution

Remark: Untersucht wurde die Verteilung und Akkumulation von radioaktiv markiertem Morpholin bei 7 maennlichen Neuseelaender Kaninchen nach i.v. Injektion von 5 mmol/kg (435 mg/kg) in 0.5 ml 0.9 % NaCl-Loesung. Nach 30 Minuten enthielt Lungengewebe 5.1 +- 1.0 mmol/kg (444 mg/kg), Leber 4.7 +- 0.9 mmol/kg (410 mg/kg) und Blut 2.3 +- 0.5 mmol/l (200 mg/l); in der Nierenrinde fanden sich 15.4 +- 2.9 mmol/kg (252 mg/kg) und im Nierenmark 36.0 +- 5.5 mmol/kg (3136 mg/kg). Eine Ansaeuerung des Urin fuehrte zu einer annaehernden Verdoppelung der Ausscheidungsgeschwindigkeit, das dabei zu 90 % der verabreichten Dosis unveraendert ausgeschieden wurde.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(155)

Type: Excretion

Remark: 14C-Morpholin wurde i.p. Meerschweinchen in einer Dosierung von 125 mg/kg (50 uCi) injiziert. Im Harn wurden 20 % der Dosis als N-Methylmorpholin-N-oxid gefunden. Nach i.p. Injektion von 125 mg/kg 14C-Morpholin betrug die Halbwertszeit bei Sprague-Dawley-Ratten 115 Minuten, bei Syrischen Goldhamstern 120 Minuten, bei Meerschweinchen (Strain II) 300 Minuten. Bei allen Tieren wurden im

24-Stunden-Harn 80 % der Dosis gefunden.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(156)

Type: Excretion

Remark: Maennlichen Neuseelaender Kaninchen wurde 14C-Morpholin i.v.injiziert. Nur 0.0008 % der verabreichten Dosis wurde als 14-CO2 ausgeatmet.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(155)

Type: Excretion

Remark: 0.5 % der verabreichten Dosis wurden bei SD-Ratten als 14CO2 exhaliert.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(156)

Type: Excretion

Remark: Die Testsubstanz wurde bei Ratten, Maeusen, Hamstern und Kaninchen im Urin nahezu vollstaendig in unmetabolisierter Form ausgeschieden.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(157)

Type: Excretion

Remark: Maennlichen Neuseelaender Kaninchen wurde 14C-Morpholin i.v.injiziert. Nur 0.0008 % der verabreichten Dosis wurde als 14-CO2 ausgeatmet.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(155)

Type: Excretion

Remark: 0.5 % der verabreichten Dosis wurden bei SD-Ratten als 14CO2 exhaliert.
Source: BASF AG Ludwigshafen

Test substance: Morpholin

(156)

Type: Excretion

Remark: Die Testsubstanz wurde bei Ratten, Maeusen, Hamstern und Kaninchen im Urin nahezu vollstaendig in unmetabolisierter Form ausgeschieden.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(157)

Type: Metabolism

Remark: Nitrosierung:
Ausfuehrliche Darstellung der Nitrosierung von Morpholin zu N-Nitrosomorpholin.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(158)

Type: Metabolism

Remark: Treatment of rats (F344) with 38.3 µmol morpholine resulted in an urinary excreation level of the metabolite of N-nitrosomorpholine (N-nitroso(2-hydroxyethyl)glycine) of 1.6 nmol. The combined administration of morpholine and nitrite (38.3 µmol and 191 µmol) resulted in an 600fold increase of this metabolite.
Source: BASF AG Ludwigshafen

(159) (160)

Type: Toxicokinetics

Remark: Untersucht wurde die prozentuale Verteilung von 14C-markiertem Morpholin nach oraler Gabe (200 mg/kg) und i.v. Injektionen (150 mg/kg) an 3 Tieren pro Gruppe. Die groessten Mengen wurden in Muskel und Darm gefunden. 90 % der Ausgangsdosis wurden nach 3 Tagen im Urin und 0.08 - 0.14 % in den Faeces gefunden.

Source: BASF AG Ludwigshafen
Test substance: Morpholin, Morpholin-Hydrochlorid und -Palmitat

(161)

Type: Toxicokinetics

Remark: Weibliche Neuseelaender Kaninchen (Zahl nicht bekannt) wurden 5 Stunden lang gegenueber 0.905 mg/l exponiert. Die hoechsten Konzentrationen nach Expositionsende wurden in Urin (324 ug/ml) und Niere (118 ug/ml) gefunden.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(162)

Type: Toxicokinetics

Remark: Ausfuehrliche Darstellung von Resorption und Verteilung, Biotransformation und Elimination.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(158)

Type: Toxicokinetics

Remark: Weibliche Neuseelaender Kaninchen (Zahl nicht bekannt) wurden 5 Stunden lang gegenueber 0.905 mg/l exponiert. Die hoechsten Konzentrationen nach Expositionsende wurden in Urin (324 ug/ml) und Niere (118 ug/ml) gefunden.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(162)

Type: Toxicokinetics

Remark: Ausfuehrliche Darstellung von Resorption und Verteilung, Biotransformation und Elimination.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(158)

Type: other

Remark: Ausfuehrliche Darstellung der Toxizitaet bei gleichzeitiger Gabe von Morpholin und Nitrit und der Wirkungen von N-Nitrosomorpholin.
Source: BASF AG Ludwigshafen

Test substance: Morpholin

(158)

Type: other

Remark: Es wurde die Auswirkung der Testsubstanz auf das Schwarmverhalten bei Fischen (Kuhlia sandvicensis) untersucht. Bis zu hoechsten geprueften Konzentration von 20ppm (20 mg/l) waren keine Auswirkungen der Testsubstanz festzustellen.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(163)

Type: other

Remark: Es wurde die Auswirkung der Testsubstanz auf das Schwarmverhalten bei Fischen (Kuhlia sandvicensis) untersucht. Bis zu hoechsten geprueften Konzentration von 20ppm (20 mg/l) waren keine Auswirkungen der Testsubstanz festzustellen.
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(163)

Type: other: Living Skin Equivalent

Remark: Title: The Living Skin Equvivalent As A Model In Vitro For Ranking The Toxic Potential Of Dermal Irritants

For the seven chemical irritants tested (including morpholine), the concentrations that inhibited MTT conversion (measure of mitochondrial function with thiazolylblue conversion assay) by 50% were approximately those threshold concentrations at which irritation was seen in human skin.
Source: BASF AG Ludwigshafen

(164)

Type: other: QSAR

Source: BASF AG Ludwigshafen
Test substance: Morpholin

(165) (166)

Type: other: QSAR

Remark: Titel: " Utility of the QSAR Modeling System for Predicting the Toxicity of Substances on the European Inventory of Existing Commercial Chemicals"
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(165)

Type: other: QSAR

Remark: Title: Quantitative Structure-Activity Relationships (QSARs)for Skin Corrosivity of Organic Acids, Bases and Phenols: Principal Components and Neural Network Analysis of Extends Datasets (Toxicology in Vitro)
Title: Quantitative Structure-Activity Relationships for skin corrosivity of organic acids, bases and phenols (Toxicology Letters)
Source: BASF AG Ludwigshafen

(167) (168)

Type: other: acute toxicity in yeast

Remark: Inhibitoric concentration on growth in Saccharomyces cerevesiae of morpholine: 50% inhibition at 94 mg/l.
Source: BASF AG Ludwigshafen

(169)

Type: other: endogenous building of N-nitrosomorpholine

Remark: Male CD-1-mice were exposed to an nominal concentration of 20 ppm 15N- NO2 (6 hours/day, 4 days and for 2 hours on day 5, and to 1 g/kg bw morpholine by gavage).
N-nitrosomorpholine was found in the whole mice (3.9 ug/27.7g mice mean). The concentration was highest in the skin and then in stomach.
Source: BASF AG Ludwigshafen

(170)

Type: other: in vitro inhibition of nitrosation

Remark: 50 µM morpholine and various concentrations of neither ß-carotine or alpha tocopherol (from ranges of 0,1 µM to 0,1mM, both substances) were exposed to 5 ppm NO2 together

with10 ppm NO for 5 minutes and then analyzed for nitrosomorpholine. From concentrations of 0.01 mM on both ß-carotine (90% inhibition at 0.1 mM) and tocopherol (60% inhibition) inhibited markedley the building of the nitroso compound.
Source: BASF AG Ludwigshafen

(171)

Type: other: in vitro toxicity to fish cells

Remark: Neutral red uptake inhibition in cultured fathead minnow cells was measured after treatment with morpholine. 8027 mg/l morpholine (no data of pH value) inhibited the uptake of neutral red to 50% in fish cells.
Source: BASF AG Ludwigshafen

(172)

Type: other: mean daily dietary exposure

Remark: Mean daily dietary exposure: 30 µg (men) and 20 µg (women), in germany.
Source: BASF AG Ludwigshafen

(173)

Type: other: occuring in human

Remark: Morpholine were occasionally found (trace quantities) in gastric juice, saliva, urine and blood.
Source: BASF AG Ludwigshafen

(174)

Type: other: physicochemically based model of skin penetration

Remark: Morpholine was identified by the theoretical model to have the potential for dermal absorption.
Source: BASF AG Ludwigshafen

(175)

Type: other: recommendation

Remark: Recommendation to morpholine costumers.
Source: BASF AG Ludwigshafen

(176)

Type: other: relationship between acute oral/inhalation toxicity

Remark: A positive correlation (0.53, $p < 0.001$) between the classification of toxicity of both routes was determined (data of 108 chemicals).
Source: BASF AG Ludwigshafen

(177)

Type: other: summarizing report

Remark: Consensus report for Morpholine and Nitrosomorpholine
Source: BASF AG Ludwigshafen

(178)

Type: other: zusammenfassende Darstellungen

Remark: Zusammenfassende Darstellungen
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(179) (158) (180) (181) (182)

Type: other: zusammenfassende Darstellungen

Remark: Zusammenfassende Darstellungen
Source: BASF AG Ludwigshafen
Test substance: Morpholin

(179) (183) (158) (180) (181) (184) (185) (182) (186)

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) MAK and BAT Values 1992, Deutsche Forschungsgemeinschaft

(2) TRGS 900 (1993)

(3) UK HSE EH40/1993

(4) ACGIH 1992

(5) ACGIH (1991-1992)

(6) Royal Society of Chemistry, UK, Chemical Safety Data Sheets Volume 3, RSC, 1989

(7) Royal Society of Chemistry (UK), Safety Data Sheets Vol 3, No 45. RSC,1989

(8) 1. Texaco report, DW Stanton. unpubl Feb 1990
2. Texaco air sampling record for period 8/2/93 to 6/8/93, Llanelli Chemical Plant, unpubl.

(9) Huels AG: Sicherheitsdatenblatt "Morpholin", Version 05 (inaktiv), 07.10.1997

(10) Stoerfall-Verordnung vom 20.09.1991

(11) 1. Application for authorisation under integrated pollution control, for UK Environmental Protection Act 1990, section 6. Texaco Llanelli Chemical Plant, Wales
Submitted 8/93
Approved 1/1/94 No AJ 9032 Texaco
No AN 0428 Huntsman of 1/5/94

2. Huntsman Corporation Llanelli Chemical Plant Quality manual and related documentation

3. Texaco/Huntsman 1993

(12) BASF AG, Sicherheitsdatenblatt Morpholin (04.01.1994)

(13) BASF AG, Analytisches Labor; unveroeffentlichte Untersuchung (J.Nr. 110079/01 vom 22.09.1989)

(14) Verschueren K., Handbook of Environmental Data on Organic Chemicals, 2nd Ed., Van Nostrand Reinhold, New York, 1983

(15) BASF AG, Labor fuer Umweltanalytik; unveroeffentlichte Untersuchung (09.01.1989)

(16) Atkinson,R., Environ. Toxicol. Chem.7, 435-442, (1988)

(17) Beratergremium fuer Umweltrelevante Altstoffe (BUA) der Gesellschaft Deutscher Chemiker (Hrsg.): 'Morpholin', Nr.56, S.85, (1990)

(18) Fraenzle,O., Schriftliche Mitteilung vom 25.10.1990 zum BUA-Stoffbericht Morpholin, Christian-Albrechts-Universitaet, Geographisches Institut, Kiel

(19) BG Chemie, Schriftliche Mitteilung zum BUA-Stoffbericht Morpholin vom 10.12.1990 mit Anlage BIA-Dokumentation MEGA-Messdaten ueber Gefahrstoffe am Arbeitsplatz, Berufsgenossenschaft der chemischen Industrie, Heidelberg, 15 S., (1990)

(20) Taft,R.M., Stroman,R.E., Health hazard evaluation determination, Report No. HE-78-131-586, Goodyear Tire and Rubber Company, Niagara Falls, New York, Hazard Evaluations and Technical Assistance Branch, NIOSH Cincinnati, Ohio, 13 S., (Order No. PB80-196736)

(21) Fajen,J.M. et al., Science 205, 1262-1264, (1979)

(22) LWA, Schriftliche Mitteilung vom 29.08.1990 zum BUA-Stoffbericht Morpholin, Landesamt fuer Wasser und Abfall Nordrhein Westfalen, Duesseldorf, 1 S., (1990)

(23) Beratergremium fuer Umweltrelevante Altstoffe (BUA) der Gesellschaft Deutscher Chemiker (Hrsg.): 'Morpholin', Nr.56, S.61, (1990)

(24) Singer,G.M., Lijinsky,W., J. Agric. Food Chem.24, 550-553, (1976)

(25) Beratergremium fuer Umweltrelevante Altstoffe (BUA) der Gesellschaft Deutscher Chemiker (Hrsg.): 'Morpholin', Nr.56, S.63, (1990)

(26) Ohnishi,T. et al., Hokuriku Koshu Eisei Gakkaishi 10, 63-67, (1983)

(27) Hoffmann,D. et al., N-Nitrosamines in tobacco carcinogenesis, in: Magee,P.N. (ed.), Nitrosamines and human cancer, Banbury Report Vol.12, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 211-225, (1982)

(28) Hotchkiss,J.H., Vecchio,A.J., J. Food Sci.48, 240-242, (1983)

(29) Hamano,T. et al., Agric. Biol. Chem.45, 2237-2243, (1981)

(30) Hoffmann,D. et al., N-Nitrosamines in tobacco carcinogenesis, in: Magee,P.N. (ed.), Nitrosamines and human cancer, Banbury Report Vol.12, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 211-225, (1982)

(31) Brunnemann,K.D. et al., Carcinogenesis 3, 693-696, (1982)

(32) BGB1, Bekanntmachung der Neufassung der Kosmetik-Verordnung vom 19.Juni 1985, Texte A500, 1083-1123, (1989)

(33) Chemisches Landesuntersuchungsamt NRW, Schriftliche Mitteilung zum BUA-Stoffbericht Morpholin vom 21.08.1990, Muenster, 2 S., (1990)

(34) Smith,J.H. et al., Environ. Sci. Technol.14, 1332-1337, (1980)

(35) Donath,G. et al., Vom Wasser 49, 221-243, (1977)

(36) Toogood,S.J., Hobson,J.A., Water Research Centre, Stevenage Lab., Stevenage/Herts, 43 p., (1980)

(37) Beratergremium fuer Umweltrelevante Altstoffe (BUA) der Gesellschaft Deutscher Chemiker (Hrsg.): 'Morpholin', Nr.56, S.90, (1990)

(38) BASF AG, Labor Oekologie; unveroeffentlichte Unter-

suchung, (Ber.v.22.09.89, 01.89/1287/20/0)

(39) BASF AG, Labor Oekologie; unveroeffentlichte Untersuchung, (Ber.v.26.09.90, 1901337)

(40) BASF AG, Labor Oekologie; unveroeffentlichte Untersuchung, (Ber.v.18.10.90, 1901337)

(41) Mills,E.J.jr., Stack,V.T.jr., Proceedings of the 8th Industrial Waste Conf., Eng. Bulletin of Purdue Univ.38, Ser.83, 492-517, (1953)

(42) Niemi,G.J. et al., Environmental Toxicology and Chemistry 6, 515-527, (1987)

(43) Knapp,J.S., Whytell,A.J., Environ. Pollut. 68, 67-79, (1990)

(44) Strotmann,U.J. et al., Chemosphere 26(9), 1729-1742, (1993)

(45) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, edited by Chemicals Inspection & Testing Institute Japan, published by Japan Chemical Industry Ecology-Toxicology & Information Center, October 1992

(46) Calamari,D. et al., Chemosphere 9, 753-762, (1980)

(47) Calamari,D.et al., Chemosphere 9, 753-762, (1980)

(48) Beratergremium fuer Umweltrelevante Altstoffe (BUA) der Gesellschaft Deutscher Chemiker (Hrsg.): 'Morpholin', Nr.56, S.87, (1990)

(49) Loeb, H.A. und Kelly, W.H.: Acute oral toxicity of 1496 chemicals force-fed to carp, U.S. Dept. of the Interior, Special Scientific Report - Fisheries No. 471, Washington D.C., September 1963, Seite 1-124

(50) Wellens H.: Z. Was. Abwas. Forsch. 49-52 (1982). Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(51) McCain J.C. et Peck J.M.: NTIS No. PB 262437 (1976)

(52) Dawson G.W. et al.: J. Hazard. Mater. 1, 303-318 (1977)

(53) Juhnke I. et Luedemann D.: Z. Was. Abwas. Forsch 11, 161 (1978)

(54) Juhnke I. and Luedemann D.: Z. Wasser und Abwasserforschung,11, 161-164 (1978) quoted in: Brandao J.C. et al.: Chemosphere, 25/4, 553-562 (1992)

(55) Calamari D. et al.: Chemosphere 9, 753-762 (1980)

(56) Bringmann,G., Kuehn,R., Zeitschrift fuer Wasser- und Abwasser-Forschung, 10(5), 161-166, (1977)

(57) Bringmann,G., Kuehn,R., Zeitschrift fuer Wasser- und Abwasser-Forschung, 15(1), 1-6, (1982)

(58) Millington,L.A., et al., Water Research 22, 1593-1597, (1988), zitiert in: BUA-Bericht Nr.56 MORPHOLIN, GDCh, S.96, 12/1990

(59) Bringmann,G., Kuehn,R., Vom Wasser 50, 45-60, (1978)

(60) Bringmann,G., Kuehn,R., Zeitschrift fuer Wasser- und Abwasser-Forschung, 10(3/4), 87-98, (1977)

(61) Millington,L.A. et al., Water Research 22, 1593-1597, (1988), zitiert in: BUA-Bericht Nr.56 MORPHOLIN, GDCh, S.96, 12/1990

(62) Adams,N. et al., Arch. Environ. Contam. Toxicol. 14, 333-345, (1985), zitiert in: BUA-Bericht Nr.56 MORPHOLIN, GDCh, S.95, 12/1990

(63) Krebs F., DGM 35, H.5/6, 161-170, 1991

(64) Kaiser,K.L.E., Palabrica,V.S., Water Poll. Res. J. Canada, Volume 26, No.3, 361-431, 1991

(65) Bringmann,G., Gesundheits-Ingenieur 94(12), 366-369, (1973)

(66) Knapp,J.S. et al., J. Appl. Bacteriol. 52, 5-13, (1982), zitiert in: BUA-Bericht Nr.56 MORPHOLIN, GDCh, S.92, 12/1990

(67) BASF AG, Labor Oekologie; unveroeffentlichte Untersuchung, (Ber.v.22.08.90, 1901337)

(68) Cech,J.S. et al., Appl. Environ. Microbiol. 54, 619-621, (1988), zitiert in: BUA-Bericht Nr.56 MORPHOLIN, GDCh, S.92, 12/1990

(69) Reynolds,T., J. Exp. Bot.40, 391-404, (1989)

(70) Kramer,V.C. et al., J. Invertebr. Pathol.42, 285-287, (1983)

(71) Shea T.E.: J. Ind. Hyg. Toxicol., 21, 236-245 (1939)

(72) Smyth H.F. et al.: Arch.Ind.Hyg.Occup.Med. 10, 61-68 (1954)

(73) BASF AG, Abteilung Toxikologie, unveroeffentlichte Untersuchung (XVI/352) vom 06.02.1967

(74) IBT (1979).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(75) Smyth, H.F. et al.: Tox. Appl. Pharmacol. 14, 340-347 (1969).
Zitiert in: "Final Report on the Safety Assessment of Morpholine", Journal of the American College of Toxicolgy 8 (4) 707-748 (1989)

(76) Smyth, H.F. et al.: Tox. Appl. Pharmacol. 17, 498-503 (1970).
Zitiert in: "Final Report on the Safety Assessment of Morpholine", Journal of the American College of Toxicolgy 8 (4) 707-748 (1989)

(77) RTECS, Update Code 9610: Toksikol. Novykh. Prom. Khim. Vesch., 10, 25, (1968)

(78) Boerzsoenyi et al.: Toxicol. Lett. 7, 285-288 (1981).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(79) Patel et al. (1985).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(80) Patel et al. (1985).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(81) TSCATS: OTS0536615, Doc. I.D: 88-920003273, 2 June 1992, Union Carbide Corp.

(82) RTECS, Update Code 8909 (Maerz 1990): Toksikol. Novykh

Prom.Khim. Veshch. 14, 90 (1975)

(83) Lam H.F. und Van Stee E.W.: Fed. Proc. 37, 679 (1978).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(84) Coate W.B.: Hazleton Laboratories America, Inc., unveroeffentlichte Untersuchung, Report No. 2147-100 vom 02.01.1981

(85) Internat. Labour Office: Encyc. Occ. Health and Safety Vol. 2, 915 (1972).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(86) Ivanov et al.: Toksikol. Nov. Prom. Khim. Veshchestv 13, 41-47 (1973).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(87) Industr. Bio-Test Lab.: Bio-fax data sheet (1970).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(88) RTECS update 9610: Raw Material Data Handbook Vol 1, 85, 1974

(89) ILO, International Labour Office (1983).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(90) Zaeva G.N. et al.: Toksikol. Nov. Prom. Khim. Veshchestv 10, 25 (1968).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(91) RTECS, Update Code 8909 (Maerz 1990): Toksikol. Novykh Prom. Khim. Veshch. 8, 60 (1966).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(92) RTECS, Update Code 8909 (Maerz 1990): Toksikol. Novykh. Prom. Khim. Veshch. 14, 90 (1975)

(93) IBT, Industrial Bio-Test Laboratories, Inc. (1979).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(94) Smyth, H.F. et al.: Arch. Ind. Hyg. Occup. Med. 10, 61-68 (1954).
Zitiert in: "Final Report on the Safety Assessment of

Morpholine", Journal of the American College of Toxicolgy 8 (4) 707-748 (1989)

(95) Landing, B.H. et al.: Cancer, 1055-1066 (1949).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(96) Kase, Y. et al.: Jpn. J. Pharmacol. 17 (3) 475-490 (1967).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(97) Stewart B.W. und Farber E.: Cancer Res. 33, 3209 (1973).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(98) Shea T.E.: J. Ind. Hyg. Toxicol. 21, 236-245 (1939)

(99) Loden et al.: FOA Report E 40023 (1985).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(100) Bellander T. et Hagmar L.: Arbete och Haelsa (1982). Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(101) Mjos K.: in Kirk-Othmer encyc. chem. techn. 3rd ed., Vol.2, 295- 308.
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(102) Kubis A. et al.: Pharmazie 36, 429-431 (1981).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(103) Wang X. und Suskind R.R.: Contact Dermatitis 19, 11-15 (1988).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(104) Wang X. und Tabor M.W.: Contact Dermatitis 19, 16-21 (1988).Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(105) Takezawa J. et Lam H.F.: Fed. Proc., 37, 247 (1978) (Abstract).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(106) Grodeckaja N.S. und Karamzina N.M.: Toksikol. Nov. Prom. Khim. Veshchestv, 13, 12-23 (1973); Kurzuebersetzung der Universitaetsbibliothek Hannover.

(107) Conaway C.C. et al.: Fundam. Appl. Toxicol. 4, 465-472 (1984)

(108) Hazleton Laboratories America, Inc., unveroeffentlichte Untersuchung, Project No. 2147-101 vom 15.10.1981

(109) Savolainen H. und Rosenberg C.: Arch. Toxicol. 53, 143-150 (1983).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(110) Migukina N.V. Toksikol. Nov. Prom. Khim. Veshhestv, 13, 92-100 (1973); Kurzuebersetzung der Universitaetsbibliothek Hannover.

(111) Harbison R.D. et al.: Fundam. Appl. Toxicol. 12, 491-507 (1989).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990) und in: Chemical Abstracts 110, 226959w (1989)

(112) Hazleton Laboratories America, Inc., unveroeffentlichte Untersuchung, Project No. 2147-102 vom 29.10.1986

(113) Texaco Petroleum Products, unveroeffentlichte Ergebnisse, "reprint copy" einer Posterpraesentation, SOT (1984)

(114) Savolainen H. und Rosenberg C.: Arch. Toxicol. 53, 143-150 (1983).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(115) TSCATS: OTS0200636-1, Doc. I.D: 89-870000054, 13 November 1986 Texaco Chemical Corp.

(116) Sander J. und Buerkle G.: Z. Krebsforsch., 73 54-66 (1969).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(117) Shibata M.-A. et al.: J. Tox. Env. Health 22, 187-194 (1987).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(118) Tombropoulos E.G. et al.: Toxicol. Appl. Pharmacol. 70, 1 (1983).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(119) Migukina N.V. Toksikol. Nov. Prom. Khim. Veshhestv, 13, 92 (1973)

(120) Haworth S. et al.: Environ. Mutagenesis Suppl. 1, 3-142 (1983)

(121) Glatt H.R. und Oesch F., Pharmakologisches Institut der Universitaet Mainz, unveroeffentlichte Untersuchung 80/490 fuer BASF AG, Abteilung Toxikologie, 30.06.1981

(122) Conaway C.C. et al.: Mut. Res. 136, 153-157 (1984)

(123) Conaway C.C. et al.: Environ. Mutagenesis 4, 390 (1982)

(124) Litton Bionetics, Inc., unveroeffentlichte Untersuchung fuerTexaco Petrochemicals, LBI Project No. 20989, Juli 1979

(125) Litton Bionetics, Inc., unveroeffentlichte Untersuchung fuerTexaco, Inc., LBI Project No. 20992, Oktober 1979

(126) Litton Bionetics, Inc., unveroeffentlichte Untersuchung fuerTexaco Petrochemicals, LBI Project No. 20992, Juni 1979

(127) Litton Bionetics, Inc., unveroeffentlichte Untersuchung fuerBASF AG, LBI Project No. 21002, Juli 1982

(128) Litton Bionetics, Inc., unveroeffentlichte Untersuchung fuerTexaco Petrochemicals, LBI Project No. 20990, Juli 1979

(129) Litton Bionetics, Inc., unveroeffentlichte Untersuchung fuerTexaco, Inc., LBI Project No. 20990, Januar 1980

(130) Spanggord, R.J. et al.: Environ. Mutagen. 4, 163-179 (1982).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(131) Monaghan (1980), zitiert in NRC, National Research Council (1983).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(132) TSCATS: OTS0200636, Doc. I.D: 88-8000294, 20 February 1980, Texaco Chemical Corp.

(133) JETOC: January 1996

(134) Perez A. et al.: Die Nahrung, 34/7, 661-664 (1990)

(135) Takahashi A. and Ono H.: Chemistry Express, 8/9, 785-788 (1993)

(136) TSCATS: OTS0200636, Doc. I.D: 88-8200402, 12 August 1982, Texaco Chemical Corp.

(137) Inui N. et al.: Int. J. Cancer 24, 356-372 (1979).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(138) Braun R. et al.: Cancer Research 37, 4572-4579 (1977).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(139) Edwards G. et al.: Mut. Research 64, 415-423 (1979).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(140) Whong et al. (1979).
Zitiert in: Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(141) Ghess M.J. et al.: WHO Inf. Bull. 13, 101 (1988).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(142) Shibata M.-A. et al.: Food. Chem. Toxicol. 25, 569-574 (1987).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(143) Shibata M.-A. et al.: Food. Chem. Toxicol. 25, 569-574 (1987).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(144) Harbison R.D. et al.: Fundam. Appl. Toxicol. 12, 491-507 (1989).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(145) Sander J.: Arzneim.-Forsch. 21, 1572-1580 (1971).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(146) Newberne P.M. und Shank R.C.: Fd. Cosmet. Toxicol. 11, 819 (1973).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(147) Greenblatt M. et al.: J. Nat. Cancer Inst. 46, 1029-1034 (1971).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(148) Shank R.C. und Newberne P.M.: Fd. Cosmet. Toxicol. 14, 1-8 (1976).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(149) Shea, T., E., Jr.; J. Ind. Hyg. Toxicol. 21, 236-245, (1939)

(150) Ivanov, N., G., Germaonva, A., L.; Zoksikol. Nov. Prom. Khim. Veshchestv 13, 41-47, (1973)

(151) Jones, W., T., Kipling, M., D.; Br. J. Ind. Med. 29, 460-461, (1972)

(152) Anon; J. Am. Coll. Toxicol. 8, 707-748, (1989)

(153) Katasova, L., D., Fomenko, V., N., Davydenko, L., N.; Gig. Tr. Prof. Zabol. 6, 35-36, (1991)

(154) Amoore, J., E., Hautala, E.; J. Appl. Toxicol. 3, 272-290, (1983)

(155) Van Stee E.W. et al.: Toxicology 20, 53-60 (1981).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(156) Sohn O.S. et al.: Toxicol. Appl. Pharmacol. 64, 486-491 (1982).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(157) Griffiths, M.H.: Biochem. J. 198, 731-740 (1968).
Zitiert in: United Nations Environment Programme (WHO), International Programme on Chemical Safety, Environmental Health Criteria for Morpholine, first draft, Maerz 1993.

(158) BUA-Stoffdossier Morpholin (Dezember 1990)

(159) Hecht S.S. and Morrison J.B.: Cancer Research, 44, 2873-2877(1984)

(160) IARC Monographs: Scientific Publication No. 57, 185-192 (1984)

(161) Tanaka A. et al.: J. Food Hyg. Soc. 19, 329-334 (1978)

(162) Tombropoulos E.G.: J. Chromatogr. 164, 95-99 (1979).
Zitiert in: BUA-Stoffbericht 56 - Morpholin (Dezember 1990)

(163) Hiatt, R.W. et al.: Biol. Bull. 104, 28-44 (1953)

(164) Gay R. et al.: Toxic. in Vitro, 6/4, 303-315 (1992)

(165) Fiedler, H. und Hutzinger, O.: Toxicological and Environmental Chemistry 28, 167-188 (1990)

(166) Titel: " Utility of the QSAR Modeling System for Predicting the Toxicity of Substances on the European Inventory of Existing Commercial Chemicals"

(167) Barrat M.D.: Toxicology Letters, 75, 169-176 (1995)

(168) Barratt M.D.: Toxicology in Vitro, 10, 85-94, 1996

(169) Koch H.P.: Pharmazie 47, 531-537 (1992)

(170) Stee, van E.W. et al.: Carcinogenesis, 16/1, 89-92 (1995)

(171) Arroyo P.L. et al.: Mutation Research, 281, 193-202 (1992)

(172) Brandao J.C. et al.: Chemosphere, 25/4, 553-562 (1992)

(173) Tricker A.R. et al.: American Chemical Society, Chapter 8 (1994)

(174) Tricker A.R. et al.: Carcinogenesis, 13/4, 563-568 (1992)

(175) Guy R.H. and Potts R.O.: American Journal of Industrial Medicine 23, 711-719 (1993)

(176) TSCATS: OTS0200636, Doc. I.D: 86-8000103, 31 December 1980, Texaco Chemical Corp.

(177) Kennedy G.L. jr. and Graepel G.J.: Toxicology Letters, 56, 317-326 (1991)

(178) National Board of Occupational Safety and Health: Arbete ochHaelsa, 36, 92-103 (1983)

(179) "Final Report on the Safety Assessment of Morpholine", Journal of the American College of Toxicolgy 8 (4) 707-748 (1989)

(180) Dynamic Corporation, Information Review Morpholine, IR-514, 14.10.1988

(181) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 47, 199-213 (1989)

(182) United Nations Environment Programme (WHO), International Programme on Chemical Safety, Environmental Health Criteria for Morpholine, first draft, Maerz 1993.

(183) American Conference of Governmental Industrial Hygienists, Inc.: TLV, Morpholine, 1991

(184) MAK Dokumentation, 1995 (Draft)

(185) Patty's Industrial Hygiene and Toxicology, 4th edition Vol II, part E, 1994

(186) United Nations Environment Programme (WHO), International Programme on Chemical Safety, Environmental Health Criteria for Morpholine, Geneva, 1995.

10.1 End Point Summary
-

10.2 Hazard Summary
-

10.3 Risk Assessment
-

201-14953B1

I U C L I D

D a t a S e t

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Existing Chemical	ID: 120-78-5
CAS No.	120-78-5
EINECS Name	di(benzothiazol-2-yl) disulphide
EINECS No.	204-424-9
TSCA Name	Benzothiazole, 2,2'-dithiobis-
Molecular Formula	C14H8N2S4

Producer Related Part
Company:
Creation date: 06-NOV-2000

Substance Related Part
Company:
Creation date: 06-NOV-2000

Memo: Data for RAPA Benzothiazole-based Thiazoles category

Printing date: 09-OCT-2001
Revision date:
Date of last Update: 26-APR-2001

Number of Pages: 67

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 7
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 OECD and Company Information
-

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information
-

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms
-

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: 180 degree C
Method: other: Handbook value
Testsubstance: other TS: purity not noted
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
26-APR-2001 (1)

Value: 168 degree C
Source: Bayer AG Leverkusen
19-APR-1993 (2)

Value: > 169 degree C
Source: Bayer AG Leverkusen
02-APR-1993 (3)

Value: 170 degree C
Source: Monsanto
Bayer AG Leverkusen
10-MAY-1994 (4)

Value: 180 - 182 degree C
Source: Bayer AG Leverkusen
19-APR-1993 (5)

2.2 Boiling Point

Value:
Decomposition: yes
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
06-NOV-2000 (2)

2.3 Density

Type: density
Value: 1.54 at 25 degree C
Method: other: Handbook value
Testsubstance: other TS: purity not noted
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
26-APR-2001 (6)

Type: density
Value: 1.34 g/cm3 at 20 degree C
Source: Bayer AG Leverkusen
02-APR-1993 (3)

Type: density
Value: 1.5 g/cm3 at 20 degree C
Source: Bayer AG Leverkusen
19-APR-1993 (2) (1)

Type: density
Value: ca. 1.51 g/cm3 at 20 degree C
Source: Bayer AG Leverkusen
02-APR-1993 (7)

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: .000000000597 hPa at 20 degree C
Method: OECD Guide-line 104 "Vapour Pressure Curve"
GLP: yes
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
06-NOV-2000 (8)

Value: .0000000543 hPa at 50 degree C
Method: OECD Guide-line 104 "Vapour Pressure Curve"
GLP: yes
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
06-NOV-2000 (8)

Value:
Remark: value:
< 2 x 10 exp -6 torr
Source: Monsanto
Bayer AG Leverkusen
26-APR-2001 (9)

2.5 Partition Coefficient

log Pow: 4.5
Method: other (measured): flask shaking method
Year: 1980
GLP: no
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
06-NOV-2000 (10)

log Pow: 4.5
Method: other (calculated)
Year:
Source: Bayer AG Leverkusen
06-NOV-2000 (9)

log Pow: 4.659 at 25 degree C
Method: other (calculated)
Year:
Flag: Critical study for SIDS endpoint
26-APR-2001 (11)

2.6.1 Water Solubility

Value: 80 - 96 mg/l at 22 degree C
pH: 5
Method: other
Remark: Value: 88 +/- 8 mg/l
Temperature: 22 °C
pH: 5
Elution through a glass bed column proviously coated with MBTS; HPLC measurement
Value: 49 +/- 2 mg/l at pH 9
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
06-NOV-2000 (12)

Value: 68 other: ppm at 22 degree C
Method: other: calculated
06-NOV-2000 (13)

Value: < .0002 g/l at 20 degree C
Source: Bayer AG Leverkusen
09-AUG-1993 (8)

Value: < 1 g/l at 21 degree C
Source: Bayer AG Leverkusen
29-APR-1993 (2)

Value: < 10 mg/l
Source: Bayer AG Leverkusen
11-AUG-1993 (14)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: 257 degree C
Type: closed cup
Method: other: DIN 51758
Year:
Source: Bayer AG Leverkusen
02-APR-1993 (3)

Value: 271 degree C
Type:
Method:
Year:
Source: Bayer AG Leverkusen
19-APR-1993 (2)

2.8 Auto Flammability

-

2.9 Flammability

-

2.10 Explosive Properties

-

2.11 Oxidizing Properties

-

2.12 Additional Remarks

Remark: Ignition temperature: > 365 degree C
Source: Bayer AG Leverkusen
30-APR-1993 (3)

3.1.1 Photodegradation

Type: water
Light source: Sun light
DIRECT PHOTOLYSIS
Halflife t1/2: 3 hour(s)
Method:
Year: GLP:
Test substance: other TS: MBTS purity = 98%
Remark: dark control 19 hours
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
26-APR-2001 (15)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .0000000003152585 cm3/(molecule * sec)
Degradation: 50 % after 24.4 minute(s)
Method: other (calculated): AOP Program (v1.89)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Flag: Critical study for SIDS endpoint
26-APR-2001 (11)

Type: air
INDIRECT PHOTOLYSIS
Rate constant: .0000000002 cm3/(molecule * sec)
Degradation: 50 % after 1.9 hour(s)
Method: other (calculated): according to Atkinson
Year: 1990 GLP:
Test substance:
Remark: no direct photolysis; sensitizer: OH-radicals
Source: Bayer AG Leverkusen
25-MAY-1993 (16)

Type:
Method:
Year: GLP:
Test substance:
Remark: UV-irradiation of bis-(2-benzothiazolyl)-disulfide (2.5 g, 7.5 mmol) in acetonitrile or ethanol (120 h) gave following products: Benzothiazole (6.8%), elemental sulphur (14.2%), 2(3H)-benzothiazolethione (29.2%), bis-(2-benzo-thiazolyl)-disulfide (17.0%), 2(3H)-benzothiazolone (30.0%).
Source: Bayer AG Leverkusen
09-JUN-1993 (17)

3.1.2 Stability in Water

Type: abiotic
Degradation: 37 % after 7 day
at pH 7
Method:
Year: GLP:
Test substance: other TS: MBTS purity = 98%
Remark: Thiofide hydrolized approximately 37% after a 7-day period in pH 7 buffered deionized water with light excluded. The sole hydrolysis product indentified was mercaptobenzthiazole.
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
06-NOV-2000 (18)

Type: abiotic
Method:
Year: GLP:
Test substance:
Remark: Hydrolysis to 2-Mercaptobenzothiazole and Benzothiazyl-2-sulfenic acid; further reaction of the sulfenic acid to 2,2'-Dithiobisbenzothiazole, Benzothiazyl-2-sulfinic acid and Benzothiazyl-2-sulfonic acid (no other information).
Source: Bayer AG Leverkusen
06-JAN-1994 (5)

Type: abiotic
Method:
Year: GLP:
Test substance:
Remark: Alkalic hydrolysis (pH 9.8-12.1) to 2-Mercaptobenzothiazole and Benzothiazyl-2-sulfenic acid; further reaction of the sulfenic acid to 2-Mercaptobenzothiazole, Benzothiazyl-2-sulfinic acid and Benzothiazyl-2-sulfonic acid. In the presence of oxidizing agents 2-Mercaptobenzothiazole reacts to MBTS, Benzothiazyl-2-sulfinic acid will be oxidized to the sulfonic acid. Based on a cyclic process Benzothiazyl-2-sulfonic acid is the major hydrolysis product of MBTS.
Source: Bayer AG Leverkusen
13-MAY-1993 (19)

3.1.3 Stability in Soil

Type: Radiolabel:
Concentration:
Cation exch.
capac.
Microbial
biomass:
Method:
Year: GLP:
Test substance:
Remark: no information
Source: Bayer AG Leverkusen
05-AUG-1992

3.2 Monitoring Data (Environment)

Type of
measurement: background concentration
Medium: other: surface water and sediment
Method:
Concentration
Remark: MBTS was not detected in 42 samples in Japan in 1978;
detection limit: - water: 0.5 ug/l
- sediment: 0.05 - 0.17 mg/kg
Source: Bayer AG Leverkusen
11-AUG-1993 (20)

Type of
measurement: concentration at contaminated site
Medium: other: waste water from MBTS production sites, USA
Method:
Concentration
Remark: untreated effluent: 0.5 - 10 ppm (no further information)
Source: Bayer AG Leverkusen
09-JUN-1993 (21)

Type of
measurement: concentration at contaminated site
Medium: other: effluent from a publicly owned treatment plant,
handling effluents from a plant manufacturing MBTS, USA
Method:
Concentration
Remark: average concentration: 11 ug/l (4 samples)
Source: Bayer AG Leverkusen
09-JUN-1993 (21)

Type of measurement:
Medium:
Method:
Concentration
Remark: no information (Germany)
Source: Bayer AG Leverkusen
05-AUG-1992

3.3.1 Transport between Environmental Compartments

Type:
Media: other: soil-air, water-air, water-soil
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method:
Year:
Remark: Based on the physico-chemical properties transport between air and water/soil has to be expected to a small extent
Source: Bayer AG Leverkusen
25-MAY-1993

3.3.2 Distribution

Media: air - biota - sediment(s) - soil - water
Method: Calculation according Mackay, Level III
Year: 1999
Result:

	Concentration (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.00014	0.814	1000	7.01e-017
Water	17.2	900	1000	1.98e-018
Soil	72.7	900	1000	2.14e-019
Sediment	10.2	3.6e+003	0	1.35e-018

Persistence Time: 1.13e+003 hr
Reaction Time: 1.4e+003 hr
Advection Time: 5.76e+003 hr
Percent Reacted: 80.4
Percent Advecte
Reliability: (2) valid with restrictions
06-NOV-2000 (11)

Media:
Method:
Year:
Remark: no information
Source: Bayer AG Leverkusen
05-AUG-1992

3.4 Mode of Degradation in Actual Use

Remark: no information
Source: Bayer AG Leverkusen
05-AUG-1992

3.5 Biodegradation

Type: aerobic
Inoculum: other: activated sludge, predominantly industrial waste water, adapted
Concentration: 100 mg/l related to Test substance
Degradation: 2 % after 28 day
Result: other: not readily biodegradable
Method: other: Manometrischer Respirationstest, Verfahren nach Richtlinie 79/831/EWG, Anhang V, Teil C (aktualisierte Fassung vom Juli 1990), Methode C.4-D
Year: 1992 GLP: yes
Test substance: other TS: purity 97.8 %
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
06-NOV-2000 (8)

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 100 mg/l related to Test substance
Degradation: 0 % after 28 day
Result: under test conditions no biodegradation observed
Method: other: MITI-Test OECD-Test Guideline 301 C; according to the EC-method: Assessment of Biodegradability of Chemicals in Water by Manometric Respirometry (DG X 1 283/82 Rev. 5)
Year: 1988 GLP: yes
Test substance: other TS: technical grade
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
06-NOV-2000 (8)

Type: aerobic
Inoculum: activated sludge, non-adapted
Concentration: 100 mg/l related to Test substance
Degradation: .8 % after 14 day
Method: other: see remarks
Year: GLP: no data
Test substance: other TS: MBTS (no information about purity)
Remark: sludge concentration: 30 mg/l
method:
"Biodegradation test of chemical substance by microorganisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test I" stipulated in the OECD Guideline for Testing of Chemicals (May 12, 1981).
Source: Bayer AG Leverkusen
06-NOV-2000 (14)

3.6 BOD5, COD or BOD5/COD Ratio

Remark: COD: 1973 mg/g
Source: Bayer AG Leverkusen
28-MAY-1993 (8)

3.7 Bioaccumulation

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .2 mg/l
BCF: 1 - 7.2
Elimination: no data
Method: other: see remarks
Year: GLP: no data
Test substance: other TS: MBTS (no information about purity
Remark: method:
"Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "305C, Bio-accumulation: Degree of Bioconcentration in Fish" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
Source: Bayer AG Leverkusen
11-AUG-1993 (14)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .02 mg/l
BCF: < 1.4 - 51
Elimination: no data
Method: other: see remarks
Year: GLP: no data
Test substance: other TS: MBTS (no information about purity)
Remark: method:
"Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "305C, Bio-accumulation: Degree of Bioconcentration in Fish" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
Source: Bayer AG Leverkusen
11-AUG-1993 (14)

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 66
Method:
Year: GLP: no data
Test substance: other TS: MBTS purity =98%
Source: Monsanto
Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
06-NOV-2000 (22)

Type: static
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: > 1000
Method:
Year: GLP: no data
Test substance: other TS: MBTS purity =98%
Source: Monsanto
Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
06-NOV-2000 (23)

Type: other: calculated
Species: other
Exposure period: 14
Unit: mg/l Analytical monitoring: no
LC50: 2.152
Method: other: ECOSAR Program (v0.99e)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
26-APR-2001 (11)

Type: other: calculated
Species: other
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: .779
Method: other: ECOSAR Program (v0.99e)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
26-APR-2001 (11)

Type:
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period:
Unit: mg/l Analytical monitoring:
LC50: 82
Method:
Year: GLP:
Test substance:
Source: Monsanto
Bayer AG Leverkusen
10-MAY-1994 (24)

Type:
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 13 day
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: In a time-independent test rainbow trout was exposed to MBTS acutely. No mortality was noted in the fish over the 13 day study period at exposure values up to 15 mg/l, the highest level tested in the study. Based on the data, MBTS was judged to not be highly toxic to the fish following acute exposure.
Source: Monsanto
Bayer AG Leverkusen
10-MAY-1994 (25)

Type:
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 19
Method: other: Japanese Industrial Standard (JIS K 0102-1986-71) "Testing methods for industrial waste water"
Year: GLP: no data
Test substance: other TS: MBTS (no information about purity)
Source: Bayer AG Leverkusen
11-AUG-1993 (14)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: Analytical monitoring: yes
Method: other: Pruefrichtlinie "Akute Toxizitaet fuer Daphnien (C.2) Richtlinie 67/548/EWG (Entwurf 1992)
Year: 1992 GLP: yes
Test substance: other TS: purity 97.8 %
Remark: No immobilization within the range of water solubility, effects could be observed only for test concentration above water solubility.
Used analytical method could not verify testing concentration.
Analytical monitoring: HPLC
Source: Bayer AG Leverkusen
Test condition: Ultra-Turrax stirred for 60 sec
pH 8.0 - 8.2
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
06-NOV-2000 (8)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC50: 82
Method:
Year: GLP: no data
Test substance: other TS: MBTS purity =98%
Source: Monsanto
Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
06-NOV-2000 (26)

Type: other: calculated
Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 1.003
Method: other: ECOSAR Program (v0.99e)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
26-APR-2001 (11)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: other: growth rate, biomass
Exposure period: 72 hour(s)
Unit: Analytical monitoring: no
Method: other: Pruefrichtlinie "Algeninhibitionstest" (C.3) Richtlinie 67/548/EWG (Entwurf 1992)
Year: 1992 GLP: yes
Test substance: other TS: purity 97.8 %
Remark: No growth inhibition of the population tested within the range of water solubility of the substance. The only tested concentration was 40 mg/l, pH 8.1 - 10.3
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
06-NOV-2000 (8)

Species: other algae
Endpoint: other: cell count
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC50: .6
Method:
Year: GLP:
Test substance: other TS: MBTS purity = 98%
Remark: Sharen - check if 0.06 or 0.6 mg/l
Source: Monsanto
Bayer AG Leverkusen
06-NOV-2000 (27)

Species: other algae
Endpoint: other: chlorophyll a
Exposure period:
Unit: mg/l Analytical monitoring:
EC50: .7
Method:
Year: GLP:
Test substance: other TS: MBTS purity = 98%
Source: Monsanto
Bayer AG Leverkusen
06-NOV-2000 (27)

Species: other algae: green algae
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: c .731
ChV : c .34
Method: other: ECOSAR Program (v0.99e)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
26-APR-2001 (11)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: > 10000
Method: other: Test for Inhibition of Oxygen Consumption by Activated Sludge, ISO 8192
Year: 1988 GLP: yes
Test substance: other TS: technical grade
Remark: Direct weight, 6 mg/l inoculum (dry weight) from a laboratory bench-scale system
Source: Bayer AG Leverkusen
11-AUG-1993 (8)

Type: aquatic
Species: activated sludge
Exposure period:
Unit: mg/l Analytical monitoring: no data
EC75 : 38
Method: other: quantitative determination of the nitrification rate, colorimetric measurement of the NO2/NO3-concentration; static test system
Year: GLP: no
Test substance:
Remark: Pre-cleaned activated sludge in particle-free communal waste water (BSB5: 250 mg/l; NH4-N/l: 50-80 mg/l); determination of the effective concentration which caused a decrease of the 1st step of the nitrification rate (NH4 to NO2) of 75 %. Exposure period: 2-4 h.
Source: Bayer AG Leverkusen
Test condition: 25 degree C; pH 7.6-7.8
02-JUN-1993 (28)

Type: aquatic
Species: activated sludge, industrial
Exposure period: 4 hour(s)
Unit: mg/l Analytical monitoring: no data
EC50: 60
Method: other: Inhibition of cell reproduction; static test system; colorimetric measurement
Year: GLP: no data
Test substance:
Source: Bayer AG Leverkusen
Test condition: 37 degree C; pH 7
02-JUN-1993 (29)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species: other
Endpoint: other
Exposure period: 30 day
Unit: mg/l Analytical monitoring: no
ChV : c .154
Method: other: ECOSAR Program (v0.99e)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
26-APR-2001 (11)

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia sp. (Crustacea)
Endpoint: other
Exposure period: 16 day
Unit: mg/l Analytical monitoring: no
EC50: .165
Method: other: ECOSAR Program (v0.99e)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
26-APR-2001 (11)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:
Species: Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint:
Exposure period: 14 day
Unit: other: ppm
LC50: 310.082
Method: other: ECOSAR Program (v0.99e)
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Remark: Chemical may not be soluble enough to measure this predicted effect.
Reliability: (2) valid with restrictions
26-APR-2001 (11)

4.6.2 Toxicity to Terrestrial Plants

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: no information
Source: Bayer AG Leverkusen
05-AUG-1992

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring

Remark: no information
Source: Bayer AG Leverkusen
05-AUG-1992

4.8 Biotransformation and Kinetics

Type:
Remark: no information
Source: Bayer AG Leverkusen
05-AUG-1992

4.9 Additional Remarks

Remark: Soil fungi, growth inhibition test:
4 d LD50 = 0.5 % related to the growth of the control
14 d LD50 = 0.75 % related to the growth of the control
Test Condition: 25 degree C, aqueous soil extract, no data on concentrations used in the test, test substance incorporated in nutrient agar
Source: Bayer AG Leverkusen
25-MAY-1993 (30)

Remark: Soil fungi:
Species: Fusarium oxysporum sp. albedinis
Growth inhibition after 5 days, test substance concentration:
41.5 mg/l = 6 %
133 mg/l = 100 %
Source: Bayer AG Leverkusen
30-APR-1993 (31)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle: other: corn oil
Value: > 7940 mg/kg bw
Method: other
Year: GLP: no data
Test substance: other TS: MBTS purity 98%; 25 % solution in corn oil
Remark: method: 7 animals tested
remark: signs of intoxication: reduced appetite and activity one to three days; no mortality; viscera appeared normal
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
06-NOV-2000 (32)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 7000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (33)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 7000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (34)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 433 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
11-APR-1995 (35)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 12000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (36)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
remarks: mortality: 0/10
Source: Bayer AG Leverkusen
22-APR-1993 (37)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: ca. 7000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (38)

Type:
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 5000 - 8000 mg/kg bw
Method: other
Year: GLP: no data
Test substance: other TS: 40 % suspension in corn oil
Remark: method: 48 animals tested
remarks: no signs of intoxication
Source: Bayer AG Leverkusen
13-MAY-1993 (39)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 7000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (34)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 4631 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
11-APR-1995 (35)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 12000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (36)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 3370 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (40)

Type: LD0
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: < 2000 mg/kg bw
Method: other
Year: GLP: no data
Test substance: other TS: 40 % suspension in corn oil
Remark: mortality: 3/24 animals
Source: Bayer AG Leverkusen
13-MAY-1993 (39)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 6200 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
11-APR-1995 (35)

Type: LD0
Species: guinea pig
Strain:
Sex:
Number of Animals:
Vehicle:
Value: < 4000 mg/kg bw
Method: other
Year: GLP: no data
Test substance: other TS: 40 % suspension in corn oil
Remark: mortality: 2/8 animals
Source: Bayer AG Leverkusen
13-MAY-1993 (39)

5.1.2 Acute Inhalation Toxicity
-

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 7940 mg/kg bw
Method: other
Year: GLP: no data
Test substance: other TS: MBTS purity 98%
Remark: method: 3 animals tested
remarks: reduced appetite and activity in 1 to 2 d; no mortality; viscera appeared normal
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
06-NOV-2000 (41)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 2600 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (34)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 3000 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (34)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value:
Method:

Year: GLP: no data
Test substance: other TS: only code designations are given (B-23, EK-5432, Y-5)
Remark: method: no data
remarks: mortality not reported
value: > 2000 mg/kg; 100-200 mg/kg
Source: Bayer AG Leverkusen
11-APR-1995 (42)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 2250 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (40)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value: = 180 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
Source: Bayer AG Leverkusen
22-APR-1993 (43)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: see remarks
Year: GLP: no data
Test substance: no data
Remark: method: 10 g/kg was applied to the skin for 24 h
Source: Bayer AG Leverkusen
22-APR-1993 (38)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: Federal Hazardous Substances Act
Year: GLP: no data
Test substance: other TS: Purity = 98%
Remark: method: 0.5 g/animal (moistened with water) was applied to the skin for 24 h
Source: Bayer AG Leverkusen
26-APR-2001 (44)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method: Draize Test
Year: GLP: no data
Test substance: no data
Remark: 4 animals tested
result: according to authors: mild irritant
Source: Bayer AG Leverkusen

13-MAY-1993 (40)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: not irritating
EC classificat.:
Method:
Year: GLP:
Test substance:
Remark: 0.0/8.0
Source: Monsanto
Bayer AG Leverkusen

10-MAY-1994 (45)

Species: human
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result:
EC classificat.:
Method: other: application of dry form or oil solution to the skin of 6 persons for 24 h
Year: GLP: no data
Test substance: no data
Remark: no symptoms were observed
Source: Bayer AG Leverkusen

22-APR-1993 (46)

Species: human
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result:
EC classificat.:
Method: other: repeated insult patch test (see also chapter 5.3)
Year: GLP: no data
Test substance: no data
Remark: The result of the first application indicated that MBTS was incapable of acting as primary irritant of the immediate type in any of the 53 individuals under test.
Source: Bayer AG Leverkusen

22-APR-1993 (47)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method: Draize Test
Year: GLP: no data
Test substance: no data
Remark: 4 animals tested
result: according to authors: strongly irritating
Source: Bayer AG Leverkusen
13-MAY-1993 (40)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method: other: Federal Hazardous Substances Act
Year: GLP: no data
Test substance: no data
Remark: method: 100 mg/animal were applied as finely ground powder to the eyes
Source: Bayer AG Leverkusen
22-APR-1993 (48)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.:
Method:
Year: GLP:
Test substance:
Remark: 0.6/110.0
Source: Monsanto
Bayer AG Leverkusen
10-MAY-1994 (45)

5.3 Sensitization

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result:
Classification:
Method: other: original procedure of Magnusson & Klingman with some modifications
Year: GLP: no data
Test substance: other TS: serial dilutions in petrolatum
Remark: A new protocol and criteria for quantitative evaluation of sensitization potencies is presented. Known sensitizers (e.g. MBTS) are tested by changing the application concentrations for induction as well as for challenge
Source: Bayer AG Leverkusen
22-JAN-1996 (49)

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result: sensitizing
Classification:
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen
02-APR-1993 (50)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method: other
Year: GLP: no data
Test substance: other TS: 1% in petrolatum
Remark: 11/46 patients with occupational rubber dermatitis had a positive patch test result with MBTS
Source: Bayer AG Leverkusen
19-JAN-1996 (51)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method: other
Year: GLP: no data
Test substance: other TS: 2% in Eucerin
Remark: 1/2 patients with rubber dermatitis had a positive patch test result with MBTS
Source: Bayer AG Leverkusen
19-JAN-1996 (52)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method: other
Year: GLP: no data
Test substance: other TS: 1% in petrolatum
Remark: 29/686 rubber sensitized patients had a positive patch test result with MBTS
Source: Bayer AG Leverkusen
19-JAN-1996 (53)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method: other
Year: GLP: no data
Test substance: other TS: serial dilutions (1-0.0032%) in petrolatum
Remark: 12 rubber-sensitive subjects were tested, significant differences from none in response to the 1 % solution is reported (no further information)
Source: Bayer AG Leverkusen
19-JAN-1996 (54)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method: other
Year: GLP: no data
Test substance: other TS: 1% in petrolatum
Remark: 0/17 thiuram sensitized patients had a positive patch test result with MBTS
Source: Bayer AG Leverkusen
22-JAN-1996 (55)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method: other
Year: GLP: no data
Test substance: other TS: 1% in petrolatum
Remark: 2/3 patients with allergic contact dermatitis from rubber footwear had a positive patch test result with MBTS
Source: Bayer AG Leverkusen
22-JAN-1996 (56)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS
Remark: result: 17 subjects allergic to mercaptobenzothiazole were found positive when tested with a 1 % solution (solvent unknown); tests were negative in 20 controls
Source: Bayer AG Leverkusen
13-MAY-1993 (57)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS
Remark: result: 3/13 persons were allergic to the upper material of safety shoes containing mercaptobenzothiazole or the disulfide; tests with the pure substances (1 %) were negative
Source: Bayer AG Leverkusen
13-MAY-1993 (58)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS
Remark: result: 5/21 persons who had a contact dermatitis when wearing certain kind of shoes were positive when tested with 1 % of the test substance in petrolatum; 4 of these 5 persons also reacted positive with mercaptobenzothiazole
Source: Bayer AG Leverkusen
13-MAY-1993 (59)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS: 5 % in petroleum or polyethylene glycol
Remark: result: an 8-year old boy with contact dermatitis against tennis shoes reacted positive when tested with the test substance or mercaptobenzothiazole
Source: Bayer AG Leverkusen
13-MAY-1993 (60)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS: 0.25 % solution in paraffine
Remark: 0/6 persons reacted positive when tested with "mercaptomix", which, among others, contained the test substance
Source: Bayer AG Leverkusen
13-MAY-1993 (61)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS
Remark: result: 50/78 men and 33/70 women were positive when tested with 1 % of the test substance (solvent unknown); in most cases a cross reaction with mercaptobenzothiazole was noted
Source: Bayer AG Leverkusen
13-MAY-1993 (62)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS
Remark: result: 25/1698 persons reacted positive when tested with 2 % of the test substance diluted in paraffin; cross reactions with other vulcanization accelerators were noted.
Source: Bayer AG Leverkusen
13-MAY-1993 (63)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: no data
Remark: result: A miner with contact eczema had a positive patch test reaction with MBTS and MBT.
Source: Bayer AG Leverkusen
22-APR-1993 (64)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS: Vulkazite DM
Remark: result: 1/5 patients with contact dermatitis against rubber reacted positive (this patient reacted positive to other accelerators too)
Source: Bayer AG Leverkusen
22-APR-1993 (65)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS: 1 % in vaseline
Remark: result: 1/21 patients with contact dermatitis reacted positive
Source: Bayer AG Leverkusen
22-APR-1993 (66)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: other TS: 1 % pet.
Remark: result: 0/15 thiuram-sensitized patients reacted positive
Source: Bayer AG Leverkusen
22-APR-1993 (55)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP: no data
Test substance: no data
Remark: method: no data
result: 10/21 contact dermatitis patients against rubber showed a positive reaction (MBT was positive too)
Source: Bayer AG Leverkusen
22-APR-1993 (67)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle: Petrolatum
Result:
Classification:
Method:
Year: GLP:
Test substance: other TS: purity: 1 % in pet.
Result: 0/9 patients with contact dermatitis due to rubber boots reacted positive
Source: Bayer AG Leverkusen
04-NOV-1998 (68)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle: Petrolatum
Result:
Classification:
Method:
Year: GLP:
Test substance: other TS: 1 % in pet.
Remark: 1/11 patients with allergic patch test reactions caused by cyclohexyl thiophthalimide showed a positive reaction with MBTS
Source: Bayer AG Leverkusen
04-NOV-1998 (69)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle: Petrolatum
Result:
Classification:
Method:
Year: GLP:
Test substance:
Remark: A 45-year-old contact dermatitis patient due to a rubber disc reacted positive with MBTS among each other.
Source: Bayer AG Leverkusen
04-NOV-1998 (70)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle: Petrolatum
Result:
Classification:
Method:
Year: GLP:
Test substance: other TS: 1 % in pet.
Remark: 0/5 patients with allergic contact dermatitis caused by thiourea compounds showed a positive reaction with MBTS
Source: Bayer AG Leverkusen
04-NOV-1998 (71)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP:
Test substance:
Remark: 309/317 (1.9 %) patients tested with the rubber tray had a positive response to MBTS. 22 % had a positive response to at least 1 of the allergens on the rubber tray.
Source: Bayer AG Leverkusen
04-NOV-1998 (72)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle: other: vaseline
Result:
Classification:
Method:
Year: GLP:
Test substance: other TS: 0.5 % in vas.
Remark: 3/135 patients with skin problems due to rubber chemicals showed a positive allergic reaction with MBT
Source: Bayer AG Leverkusen
04-NOV-1998 (73)

Type: Patch-Test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP:
Test substance:
Remark: 30/53 patients with an allergic reaction to the Mercapto Mix showed a positive reaction with MBTS
Source: Bayer AG Leverkusen
04-NOV-1998 (74)

Type: other: see remarks
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method: other: see remarks
Year: GLP: no data
Test substance: other TS: 70 % preparation in petrolatum
Remark: method: repeated insult patch test;
a series of 12 applications (each of 24 h duration) of 0.2 g on the back of 53 persons was done through weeks 1-3, during week 6 a series of 4 applications (each of 24 h duration) of 0.2 g was done on virgin sites
result: according to authors: not sensitizing
Source: Bayer AG Leverkusen
13-MAY-1993 (47)

5.4 Repeated Dose Toxicity

Species: rat Sex: no data
Strain: no data
Route of admin.: oral feed
Exposure period: 31 days
Frequency of treatment: continuously in diet
Post. obs. period: no data
Doses: 5000, 10000 or 20000 ppm (approx. 375, 750 or 1500 mg/kg bw/d)
Control Group: no data specified
Method: other
Year: GLP: no data
Test substance: no data
Result: growth retardation, no pathological changes (no further details available)
Source: Bayer AG Leverkusen
13-MAY-1993 (38)

Species: rat Sex: female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 1st-21st day of gestation
Frequency of treatment: daily
Post. obs. period: yes
Doses: 0.04; 0.2; 1 % in diet (approx. 26, 127, 596 mg/kg/d)
Control Group: yes
NOAEL: 127 mg/kg
Method: other
Year: GLP: no data
Test substance: no data
Remark: see also chapter 5.8
Result: 596 mg/kg: weight reduction until 15th day of gestation
Source: Bayer AG Leverkusen
13-MAY-1993 (75)

Species: rat Sex: male
Strain: other: Wistar Albino
Route of admin.: gavage
Exposure period: 10 days
Frequency of treatment: daily
Post. obs. period: no data
Doses: 400 or 800 mg/kg bw/d
Control Group: no data specified
Method: other
Year: GLP: no data
Test substance: no data
Remark: oil suspension
no further information available
Result: 400 mg/kg: reduced concentrations of total and reduced glutathione in blood, reduced activity of AP-enzyme in serum (78 %) and GPT-enzyme in liver (90 %) and kidneys (80 %); changes of cell proteins in liver and kidneys
800 mg/kg: reduced concentrations of total and reduced glutathione in blood, reduced activity of AP-enzyme in serum (70 %) and GPT-enzyme in liver (90 %) and kidneys (58,5 %); no information about cell proteins; unchanged weights of liver, kidneys, mill and supra-renal glands.
Source: Bayer AG Leverkusen
13-MAY-1993 (39)

Species: rat Sex: male/female
Strain: other: Albino
Route of admin.: gavage
Exposure period: females: before pregnancy on the 1st and 3rd day of estrus
males: same time as females, but twice within 3 days
Frequency of treatment: see above
Post. obs. period: until 19th day of pregnancy
Doses: 200 mg/kg bw/d
Control Group: yes
Method: other: "pseudo dominant-lethal-test" (11 females, number of males not noted; in sunflower oil)
Year: GLP: no data
Test substance: no data
Remark: see also chapter 5.8
Result: females: no visible signs of poisoning
males: no data
Source: Bayer AG Leverkusen
13-MAY-1993 (76)

Species: rat Sex: female
Strain: Wistar
Route of admin.: gavage
Exposure period: whole gestation
Frequency of treatment: daily
Post. obs. period: no data
Doses: 10 or 100 mg/kg bw/d
Control Group: yes
Method: other
Year: GLP: no data
Test substance: no data
Remark: method: 60 animals tested; suspension in sunflower oil
remarks: no further information available
Result: 100 mg/kg: increased activity of glutamatoxalacetattrans-aminase (up to 116%) and glutamatpyruvattransaminase (up to 101%) on day 21, decreased activity of the liver enzymes
10 mg/kg: similar effects like 100 mg/kg, statistically not significant
Source: Bayer AG Leverkusen
13-MAY-1993 (77)

Species: rat Sex: female
Strain: Wistar
Route of admin.: gavage
Exposure period: 3 months
Frequency of treatment: daily
Post. obs. period: no data
Doses: 100 mg/kg bw/d
Control Group: yes
Method: other
Year: GLP: no data
Test substance: no data
Remark: method: 40 animals tested
remarks: no further information available
Result: no clinical signs of intoxication; inhibition of lactate- and malate-dehydrogenase activity
Source: Bayer AG Leverkusen
13-MAY-1993 (77)

Species: mouse Sex: male/female
Strain: other: C57BL/6xC3h/Anf, C57BL/6xAKR (both F1-hybrides)
Route of admin.: other
Exposure period: 3 weeks with stomach tube followed by 17 months in diet
Frequency of treatment: daily
Post. obs. period: no
Doses: 464 mg/kg bw/d (stomach tube); approx. 237 mg/kg bw/d (in diet)
Control Group: yes
Method: other
Year: GLP: no data
Test substance: no data
Remark: the maximal tolerated doses were given;
original data: 1577 ppm in diet
see also chapter 5.7
Result: no significant effects on organs observed during external and histologic examinations of major organs (no further information)
Source: Bayer AG Leverkusen
11-APR-1995 (78)

Species: guinea pig Sex: no data
Strain: no data
Route of admin.: inhalation
Exposure period: 6 days
Frequency of treatment: 1 hour/day
Post. obs. period: no data
Doses: 0.1 mg/l
Control Group: no data specified
Method: other
Year: GLP: no data
Test substance: no data
Remark: exposure to 2,2'-dithiobisbenzothiazole-dust; concentration (no data whether analytical or nominal): 100 mg/m3; no further information available
Result: no mortality; histopathological changes in liver (fatty tissue) and kidneys; pneumonia and bronchitis
Source: Bayer AG Leverkusen
13-MAY-1993 (40)

Species: guinea pig Sex: no data
Strain: no data
Route of admin.: oral unspecified
Exposure period: no data
Frequency of treatment: 5 times
Post. obs. period: no data
Doses: 0.5 or 1 g/kg bw
Control Group: no data specified
Method: other
Year: GLP: no data
Test substance: no data
Remark: no further information available
Result: 0.5 g/kg: no symptoms were observed
1 g/kg: 1/5 animals died after 76 h, the others showed reduced mobility and extreme indolence within 48 h, fatty tissue in the liver and granulated degeneration of the renal channel epithel
Source: Bayer AG Leverkusen
13-MAY-1993 (40)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: <= 0.1 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
13-MAY-1993 (79)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration: <= 0.1 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result:
Method: other
Year: GLP: no data
Test substance: no data
Remark: result: negative without S9 mix
weakly positive with S9 mix
Source: Bayer AG Leverkusen
13-MAY-1993 (80)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration: <= 5 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
13-MAY-1993 (81)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration: <= 1 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Remark: also negative result after in vitro nitrosation
Source: Bayer AG Leverkusen
13-MAY-1993 (82)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: <= 1 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: purity 95 %
Source: Bayer AG Leverkusen
13-MAY-1993 (83) (84)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration: no data
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
13-MAY-1993 (85) (86)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 1535
Concentration: <= 10 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
13-MAY-1993 (87)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 102
Concentration: <= 10 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
13-MAY-1993 (88)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 1535, TA 1538
Concentration: <= 1.0 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: 1982 GLP: yes
Test substance: other TS: no data
Remark: GLP: Signed Quality Unit Audit Statement
Source: Bayer AG Leverkusen
19-APR-1994 (89)

Type: Ames test
System of testing: Salmonella typhimurium
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance: other TS: MBTS purity = 98%
26-APR-2001 (90) (91)

Type: Bacterial gene mutation assay
System of testing: Escherichia coli WP2uvrA-
Concentration: <= 5 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: modified Ames test
Year: GLP: no data
Test substance: other TS: 80 % purity
Source: Bayer AG Leverkusen
13-MAY-1993 (81)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary cells
Concentration: <= 10 mg/l
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: 80 % purity
Source: Bayer AG Leverkusen
13-MAY-1993 (81)

Type: DNA damage and repair assay
System of testing: Escherichia coli W3110 (pol A+) and p3078 (pol A-)
Concentration: <= 5 mg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: ambiguous
Method: other
Year: GLP: no data
Test substance: other TS: 80 % purity
Remark: solubility prevents obtaining toxic dose in plate assay
Source: Bayer AG Leverkusen
13-MAY-1993 (81)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing:
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP:
Test substance:
Source: Monsanto
Bayer AG Leverkusen
10-MAY-1994 (92)

Type: HGPRT assay
System of testing: CHO cells
Concentration: 1.25 - 80 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: no data
Year: GLP: no data
Test substance: other TS: as prescribed by chapter 1 in dataset of ELF ATOCHEM
Remark: Year: 1982-1984
Source: ELF ATOCHEM S.A., France
Bayer AG Leverkusen
10-MAY-1994 (93)

Type: HGPRT assay
System of testing: CHO cells
Concentration: 25 - 1500 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: no data
Year: 1986 GLP: no data
Test substance: other TS: as prescibed by chapter 1 in dataset of ELF ATOCHEM
Source: ELF ATOCHEM S.A., France
Bayer AG Leverkusen
10-MAY-1994 (93)

Type: Mouse lymphoma assay
System of testing: mouse lymphoma cell line L5178Y TK+/-
Concentration: <= 30 mg/l
Cytotoxic Conc.:
Metabolic activation: with and without
Result:
Method: other
Year: GLP: no data
Test substance: other TS: 80 % purity
Remark: result: negative without S9 mix
positive with S9 mix (lowest active dose: 0.015 mg/ml)
Source: Bayer AG Leverkusen
13-MAY-1993 (81)

Type: Mouse lymphoma assay
System of testing: mouse lymphoma cells (no further information)
Concentration: no data
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: purity = 98%
Source: Bayer AG Leverkusen
26-APR-2001 (94)

Type: Mouse lymphoma assay
System of testing: L5178Y cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: MBTS purity = 98%
Remark: MBTS did not significantly induce mutations in the lk locus with or without metabolic activitation
Source: Monsanto
Bayer AG Leverkusen
06-NOV-2000 (95)

Type:
System of testing: Salmonella
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance: other TS: trapped effluent samples containing phr MBTS
Source: Monsanto
Bayer AG Leverkusen
26-APR-2001 (96) (97)

5.6 Genetic Toxicity 'in Vivo'

Type: other
Species: Sex: male/female
Strain:
Route of admin.: oral unspecified
Exposure period: twice within 3 days (m); 1st 3rd day of oestrus
Doses: 200 mg/kg
Result:
Method: other
Year: GLP: no data
Test substance: other TS: Altax
Remark: Unsuitable test system (e.g. treatment of both sexes)
Result: Increased postimplantation embryonic mortality (= "index of mutagenicity")
Source: Bayer AG Leverkusen
23-JAN-1996 (76)

5.7 Carcinogenicity

Species: mouse Sex: male/female
Strain: other: C57BL/6xC3h/Anf, C57BL/6xAKR (both F1-hybrides)
Route of admin.: other
Exposure period: 3 weeks with stomach tube followed by 17 months in diet
Frequency of treatment: daily
Post. obs. period: no
Doses: 464 mg/kg bw/d (stomach tube), approx. 237 mg/kg bw/d (in diet)
Result:
Control Group: yes
Method: other
Year: GLP: no data
Test substance: no data
Remark: number of animals: 18 of each sex of each strain
necropsy: external examination with histologic examination of major organs and of all grossly visible lesions

(no further information)
strains: C57BL/6xC3h/Anf, C57BL/6xAKR (both F1-hybrides)
original data: 1577 ppm in diet
see also chapter 5.4.

Result: no significant increase of tumors
Source: Bayer AG Leverkusen
11-APR-1995 (78)

Species: mouse Sex: male/female
Strain: other: B6C3F1, B6AKF1
Route of admin.: s.c.
Exposure period: once on 18th day of life
Frequency of treatment:
Post. obs. period: 18 months
Doses: 1000 mg/kg
Result:
Control Group: yes
Method: other
Year: GLP: no data
Test substance: no data
Remark: method: 18 animals/sex tested; in gelatine
remarks: strains: B6C3F1, B6AKF1
Result: The tumor rate was not increased significantly compared to control animals (0.5 % gelatine)
Source: Bayer AG Leverkusen
13-MAY-1993 (98)

Species: other: (see method) Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method: other: celltransformation test with BALB/3T3 cells according to Kakunaga, T., Int. J. Cancer 12, 463-473 (1973); in DMSO
Year: GLP: no data
Test substance: other TS: 80 % purity
Remark: result: number of foci not increased
Source: Bayer AG Leverkusen
22-APR-1993 (81)

5.8 Toxicity to Reproduction

Type: other
Species: rat Sex: male/female
Strain: other: Albino
Route of admin.: gavage
Exposure Period: females: before pregnacy, on the 1st and 3rd day of estrus - males: at the same time as females, twice within 3 days
Frequency of treatment: see above
Duration of test: sacrifice on day 19
Doses: 200 mg/kg bw
Control Group: yes
Method: other
Year: GLP: no data
Test substance: no data
Remark: unsuitable test system (e.g. number of males not noted; treatment of both sexes)
Result: dams: no visible signs of poisoning; changes in the estrus cycle, often no conception in the next cycle, greatest retardation of cycle: 6.9+/-0.9 days
offspring: decreased body weight, decreased fertility (46 %), increased embryo mortality (56.4+/-3.8 %; controls: 10.9+/-1.6 %), increased postimplantation loss (30.8+/-4.4 %; controls: 4.6+/-1.1 %)
Source: Bayer AG Leverkusen
23-JAN-1996 (76)

Type: other: (see method)
Species: Sex:
Strain:
Route of admin.:
Exposure Period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method: other: test substance was tested for embryotoxicity and induction of malformations in three-day chicken embryos (application: injection into the air bubble of the egg or into the heart); in acetone
Year: GLP: no data
Test substance: no data
Remark: result: no effects were observed
Source: Bayer AG Leverkusen
22-APR-1993 (99) (100)

5.9 Developmental Toxicity/Teratogenicity

Species: rat Sex: female
Strain: other: Albino
Route of admin.: gavage
Exposure period: 8 days
Frequency of treatment: on day 4 and 11 of gestation
Duration of test: sacrifice on day 19
Doses: 200 mg/kg bw
Control Group: yes
Method: other
Year: GLP: no data
Test substance: no data
Remark: method: 15 animals tested; in corn oil
Result: Foetal data: decreased weight of fetuses; increase of total embryo mortality (37.8+/-3.2 %; controls:10.9+/-1.6%); Maternal general toxicity:lengthening of oestrus cycle and reduced fertility (30 %); increased postimplantation loss (15.4+/-2.7%; controls: 4.6+/-1.1 %)
Source: Bayer AG Leverkusen
06-NOV-2000 (76)

Species: rat Sex: female
Strain: Wistar
Route of admin.: gavage
Exposure period: whole gestation
Frequency of treatment: daily
Duration of test:
Doses: 10 or 100 mg/kg bw
Control Group: yes
Method: other
Year: GLP: no data
Test substance: no data
Remark: method: 30 animals/dose; in grease
Result: 10 mg/kg: no embryotoxic effects
100 mg/kg: no embryotoxic effects, changes in enzyme activities of liver and blood, increased relative organ weights of liver and kidneys, reduced RNA in liver cells, slightly dystrophic alterations in placentae
Source: Bayer AG Leverkusen
13-MAY-1993 (101)

Species: rat Sex: female
Strain: Wistar
Route of admin.: oral feed
Exposure period: 1st-21st day of gestation
Frequency of treatment: daily
Duration of test: see remarks
Doses: 0.04; 0.2; 1 % in diet (approx. 26, 127, 596 mg/kg/d)
Control Group: yes
NOAEL Maternalt.: .2 %
NOAEL Teratogen.: 1 %
Method: other
Year: GLP: no data
Test substance: no data
Remark: method: no data
NOEL (parenteral): 127 mg/kg bw
NOEL (offspring): 596 mg/kg
remarks:
follow-up period:
I. sacrifice of dams on day 21 of gestation
II. sacrifice of dams on day 21 after birth and offspring <= 7 weeks after birth
Result: 26, 127 mg/kg: no teratogenic effects;
596 mg/kg: weight reduction of dams until 15th day of gestation; no teratogenic effects
Source: Bayer AG Leverkusen
06-NOV-2000 (75)

Species: rat Sex: female
Strain: other: Wistar, Hybrid
Route of admin.: oral unspecified
Exposure period: 1st-21st, 1st-7th, 8th-12th or 13th-17th day of gestation
Frequency of treatment: daily
Duration of test:
Doses: 10 or 100 mg/kg bw/d
Control Group: yes
NOAEL Teratogen.: 10 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: method: 120 animals tested; in water solution
NOEL (parenteral): no data
NOEL (offspring): 10 mg/kg
Result: 10 mg/kg: no embryotoxic effects
100 mg/kg:
1st-21st day of gestation: increased mortality of embryos, increased frequency of autolysis, reduced weight of embryos, changes of cranium dimensions, internal hydrocephalus, intracerebral hematoma, isolated hematoma (54.5%);
13th-17th day of gestation: increased mortality of embryos, increased frequency of autolysis, reduced weight of embryos, anormal ossification of the brain;
1st-7th and 8th-12th day of gestation: anormal ossification

of the brain
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
26-APR-2001 (102)

Species: mouse Sex: female
Strain: other: N strain
Route of admin.: oral unspecified
Exposure period: whole gestation
Frequency of treatment: daily
Duration of test: sacrifice at the end of gestation
Doses: 10 or 100 mg/kg
Control Group: yes
NOAEL Teratogen.: 10 mg/kg bw
Method: other
Year: GLP: no data
Test substance: no data
Remark: method: 40 animals tested; in water solution
NOEL (offspring): 10 mg/kg
Result: 10 mg/kg: no embryotoxic or teratogenic effects
100 mg/kg: no embryotoxic effects;
teratogenic effects: exencephalia, hypognatia, edema (5.5%; control: no data), hydrocephalia (72.7%; control: 33.3%), microphtalmia (9.1%; control: 4.8%).
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
26-APR-2001 (102)

5.10 Other Relevant Information

Type: Biochemical or cellular interactions
Remark: test substance: no data
remark: The results of in vitro experiments show that MBT is the only stable compound of different mercaptobenzo-thiazoles (e.g. MBTS) when reducing sulfhydryl compounds are present; these findings may explain the cross-sensitivities reported for the mercaptobenzothiazoles.
Source: Bayer AG Leverkusen
22-APR-1993 (103)

Type: other
Remark: revision: 10/98
Source: Bayer AG Leverkusen
04-NOV-1998

Type: other: effects on blood sugar
Remark: test substance: no data
effects: 100 mg/kg i.p. in physiological sodium chloride solution tended to increase blood sugar of 3 rabbits which had alloxan derived diabetes
Source: Bayer AG Leverkusen
22-APR-1993 (104)

Type: other: enzyme activity
Remark: test substance: no data
effects: 33.25 mg/kg given by stomach tube to female rats increased the benzpyrene hydroxylase activity in the liver after 48 h (1.5 fold in comparison with controls), but not in the lung
Source: Bayer AG Leverkusen
04-NOV-1998 (105)

Type: other: enzyme activity
Remark: test substance: no data
effects: < 2.33 mg/l in vitro did not have an activation effect on the carbohydrate metabolism of Ehrlich Ascites tumor cells
Source: Bayer AG Leverkusen
22-APR-1993 (106)

Type: other: metabolism/pharmacokinetics
Remark: test substance: purity of unlabeled test substance 94-99.4%; radiochemical purity 94.1-100%
effects: F 344 rats (4m/4f) were dosed by gavage with 0.547 mg/kg bw/d in corn oil for 14 d. Then they received a single oral dose of 0.73 mg/kg bw of the 14C-labeled test substance. After 96 h 60.8% (m) or 81.7% (f) of the radioactivity were found in urine and 8.6% (m) or 3.5% (f) in the feces, indicating that the test substance is well absorbed from the gastro-intestinal tract.
8 h after application of the labeled dose elevated levels of radioactivity were found in the thyroid glands and in the erythrocytes and kidneys; comparably low concentrations were found in the gonads and spleen. After 96 h tissue concentrations were generally low; the highest concentrations were in whole blood and thyroid.
Elimination half-life values (h) were as follows:

	alpha phase	beta phase
whole blood:	not discernable	239 (m), 3840 (f)
plasma:	4.32 (m), 3.91 (f)	102 (m), 138 (f)

Radioactivity excreted in the urine was confined to two polar metabolites being most probably a thioglucuronide and a sulfonic acid derivative of the monomer 2-mercaptobenzo-thiazole.
Source: Bayer AG Leverkusen
22-APR-1993 (107)

Type: other: metabolism/pharmacokinetics
Remark: test substance: purity of unlabeled test substance, as far as stated; analytical grade
effects: F 344 rats (4/dose/sex) were dosed by gavage with 0.438 or 51.1 mg/kg bw of the 14C-labeled test substance in corn oil. After 96 h most of the radioactivity was found in the urine (low dose: 95.8% (m), 82.9% (f); high dose: 94.3% (m), 90.7% (f)) and minor amounts in the feces (low dose: 7.27% (m), 4.91% (f); high dose: 10.3% (m), 4.94% (f)).
Elimination half-life values (h) were as follows:

	alpha phase	beta phase
low dose:		
whole blood:	7.63 (m), 4.58 (f)	7500 (m), 289 (f)
plasma:	4.32 (m), 3.91 (f)	102 (m), 138 (f)
high dose:		
whole blood:	6.39 (m), 8.03 (f)	25400 (m), 9610 (f)
plasma:	4.78 (m), 4.18 (f)	50200 (m), 6490 (f)

7 not identified metabolites were found in the urine.
Source: Bayer AG Leverkusen
22-APR-1993 (108)

Type: other: metabolism/pharmacokinetics
Remark: test substance: test substance contained 6-17% 2-mercapto-benzothiazole resulting from the peroxidizing activity of the solvent tetrahydrofuran.
effects: F 344 rats (4 animals/sex) were injected a single dose of the 14C-labeled test substance (0.571 mg/kg bw) into the tail vein. After 72 h most of the radio activity was found in the urine (92.9% (m), 101.9% (f)) and minor amounts in the feces (9.64% (m), 3.82% (f)).
Elimination half-life values (h) were as follows:

	alpha phase	beta phase
whole blood:	0.87 (m), 0.47 (f)	89.9 (m), 55.1(f)
plasma:	1.29 (m), 0.64 (f)	18.9 (m), 13.2 (f)

Source: Bayer AG Leverkusen
22-APR-1993 (107)

Type: other: metabolism/pharmacokinetics
Remark: test substance: purity of unlabeled test substance 94-99.4%; radiochemical purity: 94.1-100%
effects: 96 h after occlusive application of a single dose of the 14C-labeled test substance in tetrahydrofuran (0.034 mg/animal) on the scarified skin (area: 2 cmE2) of F 344 rats (4 animals/sex) 88.2% (m) resp. 92.8% (f) of the total absorbed dose were found in urine and 8.7% (m) resp. 5.3% (f) in the feces.
Elimination half-life values (h) were as follows:

	alpha phase	beta phase
whole blood:	0.87 (m), 0.47 (f)	89.9 (m), 55.1 (f)
plasma:	1.29 (m), 0.64 (f)	18.9 (m), 13.2 (f)

Source: Bayer AG Leverkusen
22-APR-1993 (107)

Type: other: metabolism/pharmacokinetics
Remark: test substance: purity of unlabeled test substance 94-99.4% radiochemical purity 94.1-100%.
effects: 96 h after occlusive application of a single dose of the 14C-labeled test substance in tetrahydrofuran (0.034 mg/animal) on the scarified skin (area: 5 cmE2) of 3 female guinea pigs (Hartley) 96.7% of the total absorbed dose were found in the urine and 2.3% in the feces.
Source: Bayer AG Leverkusen
22-APR-1993 (107)

Type: other: metabolism/pharmacokinetics
Remark: After a single dose of 25 mg 14C-MBTS/rat over 90% of the S atoms of urinary metabolites were derived from the parent compound (no detailed information on the metabolites).
Excretion predominately into faeces (71.9% radioactivity).
Source: Bayer AG Leverkusen
23-JAN-1996 (109)

Type: other: metabolism/pharmacokinetics
Remark: A single oral dose of 125 mg 14C-MBTS/kg (3m): ca. 21% radioactivity in urine and 72% in faeces (total recovery after 3 days = 93%)
Single injection of 14C-MBTS into the jejunal loop: The radioactivity absorbed was ca. 6.4% shared between MBT and MBTS with a ratio of 1:3 in the plasma.
Incubation with rat liver/kidney homogenate: Transformation to MBT and its glucoronide and sulfate.
Source: Bayer AG Leverkusen
24-JAN-1996 (110)

5.11 Experience with Human Exposure

Remark: In a repeat insult patch test conducted with 53 human volunteers, MBTS did not demonstrate that it was a primary or a cummulative irritant or a skin sensitizer.
Source: Monsanto
Bayer AG Leverkusen
10-MAY-1994 (111)

(1) Windholz, M., The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals, 10th ed. Rahway, New York, 492-493 (1983)

(2) Keith, L.H. & Walters, D.B., Compendium of Safety Data Sheets for Research and Industrial Chemicals, VCH, Verlagsgesellschaft mbH, Weinheim, 2462-2465 (1987)

(3) Bayer data, DIN-Sicherheitsdatenblatt Dibenzothiazyldisulfid (MBTS), Bayer AG, Leverkusen (1988)

(4) Monsanto data

(5) Boberg, M. et al., Thiazole und Isothiazole; Benzothiazole, cited in: Ullmanns Enzyklopaedie der technischen Chemie, 4. Aufl., Bd. 23, Verlag Chemie, 143-151 (1983)

(6) Merck Index (1989)

(7) Kempermann, T. & Eholzer, U., Bayer AG, Leverkusen, T.I.B. Kautschuk-Chemikalien, Nr. 1.8., 8 pp. (1983)

(8) Bayer AG data

(9) Monsanto Studies SR-83X-64 and SR-85-X017

(10) SRI International, Project No. 8669 from 20.8.1980

(11) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(12) SRI International, Project No. 8669 from 20.8.1990

(13) Monsanto SR-83-64, SR 85-017 SRI International, 1983 and 1985.

(14) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Compiled under the Supervision of Chemical Products Safety Division, Basic Industries Bureau MITI, Ed. by CITI, October 1992. Published by Japan Chemical Industry Ecology-Toxicology & Information Center

(15) Monsanto Studies SR-83X-64 and SR-85-X017 (1983 and 1985)

(16) Behnke, W., Berechnung nach Atkinson zum photochemischen Abbau in der Athmosphaere. Unveroeffentlichte Berechnung, Fraunhofer-Institut fuer Toxikologie und Aerosolfoschung, Abt. Physikalische Chemie, Hannover (1990)

(17) Abdou, W.M. et al., Z. Naturforsch. 42b, 1153-1158 (1987)

(18) Monsanto Study AB-84X-129 (ES-80-SS-42), Analytic Bio-Chemistry Lab, 1984

(19) Monsanto Co. data, NTIS OTS0206761, EPA OTS document

(20) Environmental Agency Japan, Background paper on the experience of the environmental monitoring of chemical substances in Japan. Proceedings of the workshop on the control of existing chemicals under the patronage of the OECD. Umweltbehoerde Japan, Umweltbundesamt Berlin, 165 - 189 (1981)

(21) Bosch et al., Technical support document 2-Mercaptobenzthiazoles (SRC-TR-85-104; Contract No. 68-02-4209). Syracuse Research Corporation, Syracuse, New York (1985)

(22) Monsanto Study BN-76-170, EG&G Bionomics (1976)

(23) Monsanto Study BN-79-219, EG&G Bionomics (1979)

(24) Monsanto Study BN-76-170

(25) Monsanto Study SR-83X-64 and SR-85-X017

(26) Monsanto Study BN-79-220, EG&G Bionomics (1979)

(27) Monsanto Study BN-79-218, EG&G Bionomics (1979)

(28) Tomlinson, T.G. et al., J. Appl. Bact. 29, 266-291 (1966)

(29) Suzuki, S. & Nakajima, T., Kogyo Yosui 103, 50-53 (1967)

(30) Williams, G.R., Int. Biodeterior. 20, 173-175 (1984)

(31) Bounaga, N., Phytopath. Z. 98, 210-217 (1980)

(32) Younger Laboratories, Monsanto Co., St. Louis, Missouri (1973); Monsanto Study Y-73-190

(33) Vanderbilt data, Material Safety Data Sheet for Benzothiazyl Disulfide, R.T. Vanderbilt Co., Inc., Norwalk, Connecticut (1990)

(34) Food Preserves Hygiene Council Reports No. 22, 17 (1973); cited in: Takahashi, A., Int. Polym. Sci. Techn. 3, 93-105 (1976)

(35) Vaisman, Y.I. et al., Gig. Sanit. 30, 17-21 (1973)

(36) Vernot, E.H. et al., Toxicol. Appl. Pharmacol. 42, 417-423 (1977)

(37) Sumitomo data, Acute oral toxicity of Soxinol DM in rats, Sumitomo Chemical Co. LTD., report No. PDT-No. C-77-114 (1977)

(38) Amer. Cyan. Co.; cited in: McCormick, W.E., Rubber Chem. Technol. 44, 512-533 (1971)

(39) Radeva, M., Chig. Chran. 23, 326-330 (1980) (in Bulgarisch; dtsch. Kurzuebersetzung)

(40) Kowalski, Z. & Bassendowska, E., Medycina Pracy 16, 35-43 (1965) (in Polnisch; dtsch. Kurzuebersetzung)

(41) Younger Laboratories, Monsanto Co., St. Louis, Missouri (1973); Monsanto Study Y-73-190 and Y-72-327

(42) Doull, J. et al., Armed Services Technical Information Agency, Arlington, Virginia, NTIS-Publication No. AD 277-689 (1962)

(43) US Army data; cited in: RTECS data base (1992)

(44) Younger Laboratories, Monsanto Co., St. Louis, Missouri (1973) Study# Y-73-190

(45) Monsanto Study Y-73-190

(46) IG Farben, Mitteilung des Gewerbehygienischen I. G. Labors vom 30.7.31 (unpublished). Ludwigshafen (1931)

(47) Monsanto data, Monsanto Company, St. Louis, Missouri, report No. PI 2600, 30 pp. (1982)

(48) Younger Laboratories, Monsanto Co., St. Louis, Missouri (1973)

(49) Nakamura, A. et al., Contact Dermatitis 31, 72-85 (1994)

(50) Kaniwa, M.-A. et al., Contact Dermatitis 27, 166-173 (1992)

(51) Kiec-Swierczynska, Contact Dermatitis 32, 171-172 (1995)

(52) Bandmann, H.J. & Nasemann, Th., Der Hautarzt 9, 40-41 (1958)

(53) Conde-Salazar, L. et al., Journal of the American Academy of Dermatology 29, 176-180 (1993)

(54) Emmet, E.A. et al., Contact Dermatitis 30, 85-90 (1994)

(55) Knudsen, B.B. et al., Contact Dermatitis 28, 63-69 (1993)

(56) Kaniwa, M.-A. et al., Contact Dermatitis 30, 26-34 (1994)

(57) Foussereau, J. et al., Contact Dermat. 9, 514-516 (1983)

(58) Foussereau, J. et al., Contact Dermat. 14, 233-236 (1986)

(59) Blank, I.H. & Miller, O.G., J. Am. Med. Assoc. 149, 1371-1374 (1952)

(60) Jung, J.H. et al., Contact Dermat. 19, 254-259 (1988)

(61) Te Lintum, J.C.A. & Nater, J.P., Berufsdermatosen 21, 16-22 (1973)

(62) Cronin, E., Churchill Livingstone, Edinburgh, London, New York, 915 pp. (1980)

(63) Rudzki, E. et al., Contact Dermatitis 2, 24-27 (1976)

(64) Hegyi, E. Prac. Lek. 42 (10), 436-437 (1990)

(65) Bandmann, H.-J., Hautarzt 7, 419-421 (1956)

(66) Frosch, P.J. et al., Hautarzt 38, 210-217 (1987)

(67) Schultheiss, E., Berufsdermatosen 7, 76-97 (1959)

(68) Nishioka, K. et al., Contact Dermatitis 35, 241-245 (1996)

(69) Kanerva, L. et al., Contact Dermatitis 34, 23-26 (1996)

(70) Mitxelena, J. et al., Contact Dermatitis 38, 181-182 (1998)

(71) Kanerva, L. et al., Contact Dermatitis 31, 242-248 (1994)

(72) Holness, D.L. & Nethercott, J.R., Contact Dermatitis 36, 207-211 (1997)

(73) Heise, H. et al., Dermatosen 45, 226-228 (1997)

(74) Geier, J. & Gefeller, O., Am. J. Contact Dermatitis 6, 143-149 (1995)

(75) Ema, M. et al., J. Appl. Toxicol. 9, 413-417 (1989)

(76) Aleksandrov, S.E., Byull. Eks. Biol. Med. 93, 87-88 (1982) (in Russisch; engl. Uebersetzung)

(77) Mirkova, E., Chig. Zdraveop. 23, 414-419 (1980) (in Bulgarisch; dtsch. Kurzuebersetzung)

(78) Innes, J.R.M. et al., J. Nat. Cancer Inst. 42, 1101-1114 (1969)

(79) Goodyear data, laboratory report No. 79-58, Akron., Ohio, November 8 (1979)

(80) You, X. et al., Huanjing Kexue 3, 39-42 (1982) (in Chinesisch; dtsch. Uebersetzung)

(81) Hinderer, R.K. et al., Environ. Mutagenesis 5, 193-215 (1983)

(82) Crebelli, R. et al., Toxicol. Lett. 23, 307-313 (1984)

(83) Crebelli, R. et al., Brit. J. Ind. Med. 42, 481-487 (1985)

(84) Crebelli, R. et al., IARC Sci. Publ. 59, 289-295 (1984)

(85) Donner, M. et al., Scand. J. Work Environ. Health 9, 27-37 (1983)

(86) Rannug, A. et al., Prog. Clin. Biol. Res. 141, 407-419 (1984)

(87) Zeiger, E., Environ. Mol. Mutagen. 11, Suppl. 12, 1-158 (1988)

(88) Hinderer, R.K., Ames Salmonella Microsome, BFG Quality Assurance Unit (1984)

(89) The BF Goodrich Company data, 12-15-1982, Laboratory Identification Number 14

(90) Industrial Hazards of Plastics & Synthetic Elastomers (1984)

(91) Monsanto BO-76-178, Litton Bionetics (1976)

(92) Monsanto Study BO-76-178

(93) ELF ATOCHEM, Synopsis of Mutagenicity Data, 2-Mercaptobenzothiazole disulfide, August 1986

(94) Monsanto data (1982); cited in: Bosch, S.J. et al., Technical Support Document: 2-Mercaptobenzothiazoles. Syracuse Research Corporation, New York (1985)

(95) Monsanto Study BO-78-239, Litton Bionetics (1978)

(96) Monsanto Study ML-79-39

(97) Monsanto Study ML-79-44

(98) NCI, Public Health Service Publication No. 149, National Cancer Institute, Washington, D.C., Government Printing Office (1968), cited in: Holleman, J., Chemical Hazard Information Profile (Draft Report): Mercaptobenzothiazole disulfide (MBTS) (CAS-No. 120-78-5). Chemical Effects Information Center, Oak Ridge National Laboratory, 32 pp (1983).

(99) Korhonen, A. et al., Arch. Environ. Contam. Toxicol. 11, 735-759 (1982)

(100) Korhonen, A. et al., Scand. J. Work Environ. Health 9, 115-119 (1983)

(101) Radeva, M. & Dinoeva, S., Chig. Zdraveop. 26, 51-55 (1983) (in Bulgarisch; dtsch. Kurzuebersetzung)

(102) Mirkova, E., Probl. Higien. 5, 83-91 (1980) (in Russisch; engl. Uebersetzung)

(103) Hansson, C. and Agrup, G., Contact Dermatitis 28, 29-34 (1993)

(104) Chiba, T., Yakugaku Zasshi 89, 1138-1143 (1969) (in Japanisch; dtsch. Kurzuebersetzung)

(105) Wattenberg, L.W. et al., Cancer Res. 28, 2539-2544 (1968)

(106) Grassetti, D.R. et al., J. Med. Chem. 13, 273-276 (1970)

(107) El Dareer, S.M. et al., J. Toxicol. Environ. Health 27, 65-84 (1989)

(108) Hill, D.L., Disposition of 2-mercaptobenzothiazole-ring-UL-14C and 2-mercaptobenzothiazole disulfide-ring-UL-14C in Fischer-344 male and female rats dosed orally. Southern Research Institute, Birmingham, Alabama, 46 pp. (Report 5873-I) (1986)

(109) Fukuoka, M. & Tanaka, A., Arch. Toxicol. 61, 158-160 (1987)

(110) Fukuoka, M. et al., Arch. Toxicol. 70, 1-9 (1995)

(111) Monsanto Study SH-82-9

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

201-14953B1

IUCLID

Data Set

RECEIVED
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Existing Chemical	:	ID: 149-30-4
CAS No.	:	149-30-4
EINECS Name	:	benzothiazole-2-thiol
EC No.	:	205-736-8
TSCA Name	:	2(3H)-Benzothiazolethione
Molecular Formula	:	C7H5NS2

Producer related part

Company	:	Bayer Corporation
Creation date	:	15.07.1999

Substance related part

Company	:	Bayer Corporation
Creation date	:	15.07.1999
Status	:	
Memo	:	American Chemistry Council, Rubber and Plastic Additives Panel, Benzothiazole-based Thiazoles Category
Printing date	:	18.06.2003
Revision date	:	
Date of last update	:	18.06.2003
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

Type	:	lead organisation
Name	:	American Chemistry Council - Rubber and Plastics Additives Panel (RAPA)
Contact person	:	
Date	:	
Street	:	1300 Wilson Boulevard
Town	:	22209 Arlington, VA
Country	:	United States
Phone	:	703-741-5600
Telefax	:	703-741-6091

26.04.2001

Type	:	cooperating company
Name	:	Bayer Polymers LLC (a wholly-owned subsidiary of Bayer Corporation
Contact person	:	
Date	:	
Street	:	100 Bayer Road
Town	:	PA 15205-9741 Pittsburgh
Country	:	United States

15.05.2003

Type	:	cooperating company
Name	:	Crompton Corporation
Contact person	:	
Date	:	
Street	:	Benson Road
Town	:	06749 Middlebury, CT
Country	:	United States

15.05.2003

Type	:	cooperating company
Name	:	Flexsys America L.P.
Contact person	:	
Date	:	
Street	:	260 Springside Drive
Town	:	44333-0444 Akron, OH
Country	:	United States

16.05.2003

Type	:	cooperating company
Name	:	Noveon, Inc.
Contact person	:	
Date	:	
Street	:	9911 Brecksville Road
Town	:	44141-3247 Cleveland, OH
Country	:	United States

16.05.2003

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	:	2(3H)-Benzothiazolethione
Smiles Code	:	N(c(c(S1)ccc2)c2)=C1S
Molecular formula	:	C7 H5 N1 S2
Molecular weight	:	167.24
Petrol class	:	

15.05.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	organic
Physical status	:	solid
Purity	:	> 96 - % w/w
Colour	:	
Odour	:	

15.05.2003

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

2(3H)-benzothiazolethione

20.10.1999

2-mercaptobenzothiazole

20.10.1999

MBT

20.10.1999

1.3 IMPURITIES

Purity	:	
CAS-No	:	7704-34-9
EC-No	:	231-722-6
EINECS-Name	:	sulphur
Molecular formula	:	
Value	:	< 1 - % w/w

15.05.2003

Purity	:	
CAS-No	:	
EC-No	:	
EINECS-Name	:	N-Phenyl-2-benzothiazolamine
Molecular formula	:	
Value	:	< 1 - % w/w

15.05.2003

Purity	:	
CAS-No	:	934-34-9
EC-No	:	213-281-1
EINECS-Name	:	benzothiazol-2(3H)-one
Molecular formula	:	
Value	:	< .5 - % w/w

15.05.2003

1.4 ADDITIVES

Purity type	:	
CAS-No	:	8042-47-5
EC-No	:	232-455-8
EINECS-Name	:	White mineral oil (petroleum)
Molecular formula	:	
Value	:	0 - 2 % w/w
Function of additive	:	Dust control agent

15.05.2003

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

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	:	TSCA
Additional information	:	

15.05.2003

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

2.1 MELTING POINT

Value : 181 - °C
Sublimation :
Method : other: Handbook value
Year :
GLP :
Test substance :

Reliability : (2) valid with restrictions
Data from Handbook or collection of data
Flag : Critical study for SIDS endpoint
06.11.2000 (1)

Value : = 180.2 - 181.7 °C
Decomposition : no, at - °C
Sublimation :
Method : other: Handbook value
Year :
GLP :
Test substance :

Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Data from Handbook or collection of data
Flag : Critical study for SIDS endpoint
26.04.2001 (2)

2.2 BOILING POINT

Value : > 260 - °C at 1013 hPa
Decomposition : yes
Method :
Year :
GLP : no data
Test substance : other TS: 2-mercaptobenzothiazole (CAS# 149-30-4); purity not noted

Remark : Decomposes above 260 degrees centigrade.
Source : Bayer AG Leverkusen
Reliability : (3) invalid
Documentation insufficient for assessment
Flag : Critical study for SIDS endpoint
15.05.2003 (3)

2.3 DENSITY

Type : density
Value : = 1.42 - g/cm3 at 20 °C
Method : other: Handbook value
GLP : no data
Test substance :

Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Data from Handbook or collection of data
Flag : Critical study for SIDS endpoint
06.11.2000 (1) (4)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	< .000003 - hPa at 25 °C
Decomposition	:	
Method	:	OECD Guide-line 104 "Vapour Pressure Curve"
Year	:	1981
GLP	:	yes
Test substance	:	
Remark	:	Method similar to OECD test method 104. This procedure employed the gas saturation technique.
Source	:	Bayer AG Leverkusen
Reliability	:	(1) valid without restriction GLP Guideline study
Flag	:	Critical study for SIDS endpoint

06.11.2000 (5)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	
Log pow	:	= 2.34 - 2.5 at °C
pH value	:	-
Method	:	other (measured)
Year	:	1980
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Bayer AG Leverkusen
Reliability	:	(2) valid with restrictions Method did not follow OECD guidelines. Samples analyzed at one test concentration only.
Flag	:	Critical study for SIDS endpoint

15.05.2003 (6)

Partition coefficient	:	
Log pow	:	2.41 - at °C
pH value	:	-
Method	:	other (measured)
Year	:	
GLP	:	no data
Test substance	:	other TS: 2-mercaptobenzothiazole (CAS# 149-30-4); purity not noted
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment

15.05.2003 (7)

Partition coefficient	:	
Log pow	:	2.862 - at 25 °C
pH value	:	-
Method	:	other (calculated): KOWWIN Program (v1.65)
GLP	:	no
Test substance	:	other TS: molecular structure
Reliability	:	(2) valid with restrictions Accepted calculation method

15.05.2003 (8)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 118 - mg/l at 25 °C
pH value	:	= 7 -
concentration	:	at °C
Temperature effects	:	Not measured; pH effect measured
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	not measured
Method	:	other: Campbell Method; Campbell A.N., J. Chem. Soc. London, Part I, 179 - 180, 1930
Year	:	1980
GLP	:	yes
Test substance	:	other TS: As prescribed by 1.1-1.4, purity >97%
Remark	:	Equilibration was done with the apparatus wrapped in foil to exclude all light and prevent photodegradation.
Result	:	Water solubility measured at: pH 5 = 51 ppm pH 7 = 118 ppm pH 9 = 900 ppm
Reliability	:	(2) valid with restrictions GLP study
Flag	:	Critical study for SIDS endpoint

16.05.2003 (9)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value	:	ca. 252 °C
Type	:	open cup
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	
Source	:	Bayer AG Leverkusen

19.05.1994 (3)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	water
Light source	:	Sun light
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
Conc. of substance	:	.495 mg/l at 36 °C
DIRECT PHOTOLYSIS		
Halflife t1/2	:	31.1 - minute(s)
Degradation	:	86 - % after 90 minute(s)
Quantum yield	:	
INDIRECT PHOTOLYSIS		
Sensitizer	:	water with additives
Conc. of sensitizer	:	
Rate constant	:	cm^3/(molecule*sec)
Degradation	:	= 91 - % after 90 minute(s)
Deg. product	:	
Method	:	EPA OTS 795.7000
Year	:	1989
GLP	:	yes
Test substance	:	other TS: 2-mercaptobenzothizole; purity = 98.2%
Method	:	Federal register 53(173) page 34522-34530.
Test condition	:	Indirect photolysis measurement was with added humic acid. Half-life estimated to be 27.4 minutes.
Reliability	:	(1) valid without restriction GLP Guideline study
Flag	:	Critical study for SIDS endpoint

18.06.2003 (10)

Type	:	air
Light source	:	
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1560000 molecule/cm3
Rate constant	:	.0000000000406348 cm^3/(molecule*sec)
Degradation	:	50 - % after 3.2 hour(s)
Deg. product	:	
Method	:	other (calculated): AOP Program (v1.89)
Year	:	1999
GLP	:	no
Test substance	:	other TS: molecular structure
Reliability	:	(2) valid with restrictions Accepted calculation method
Flag	:	Critical study for SIDS endpoint

15.05.2003 (8)

Type	:	other: dilute phosphate buffer
Light source	:	Sun light
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
Conc. of substance	:	11.1 mg/l at 20 °C
DIRECT PHOTOLYSIS		
Halflife t1/2	:	.1 - .2 day(s)
Degradation	:	100 - % after
Quantum yield	:	0

INDIRECT PHOTOLYSIS

Sensitizer	:	other: dissolved organic matter
Conc. of sensitizer	:	10 mg/l
Rate constant	:	ca. 3.1 cm^3/(molecule*sec)
Degradation	:	98 - % after
Deg. product	:	yes
Method	:	other (measured): test conditions undocumented
Year	:	1992
GLP	:	no data
Test substance	:	no data
Remark	:	for direct photolysis: pH 7, rate constant 8.1-8.7; for indirect photolysis: initial conc.=1.9 mg/l, temp=1-10C, total solar radiation=36.3E/m2, pH=7, t 1/2=.28-.44 day, quantum yield=.0013; similar results obtained when natural water was used: quantum yield=.0015 and 100% reduction; Products formed with and without sensitizer and in natural water: benzothiazole (28-47%), 2-hydroybenzothiazole (4-5%) and unidentified product
Source	:	Bayer AG Leverkusen

18.06.2003 (11)

Type	:	other: ethanol
Light source	:	other: Hanovia mercury lamp-UV irradiation
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
Conc. of substance	:	860 mg/l at °C
Method	:	other (measured): Parkanyi, C. et al protocol; see test conditions
Year	:	1985
GLP	:	no data
Test substance	:	no data
Remark	:	Final product was benzothiazole sulfate with solutions of methanol, ethanol or acetonitrile; When dry benzene or toluene was the reaction medium bis-(2-benzothiazolyl) disulfide was formed that could then be degraded to benzothiazole; oxygen is necessary for this reaction to take place and water is needed for last step
Source	:	Bayer AG Leverkusen
Test condition	:	immersion-well type; water cooled Ace Glass photochemical reactor; air saturated 96% ethanol; irradiated 22 hours; 450 watts

03.03.1994 (12)

Type	:	other: filter paper
Light source	:	other: germicidal lamp
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
Method	:	other (measured): Mitchell, E.C. protocol; see test conditions
Year	:	1961
GLP	:	no data
Test substance	:	no data
Remark	:	classified as "little or no degradation"
Source	:	Bayer AG Leverkusen
Test condition	:	10 mg quantities of a pesticide chemical are spotted on filter paper and the spot is exposed to a germicidal light (30 watt)

03.03.1994 (13)

Type	:	water
Light source	:	Sun light
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
Conc. of substance	:	1.1 mg/l at °C
DIRECT PHOTOLYSIS		
Halflife t1/2	:	3.7 - hour(s)
Degradation	:	- % after
Quantum yield	:	
Deg. product	:	
Method	:	other (measured): test conditions undocumented
Year	:	1980
GLP	:	yes
Test substance	:	other TS: mecaptobanzothiazole; purity 98%
Remark	:	Dark control T1/2 = 100 hours. Four photodegradation by-products were observed.

15.05.2003 (9)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	- at °C
t1/2 pH7	:	- at °C
t1/2 pH9	:	- at °C
Degradation	:	15 - % after 7 day(s) at pH 7 and °C
Deg. product	:	
Method	:	other: Monsanto protocol
Year	:	1985
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Bayer AG Leverkusen
Reliability	:	(1) valid without restriction GLP study
Flag	:	Critical study for SIDS endpoint

15.05.2003 (14)

Type	:	abiotic
t1/2 pH4	:	- at °C
t1/2 pH7	:	- at °C
t1/2 pH9	:	- at °C
Degradation	:	- 0 % after 7 day(s) at pH and °C
Deg. product	:	
Method	:	other: according to Analytic Bio-Chemistry Labs Protocol
Year	:	1984
GLP	:	no data
Test substance	:	other TS: 2-mercaptobenzothiazole, purity = 98%
Remark	:	No measurable hydrolysis after 7 days
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment

15.05.2003 (15)

Type	:	biotic
t1/2 pH4	:	- at °C
t1/2 pH7	:	- at °C
t1/2 pH9	:	- at °C
Deg. product	:	

Method : other: test conditions undocumented
Year : 1992
GLP : no data
Test substance : no data

Remark : 6 mg chemical; sediment 1.33 g dry weight/l H2O; Converted in low yield to 2-(methylthiobenzothiazole)
Source : Bayer AG Leverkusen
Reliability : (3) invalid
Documentation insufficient for assessment
15.05.2003 (11)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement : other: monitoring paper mill
Media : other: effluent
Concentration : -
Method :

Remark : 4 samples taken at various stages of treatment; conc. ranged from .025-.035 mg/l
Source : Bayer AG Leverkusen
03.03.1994 (16)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : adsorption
Media : water - soil
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: Springborn Laboratories protocol; see test conditions
Year : 1989

Result : Results:

	Kd	Koc	Slope (1/n)	%Organic Matter
California Sandy Loam	4.38	677	0.855	1.1
California Clay Loam	5.73	326	0.808	3.0
California Sand	0.799	1360	1.137	0.1
Carver Sandy Loam	18.8	2130	0.594	1.5
Dartmouth Sand	23.0	3560	0.861	1.1
Weweantic Sand	18.3	2590	0.763	1.2

Kd = adsorprtion coefficient
Koc = adsorprtion coefficient based on organic carbon content
Test condition : Protocol followed US TSCA Test Standard 40 CFR Chapter 1, paragraph 796.2750.
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
16.05.2003 (17)

Type : fugacity model level III
Media : other: air, water, soil, sediment
Method : other: EPIWIN Level III Fugacity Model
Year : 1999

Remark : Modeling was performed using equal releases (1,000 kg/hr) and equal distribution to all compartments.

Result :

	Distribution (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.507	6.32	1000	7.72e-012
Water	35.9	360	1000	4.06e-013
Soil	63.4	360	1000	2.76e-012
Sediment	0.172	1.44e+003	0	2.71e-013

Persistence Time: 347 hr
Reaction Time: 405 hr
Advection Time: 2.44e+003 hr
Percent Reacted: 85.8
Percent Advected: 14.2

Reliability : (2) valid with restrictions
Accepted calculation method

Flag : Critical study for SIDS endpoint

18.06.2003 (8)

Type : adsorption
Media : water - soil
Method :
Year :

Method : Aqueous solutions of MBT, initial concentrations ranging from 0.1 to 1.0 ppm, were equilibrated for 24 hours with four soils. K (adsorption coefficient) was calculated using the following equation
K= equilibrium concentration in soil / equilibrium concentration in water

The concentration in the water was measured using analytical method ES-80-M-15. The concentration in the soil was calculated by the difference.

Result :

Soil	K	95% confidence limits
Drummer silty clay loam	18	13-23
Spinks sandy loam	12	8-19
Ray silt loam	10	6-16
Lintonia sandy loam	7.5	5-11
Mean =	12	

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment

16.05.2003 (18)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 23.8 mg/l related to Test substance
Contact time : 28 days

Degradation : < 1 - (±) % after 28 day(s)
Result : under test conditions no biodegradation observed
Deg. product :
Method : EPA OTS 796.3100
Year : 1989
GLP : yes
Test substance : other TS: 2-mercaptobenzothiazole, purity = 98%

Remark : Gledhill method listed in U.S. TSCA regulations 40 CFR Ch 1 subpart D paragraph 796.3100
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
15.05.2003 (19)

Type : aerobic
Inoculum : other: sludge samplings from different sewage plants, rivers, bays and a lake
Concentration : 100 mg/l related to Test substance
Contact time :
Degradation : 2.5 - (±) % after 14 day(s)
Result :
Deg. product :
Method : OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year : 1981
GLP : no data
Test substance : no data

Remark : related to BOD; sludge conc.: 30 mg/l
Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
15.05.2003 (20)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 18 mg/l related to Test substance
Contact time :
Degradation : 0 - 5 (±) % after 35 day(s)
Result : under test conditions no biodegradation observed
Deg. product :
Method : other: CO2 evolution method listed in U.S. TSCA regulations 40 CFR Ch 1 subpart D paragraph 796.3100.
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Sample run in triplicate; 0%, 2%, and 5% theoretical carbon dioxide evolution obtained with an average of 2%.
Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
Guideline study
15.05.2003 (21)

Type : aerobic
Inoculum : other: water and sediment from nearby creek, agricultural land and industrial site with sediment.
Concentration : 1 mg/l related to Test substance
Contact time :
Degradation : 81 - (±) % after 56 day(s)

Result : other: Primary degradation was estimated to be 81% after 8 weeks.Sterile samples also degraded.
Deg. product :
Method : other: SRI protocol; see test conditions
Year : 1985
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer AG Leverkusen
Test condition : River die-away test.
18.01.1995 (22)

Type : aerobic
Inoculum : activated sludge
Concentration : 3 mg/l related to Test substance
Contact time :
Degradation : - (±) % after
Result : other: 3 mg/l inhibited oxidation of ammonia by 75%.
Deg. product :
Method : other: see test conditions
Year : 1966
GLP : no data
Test substance : no data

Remark : The concentration of the oxidized form, benzothiazole disulphide, had to be about 10 times greater than that of MBT to give 75% inhibition of ammonia oxidation.
Source : Bayer AG Leverkusen
Test condition : 250 ml flasks at 25 degrees Celsius shaker for 2-4 hours.
18.01.1995 (23)

Type : aerobic
Inoculum : activated sludge
Concentration : 5 mg/l related to Test substance
Contact time :
Degradation : - (±) % after
Result : other: 74% inhibition of the nitrifying activity of activated sludge
Deg. product :
Method : other: see test conditions
Year : 1966
GLP : no data
Test substance : no data

Remark : 5 mg/l MBT produced 74% inhibition, but in the presence of 5 mg/l zinc as zinc sulphate, which itself was not inhibitory, MBT was noninhibitory.
Source : Bayer AG Leverkusen
Test condition : 250 ml flasks at 25C in a shaker for 2-4 hours.
26.04.1994 (23)

Type : aerobic
Inoculum : activated sludge
Concentration : 20 mg/l related to Test substance
Deg. product :
Method : other: see test conditions
Year : 1966
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
Test condition : Sewage containing MBT was supplied daily to a fill-and-draw plant. Initial period of 9 weeks MBT conc 2 mg/L, was

increased to 20 mg/L for 7 weeks. Results suggest that during experiment, a strain of Nitrosomonas developed which was far less susceptible to MBT than that in the control sludge. Whereas 2 mg/L MBT inhibited control sludge by 75%, over 40 mg/L was necessary to produce the same effect on sludge which was previously exposed to 20 mg/L MBT. There was no evidence MBT was being decomposed in the sewage.

03.03.1994 (23)

Type : aerobic
Inoculum : other: soil
Concentration : 1 g/l related to Test substance
Contact time :
Degradation : - (±) % after
Result : other: completely retarded microbial growth of soil microbes at 0.1%
Deg. product :
Method : other: see test conditions
Year : 1984
GLP : no data
Test substance : no data

Remark : After three months, MBT completely retarded microbial growth of soil microbes at 0.1%. Toxicity level for MBT in agar: 4-day LD50 & 14-day LD50 < = 0.1%.
Source : Bayer AG Leverkusen
Test condition : Three techniques used for exposing rubber additives to John Innes No. 1 Soil. 1st involved placing powdered additives onto non-biodegradable polycarbonate membranes w/a 12 um pore diameter & placing membranes onto the soil w/powders on the upper surface. 2nd involved embedding powdered additives onto a thin layer (0.3 cm) of epoxy resin poured onto aluminum foil. During the curing process, excess of powder was poured onto resin. When cured, excess powder was shaken off resin which was cut and placed with the additive in contact with the soil. 3rd technique involved incorporating additives into an agar medium & inoculating medium with soil extract.

26.04.1994 (24)

Type : aerobic
Inoculum :
Concentration : 20 mg/l related to Test substance
Contact time :
Degradation : 0 - 12 (±) % after 3 day(s)
Result :
Deg. product :
Method : other: see test conditions
Year :
GLP : no data
Test substance : no data

Remark : 2-MBT was tested for degradability in river water by 4 different institutes. The results were 0%, 3%, 11% & 12%. It was also tested in sea water with the following results: 0%, 21%, 41%, 10%.
Partial translation (abstract and results table) of a Japanese article.
Source : Bayer AG Leverkusen
Test condition : Method was listed as the "cultivation method".

18.01.1995 (25)

Type : aerobic
Inoculum :
Contact time :
Degradation : - (±) % after
Result : other: listed as resistant substance in U.K.
Deg. product :
Method : other: test conditions undocumented
Year : 1975
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
03.03.1994 (26)

Contact time :
Degradation : - (±) % after
Result : other: listed as degradation resistant
Deg. product :
Method : other: MITI
Year :
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
26.04.1994 (27)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species : Cyprinus carpio (Fish, fresh water)
Exposure period : 42 day(s) at °C
Concentration : .1 mg/l
BCF : < .8 -
Elimination : no data
Method : OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year : 1981
GLP : no data
Test substance : no data

Remark : when test conc. .01 mg/l BCF < 8.0
Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
Guideline study
15.05.2003 (20)

Species : Cyprinus carpio (Fish, fresh water)
Exposure period : at 15 °C
Concentration : .56 mg/l
Elimination : yes
Method : other: Hashimoto, K. et al protocol; see test conditions
Year : 1978
GLP : no data
Test substance : other TS: 14C; 98.5% pure

Remark : about 20% excreted at 1h, 35% at 2h, 75% at 24h and 77% at 72h; fish that were fed had 100% excretion at 72hr; chemical oxidized to C-2,2,dithiobis[benzothiazole]
Source : Bayer AG Leverkusen
Test condition : fish starved 2 days prior to test; 30L water; water renewed at periodic intervals, some fish fed after administration of

chemical, chemical administered with a catheter into intestine

15.05.2003 (28)

Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	56 day(s) at 25 °C
Concentration	:	
Elimination	:	no data
Method	:	other: test conditions undocumented
Year	:	1978
GLP	:	no data
Test substance	:	no data
Remark	:	"confirmed to be non accumulative or low accumulative" ie. BCF did not increase a few hundred times during the 56 day exposure
Source	:	Bayer AG Leverkusen
Test condition	:	length 10 cm; weight 30 g; DO 7 mg/l
Reliability	:	(3) invalid Documentation insufficient for assessment

15.05.2003 (29)

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 : 4.2 -
LC50 : 11 -
Limit test :
Analytical monitoring : no
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1984
GLP : yes
Test substance : other TS: 2-mercaptobenzothiazole, purity = 98%

Remark : all conc. tested were above solubility
C.I. 8.3-15 mg/l; 24h-LC50: 18 mg/l; 48h-LC50: 13mg/l
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
15.05.2003 (30)

Type : static
Species : Brachydanio rerio (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC0 : .8 -
LC100 : 3.2 -
Limit test :
Analytical monitoring : yes
Method : other: UBA-Verfahrensvorschlag "Lethale Wirkung beim ZebrabaerblingBrachydanio rerio (LC0, LC50< LC100, 48-96 h), Mai 1984
Year : 1984
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : geometric mean: 1.6 mg/l
Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
15.05.2003 (31)

Type : flow through
Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 8 day(s)
Unit : mg/l
NOEC : 2 -
LC50 : .67 -
Limit test :
Analytical monitoring : yes
Method : other: Springborn Laboratory protocol; see test conditions
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : C.I. 0.54-0.83 mg/l; 24h-LC50: 1.14 mg/l; 48h-LC50: 0.73 mg/l
Source : Bayer AG Leverkusen

Test condition : continuous flow; 19L aquaria; 10 fish/conc; fed brine shrimp daily
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
15.05.2003 (32)

Type : static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 1.5 -
Limit test :
Analytical monitoring : no
Method : other: Bionomics Laboratroy protocol; see test conditions
Year : 1976
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : C.I. 1.2-1.9 mg/l; 24h-LC50: 3.4 mg/l; 48h-LC50: 2.1 mg/l
Source : Bayer AG Leverkusen
Test condition : carrier-acetone; 15L water; 10 fish/vessel; length 3.8 cm; no food; no aeration; temp 22 degrees Celsius
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
15.05.2003 (33)

Type : static
Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : .75 -
Analytical monitoring : no
Method : other: Bionomics Laboratory protocol; see test conditions
Year : 1976
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : C.I. 0.55-1 mg/l; 24h-LC50: 0.92 mg/l; 48h-LC50: 0.75 mg/l
Test condition : carrier-acetone; 15L water; 10 fish/vessel; length 3.7 cm; no food; no aeration; temp 12 degrees Celsius
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
15.05.2003 (34)

Type : semistatic
Species : Cyprinus auratus
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : 2 -
Analytical monitoring : no data
Method : other: test conditions undocumented
Year : 1983
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
Reliability : (3) invalid
Documentation insufficient for assessment
15.05.2003 (35)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	1.9 -
EC50	:	2.9 -
Analytical monitoring	:	yes
Method	:	other: "Protocol for Conducting a Static Acute Toxicity Test with Daphnia magna Following FIFRA Guideline 72", SLI Protocol #010190/FIFRA 72-2 DM SA and protocol amendment #1 dated 9 January 1992
Year	:	1992
GLP	:	yes
Test substance	:	other TS: 100 % (2-Mercaptobenzothiazole (ROKON), Lot #N9H 211)
Remark	:	24h-EC 50: 3.9 mg/l Analytical monitoring: HPLC
Reliability	:	(1) valid without restriction GLP Guideline study
Flag	:	Critical study for SIDS endpoint

16.05.2003 (36)

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	1.8 -
EC50	:	4.1 -
Analytical monitoring	:	no
Method	:	other: Methods of Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, 1975, EPA 660/3-75009
Year	:	1975
GLP	:	yes
Test substance	:	other TS: As prescribed by 1.1-1.4, purity = 98%
Remark	:	An initial rangefinding experiment preceded the definitive test. Concentrations of the test substance (0, 1.0, 1.8, 3.2, 5.6 and 10.0 mg/l) were prepared in reagent-grade acetone. Acetone was used as the solvent control. Water quality parameters of temperature, dissolved oxygen, pH, hardness and alkalinity were monitored throughout the test and remained within acceptable limits. The EC50 value and 95% confidence limits were calculated using the statistical methods of Litchfield and Wilcoxon (1949).
Result	:	EC50 (24h) = 7.0 mg/l EC50 (48h) = 4.1 mg/l (C.I. for EC50: 3.6-4.7 mg/l) NOEC = 1.8 mg/l
Reliability	:	(1) valid without restriction GLP Guideline study
Flag	:	Critical study for SIDS endpoint

18.06.2003 (37)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	biomass
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	.25 -
Analytical monitoring	:	no

Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1984
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Biomass 96 hr EC50 = 0.25 mg/l C.I. 0.06-0.98 mg/l;

in vivo chlorophyll results:
24 hr EC50 = >0.3<0.6 mg/l
48 hr EC50 = >0.3<0.6 mg/l
96 hr EC50 = 0.23 mg/l

Test condition : temp 24 degrees Celsius; 4000 lux; Algal Assay Media; init. inoc. 10000 cells/ml; "cool" white lights
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
18.06.2003 (38)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : Tetrahymena sp. (Protozoa)
Exposure period : 24 hour(s)
Unit : mg/l
EC50 : 10 -
Analytical monitoring : no
Method : other: Yoshioka, Y. protocol; see test conditions
Year : 1985
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
Test condition : temp. 30 degrees Celsius; sterile medium of 2% protose peptone; 60 umol/l; no agitation; count cell numbers; conc. ratio of 1.8 in 10 ml media
18.01.1995 (39)

Type : other: undefined and synthetic media
Species : other bacteria: several genera
Exposure period :
Unit :
Analytical monitoring : no data
Method : other: test conditions undocumented
Year : 1976
GLP : no data
Test substance : no data

Remark : complete inhibition at 50-1000 ug/ml; partial inhibition from 25-1000 ug/ml
Source : Bayer AG Leverkusen
18.01.1995 (40)

Type : other: unknown
Species : Aspergillus niger (Fungi)
Exposure period :
Unit :
Analytical monitoring : no data
Method : other: test conditions undocumented
Year : 1975
GLP : no data

Test substance : no data

Remark : Inhibits sporulation; also inhibits several other bacteria
Source : Bayer AG Leverkusen
04.05.1994 (41)

4.5.1 CHRONIC TOXICITY TO FISH

Species : Oncorhynchus sp.
Endpoint : other: embryo survival,viability, length
Exposure period : 89 day(s)
Unit : mg/l
MATC : .041 - .078
Analytical monitoring : yes
Method : other: according to Federal Register 50:797.1600
Year : 1989
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : max. accept. tox. concentration for larval length; no effect on embryo viability or survival.
Test condition : test lasted 60 days post hatch; 24-80 foot candles; temp. 12 degrees Celsius
Reliability : (1) valid without restriction
GLP Guideline study
15.05.2003 (42)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Daphnia magna (Crustacea)
Endpoint : reproduction rate
Exposure period : 21 day(s)
Unit : mg/l
NOEC : .34 -
EC50 : > .47 -
Analytical monitoring : yes
Method : OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test"
Year : 1989
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Maximum accept. conc.>0.25<0.47 mg/l; geometric mean: 0.34 mg active ingredient/liter
Test condition : carrier acetone; 50% dilutions; 1.8L vessels; 30-70 foot candles; 16 hours light; temp. 20 degrees Celsius
Reliability : (1) valid without restriction
GLP Guideline study
15.05.2003 (43)

Species : Daphnia magna (Crustacea)
Endpoint : reproduction rate
Exposure period : 21 day(s)
Unit : mg/l
NOEC : ca. .22 -
EC50 : ca. 2.22 -
Analytical monitoring : no
Method : OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test"

Year	:	1987
GLP	:	no
Test substance	:	other TS: 99.45 %
Source	:	Bayer AG Leverkusen
Test condition	:	concentrations tested: 0.07, 0.22, 0.7, 2.22, and 7 mg/l. Preparation of stock solution: 100 mg of test substance were weighed into 1 l of water and dissolved over night by means of a magnetic stirrer.
Reliability	:	(1) valid without restriction Guideline study

15.05.2003 (31)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : = 3800 - mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 20
Vehicle : other: Corn Oil (20% suspension)
Doses : 3160, 3980, 5010 or 6310 mg/kg bw
Method : other: Single Oral Dose, Younger Laboratories Protocol, 1975
Year : 1975
GLP : no data
Test substance : other TS: As prescribed by 1.1-1.4; purity = 98%

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag : Critical study for SIDS endpoint
16.05.2003 (44)

Type : LD50
Value : = 2830 - mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 20
Vehicle : other: Corn Oil (20% suspension)
Doses : 2000, 2510, 3160 or 3980 mg/kg bw
Method : other: Single Oral Dose, Younger Laboratories Protocol
Year : 1973
GLP : no data
Test substance : other TS: as prescribed by 1.1 - 1.4; purity >97%

Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag : Critical study for SIDS endpoint
16.05.2003 (45)

Type : LDLo
Value : = 7500 - 8750 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 5
Vehicle : other: Water (25% aqueous suspension)
Doses : 5.0, 6.25, 7.5, 8.75 or 10.0 g/kg bw
Method : other: Minimum Lethal Dose Protocol, Scientific Associates
Year : 1955
GLP : no data
Test substance : other TS: as prescribed by 1.1 - 1.4; purity = Commercial grade

16.05.2003 (46)

Type : LD50
Value : > 500 - mg/kg bw
Species : rat

Strain :
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Method :
Year :
GLP :
Test substance : other TS: 2-mercaptobenzothiazole (purity not noted)

15.05.2003 (47)

Type : LD50
Value : 2000 - mg/kg bw
Species : mouse
Strain :
Sex : male
Number of animals :
Vehicle : other: 0.5% carboxymethyl cellulose in normal saline
Doses :
Method :
Year :
GLP :
Test substance : other TS: ROTAX (purified MBT)

Method : Mice were observed for 72 hours after a single oral exposure. LD50 values were calculated by the Cornfield and Mantel modification (1950) of the Karber method.

15.05.2003 (48)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC50
Value : > 1.27 - mg/l
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : other: IBT protocol
Year : 1977
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment; age of study, lack of details

18.06.2003 (49)

Type : LC50
Value : > .722 - mg/l
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Exposure time : 7 hour(s)
Method : other: Acute Inhalation Toxicity
Year : 1961
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment; age of study, lack of details
18.06.2003 (50)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : > 7940 - mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 3
Vehicle : other: Corn Oil (40% suspension)
Doses : 5010 or 7940 mg/kg bw
Method : other: Single Dermal Dose, Younger Laboratories Protocol
Year : 1975
GLP : no data
Test substance : other TS: As prescribed by 1.1-1.4, purity = 98%

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag : Critical study for SIDS endpoint
16.05.2003 (44)

Type : LD50
Value : > 7940 - mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 3
Vehicle : other: Corn Oil (40% suspension)
Doses : 5010 or 7940 mg/kg bw
Method : other: Single Dermal Dose, Younger Laboratories Protocol
Year : 1973
GLP : no data
Test substance : other TS: as prescribed by 1.1 - 1.4; purity >97%

Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
16.05.2003 (51)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50
Value : 437 - mg/kg bw
Species : mouse
Strain :

Sex	:	male
Number of animals	:	
Vehicle	:	other: 0.5% carboxymethyl cellulose in normal saline
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: ROTAX (purified MBT)
Method	:	Mice were observed for 72 hours after a single i.p. injection. LD50 values were calculated by the Cornfield and Mantel modification (1950) of the Karber method.

03.11.2000 (48)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	other: Water (0.5g test compound moistened with water)
PDII	:	0
Result	:	not irritating
Classification	:	not irritating
Method	:	Draize Test
Year	:	1975
GLP	:	no data
Test substance	:	other TS: As prescribed by 1.1-1.4; purity = 98%
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment

16.05.2003 (44)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	
Year	:	1973
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

15.05.2003 (52)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	100 other: mg

Exposure time : 24 hour(s)
Comment : not rinsed
Number of animals : 6
Vehicle : none
Result : slightly irritating
Classification : not irritating
Method : Draize Test
Year : 1975
GLP : no data
Test substance : other TS: As prescribed by 1.1-1.4, purity = 98%

Remark : Test substance, as a finely ground powder, was introduced into one eye of each animal; the other eye was left untreated and served an a control. Scoring was done via the Draize Method. Score was 3.2 / 110.0 (Slightly irritating).
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
18.06.2003 (44)

Species : rabbit
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : not irritating
Classification :
Method : other
Year : 1973
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer AG Leverkusen
15.05.2003 (52)

5.3 SENSITIZATION

Type : Buehler Test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method : OECD Guide-line 406 "Skin Sensitization"
Year : 1992
GLP : no data
Test substance : other TS: 98 % purity

Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
Guideline study
18.06.2003 (53)

Type : Buehler Test
Species : guinea pig
Number of animals :
Vehicle : petrolatum
Result : sensitizing

Classification :
Method : other
Year : 1988
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : 0/10 animals reacted to 0.1%, 2/10 reacted to 0.5%, 7/10 reacted to 2%.
15.05.2003 (54)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method : OECD Guide-line 406 "Skin Sensitization"
Year : 1992
GLP : no data
Test substance : other TS: 98 % purity

Source : Bayer AG Leverkusen
01.09.1994 (53) (55) (56)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification : sensitizing
Method : other
Year : 1970
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer AG Leverkusen
23.02.1994 (57)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification : sensitizing
Method : other
Year : 1968
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer AG Leverkusen
23.02.1994 (58)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method :
Year : 1992
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
01.09.1994 (59)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method :
Year : 1972
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
06.09.1994 (60)

Type : Mouse local lymphnode assay
Species : mouse
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method : other
Year : 1993
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer AG Leverkusen
02.09.1994 (61)

Type : Mouse local lymphnode assay
Species : mouse
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method : other: Skin Sensitization Test
Year : 1992
GLP : no data
Test substance : other TS: 98 % purity; dissolved in dimethyl formamide

Source : Bayer AG Leverkusen
01.09.1994 (53) (55) (56)

Type : Mouse local lymphnode assay
Species : mouse
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method :
Year : 1989
GLP : no data
Test substance : other TS: dissolved either in DMSO or aqueous solvent

Source : Bayer AG Leverkusen
01.09.1994 (62)

Type : Patch-Test
Species : human
Number of animals :

Vehicle :
Result : not sensitizing
Classification : not sensitizing
Method : other
Year : 1976
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer AG Leverkusen
23.02.1994 (63)

Type : other
Species : other
Number of animals :
Vehicle :
Result :
Classification :
Method : other
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : No T-cell response was noted in an in-vitro lymphocyte transformation assay.
Source : Bayer AG Leverkusen
02.06.1994 (64)

Type : other: occlusive epicutaneous test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method : other: Skin Sensitization Test according to Brulos
Year : 1976
GLP : no data
Test substance : no data

Remark : Animals were applied 0.5 g test substance (in 1 % vaseline) to the interscapular region on alternate days for 4 weeks (10 applications, occlusive). At the first day of week 1 and 2, 0.1 ml Freund's adjuvans was injected intradermally. One week after the last application animals were challenged with 0.5 g test compound epicutaneously (occlusive). The mean sensitizing index was 1.1 of 3.0 (maximal score). 50 % of animals were sensitized. Test substance was considered to be moderate sensitizing.
Source : Bayer AG Leverkusen
01.09.1994 (65)

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 4 weeks
Frequency of treatm. : ad libitum
Post exposure period :

Doses : 5000, 10000, 15000, 20000, or 25000 ppm (57, 714, 1071, 1429, 1786 mg/kg bw/d)
Control group : yes
NOAEL : = 714 - mg/kg bw
LOAEL : = 1071 - mg/kg bw
Method : other
Year : 1988
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : 5000, 10000, 15000, 20000, 25000 ppm =
57, 714, 1071, 1429, 1786 mg/kg bw/d
(conversion factor is 14)
Result : Dose: Observations
5000 ppm: NOEL; no effect
10000 ppm: NOEL; no effects
15000 ppm: LOEL; decr bw gain (male); decr food consumption
20000 ppm: decr bw gain; decr food consumption
25000 ppm: decr bw gain; decr food consumption
Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
GLP study
Flag : Critical study for SIDS endpoint
15.05.2003 (66)

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : 13 weeks
Frequency of treatm. : 5 days/week
Post exposure period : 3 days
Doses : 0, 188, 375, 750, 1500, or 3000 mg/kg bw
Control group : yes
NOAEL : = 375 - mg/kg bw
LOAEL : = 750 - mg/kg bw
Method : other
Year :
GLP : yes
Test substance : other TS: mecaptobenzothizole, purity = 96.3%

Remark : Because the hepatomegaly was not associated with histopathological findings, those dose levels with hepatomegaly but no other toxicity findings are considered to be no observable adverse effect levels (NOAELs) and are reported as NOELs.
Result : Dose: Observations
188 mg/kg bw/d: hepatomegaly, (female)
375 mg/kg bw/d: NOAEL; hepatomegaly, (female)
750 mg/kg bw/d: LOAEL; bw, decr; hepatomegaly, (female)
1500 mg/kg bw/d: bw, decr; hepatomegaly.
Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag : Critical study for SIDS endpoint
15.05.2003 (67) (68)

Type :
Species : rat
Sex : male/female

Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 4 weeks
Frequency of treatm. : continuous
Post exposure period :
Doses : 4300, 9000, 14000, 19000, 25000 ppm
Control group : yes, concurrent vehicle
Method : other
Year :
GLP : no data
Test substance : other TS: 2-mercaptobenzothiazole (lot No. N8F-228)

Method : 2-mercaptobenzothiazole (lot No. N8F-228) was administered to Sprague-Dawley rats at target levels of 0, 5000, 10000, 15000, 20000, 25000 ppm in feed for 4 weeks. The test material was analysed neat and mixed with the diet. Averages for consumption were 425, 839, 1232, 1696, 2143 mg/kg (males) and 432, 874, 1320, 1703, 2058 mg/kg (females).

All animals were observed twice daily for mortality and moribundity. Detailed clinical observations and body weights were done weekly. All animals were given a thorough necropsy and livers were weighed.

Result : Observations included decreased weight gain and reduced food consumption, which were statistically significant in males at 15000 ppm and females at 20000 and 25000 ppm. Slightly heavier livers occurred in animals of both sexes at all levels.

15.05.2003 (69)

Type : Sub-chronic
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 13 weeks
Frequency of treatm. : 5 days/week
Post exposure period : 3 days
Doses : 94, 188, 375, 750, or 1500 mg/kg bw
Control group : yes
NOAEL : = 375 - mg/kg bw
LOAEL : = 750 - mg/kg bw
Method : other: well documented in Physiolological Research Laboratories 78-60-106002 (1981)
Year :
GLP : yes
Test substance : other TS: mecaptobenzothizole, purity = 96.3%

Result :

Dose:	Observations
94 mg/kg bw/d:	no effects
188 mg/kg bw/d:	no effects
375 mg/kg bw/d:	NOEL; no effects
750 mg/kg bw/d:	LOEL; death (female)
1500 mg/kg bw/d:	deaths.

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment

18.06.2003 (67) (70)

Type	:	
Species	:	mouse
Sex	:	male/female
Strain	:	other: Slc: ddY
Route of admin.	:	oral feed
Exposure period	:	20 months
Frequency of treatm.	:	daily
Post exposure period	:	
Doses	:	30, 120, 480 or 1920 ppm (males: 3.6, 14.7, 57.9 or 289.4 mg/kg bw day; females: 3.6, 13.5, 58.9 or 248.0 mg/kg bw/day
Control group	:	yes
NOAEL	:	= 120 - ppm
Method	:	other: Repeated Dose Toxicity
Year	:	1989
GLP	:	no data
Test substance	:	other TS: technical grade
Result	:	Inhibition of body weight gain was observed in the 1920 ppm-group of males from the initial stage of the treatment. No signigicant changes were seen between the controls and the treated groups in weights of organs and in several biochemical parameters of serum. Histopathologically, cell infiltration in the interstitium of kidney in the 1920 and 480 ppm groups of the males was found at the 20th month.
Source	:	Bayer AG Leverkusen

18.06.2003 (71)

Type	:	
Species	:	mouse
Sex	:	male
Strain	:	other: white
Route of admin.	:	i.p.
Exposure period	:	1 week
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	55 and 110 mg/kg
Control group	:	yes, concurrent vehicle
NOAEL	:	55 - mg/kg bw
LOAEL	:	110 - mg/kg bw
Method	:	other
Year	:	
GLP	:	
Test substance	:	other TS: ROTAX (purified MBT)
Method	:	Groups of male mice were dosed daily for one week by the i.p. route with oil suspensions of MBT. Control animals received daily injections of the same volume of cottonseed oil. At the end of one week, the animals were sacrificed, tissues were removed and examined histopathologically.
Result	:	There were no gross signs of toxicity at either dose level. All animals exhibited normal weight gain and behavior. Gross examination at necropsy revealed no significant injury to the vital organs. Microscopic examination of lungs, heart, thyroid and testes were normal. The kidney showed cloudy swelling and the livers revealed severe damage at the 110 mg/kg dose level.

15.05.2003 (48)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Salmonella typhimuriumTA 97, TA98, TA100, TA102
Test concentration : 1, 10, 100, 500, 1000, 5000 ug/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year : 1983
GLP : yes
Test substance : other TS: MBT (purity not noted)

Result : There was no significant increase in revertant colonies and therefore no evidence for mutagenic activity in these assays. There was a toxic response to the test material at 5000 ug/plate and in most cases at 1000 ug/plate. The positive and negative controls were within acceptable limits.
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
15.05.2003 (72)

Type : HGPRT assay
System of testing : Chinese Hamster Ovary cells
Test concentration : up to 333.33 ug/ml with S9 and up to 33.33 ug/ml without S9
Cycotoxic concentr. : with metabolic activation = 1000 ug/ml;
without metabolic activation = 333.33 ug/ml
Metabolic activation : with and without
Result : negative
Method : EPA OTS 798.5300
Year : 1986
GLP : yes
Test substance : other TS: MBT; lot #39-14B; purity not noted

Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
15.05.2003 (73)

Type : Mouse lymphoma assay
System of testing : L5178Y mouse lymphoma cells
Test concentration : up to 60ug/ml (with) and 70 ug/ml (without)
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 476
Year : 1984
GLP : no data
Test substance : other TS: 2-mercaptobenzothiazole (purity not stated)

Reliability : (1) valid without restriction
Guideline study
15.05.2003 (74)

Type : Sister chromatid exchange assay
System of testing : Chinese hamster ovary cells
Test concentration : up to 500.5 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without

Result : negative
Method : other: BrdUrd/dye technique
Year : 1988
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
15.05.2003 (67)

Type : Cytogenetic assay
System of testing : Chinese hamster ovary cells
Test concentration : up to 500.5 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result :
Method : other: Chromosome Aberration Test
Year : 1988
GLP : no data
Test substance : no data

Remark : result: negative (-S9 mix)
positive at > = 373,5 ug/ml (+ S9 mix)
Source : Bayer AG Leverkusen
15.05.2003 (67)

Type : Mouse lymphoma assay
System of testing : L5178Y
Test concentration : up to 150 ug/ml with S9 and up to 100 ug/ml without S9
Cycotoxic concentr. :
Metabolic activation : with and without
Result : ambiguous
Method : EPA OTS 798.5300
Year : 1986
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Small increases in mutant frequency were observed but only at concentrations that also produced cytotoxicity.
Reliability : (1) valid without restriction
GLP Guideline study
15.05.2003 (75)

Type : Ames test
System of testing : TA98, TA100, TA1535, TA1537, TA1538
Test concentration : up to 500 ug/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1976
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer AG Leverkusen
15.05.2003 (76)

Type : Ames test
System of testing : TA98, TA100, TA1535, TA1537, TA1538
Test concentration : up to 300 ug/plate

Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : EPA OTS 798.5265
Year : 1986
GLP : yes
Test substance : other TS: MBT; lot #39-14B; purity = 98%

Reliability : (1) valid without restriction
GLP Guideline study
16.05.2003 (77)

Type : Escherichia coli reverse mutation assay
System of testing : Escherichia coli SD-4-73
Test concentration : no data
Cycotoxic concentr. :
Metabolic activation : without
Result : negative
Method : other: Paper Disk Method
Year : 1958
GLP : no data
Test substance : no data

15.05.2003 (78)

Type : Gene mutation in Saccharomyces cerevisiae
System of testing : D4 strain
Test concentration : up to 500 ug/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1976
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer AG Leverkusen
15.05.2003 (76)

Type : HGPRT assay
System of testing : V79 Chinese hamster cells
Test concentration : 50 - 300 ug/ml
Cycotoxic concentr. :
Metabolic activation : without
Result : negative
Method : other: 6-thioguanine Resistance Assay
Year : 1976
GLP : no data
Test substance : no data

Source : Bayer AG Leverkusen
15.05.2003 (79)

Type : Mouse lymphoma assay
System of testing : L5178Y
Test concentration : up to 100 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1978
GLP : no data

Test substance : as prescribed by 1.1 - 1.4

16.05.2003 (80)

Type : Mouse lymphoma assay
System of testing : L5178Y
Test concentration : 3.75 - 150 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result :
Method : other: TK Test
Year : 1985
GLP : yes
Test substance : other TS: solvent: DMSO

Remark : - S9: 1.8- to 8.7fold increases in the mutant frequency for treatments causing very high toxicity (less than 10 % relative growth).
+ S9: 1.7- to 2.7fold increases in the mutant frequency in the 7 - 20 % relative growth range; treatments with 150 ug/ml were lethal.
The results were evaluated as showing the test material to be weakly mutagenic at high toxicity.
Source : Bayer AG Leverkusen
15.05.2003 (81)

Type : Mouse lymphoma assay
System of testing : L5178Y
Test concentration : up to 150 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result :
Method : other: TK Test
Year : 1985
GLP : no data
Test substance : other TS: dissolved in ethanol

Remark : result: negative (- S9 mix)
positive at > = 5 ug/ml (+ S9 mix)
Source : Bayer AG Leverkusen
15.05.2003 (82)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Dominant lethal assay
Species : rat
Sex : male
Strain : CD-1
Route of admin. : oral feed
Exposure period : 13 weeks
Doses : 2500, 8750, or 15000 ppm
Result : negative
Method : EPA OPPTS 870.5450
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : There were no findings that were indicative of dominant lethality.
Reliability : (1) valid without restriction

GLP Guideline study
Flag : Critical study for SIDS endpoint
15.05.2003 (83)

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : CD-1
Route of admin. : i.p.
Exposure period : single dose
Doses : 300 mg/kg bw
Result : negative
Method : EPA OTS 798.5395
Year : 1986
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : There was no increase in micronucleated cells as compared to control. MBT was considered not to be clastogenic in this assay.
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
19.05.2003 (84)

Type : other: In vivo DNA binding study
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : single dose
Doses : 375 mg/kg
Result : negative
Method : other
Year :
GLP :
Test substance : other TS: radio-labelled 2-mercaptobenzothiazole (purity not noted)

Method : Male and female Fischer 344 rats were gavaged with 375 mg/kg MBT and sacrificed 8 hours later. DNA was extracted from the liver, adrenal glands, pituitary gland, pancreas, and bone marrow using standard exhaustive solvent extraction techniques. The amount of radioactivity associated with the DNA was determined.
Result : There was little or no binding of MBT with DNA in any of the tissues examined.
15.05.2003 (85)

Type : other: Drosophila mutagenicity assay
Species : Drosophila melanogaster
Sex : no data
Strain : no data
Route of admin. : oral feed
Exposure period : 8 - 10 days
Doses : 20 - 40 mg/ml
Result :
Method : other: no data
Year : 1968
GLP : no data
Test substance : no data

Remark : The mutagenic activity included lethal, sublethal and visible mutations.

Result : mutation frequency: 2.5 +- 0.49 %;
no control group mentioned
Source : Bayer AG Leverkusen
15.05.2003 (86)

5.7 CARCINOGENICITY

Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : 2 years
Frequency of treatm. : 5 days/week
Post exposure period :
Doses : 0, 375 or 750 mg/kg bw for males; 0, 188 or 375 mg/kg bw for females
Result :
Control group : yes
Method : other
Year : 1988
GLP : yes
Test substance : other TS: as prescribed by 1.1 - 1.4; purity = 98%

Remark : The NTP report concluded that "there was some evidence of carcinogenic activity" in male and female rats.
Result : Survival was decreased for male rats. No effects were noted in rats in body weight gain. Non-neoplastic histopathological changes included forestomach lesions in male and female rats and nephropathy in male rats only.

Dose:	Observations
188 mg/kg bw/d:	NOEL; no effect
375 mg/kg bw/d:	LOEL; forestomach, lesions; mononuclear cell, leukemia (male); pancreatic acinar cell, adenoma (male); pituitary, adenoma (female); adrenal, pheochromocytoma (female)
750 mg/kg bw/d:	forestomach, lesions (male); adrenal, pheochromocytoma (male); benign and carcinoma (male)

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
19.05.2003 (87)

Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : oral feed
Exposure period : 2 years
Frequency of treatm. : 5 days/week
Post exposure period :
Doses : 0, 375 or 750 mg/kg bw
Result :
Control group : yes
Method : other
Year : 1988
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

: The NTP report concluded that "there was equivocal evidence

Remark for carcinogenic activity" in female mice and no evidence for carcinogenic activity in male mice.
Result : Dose: Observations
375 mg/kg bw/d: liver, adenoma (female); liver, carcinoma (female)
750 mg/kg bw/d: no effect.
Source : Bayer AG Leverkusen
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
16.05.2003 (88)

Species : mouse
Sex : male/female
Strain : other: Slc: ddY
Route of admin. : oral feed
Exposure period : 20 months
Frequency of treatm. : daily
Post exposure period :
Doses : 30, 120, 480 or 1920 ppm (males: 3.6, 14.7, 57.9 or 289.4 mg/kg bw day; females: 3.6, 13.5, 58.9 or 284.0 mg/kg bw day
Result :
Control group : yes
Method : other
Year : 1989
GLP : no data
Test substance : other TS: technical grade

Remark : see also chapter 5.4
Result : no significant increase in the tumour incidences
Source : Bayer AG Leverkusen
06.09.1994 (71)

Species : mouse
Sex : male/female
Strain : other: C57BL/6xC3H/Anf or C57BL/6xAKR hybrids
Route of admin. : other: gavage for 3 weeks and subsequently oral feed for 17 months
Exposure period : 18 months
Frequency of treatm. : daily
Post exposure period :
Doses : 100 mg/kg bw/day (gavage) and 323 ppm (oral feed: 50 mg/kg bw/day)
Result :
Control group : no data specified
Method :
Year : 1969
GLP : no data
Test substance : other TS: vehicle: 0.5 % gelantine

Remark : Rats were given 100 mg/kg bw/day in a suspension of the vehicle by gavage, beginning when the mice were 7 days of age until 4 weeks of age. After the mice were weaned at 4 weeks of age, the test substance was mixed directly with the diet (no vehicle was used) at a concentration of 323 ppm (50 mg/kg bw/day) for 17 months; 18 animals sex/strain/dose group.
Result : no significant increase in the incidence of tumors after oral administration of 2-mercaptobenzothiazole
Source : Bayer AG Leverkusen
01.09.1994 (89) (90)

Species : mouse
Sex : male/female

Strain	:	other: B6C3F1 or B6AKF1 hybrids
Route of admin.	:	s.c.
Exposure period	:	see remark
Frequency of treatm.	:	single injection
Post exposure period	:	17 months
Doses	:	215 mg/kg bw
Result	:	
Control group	:	other: yes, concurrent vehicle and concurrent no treatment
Method	:	other: Carcinogenicity Test
Year	:	1968
GLP	:	no data
Test substance	:	other TS: dissolved in 0.5 % gelantine
Remark	:	single s.c. injection in nape of neck at 28th day of age; 18 animals/sex/strain/dose and control group.
Result	:	No significant increase in the incidence of tumors was found.
Source	:	Bayer AG Leverkusen

01.09.1994 (89)

Species	:	other
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	18.46 - 110.76 ug/ml
Result	:	
Control group	:	
Method	:	other: Cell transformation assay
Year	:	1982
GLP	:	yes
Test substance	:	no data
Result	:	no increased number of transformed foci
Source	:	Bayer AG Leverkusen

06.09.1994 (81)

5.8.1 TOXICITY TO FERTILITY

Type	:	Two generation study
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	10 weeks before mating, through gestation and lactation until sacrifice
Frequency of treatm.	:	ad libitum
Premating exposure period		
Male	:	10 weeks
Female	:	10 weeks
Duration of test	:	approximately 88 days past weaning
No. of generation studies	:	
Doses	:	0, 2500, 8750, or 15000 ppm (0, 179, 625, and 1071 mg/kg bw/d)
Control group	:	yes
NOAEL parental	:	< 2500 - ppm
NOAEL F1 offspring	:	< 2500 - ppm
NOAEL F2 offspring	:	< 2500 - ppm
Result	:	No observed adverse effects on reproductive parameters.

Method : EPA OTS 798.4700
Year : 1991
GLP : yes
Test substance : other TS: MBT; purity = 98.1%

Remark : 2500, 8750, and 15000 ppm = 179, 625, and 1071 mg/kg bw/d
conversion number is 14
Result : Body weights were dose-dependently reduced for all treated F0 males and for mid- and high-exposure females. Body weights were reduced in the F1 pups from the mid- and high-exposure groups and in F2 pups from all dose levels beginning on Day 14 of lactation.

Dose:	Observations
2500 ppm:	F0: decr. bw (male)
	F1: decr. bw
	F2: decr. bw
8750 ppm:	F0: decr. bw; decr. food consumption, decr. kidney weight
	F1: decr. bw; decr. kidney weight (male); kidney, brown pigmentation; incr. liver weight; liver, hepatocellular hypertrophy
	F2: decr. bw
15000 ppm:	F0: decr. bw; decr. food consumption; decr. kidney weight
	F1: decr. bw; decr. kidney weight; kidney, brown pigmentation; incr. liver weight; liver, hepatocellular hypertrophy
	F2: decr. bw

Conclusion : There was no observation of adverse effects on reproductive parameters observed in this study.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.05.2003 (91)

Type : other
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : gestation and lactation and 35-days post-weaning
Frequency of treatm. : daily
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies :
Doses : 5000, 10000, or 15000 ppm
Control group : yes
NOAEL parental : < 5000 - ppm
NOAEL F1 offspring : < 5000 - ppm
Method : other
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : This was a rangefinding study.
5000, 10000, and 15000 ppm = 357, 714, and 1071 mg/kg bw/d
conversion number is 14
In the study report, there is reference to two different

groups of F0 female rats. The first group, called Group 2, received MBT in the diet at a level of 15000 ppm throughout gestation and lactation. The F1 pups from these dams were exposed to 15000 ppm postweaning. The second group of F0 dams, called Group 3, received MBT in the diet at a level of 15000 ppm during gestation and the first week of lactation, 10000 ppm during the second week of lactation, and 5000 ppm during the third week of lactation. The F1 pups from these dams were exposed to 5000 ppm postweaning.

Result : Group 2 F0 dams: decr. bw; decr. food consumption
F1 pups: decr. bw
Group 3 F0 dams: decr. bw; decr. food consumption
F1 pups: decr. bw

Source : Bayer AG Leverkusen

15.05.2003 (92)

Type : other: see Method
Species : rat
Sex : male/female
Strain : no data
Route of admin. : unspecified
Exposure period : see Method
Frequency of treatm. :
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies :
Doses :
Control group :
Method :
Year :
GLP :
Test substance : other TS: Captax, purity not noted

Method : Trial #1: 5-7 days before mating in males and at estrus state in females. Mating occurred during next estrus.
Trial #2: females exposed on day 4 and 11 of pregnancy after mating with untreated males.

Females sacfificed on 19th day of pregnancy.
Obervations: number of yellow bodies (corpora lutea), number of live and dead fetuses, weight and length of fetuses.

Result : All accelerators tested had some effect on the development of the fetus.

Reliability : (4) not assignable
abstract only; translation from Russian

27.04.2001 (93)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : Day 6-15 of gestation
Frequency of treatm. : daily
Duration of test : up to Day 20 of gestation
Doses : 300, 1200, or 1800 mg/kg bw/d

Control group : yes
NOAEL maternal tox. : = 300 - mg/kg bw
NOAEL teratogen. : = 1800 - mg/kg bw
Method : EPA OTS 798.4900
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : The post-implantation loss was judged to be equivocal since it was not observed at 1200 mg/kg bw/d. There were no other indications that MBT was fetotoxic or teratogenic.

Result :

Dose:	Observation
300 mg/kg bw/d:	PI loss.
1200 mg/kg bw/d:	salivation (female); urine staining (female); dark red material around mouth (female)
1800 mg/kg bw/d:	PI loss; salivation (female); urine staining (female); dark red material around mouth (female); decr. activity (female); decr. bw (female); decr. food consumption (female) Days 6-9.

Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
16.05.2003 (94)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : gavage
Exposure period : Day 6-18 of gestation
Frequency of treatm. : daily
Duration of test : up to Day 29 of gestation
Doses : 0, 50, 150, or 300 mg/kg bw/d
Control group : yes
NOAEL maternal tox. : = 300 - mg/kg bw
NOAEL teratogen. : = 300 - mg/kg bw
Result : No indication of fetotoxicity or teratogenicity compared to controls.
Method : EPA OTS 798.4900
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Quality Assurance Statement signed.
Result : No indication of fetotoxicity or teratogenicity compared to controls.
Maternal general toxicity: Slightly reduced body weight gain at 300 mg/kg (not statistically significant).

Dose:	Observation
50 mg/kg bw/d:	no effect.
150 mg/kg bw/d:	NOEL; no effect.
300 mg/kg bw/d:	incr. liver weight, (maternal); decr. bw (maternal).

Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
19.05.2003 (95)

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : Day 6-15 of gestation
Frequency of treatm. : daily
Duration of test : up to Day 20 of gestation
Doses : 0, 300, 600, 1000, 1500, or 2200 mg/kg bw/d
Control group : yes
NOAEL maternal tox. : = 1000 - mg/kg bw
NOAEL teratogen. : = 2200 - mg/kg bw
Method : EPA OTS 798.4900
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Quality Assurance Statement signed.
This was a range-finding study. There was no observation of external abnormalities in fetuses.

Result :

Dose:	Observations
300 mg/kg bw/d:	no effect.
600 mg/kg bw/d:	no effect.
1000 mg/kg bw/d:	NOEL; no effect.
1500 mg/kg bw/d:	decr. bw (female)
2200 mg/kg bw/d:	decr. bw (female); mortality (female)

Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
GLP Guideline study

16.05.2003 (96)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : gavage
Exposure period : Day 6-18 of gestation
Frequency of treatm. : daily
Duration of test : up to Day 29 of gestation
Doses : 150, 300, 600, 1000, or 1500 mg/kg bw/d
Control group : yes
NOAEL maternal tox. : < 150 - mg/kg bw
NOAEL teratogen. : = 300 - mg/kg bw
Method : other
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : This was a range-finding study. There was no observation of treatment-induced external abnormalities in fetuses.

Result : 5) 1500 mg/kg bw/d:
mortality, F.

Dose:	Observation
150 mg/kg bw/d:	decr. bw (female); decr. viability (fetal); decr.bw (fetal).
300 mg/kg bw/d:	decr. bw (female); decr. viability (fetal); decr.bw (fetal).
600 mg/kg/bw d:	decr. bw (female); decr. viability (fetal); decr.bw (fetal).
1000 mg/kg bw/d:	mortality (female).
1500 mg/kg bw/d:	mortality (female).

Source : Bayer AG Leverkusen
Reliability : (1) valid without restriction
GLP Guideline study
16.05.2003 (97)

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : i.p.
Exposure period : Days 1-15 of gestation
Frequency of treatm. :
Duration of test :
Doses : 200 mg/kg
Control group :
NOAEL maternal tox. : 200 - mg/kg bw
NOAEL teratogen. : 200 - mg/kg bw
Method : other: Hardin BD, Bond GP, Sikov MR, Andrew FD, Beliles RP, Niemeier RW. (1981) Scan. J. Work Environ. Hlth. 7(S4):66-75
Year :
GLP : no data
Test substance : other TS: 2-mercaptobenothiazole; purity not noted

27.04.2001 (98)

Species : rat
Sex : male/female
Strain : no data
Route of admin. : unspecified
Exposure period : see method
Frequency of treatm. :
Duration of test :
Doses : not specified
Control group :
Method :
Year :
GLP :
Test substance : other TS: Captax, purity not noted

Method : Trial #1: 5-7 days before mating in males and at estrus state in females. Mating occurred during next estrus.
Trial #2: females exposed on day 4 and 11 of pregnancy after mating with untreated males.

Females sacfific ed on 19th day of pregnancy.
Obervations: number of yellow bodies (corpora lutea), number of live and dead fetuses, weight and length of fetuses.
Result : All accelerators tested had some effect on the development of the fetus.
Reliability : (4) not assignable
abstract only; translation from Russian
27.04.2001 (93)

Species : other: chicken embryo
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Duration of test :
Doses : 0.10, 0.50, 1.0, 1.5, 2.0 umoles/egg
Control group :
Method :

Year :
GLP :
Test substance : other TS: Vulkacit Mercapto; technical grade

Method : Three day chicken embryos were selected by candling. 5ul of a solution of the test substance in acetone was injected onto the heart of the embryo (Korhonen et al. 1982. Scand. J. Work Environ. Hlth. 8:63). 5ul of acetone was used as a control substance. After 2 days the eggs were candled and dead embryos were discarded. Eggs were again candled every 2 or 3 days; those containing dead embryos were opened and checked for external malformations and the developmental stage. The incubation was terminated 11 days after injection and embryos inspected for survival and external malformations.

Result :

Treatment (umoles/egg)	n=	early deaths	late deaths normal	late deaths malformed	malformed survivors	% affected
0.10	9	0	0	0	1	11%
0.50	30	0	0	0	5	17%
1.0	40	7	0	1	7	38%
1.5	30	6	0	0	6	40%
2.0	30	4	0	0	9	43%

Median effective dose (ED50) = 2.0 umole/egg

27.04.2001 (99) (100)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : A mortality study of workers (2410 employees: 2160 men; 250 women) employed at a manufacturing chemicals plant for the rubber industries in the United Kingdom in the period 1955 - 1986 was performed. The eight hour time weighted average exposures to 2-mercaptobenzothiazole and its derivatives were estimated for different years and for each job and department title. Jobs attracted either zero exposure, very low (0 - 1 mg/m3), low (1 - 2.5 mg/m3), medium (2.5 - 6 mg/m3), or high exposure (6 - 20 mg/m3). The standardized mortality ratios (SMR) for all causes and the SMRs for mortality from cancer were not significantly different from 100. In this study estimated cumulative exposure to 2-mercaptobenzothiazole was not found to be a risk factor.

Source : Bayer AG Leverkusen

01.09.1994 (101)

Remark : Mortality trends for 1059 production workers at a rubber chemical plant in Nitro, West Virginia (USA) during 1955 - 1987 were examined to find whether they had increased mortality from cancer associated with exposure to 2-mercaptobenzothiazole. This chemical has been manufactured at the plant since 1935. Analyses were conducted on 2-mercaptobenzothiazole exposed employees by cumulative exposure and time since first exposure, and were also stratified by past assignment to p-aminobiphenyl-related departments; p-aminobiphenyl is a potent bladder carcinogen,

that was used at the plant between 1935 and 1955. An excess of bladder cancer was seen in 2-mercaptobenzothiazole workers who also had job assignments with exposure to p-aminobiphenyl. In workers without a job assignment with exposure to p-aminobiphenyl, there were no associations between exposure to 2-mercaptobenzothiazole and increased rates of most malignant neoplasms. The standardized mortality ratio (SMR) for bladder cancer was raised, although there were too few deaths to evaluate trends exposure category. There were no deaths from bladder cancer among 2-mercaptobenzothiazole workers hired after the end of p-aminobiphenyl use at the plant although only 0.03 deaths were expected.

Source : Bayer AG Leverkusen
02.09.1994 (102)

5.11 ADDITIONAL REMARKS

Type : Chemobiokinetics general studies

Remark : 72 % radioactivity excreted in urine and 4 % in feces in 96 hr.
Male and female Fischer 344 rats were dosed orally with 0.592 or 55.5 mg/kg of 14C-labelled MBT, then sacrificed at 8, 24, 72, or 96 hr post-dosing.

Source : Bayer AG Leverkusen
06.11.2000 (103)

Type : Chemobiokinetics general studies

Remark : Male and female rats and female guinea pigs were topically exposed to 14C-MBT at approximately 36.1% ug/animal. A separate set of rats were also dosed orally for 14 days with unlabelled MBT at 0.51 mg/kg/day prior to a single dose with 0.503 mg/kg of radiolabelled material. A third set of rats received radiolabelled MBT iv at a dosage of 0.602 mg/kg. Urine excretion of the absorbed dose was > 91 %.

Source : Bayer AG Leverkusen
02.06.1994 (104)

Type : Neurotoxicity

Remark : Decreased motor activity was noted.
This study was a rangefinding study. Male and female Sprague-Dawley rats were given MBT by gavage in a corn oil vehicle at dosage levels of 0 or 2750 mg/kg and then observed for 24 hr in a motor activity assessment.

Source : Bayer AG Leverkusen
03.11.2000 (105)

Type : Neurotoxicity

Remark : Male and female Sprague-Dawley rats were dosed once by gavage with MBT in a corn oil vehicle at levels of 0, 500, 1250, or 2750 mg/kg bw and then observed for 14 days. Motor activity testing and a functional observational battery were performed.

Based on the findings, it was concluded that the effects seen may be related to an acute, non-specific toxicity

without apparent neurotoxicity.

Source : Bayer AG Leverkusen
03.11.2000 (106)

Type : Neurotoxicity

Remark : 5000 ppm: NOEL; no effect.
In a three-month study, MBT was administered to Sprague-Dawley rats in the diet at levels of 0, 5000, 15000, or 25000 ppm. [5000, 15000, and 25000 ppm = 357, 2500, and 1786 mg/kg be, conversion number is 14.] Motor activity, functional observational battery, and gross and microscopic evaluations were performed.

Source : Bayer AG Leverkusen
03.11.2000 (107)

Type : other

Remark : Revision of chapter 5 (without inquiry): September 94

Source : Bayer AG Leverkusen
06.09.1994

Type : other: DNA binding study

Remark : Male and female Fischer 344 rats received a single dose of 375 mg [14C]2-mercaptobenzothiazole/kg bw by gavage; after 8 hours rats were killed, DNA was extracted from liver, adrenals, pituitary gland, pancreas and bone marrow and the amount of DNA associated radioactivity was determined. 2-mercaptobenzothiazole does not significantly bind to DNA from any of the tissues examined. The covalent binding index (CBI) for liver was approximately 1 to 3. The covalent binding indices for the other tissues were below 1. Strong hepatocarcinogens such as dimethylnitrosamine and aflatoxin have CBI values ranging from 6000 to greater than 20000.

Source : Bayer AG Leverkusen
01.09.1994 (108)

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**

9. References

(1) CRC Handbook of Chemistry and Physics. 80th edition (1999-2000) David R. Lide, ed. CRC Press, New York. p3-80, No. 2866.

(2) The Merck Index Eleventh Edition - 1989.

(3) Monsanto manufacturing data.

(4) The Merck Index Eleventh Edition - 1989.
Nine-volume 2nd edition of the CRC handbook of data on organic compounds.

(5) Monsanto study number SR-85-X017.

(6) Monsanto report number SR-85-X017.

(7) Environ Toxicol Chem 11:1153-68

(8) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(9) Monsanto. 1985. Report #SR-85-X017 SRI International.

(10) Springborn Laboratories Report # 89-9-3094. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule.

(11) Brownlee, B.G. J.H. Carey, G.A. MacInnis and I.T. Pellizzari (1992), Aquatic environmental chemistry of 2-(thiocyanomethylthio) benzothiazole and related benzothiazoles, Environmental Toxicology and Chemistry 11, 1153-1168.

(12) Parkanyi, C. and A.O. Abdelhamid (1985), Photodegradation of pesticides: photolysis of 2-mercaptobenzothiazole and 2-mercaptobenzimidazole, Heterocycles 23(11), 2917-2926.

(13) Mitchell, L.C. (1961), The effect of ultraviolet light (2537A) on 141 pesticide chemicals by paper chromatography, Journal Association of Official Agricultural Chemistry 44:643-712.

(14) Monsanto report AB-85-X016.

(15) Monsanto. 1984. Report# AB-84-X134 Analytic Bio-Chemistry Labs.

(16) Keith, L.H. (1976), Identification of organic compounds in unbleached treated Kraft paper mill wastewaters, Environmental Science and Technology 10(6), 555-564.

(17) Springborn Laboratories Report # 89-9-3086. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule.

(18) Monsanto Study #AN6405; August 19, 1980

(19) Springborn Laboratories Report # 89-9-3087. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule.

(20) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Compiled under the Supervision of Chemical Products Safety Division, Basic Industries Bureau MITI, Ed. by CITI, October 1992. Published by Japan Chemical Industry Ecology-Toxicology & Information Center

(21) Monsanto report MO-92-9056

(22) Monsanto report SR-85-0017.

(23) Tomlinson, T.G., A.G. Boon and C.N.A. Trotman (1966), Inhibition of nitrification in the activated sludge process of sewage disposal, Journal of Applied Bacteriology, 29(2), 266-291.

(24) Williams, G.R. (1984), The Effect of both powdered and liquid rubber additives on the growth of soil microorganisms, International Biodeterioration 20(3),173-5.

(25) Kondo, M., T. Nishihara, T. Shimamoto, T. Koshiwaka, T. Ii O, R. Sawamura,and K. Tanaka (1988A), Biodegradation Test of Chemicals by Cultivation Method, Eisei Kagaku 34,188-195.

(26) Thom, N.S. and A.R. Agg (1975), The breakdown of synthetic organic compounds in biological processes, Proceedings of the Royal Society London B. 189, 347-357.

(27) M. Kawasaki (1980), Experiences with the test scheme under the chemical control law of Japan: an approach to structure-activity correlations, Ecotoxicology and Environmental Safety 4, 444-454.

(28) Hashimoto, K., Y. Sasaki, Y. Ohara, and T. Matsuzawa (1978), Absorption, distribution and excretion of 2-mercaptobenzothiazole in carp, Bulletin Japanese Society of Scientific Fisheries 44(6), 623-629.

(29) Sasaki, S. (1979), The scientific aspects of the chemical substance control law in Japan, in Aquatic Pollutants: Transformation and Biological Effects. Hutzinger, O. et al (eds). Oxford: Pergamon Press. pp283-298.

(30) Monsanto. 1979. Report # AB-79-315 Analytic Bio-Chemistry.

(31) Bayer AG report

(32) Monsanto report SR-83-X062

(33) Monsanto report BN-76-0169

(34) Monsanto. 1976. Report# BN-76-169 EG&G Bionomics.

(35) Sollmann, T. (1949), Correlation of the aquarium goldfish toxicities of some phenols, quinones, and other benzene derivatives with their inhibition of autooxidative reactions, Journal General Physiology 32, 671-679.

Verschueren, K. (1983), Handbook of Environmental Data on Organic Chemicals. Van Nostrand Reinhold Company, Inc. NY.

(36) (2-Mercaptobenzothiazole (ROKON)) - Acute Toxicity to Daphnids (Daphnia magna) under Static Conditions (Final Report), EPA/OTS; Doc #86-920000843 (1992)

(37) Monsanto. 1979. Report # AB-79-314 Analytical Bio-Chemistry Laboratories

(38) Monsanto. 1979. Report # BN-79-313 EG&G Bionomics.

(39) Yoshioka, Y. (1985), Testing for the toxicity of chemicals with Tetrahymena pyriformis, The Science of the Total Environment 43, 149-157.

(40) Santodonato, J., L.N. Davis, P.H. Howard and J. Saxena (1976), Investigation of selected potential environmental contaminants: mercaptobenzothiazoles, EPA-560/2-76-006.

(41) Brown, S.L., F.Y. Chan, J.L. Jones (1975), Research program on hazard priority ranking of manufactured chemicals (chemicals 41-60), Stanford Research Institute. Menlo Park, CA 191 NSF-RA-E-75-190C.

(42) Springborn Laboratories Report # 89-9-3083. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule.

(43) Springborn Laboratories Report # 89-9-3082. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule.

(44) Monsanto. 1975. Report # Y-75-237 Younger Laboratories.

(45) Monsanto. 1973. Report Y-73-288, Younger Laboratories.

(46) Monsanto. 1956. Report SA-55-0074, Scientific Associates.

(47) McCormick, WE. Rubber Chemistry and Tehnology 44(2): 512-530. (1971)

(48) Guess WL and O'Leary RK. Toxicol and Appl Pharm. 14: 221-231 (1969)

(49) Industrial Bio-TEST-Laboratories Inc. (1977): IBT No. 8562-10075
In: Ciba Geigy Corp. (1985): NTIS/OTS 0206754

(50) DOW Chemical Co. (1961): Results of range finding toxicological tests on 2 mercaptobenzothiazole (Captex) cited in: Syracuse Research Corporation (1985): Technical Support Document 2-Mercaptobenzothiazole

(51) Monsanto. 1974. Report Y-73-0288 Younger Laboratories.

(52) Monsanto. 1973. Report Y-73-0288.

(53) Basketter, D.A. et al. (1993): Food Chem. Toxicol. 31, 63 - 67

(54) Wang, X. and Suskind, R.R. 1988. Comparative studies of the sensitization potential of morpholine, 2-mercaptobenzothiazole and 2 of their derivatives in guinea pigs. Contact Dermatitis. 19:11-15.

(55) Basketter, D.A., Scholes, E.W. (1992): Food Chem. Toxicol. 30, 65 - 69

(56) Scholes, E.W. et al. (1992): J. Appl. Toxicol. 12, 217 - 222

(57) Magnusson, B. and Kligman, A.M. (1970), Allergic Contact Dermatitis in the Guinea Pig, C.C. Thomas, ed., Springfield, IL.

(58) Magnusson, B. and Kligman, A.M. (1968), The identification of contact allergens by animal assay, the guinea pig maximization test method, Journal of Investigative Dermatology, 52, 268-276.

(59) Kaniwa, M.-A. et al. (1992): Contact Dermatitis 27, 166 - 173

(60) Ziegler, V. et al. (1972): Allergie und Immunologie 18, 203 - 208

(61) Ikarashi, Y. et al (1993), Evaluation of contact sensitivity of rubber chemicals using the murine local lymph node assay, Contact Deramtitis, 28, 77-80.

(62) Kammueller, M.E. et al. (1989): Int. J. Immunopharmac. 11, 293 - 300

(63) Monsanto report SH-76-0005

(64) Monsanto report ML-87-0068

(65) Bourrinet, P. et al. (1979): J. Pharm. Belg. 34, 21 - 26

(66) Monsanto report ML-88-0426

(67) National Toxicology Program report NTP TR 332.

(68) Physiolological Research Laboratories 78-60-106002 (1981)

(69) Monsanto Report MSL-8968

(70) Physiolological research Laboratories 78-60-106002 (1981)

(71) Ogawa, Y. et al. (1989): Bull. Natl. Inst. Hyg. Sci. 107, 44 - 50

(72) BF Goodrich Study No. 22 (1984)

(73) Monsanto. 1986. Report PK-86-9006 Pharmakon Research International. Jointly sponsored through the Chemical Manufacturer's Association, study No. PH 314-CMA-001-83.

(74) WTR International Work Group on the Toxicology of Rubber. Central Toxicology Laboratory Study No. CTL/5548. (1997)

(75) Monsanto report LB-86-9004. Jointly sponsored study through the Chemical Manufacturer's Association. Litton Bionetics, Inc. Project No. 20989.

(76) Monsanto report BO-76-0177

(77) Monsanto. 1986. Report PK-86-9005 Pharmakon Research International. Jointly sponsored through the Chemical Manufacturer's Association.

(78) Szybalski, W. (1958): Ann. N.Y. Acad. Sci. 76, 475 - 489

(79) Donner, M. et al. (1983): Scand. J. Work Environ. Health 9, Suppl. 2, 27 - 37

(80) Monsanto report BO-78-0240

(81) Litton Bionetics, Inc. (1985): LBI Project No. 20989

(82) Myhr, B. et al. (1990): Environ. Mol. Mutagen. 16, Suppl. 18, 138 - 144, 156

(83) Monsanto report SB-91-9705. SLS Study No. 3205.6 Jointly sponsored by the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule study. Springborn Laboratories Study No. 3205.5, 3205.6, 3205.7

(84) Monsanto. 1986. Report PK-86-9007 Pharmakon Research International. Jointly sponsored through the Chemical Manufacturer's Association, study No. PH 309A-CMA-001-83.

(85) Monsanto Environmental Health Lab Study No. 87134 (1988)

(86) Revazova, Y.A. (1968): Toksikol. Nov. Khim. Veshchestv, Vnedryaemykh Rezin. Shinnuyu Prom., 196 - 203 In: Chemical Abstr. 71, 47071e (1969)

(87) National Toxicology Program report NTP TR 332; NIH Publication No. 88-2588

(88) Monsanto report XX-86-9079. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule.

(89) Bionetics Research Laboratories, Inc. (1968): NTIS/PB 223159

(90) Innes, J.R.M. et al. (1969): J. Natl. Cancer Inst. 42, 1101 - 1114

(91) Springborn Laboratories, study No. 3205.5, Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule.

(92) Monsanto report SB-91-9708. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule SLS Study No. 3205.7

(93) Alexandrov, SE. (1974) Tezisy Dokl. Nauchn. Sess. Khim. Teknol. Org. Soedin. Sery Sernistykh Neftei. 13:98-99

(94) Monsanto report SB-91-9702. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule. Rodwell, D.E. et al (1990), Developmental toxicity study of 2-mercaptobenzothiazole (MBT) in two species, Teratology, p. 587 (abstract).

(95) Monsanto report SB-91-9704. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule. SLS Study No. 3205.4 Rodwell, D.E. et al (1990), Developmental toxicity study of 2-mercaptobenzothiazole (MBT) in two species, Teratology, p. 587 (abstract).

(96) Monsanto report SB-91-9701. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule, SLS Study No. 3205.2

(97) Monsanto report SB-91-9703. Jointly sponsored through the Chemical Manufacturer's Association as part of a TSCA Section 4 test rule, SLS study No.3205.1

(98) Hardin BD, Bond GP, Sikov MR, Andrew FD, Beliles RP, Niemeier RW. (1981) Scan. J. Work Environ. Hlth. 7(S4):66-75

(99) Korhonen A, Hemminki K, Vainio H. (1982) Arch. Environ. Contam. Toxicol. 11:753-759.

(100) Korhonen A, Hemminki K, Vainio H. (1983) Scan. J. Work Environ. Hlth. 9:115-119

(101) Sorahan, T., Pope, D. (1993): Br. J. Ind. Med. 50, 998 - 1002

(102) Strauss, M.E. et al. (1993): Br. J. Ind. Med. 50, 888 - 893

(103) Monsanto report SR-92-9055. Jointly sponsored through the Chemical Manufacturers Association as part of U. S. EPA TSCA Section 4 test rule.

(104) El Dareer, S.M., et al (1989), Disposition of 2-mercaptobenzothiazole and 2-mercaptobenzothiazole disulfide in rats dosed intravenously, orally, and topically and in guinea pigs dosed topically, Journal of Toxicology and Environmental Health, 27, 65-84.

(105) Monsanto Study BR-91-9707. Jointly sponsored through the Chemical Manufacturers Association as part of U. S. EPA TSCA Section 4 test rule, Project No. 83800

(106) Monsanto Study BR-91-9706. Jointly sponsored through the Chemical Manufacturers Association as part of U. S. EPA TSCA Section 4 test rule, Project No. 83801.
Bannister, R.M. et al (1991), Acute and subchronic neurotoxicity evaluation of 2-mercaptobenzothiazole (MBT) in rats, The Toxicologist, 11, 117 (Abstract).

(107) Monsanto Study XX-90-9513. Jointly sponsored through the Chemical Manufacturers Association as part of U. S. EPA TSCA Section 4 test rule.
Bannister, R.M. et al (1991), Acute and subchronic neurotoxicity evaluation of 2-mercaptobenzothiazole (MBT) in rats, The Toxicologist, 11, 117 (Abstract).

(108) Brewster, D.W. et al. (1989): Biochem. Biophys. Res. Commun. 165, 342 - 348

10. Summary and Evaluation

Id 149-30-4
Date 18.06.2003

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT