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Existing Chemical ID: 13752-51-7
CAS No. 13752-51-7
CAS Name N-oxodiethylenethiocarbamyl-N-oxodiethylsulfenamide
EINECS No. 237-335-9

Producer Related Part
Company:
Creation date: 19-AUG-2003 revised

Substance Related Part
Company:
Creation date: 19-AUG-2003 revised

Memo: Rubber and Plastic Additives (RAPA) HPV Panel

Printing date: 19-AUG-2003 revised
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Chapter (profile): Chapter: 1, 2, 3, 4, 5, 7
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Flags (profile): Flags: without flag, confidential, non confidential, WGK
(DE), TA-Luft (DE), Material Safety Dataset, Risk
Assessment, Directive 67/548/EEC, SIDS

1. General Information

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
Telefax: 703-741-6091

Type: cooperating company
Name: Alco Chemical Corporation
Country: United States

Type: cooperating company
Name: Bayer Polymers LLC
Country: United States

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

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

Type: cooperating company
Name: Eliokem, Inc.
Country: United States

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

Type: cooperating company
Name: Noveon, Inc (formerly BF Goodrich)
Country: United States

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

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

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

1. General Information

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 - 99 % w/w

1.1.0 Details on Template

1.1.1 Spectra

1.2 Synonyms

Morpholine, 4-[(morpholinthiocarbonyl)thio]-

Cure-Rite® 18

Good-Rite® 3030x18

1.3 Impurities

CAS-No: 729-46-4
EINECS-No:
EINECS-Name: Dimorpholine Thiuram Disulfide
Contents: < 5 % w/w

CAS-No: 34986-62-4
EINECS-No:
EINECS-Name: [4-(4'-morpholinodithion) thioxomethyl-morpholine]
Contents: < .5 % w/w

CAS-No: 110-91-8
EINECS-No: 203-815-1
EINECS-Name: morpholine
Contents: < .02 % w/w

CAS-No: 59-89-2
EINECS-No:
EINECS-Name: N-nitrosomorpholine
Contents: < .005 % w/w

1. General Information

- 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. Physico-chemical Data

2.1 Melting Point

Value: 130.0 -140.0 degree C
Method: Capillary melt point tube and Thomas Hoover Melt Point Apparatus
Year: 2003
GLP: no
Test substance: Commercial Cure-Rite® 18
Remark: The specification for Commercial Cure-Rite® 18 is 130.0 -140.0 degree C. The test is conducted using a capillary melt point tube and Thomas Hoover Melt Point Apparatus. The test material is ground and packed 3 mm to 6 mm high in the capillary tube. Bath temperature is started 10-15° C below expected melt point. Temperature automatically increases at a rate of 1.5° C/minute. The initial melt point is the temperature where liquid forms a meniscus. The final melt point is the temperature where no further melting is observed.
Result: 130.0 -140.0 degree C
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
Reference: (1)

Melting Point

Value: 124.3 degree C
Method: other: (calculated) MPBPWIN (v1.31)
Year: 1999
GLP: no
Test substance: other TS: molecular structure
Remark: Comparable to BFG MSDS data of ≥ 132 °C
Result: Melting Point: 251.84 deg C (Adapted Joback Method)
Melting Point: 92.44 deg C (Gold and Ogle Method)
Mean Melt Pt : 172.14 deg C (Joback; Gold,Ogle Methods)
Selected MP: 124.32 deg C (Weighted Value)
Reliability:
Reference: (2)

2.2 Boiling Point

Value: 130.0 -140.0 degree C (Decomposition)
Method: other: See Melting Point.
Year: 2003
GLP: no
Test substance: Commercial Cure-Rite® 18
Remark: Commercial Cure-Rite® 18 decomposes before it can boil. Decomposition starts at the melting point.
Reliability: (2) valid with restrictions

Flag: Critical study for SIDS endpoint
Reference: (1)

Boiling Point

Value: 353 degree C
Method: other: (calculated) MPBPWIN (v1.31) - Adapted Stein and Brown Method
Year: 1999
GLP: no
Test substance: other TS: molecular structure
Remark:
Reliability:
Reference: (2)

2.3 Density

Type: density
Value: 0.6 g/cm³
Method: other: historical data
Test substance: as prescribed by 1.1 - 1.4
Remark: Historical data
Reliability:
Reference: (3)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: 0.0000153 hPa at 25 degree C
Method: other (calculated): MPBPWIN (v1.31)
Year: 1999
GLP: no
Test substance: other TS: molecular structure
Result: Vapor Pressure Estimations (25 deg C):
(Using BP: 352.97 deg C (estimated))
(Using MP: 124.32 deg C (estimated))
VP: 5.17E-006 mm Hg (Antoine Method)
VP: 1.15E-005 mm Hg (Modified Grain Method)
VP: 2.32E-005 mm Hg (Mackay Method)
Selected VP: 1.15E-005 mm Hg (Modified Grain Method)
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
Reference: (2)

2.5 Partition Coefficient

log Pow: -0.84
Method: other (calculated): KOWWIN Program (v1.65)
Year: 1999
GLP: no
Test substance: other TS: molecular structure

2. Physico-chemical Data

ID: 13752-51-7

Reliability: (2) valid with restrictions
 Accepted calculation method
 Flag: Critical study for SIDS endpoint
 Reference: (2)

2.6.1 Water Solubility

Value: 62.85 g/l at 25 degree C
 Method: other: (calculated) WSKOW (v1.36)
 Year: 1999
 GLP: no
 Test substance: other TS: molecular structure
 Result: Log Kow (estimated) : -0.84
 Log Kow (experimental): not available from database
 Log Kow used by Water solubility estimates: -0.84

Equation Used to Make Water Sol estimate:

$$\text{Log S (mol/L)} = 0.796 - 0.854 \log \text{Kow} - 0.00728 \text{ MW} +$$

Correction (used when Melting Point NOT available)

Correction(s): Value

----- ----

Amine, aliphatic 1.008

Multi-Nitrogen Type -1.310

Log Water Solubility (in moles/L) : -0.597

Water Solubility at 25 deg C (mg/L): 6.285e+004

Reliability: (2) valid with restrictions
 Accepted calculation method
 Flag: Critical study for SIDS endpoint
 Reference: (2)

2.6.2 Surface Tension

2.7 Flash Point

2.8 Auto Flammability

Value: 275 degree C
 Remark: Self-Ignition Temperature (2)

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: 0.00000000002156 cm³/(molecule * sec)
 Degradation: 50 % after .6 hour(s)
 Method: other (calculated): AOP (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
 Reference: (2)

3.1.2 Stability in Water

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:

| Media | Concentration (percent) | Half-Life (hr) | Emissions (kg/hr) | Fugacity (atm) |
|----------|----------------------------|-------------------|----------------------|-------------------|
| Air | 0.00657 | 1.19 | 1000 | 1.47e-013 |
| Water | 50.2 | 900 | 1000 | 9.26e-015 |
| Soil | 49.7 | 900 | 1000 | 3.38e-013 |
| Sediment | 0.0927 | 3.6e+003 | 0 | 8.53e-015 |

Persistence Time: 763 hr
 Reaction Time: 1.24e+003 hr
 Advection Time: 1.99e+003 hr
 Percent Reacted: 61.6
 Percent Advected: 38.4
 Reliability: (2) valid with restrictions
 Accepted calculation method
 Flag: Critical study for SIDS endpoint
 Reference: (2)

3.3.2 Distribution

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

3.6 BOD₅, COD or BOD₅/COD Ratio

3.7 Bioaccumulation

Species: other: calculation

Exposure period:

Concentration:

BCF: 3.16

Elimination:

Method: other: BCF Program (v2.13)

Year: 1999 GLP: no

Test substance: other TS: molecular structure

Result: Log Kow (estimated) : -0.84

Log Kow (experimental): not available from database

Log Kow used by BCF estimates: -0.84

Equation Used to Make BCF estimate:

Log BCF = 0.50

Correction(s): Correction Factors Not Used for Log Kow < 1

Estimated Log BCF = 0.500 (BCF = 3.162)

Reference:

(2)

3.8 Additional Remarks

-

4. Ecotoxicity

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: other: calculation
Species: other: Fish
Exposure period: 96 hour(s)
Unit: g/l Analytical monitoring: no
LC50: 86.036
Method: other: ECOSAR 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:
Reference: (2)

Type: other: calculation
Species: other: Saltwater Fish
Exposure period: 96 hour(s)
Unit: g/l Analytical monitoring: no
LC50: 4.992
Method: other: ECOSAR 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:
Reference: (2)

Type: other: calculation
Species: other: Fish
Exposure period: 14 day
Unit: g/l Analytical monitoring: no
LC50: 99.248
Method: other: ECOSAR 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:
Reference: (2)

4. Ecotoxicity

4.2 Acute Toxicity to Aquatic Invertebrates

Type: other: calculation
Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: g/l Analytical monitoring: no
LC50: 75.767
Method: other: ECOSAR 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:
Reference: (2)

Type: other: calculation
Species: Mysidopsis bahia (Crustacea)
Exposure period: 96 hour(s)
Unit: g/l Analytical monitoring: no
LC50 : 188
Method: other: ECOSAR 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:
Reference: (2)

Type: other: calculation
Species: Daphnia sp. (Crustacea)
Exposure period: 16 day
Unit: mg/l Analytical monitoring: no
EC50: 1121
Method: other: ECOSAR 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:
Reference: (2)

4. Ecotoxicity

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: other algae: green algae
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: g/l Analytical monitoring: no
EC50: 40.223
ChV : 0.779
Method: other: ECOSAR v0.99e
Year: GLP: no
Test substance: other TS: molecular structure
Remark: Chemical may not be soluble enough to measure this predicted effect.
Reliability:
Reference: (2)

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: other
Exposure period: 30 day
Unit: mg/l Analytical monitoring: no
ChV : 7012
Method: other: ECOSAR 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:
Reference: (2)

4.5.2 Chronic Toxicity to Aquatic Invertebrates

4. Ecotoxicity

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type: other: calculation
Species: Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint: mortality
Exposure period: 14 day
Unit: other: ppm
LC50: 11449
Method: other: ECOSAR 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:
Reference: (2)

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. Toxicity

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: CD® Sprague-Dawley (Charles River)
Sex: Male and Female
Number of
Animals: 10/sex/dose for both suppliers
Vehicle: corn oil
Value: 5200 mg/kg bw 5000 mg/kg bw (+/- 1,200 mg/kg) Taconic
Method: other: 40CFR Part 163.81-1
Year: GLP: yes
Test substance: other TS: Cure-Rite® 18, purity: not noted
Remark: Groups of albino rats (5 males/group) were administered doses of 1800, 2700, 4050, 6075, or 9112 mg/kg by gavage as a 50% suspension in corn oil. All animals were observed closely for signs of systemic toxicity and mortality at frequent intervals during the day of dosing and daily thereafter for 14 days. Gross necropsies were performed on the animals that died. At the end of the 14-day post exposure observation period the surviving animals were weighed, sacrificed, and subjected to gross necropsies.
Discriminating dose: LD0 = 2,700 mg/kg
Reliability: (1) valid without restriction
GLP study, Meets National standards method
Flag: Critical study for SIDS endpoint
Reference: (4)

Type: LD50
Species: mouse
Strain: CD-1
Sex: male/female
Number of
Animals: 10/sex/group
Vehicle: corn oil
Value: 9000 mg/kg bw
Method: other: 40CFR Part 163.81-1
Year: GLP: yes
Test substance: other TS: Cure-Rite® 18; purity: not noted
Remark: Groups of albino rats (5 males/group) were administered doses of 25, 50, 100, 1800, 2700, 4050, 6075, or 9112 mg/kg by gavage as a 50% suspension in corn oil. All animals were observed closely for signs of systemic toxicity and mortality at frequent intervals during the day of dosing and daily thereafter for 14 days. Gross necropsies were performed on the animals that died. At the end of the 14-day post exposure observation period the surviving animals were weighed, sacrificed, and subjected to gross necropsies.

Discriminating dose: LD0 = 4,050 mg/kg

5. Toxicity

LD50 (95% conf. Limits) = 11,000 mg/kg (5,100-16,900 mg/kg) for males and 7,000 mg/kg (4,900-9,100 mg/kg) for females

Reliability: (1) valid without restriction
GLP study, Meets National standards method

Flag: Critical study for SIDS endpoint

Reference: (5)

Type: LD50

Species: rat

Strain: Unknown

ex: Males

Number of

Animals: 5/group

Vehicle: Corn oil

Value: 5110 mg/kg bw

Method: other: Federal Hazardous Substances Act (Revised, Fed. Reg.,
September 17, 1964

Year: 1971 GLP: no

Test substance: other TS: Good-Rite® 3030x18 (Cure-Rite® 18) ; purity: not noted

Remark: Groups of albino rats (5 males/group) were administered doses of 464, 1000, 2150, 4640, and 10,000 mg/kg by gavage as a 50% suspension in corn oil. All animals were observed closely for signs of systemic toxicity and mortality at frequent intervals during the day of dosing and at least once daily thereafter for 14 days. Gross necropsies were performed on the animals that died. At the end of the 14-ay post exposure observation period the surviving animals were weighed, sacrificed, and subjected to gross necropsies.

Discriminating dose: LD0 = 1,000 mg/kg

Reliability: (2) valid with restrictions

Reference: (6)

Type: LD50

Species: rat

Strain: CD® Sprague-Dawley (Taconic Farms)

Sex: Male and Female

Number of

Animals: 10/sex/group

Vehicle: Corn oil

Value: 5000 mg/kg bw

Method: other: 40CFR Part 163.81-1

Year: GLP: yes

Test substance: other TS: Cure-Rite® 18; purity: not noted

Remark: Groups of albino rats (5 males/group) were administered doses of 1800, 2700, 4050, 6075, or 9112 mg/kg by gavage as a 50% suspension in corn oil. All animals were observed closely for signs of systemic toxicity and mortality at frequent intervals during the day of dosing and daily thereafter for 14 days. Gross necropsies were performed on the animals that died. At the end of the 14-ay post exposure observation period the surviving animals were weighed, sacrificed, and subjected to gross necropsies.

Discriminating dose: LD0 = 2,700 mg/kg

5. Toxicity

Reliability: (1) valid without restriction
GLP study, Meets National standards method
Reference: (4)

5.1.2 Acute Inhalation Toxicity

Type: LC0
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 1 hour(s)
Value: 164.4 mg/l
Method: other: Federal Hazardous Substances Act (Revised, Fed. Reg.,
September 17, 1964)
Year: 1971 GLP: no
Test substance: other TS: Good-Rite® 3030x18 (Cure-Rite® 18); purity: not noted
Remark: A group of 10 male albino rats were exposed to 164.4 mg/l (calculated) for 1 hour..
All animals were observed closely for signs of systemic toxicity and mortality at
during the exposure period and at frequent intervals daily thereafter for 14 days. At
the end of the 14-ay post exposure observation period the surviving animals were
weighed, sacrificed, and subjected to gross necropsies.

No evidence of systemic toxicity or mortality was observed.

Test substances measured not analysed.

Reliability: (1) valid without restriction
Meets National standards method
Flag: Critical study for SIDS endpoint
Reference: (6)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Strain:
Sex:
Number of
Animals:
Vehicle:
Value: > 10000 mg/kg bw
Method: other:) Federal Hazardous Substances Act (Revised, Fed. Reg.,
September 17, 1964)
Year: 1971 GLP: no
Test substance: other TS: Good-Rite® 3030x18 (Cure-Rite® 18); purity: not noted
Remarks: Groups of albino rabbits (2/sex/group) were administered doses of 1000, 2150,
4640, and 10,000 mg/kg to the abraded and intact skin and then wrapped with a

5. Toxicity

semi-occlusive bandage. After 24 hours the bandages were removed. All animals were observed closely for signs of systemic toxicity and mortality, and irritation. Examinations for gross signs of toxicity and dermal irritation were conducted at frequent intervals during the 14 day post exposure period. Gross necropsies were performed on the animal (1,000 mg/kg group) that died. At the end of the 14-day post exposure observation period the surviving animals were weighed, sacrificed, and subjected to gross necropsies.

Reliability: (1) valid without restriction
Meets National standards method
Flag: Critical study for SIDS endpoint
Reference: (6)

5.1.4 Acute Toxicity, other Routes

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of
Animals:
Result: not irritating
EC classificat.:
Method: other: Section 1500.42, Federal Hazardous Substances Act
Regulations, CFR 16, p. 125
Year: 1981 GLP: yes
Test substance: other TS: Cure-Rite® 18; purity: not noted
Result: No positive scores; one animal had scores of "1" for redness
and chemosis at day one.
Reliability: (1) valid without restriction
GLP study, Meets National standards method
Reference: (7)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of
Animals:
Result: irritating
EC classification:

5. Toxicity

Method: other: Federal Hazardous Substances Act (Revised, Fed. Reg.,
September 17, 1964)
Year: 1964 GLP: no
Test substance: other TS: Good-Rite® 3030x18 (Cure-Rite® 18); purity: not
noted
Reliability: (1) valid without restriction
Meets National standards method
Reference: (5)

5.3 Sensitization

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure period: 2 years
Frequency of
treatment: continuous daily
Post. obs.
period: none
Doses: 0, 20, 60, 200, or 600 ppm
Control Group: yes, concurrent no treatment
NOAEL: 200 ppm
LOAEL: 600 ppm
Method: EPA OPP 82-5
Year: 1986 GLP: yes
Test substance: other TS: Commercial Cure-Rite® 18; purity: 96.8%
Result: Diets containing 0, 20, 60, or 600 ppm of the test material were administered to groups (60/sex/group) of Sprague-Dawley rats for 112 weeks. Ten rats/sex/group were identified for a 12 month interim sacrifice. Animals were checked twice dail for mortality and gross signs of toxicity. A detailed physical exam palpation for tissue masses was performed weekly. Body weight and feed consumption were measured weekly through week 12 and biweekly from week 13 to 26 and monthly thereafter. Hematology, clinical chemistry, and urinalysis were conducted pretest on 15 animals/sex and at months 6, 12, 18, and 24. Animals were given a complete gross post mortem examination following spontaneous death, death *in extremis*, or scheduled sacrifices. A full set of organs were subjected to gross and histological examination. All tissues from the control and high dose were processed for pathological examination at 12 months and termination. Tissues in mid and low dose groups were identified for pathological evaluation based on the pathological evaluations in the controls and high dose groups. Organs also were weighed. Furthermore, the testes from 3 of the 10 males at 12 months were processed for electron and light microscopy examination. Statistical analyses were conducted on the end points.

5. Toxicity

A compound related increase in tumors of the urinary system was observed in the high dose group: males (**kidney**: urothelia carcinoma, 2/60; squamous cell carcinoma, 1/60; **ureters**: urothelial carcinoma 4/6 [2 in one male]; **urinary bladder**: urothelial papilloma, 3/59; urothelial carcinoma, 4/59; squamous cell papilloma, 1/59; squamous cell carcinoma, 2/59; **combined total neoplasms**: 17 vs 1 urothelial papilloma in the control); females (**kidney**: urothelial papilloma, 1/60; urothelia carcinoma, 3/60; squamous cell carcinoma, 3/60; **ureters**: urothelial carcinoma 2/8; **urinary bladder**: urothelial papilloma, 3/59; urothelial carcinoma, 2/59; squamous cell papilloma, 2/59; squamous cell carcinoma, 1/59; **combined total neoplasms**: 15 vs 0 in the control). Tumors of the urinary system were not found in the mid and low dose groups. Ureters were not evaluated in the controls, low or mid dose groups.

Kidney weights, non-neoplastic urinary tract abnormalities, and rales was observed in the high dose males and females. Body weights also were significantly lower in the high dose males and females. No compound-related effects on hematology, clinical chemistry, or urinalysis were noted.

Reliability: (1) valid without restriction

GLP guideline study

Flag: Critical study for SIDS endpoint

Reference:

(8)

5.5 Genetic Toxicity 'in Vitro'

Type: Bacterial reverse mutation assay

System of testing:

Salmonella typhimurium strains TA-1535, TA-1537, TA-1538, TA-98, TA-100

Concentration: 0.5 to 1,000 ug/plate

Cytotoxic Conc.: With metabolic activation: 0.5 to 100 ug/plate (little to no toxicity)

Without metabolic activation: 0.5 to 100 ug/plate (little to no toxicity)

Metabolic

activation: with and without

Result: negative

Method: other: according to other: according to Ames et al (1975)

Mutation Res. 31:347-364; McCann et al. (1975) Proc. Nat.

Acad. Sci. 72:5135-5139

Year: 1975 GLP: no data

Test substance: other TS: Commercial Cure-Rite® 18 (Purified); purity: 97.5%

Remark: 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 typhimurium* strains TA-1535, TA-1537, TA-1538, TA-98 and TA-100 were obtained from Dr. Bruce Ames. All indicator strains were kept at 4°C 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 37°C 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 MgCL₂, 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 ----.”

Signed QA assurance statement provided

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

Flag: Critical study for SIDS endpoint (9) (10)

Type: Bacterial reverse mutation assay

System of testing: Escherichia coli strain WP2urvA-

Concentration: 0.5 to 1,000 ug/plate

Cytotoxic Conc.: With metabolic activation: 0.5 to 100 ug/plate (little to no toxicity)
Without metabolic activation: 0.5 to 100 ug/plate (little to no toxicity)

Metabolic activation: with and without

Result: negative

Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath,
S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983)
Environ. Mutagen. 5:193-215

Year: 1983 GLP: no data

Test substance: other TS: Cure-Rite® 18 (purified), purity: 97.5%

Remark: "The *E. coli* strain WP₂ uvrA⁻ was obtained from Dr. M.H.L. Green, MRC Cell Mutation Unit, University of Sussex, England. The indicator strain was kept at 4°C on standard methods agar plates or minimal medium plates supplemented with an excess triptophan. Laboratory cultures were grown at 37°C 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.

A signed QA assurance statement was provided.

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

Flag: Critical study for SIDS endpoint

Reference: (9) (10)

Type: Cytogenetic assay

System of testing: Chinese Hamster Ovary (CHO) Cells

Concentration: 2.500 to 20.000 µg/ml

Cytotoxic Conc.: concentration used based on mouse lymphoma L5178Y cells

Metabolic activation: with and without

Result: positive

Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath, S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983) Environ. Mutagen. 5:193-215

Year: 1983 GLP:

Test substance: other TS: Cure-Rite® 18 (purified); purity = 97.5%.

Remark: CHO cells were obtained from the American Culture Collection, Repository No. CCL61, Rockville, MD. CHO cells were grown in McCoy's 5a medium supplemented with 10% fetal calf serum, L-glutamine, and penicillin-streptomycin. Cultures were set up approximately 24 hours prior to treatment by seeding 8x10⁵ cells per 75-cm² plastic flask in 10 ml of fresh medium.

The test chemical were dissolved in DMSO. Untreated and solvent (1% final concentration) control cultures were used and the positive controls were triethylenemelamine (0.5, 0.75, or 1.0 µg.ml) without activation or cyclophosphamide (62.25, 130.5, or 261 µg/ml) with S-9 activation. The dose

range was selected on the basis of survival of L5178Y cells 24 hours after treatment in the mouse lymphoma forward mutation assay, considering that the exposure period in the CHO assay (2 hours) is shorter than the mouse lymphoma assay (4 hours). The highest dose for cytogenetics assay was selected to produce little or no toxicity.

In the nonactivation assay, approximately $2-3 \times 10^6$ cells were treated with the test chemical for two hours at 37°C in growth medium. The exposure period was terminated by washing the cells twice with saline containing 10% FBS and then adding fresh medium. Incubation continued for 17 hours. Colcemid was added for the last two hours of incubation (2×10^{-7} M final concentration), and metaphase cells were collected by mitotic shake-off. The cells were treated with 0.075 M KCl hypotonic solution, washed three times in fixative (methanol:acetic acid, 3:1 v/v), dropped into slides, and air-dried. The slides were stained with 10% Giemsa at pH 6.8. Fifty or 100 cells were scored at each dose level.

The activation assay differed from the nonactivation assay in that the S-9 reaction mixture (2.4 mg NADP, 4.5 mg isocitric acid and 15 μl S-9 fraction per ml) was added to the growth medium, together with the test chemical, for two hours. After exposure the cultures were treated as above.

Statistical evaluations were conducted using the Student t-test.

Signed QA assurance statement provided

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

Flag: Critical study for SIDS endpoint

Reference: (9) (11)

Type: DNA damage and repair assay

System of testing: *Escherichia coli* strains W3110 (pol A+) and W3078 (pol A-)

Concentration: 100 to 5,000 $\mu\text{g}/\text{plate}$

Cytotoxic Conc.: With metabolic activation: 0.5 to 100 $\mu\text{g}/\text{plate}$ (little or no toxicity)
Without metabolic activation: 0.5 to 100 $\mu\text{g}/\text{plate}$ (little or no toxicity)

Metabolic activation: with and without

Result: positive

Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath, S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983) *Environ. Mutagen.* 5:193-215

Year: 1983 GLP:

Test substance: other TS: Cure-Rite® 18.(purified); purity: 97.5%

Remark: Repair competent *E. coli* strain W3110 (polA⁺) and repair deficient strain *E. coli* p3078 (polA⁻) were obtained from Dr. RosenKrantz, Columbia University, New York. The indicator strains were kept at 4°C on standard methods agar plates or HA + T medium. For each experiment, the bacterial strains were cultured overnight at 37°C in HA + T medium without agar. A thymine-supplemented HA agar was used as the selective medium.

5. Toxicity

The procedure was based on the method of Slater et al. (1971). Test material was dissolved in DMSO. Positive controls (10 µl methylmethane sulfonate without S-9 and 100µl dimethylnitrosamine with S-9) and solvent controls (50 µl DMSO) were used. In order, 2.0 ml of HA + T overlay agar and 0.1 ml – 0.2 ml of indicator organisms were added to a sterile test tube in a 45°C water bath. Equal volumes of at least 4 doses of the test material and a single dose of the control chemicals were added to wells of uniform diameter in the agar in the appropriate plates. For noactivation assays, 0.05 ml of phosphate buffer, pH 7.4 was added to each well. For activation assays, 0.05 of the S-9 mix was added. The plates were incubated at 37°C for approximately 24 hours. The zones of inhibition were measured and recorded in millimeters.

A differential of 4 mm or greater between the competent and noncompetent strains was considered to have produced a DNA-modifying effect. If no zones were induced, the results were considered to be a no-test. Additional criteria such as reproducibility also were considered.

Reliability: Signed QA assurance statement provided
(2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment

Flag: Critical study for SIDS endpoint

Reference: (9) (10)

Type: Mammalian cell gene mutation assay

System of testing: BALB 3T3 Mouse Cells

Concentration: 0.01000 to 0.20000 ug/ml

Cytotoxic Conc.: 0.488 ug/ml

Metabolic activation: without

Result: positive

Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath, S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983) Environ. Mutagen. 5:193-215

Year: 1983 GLP:

Test substance: other TS: Cure-Rite® 18 (purified); purity = 97.5%.

Remark: Clone 113 of BALB/3T3 mouse cells was obtained from Dr. Takeo Kakunga, NCI, Bethesda, MD. Subclones that were selected for low spontaneous frequencies of foci formation were used, Stocks were maintained in liquid nitrogen, and laboratory cultures were checked periodically for mycoplasma contamination. Cultures were grown and passed weekly in Eagle's Minimum Essential Medium (EMEM) supplemented with 10% fetal bovine serum.

The test chemical was dissolved in a small quantity of DMSO and then diluted with EMEM so the final concentration of DMSO was less than 0.5%. Lower concentrations were obtained by serial dilutions with EMEM. The dose range was based on the results of a clonal toxicity assay in which a series of 200 cells/dish were

5. Toxicity

exposed in triplicate to a wide range of test chemical concentrations for 3 days. Five doses were selected to cover a wide range of toxicities from little or no reduction in colony-forming ability to a 50% reduction in the colony number. A negative control consisting of cells exposed to 0.5% DMSO in EMEM and a positive control treatment of 5 µg/ml 3-methylcholanthrene (3-MCA) were also employed.

The transformation assay was based on the method of Kakunga (1973). Twenty four hours prior to treatment, a series of 25-cm² flasks was seeded with 10⁴ cells/flask and incubated. Fifteen flasks then were treated for each test dose, positive control, and negative control. The flasks were incubated for a three-day period at 37°C in a humidified atmosphere containing 5% CO₂. The cells were then washed, and the incubation was continued for 4 weeks with refeeding twice a week. The assay was terminated by fixing the cell monolayers with methanol and staining Giemsa. The stained flasks were examined by eye and by microscope to determine the number of foci of transformed cells. The foci consisted of piled up and randomly oriented cells, sometimes with necrotic centers, on surrounding monolayers of normal cells.

Statistical tables provided by Kastenbaum and Bowman (1970) were used to determine statistical significance.

Precipitation conc: >250 ug/ml
Signed QA assurance statement provided.
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented
and acceptable for assessment
Flag: Critical study for SIDS endpoint
Reference: (9) (12)

Type: Mouse lymphoma assay
System of testing: Mouse Lymphoma cell line L5178Y TK+/-
Concentration: 1.250 to 25.0 ug/ml
Cytotoxic Conc.: With metabolic activation: Percent relative growth was 64.9%
at 1.560 ug/ml and 5.2% at 25.0 ug/ml
Without metabolic activation: Percent relative growth was
29.7% at 1.250 ug/ml and 7.7-11.2% at 5.0-20.0 ug/ml
Metabolic activation: with and without
Result: positive with and without
Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath,
S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983)
Environ. Mutagen. 5:193-215
Year: 1983 GLP:

Test substance: other TS: Cure-Rite® 18 (purified); purity = 97.5%.

Remark: Mouse Lymphoma cells (L5178Y TK^{+/-}, clone 3.7.2C derived from the Fischer line from Dr. Donald Clive) were treated with doses of 0, 1.25, 5, 15, and 20 µg/ml. The negative solvent control was prepared by adding 0.1 DMSO per 10 ml of culture. The positive control was 0.5 µl/ml ethyl methanesulfonate under nonactivation conditions and) and 0.3 µl/ml dimethylnitrosamine under activation conditions. The assay procedure was very similar to the method of Clive and Spector (1975). Each treated culture consisted

5. Toxicity

of 3×10^6 cells suspended in 10 ml final volumes in 15 ml centrifuge tubes. Nonactivation and activation assays were conducted the same except the cell cultures in the activation assay contained the S-9, Aroclor 1254-induced liver preparation with cofactors. The cells were exposed to the test material dose for 4 hours, were washed, and were allowed an expression time of two days in growth medium. At the end of the expression period, 3×10^6 cells from each treated culture were seeded in the selection medium (1×10^6 cells per 100 mm dish). Cloning efficiency was determined by serially diluting a portion of the cells and seeding 300 cells in the nonselective cloning medium at 100 cells per 100 mm dish. BrdUrd-resistant colonies (TK^{-/-} mutants) and viable colonies (nonselective medium) were counted after 10 days incubation at 37°C in a humidified atmosphere containing 5% CO₂. The ratio of resistant to viable colonies yielded the mutant frequency in units of 10⁻⁴. The average of the solvent and untreated negative control mutant frequencies was used as the background or spontaneous mutant frequency for each trial. A treated culture was considered to have a significantly elevated mutation frequency if the frequency exceeded 10×10^{-6} plus 1.5 times the background frequency. Additional criteria such as a dose or toxicity related response and repeatability between trial were also used to determine the presence of mutagenic activity.

The test substance was positive with and without activation but only at doses that were very toxic.

Precipitation conc: >250 ug/ml
Signed QA assurance statement provided.

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

Flag: Critical study for SIDS endpoint

Reference: (9) (10)

Type: Bacterial reverse mutation assay

System of

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

Concentration: 0.5 to 5,000 ug/plate

Cytotoxic Conc.: With metabolic activation: 0.5 to 100 ug/plate (little to no
toxicity)

Without metabolic activation: 0.5 to 100 ug/plate (little to
no toxicity)

Metabolic

activation: with and without

Result: negative

Method: other: according to Ames et al (1975) Mutation Res.
31:347-364; McCann et al. (1975) Proc. Nat. Acad. Sci.
72:5135-5139

Year: 1975 GLP:

Test substance: other TS: Commercial Cure-Rite® 18, purity: 95.6%

Remark: 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:

5. Toxicity

“*Salmonella typhimurium* strains TA-1535, TA-1537, TA-1538, TA-98 and TA-100 were obtained from Dr. Bruce Ames. All indicator strains were kept at 4°C on minimal medium plates supplemented with a trace of biotin and an excess of histidine (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 37°C 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 Bionetics 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 MgCl₂, 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 ----.”

Signed QA assurance statement provided

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

Reference: (9) (10)

Type: Bacterial reverse mutation assay

System of testing: *Salmonella typhimurium* strains TA-1535, TA-1537, TA-1538, TA-98, TA-100 and *Saccharomyces* strain D4

Concentration: 0.5 to 1,000 ug/plate

Cytotoxic Conc.: With metabolic activation: 1000 ug/plate (TA-98); 1000 ug/plate, 500 ug/plate, and 100 ug/plate (D4)
Without metabolic activation: 1000 ug/plate (TA-98); 1000 ug/plate, 500 ug/plate, and 100 ug/plate (D4)

Metabolic activation: with and without

Result: negative

5. Toxicity

Method: other: according to Ames et al (1975) Mutation Res.
31:347-364; McCann et al. (1975) Proc. Nat. Acad. Sci.
72:5135-5139

Year: 1975 GLP:

Test substance: other TS: Commercial Cure-Rite® 18; purity: not noted

Remark: 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 typhimurium* strains TA-1535, TA-1537, TA-1538, TA-98 and TA-100 were obtained from Dr. Bruce Ames. All indicator strains were kept at 4°C 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 37°C 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 MgCL₂, 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 ----.”

Signed QA assurance statement provided

Saccharomyces strain D4 not reported in referenced publication.

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

Reference: (9) (10)

5. Toxicity

Type: Bacterial reverse mutation assay
System of testing: Escherichia coli strain WP2uvrA
Concentration: 0.5 to 1,000 ug/plate
Cytotoxic Conc.: With metabolic activation: 0.5 to 100 ug/plate (little or no toxicity) Without metabolic activation: 0.5 to 100 ug/plate (little or no toxicity)
Metabolic activation: with and without
Result: negative
Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath, S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983) Environ. Mutagen. 5:193-215
Year: 1983 GLP:
Test substance: other TS: Commercial Cure-Rite® 18, purity: 95.6%

Remarks: "The *E. coli* strain WP₂ uvrA⁻ was obtained from Dr. M.H.L. Green, MRC Cell Mutation Unit, University of Sussex, England. The indicator strain was kept at 4°C on standard methods agar plates or minimal medium plates supplemented with an excess triptophan. Laboratory cultures were grown at 37°C 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.

A signed QA assurance statement was provided.

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

Reference: (9) (10)

Type: Cytogenetic assay
System of testing: Chinese Hamster Ovary (CHO) Cells
Concentration: 0.313 to 5.000 ug/ml
Cytotoxic Conc.: concentration used based on mouse lymphoma L5178Y cells
Metabolic activation: with and without
Result:

5. Toxicity

Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath,
S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983)
Environ. Mutagen. 5:193-215

Year: 1983 GLP:

Test substance: other TS: Commercial Cure-Rite® 18; purity = 95.6%.

Remark: CHO cells were obtained from the American Culture Collection, Repository No. CCL61, Rockville, MD. CHO cells were grown in McCoy's 5a medium supplemented with 10% fetal calf serum, L-glutamine, and penicillin-streptomycin. Cultures were set up approximately 24 hours prior to treatment by seeding 8×10^5 cells per 75-cm² plastic flask in 10 ml of fresh medium.

The test chemical were dissolved in DMSO. Untreated and solvent (1% final concentration) control cultures were used and the positive controls were triethylenemelamine (0.5, 0.75, or 1.0 µg.ml) without activation or cyclophosphamide (62.25, 130.5, or 261 µg/ml) with S-9 activation. The dose range was selected on the basis of survival of L5178Y cells 24 hours after treatment in the mouse lymphoma forward mutation assay, considering that the exposure period in the CHO assay (2 hours) is shorter than the mouse lymphoma assay (4 hours). The highest dose for cytogenetics assay was selected to produce little or no toxicity.

In the nonactivation assay, approximately $2-3 \times 10^6$ cells were treated with the test chemical for two hours at 37° C in growth medium. The exposure period was terminated by washing the cells twice with saline containing 10% FBS and then adding fresh medium. Incubation continued for 17 hours. Colcemid was added for the last two hours of incubation (2×10^{-7} M final concentration), and metaphase cells were collected by mitotic shake-off. The cells were treated with 0.075 M KCl hypotonic solution, washed three times in fixative (methanol:acetic acid, 3:1 v/v), dropped into slides, and air-dried. The slides were stained with 10% Giemsa at pH 6.8. Fifty or 100 cells were scored at each dose level.

The activation assay differed from the nonactivation assay in that the S-9 reaction mixture (2.4 mg NADP, 4.5 mg isocitric acid and 15 µl S-9 fraction per ml) was added to the growth medium, together with the test chemical, for two hours. After exposure the cultures were treated as above.

Statistical evaluations were conducted using the Student t-test.

Signed QA assurance statement provided

Result: Genotoxic effects: With metabolic activation: negative
Without metabolic activation: positive

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

Reference: (9) (11)

5. Toxicity

Type: DNA damage and repair assay
System of testing: Escherichia coli strains W3110 (pol A+) and W3078 (pol A-)
Concentration: 100 to 5,000 ug/plate
Cytotoxic Conc.: With metabolic activation: 0.5 to 100 ug/plate (little or no toxicity)
Without metabolic activation: 0.5 to 100 ug/plate (little or no toxicity)

Metabolic

activation: with and without

Result: positive

Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath,
S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983)
Environ. Mutagen. 5:193-215

Year: 1983 GLP:

Test substance: other TS: Commercial Cure-Rite® 18, purity: 95.6%

Remark: Repair competent *E. coli* strain W3110 (polA⁺) and repair deficient strain *E. coli* p3078 (polA⁻) were obtained from Dr. RosenKrantz, Columbia University, New York. The indicator strains were kept at 4°C on standard methods agar plates or HA + T medium. For each experiment, the bacterial strains were cultured overnight at 37°C in HA + T medium without agar. A thymine-supplemented HA agar was used as the selective medium.

The procedure was based on the method of Slater et al. (1971). Test material was dissolved in DMSO. Positive controls (10 µl methylmethane sulfonate without S-9 and 100µl dimethylnitrosamine with S-9) and solvent controls (50 µl DMSO) were used. In order, 2.0 ml of HA + T overlay agar and 0.1 ml – 0.2 ml of indicator organisms were added to a sterile test tube in a 45°C water bath. Equal volumes of at least 4 doses of the test material and a single dose of the control chemicals were added to wells of uniform diameter in the agar in the appropriate plates. For noactivation assays. 0.05 ml of phosphate buffer, pH 7.4 was added to each well. For activation assays, 0.05 of the S-9 mix was added. The plates were incubated at 37°C for approximately 24 hours. The zones of inhibition were measured and recorded in millimeters.

A differential of 4 mm or greater between the competent and noncompetent strains was considered to have produced a DNA-modifying effect. If no zones were induced, the results were considered to be a no-test. Additional criteria such as reproducibility also were considered.

Signed QA assurance statement provided

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

Reference: (9) (10)

5. Toxicity

Type: Mammalian cell gene mutation assay
System of testing: BALB 3T3 Mouse Cells
Concentration: 0.05000 to 0.10000 ug/ml
Cytotoxic Conc.: 0.488 ug/ml
Metabolic activation: without
Result: negative
Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath, S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983) Environ. Mutagen. 5:193-215
Year: 1983 GLP:
Test substance: other TS: Commercial Cure-Rite® 18; purity = 95.6%.
Remark: Clone 113 of BALB/3T3 mouse cells was obtained from Dr. Takeo Kakunga, NCI, Bethesda, MD. Subclones that were selected for low spontaneous frequencies of foci formation were used, Stocks were maintained in liquid nitrogen, and laboratory cultures were checked periodically for mycoplasma contamination. Cultures were grown and passed weekly in Eagle's Minimum Essential Medium (EMEM) supplemented with 10% fetal bovine serum.

The test chemical was dissolved in a small quantity of DMSO and then diluted with EMEM so the final concentration of DMSO was less than 0.5%. Lower concentrations were obtained by serial dilutions with EMEM. The dose range was based on the results of a clonal toxicity assay in which a series of 200 cells/dish were exposed in triplicate to a wide range of test chemical concentrations for 3 days. Five doses were selected to cover a wide range of toxicities from little or no reduction in colony-forming ability to a 50% reduction in the colony number. A negative control consisting of cells exposed to 0.5% DMSO in EMEM and a positive control treatment of 5µg/ml 3-methylcholanthrene (3-MCA) were also employed.

The transformation assay was based on the method of Kakunga (1973). Twenty four hours prior to treatment, a series of 25-cm² flasks was seeded with 10⁴ cells/flask and incubated. Fifteen flasks then were treated for each test dose, positive control, and negative control. The flasks were incubated for a three-day period at 37°C in a humidified atmosphere containing 5% CO₂. The cells were then washed, and the incubation was continued for 4 weeks with refeeding twice a week. The assay was terminated by fixing the cell monolayers with methanol and staining Giemsa. The stained flasks were examined by eye and by microscope to determine the number of foci of transformed cells. The foci consisted of piled up and randomly oriented cells, sometimes with necrotic centers, on surrounding monolayers of normal cells.

Statistical tables provided by Kastenbaum and Bowman (1970) were used to determine statistical significance.

Precipitation conc: >250 ug/ml
Signed QA assurance statement provided.

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

Reference: (9) (12)

Type: Mammalian cell gene mutation assay
System of testing: BALB 3T3 Mouse Cells
Concentration: 0.00625 to 0.10000 ug/ml
Cytotoxic Conc.: 0.244 ug/ml
Metabolic activation: without
Result: positive
Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath, S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983) Environ. Mutagen. 5:193-215
Year: 1983 GLP:
Test substance: other TS: Commercial Cure-Rite® 18, purity: Not noted
Remark: Clone 113 of BALB/3T3 mouse cells was obtained from Dr. Takeo Kakunga, NCI, Bethesda, MD. Subclones that were selected for low spontaneous frequencies of foci formation were used, Stocks were maintained in liquid nitrogen, and laboratory cultures were checked periodically for mycoplasma contamination. Cultures were grown and passed weekly in Eagle's Minimum Essential Medium (EMEM) supplemented with 10% fetal bovine serum.

The test chemical was dissolved in a small quantity of DMSO and then diluted with EMEM so the final concentration of DMSO was less than 0.5%. Lower concentrations were obtained by serial dilutions with EMEM. The dose range was based on the results of a clonal toxicity assay in which a series of 200 cells/dish were exposed in triplicate to a wide range of test chemical concentrations for 3 days. Five doses were selected to cover a wide range of toxicities from little or no reduction in colony-forming ability to a 50% reduction in the colony number. A negative control consisting of cells exposed to 0.5% DMSO in EMEM and a positive control treatment of 5µg/ml 3-methylcholanthrene (3-MCA) were also employed.

The transformation assay was based on the method of Kakunga (1973). Twenty four hours prior to treatment, a series of 25-cm² flasks was seeded with 10⁴ cells/flask and incubated. Fifteen flasks then were treated for each test dose, positive control, and negative control. The flasks were incubated for a three-day period at 37°C in a humidified atmosphere containing 5% CO₂. The cells were then washed, and the incubation was continued for 4 weeks with refeeding twice a week. The assay was terminated by fixing the cell monolayers with methanol and staining Giemsa. The stained flasks were examined by eye and by microscope to determine the number of foci of transformed cells. The foci consisted of piled up and randomly oriented cells, sometimes with necrotic centers, on surrounding monolayers of normal cells.

Statistical tables provided by Kastenbaum and Bowman (1970) were used to determine statistical significance.

Precipitation conc: >250 ug/ml
Signed QA assurance statement provided.

Weakly active.

Signed QA assurance statement provided.

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

Reference: (9) (12)

Type: Mouse lymphoma assay

System of

testing: Mouse Lymphoma cell line L5178Y TK+/-

Concentration: 0.313 to 35.0 ug/ml

Cytotoxic Conc.: With metabolic activation: Percent relative growth was 78.1%
at 20.0 ug/ml and 5.7% at 35.0 ug/ml

Without metabolic activation: Percent relative growth was 25.6%
at 0.313 ug/ml and 3.8% at 1.880 ug/ml

Metabolic

activation: with and without

Result: positive

Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath,
S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983)

Environ. Mutagen. 5:193-215

Year: 1983 GLP:

Test substance: other TS: Commercial Cure-Rite® 18; purity = 95.6%.

Remark: Mouse Lymphoma cells (L5178Y TK^{+/-}, clone 3.7.2C derived from the Fischer line from Dr. Donald Clive) were treated with doses of 0, 1.25, 5, 15, and 20 µg/ml. The negative solvent control was prepared by adding 0.1 DMSO per 10 ml of culture. The positive control was 0.5 µl/ml ethyl methanesulfonate under nonactivation conditions and) and 0.3 µl/ml dimethylnitrosamine under activation conditions. The assay procedure was very similar to the method of Clive and Spector (1975). Each treated culture consisted of 3x10⁶ cells suspended in 10 ml final volumes in 15 ml centrifuge tubes. Nonactivation and activation assays were conducted the same except the cell cultures in the activation assay contained the S-9, Aroclor 1254-induced liver preparation with cofactors. The cells were exposed to the test material dose for 4 hours, were washed, and were allowed an expression time of two days in growth medium. At the end of the expression period, 3x10⁶ cells from each treated culture were seeded in the selection medium (1x10⁶ cells per 100 mm dish). Cloning efficiency was determined by serially diluting a portion of the cells and seeding 300 cells in the nonselective cloning medium at 100 cells per 100 mm dish. BrdUrd-resistant colonies (TK^{-/-} mutants) and viable colonies (nonselective medium) were counted after 10 days incubation at 37°C in a humidified atmosphere containing 5% CO₂. The ratio of resistant to viable colonies yielded the mutant frequency in units of 10⁻⁴. The average of the solvent and untreated negative control mutant frequencies was used as the background or spontaneous mutant frequency for each trial. A treated culture was considered to have a significantly elevated mutation frequency if the frequency exceeded 10x10⁻⁶ plus 1.5 times the background frequency. Additional criteria such as a dose or toxicity related response and repeatability between trial were also used to determine the presence of mutagenic activity.

The test substance was positive with and without activation but only at doses that were very toxic.

5. Toxicity

Date: 19-AUG-2003 revised
ID: 13752-51-7

Precipitation conc: >250 ug/ml
Signed QA assurance statement provided.
Weakly active.

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

Reference: (9) (10)

Type: Mouse lymphoma assay

System of

testing: Mouse Lymphoma cell line L5178Y TK+/-

Concentration: 0.313 to 50.0 ug/ml

Cytotoxic Conc.: With metabolic activation: Percent relative growth was 43.2%
at 12.50 ug/ml and 4.2% at 50.0 ug/ml

Without metabolic activation: Percent relative growth was
80.9% at 0.313 ug/ml and 7.9% at 1.880 ug/ml

Metabolic

ctivation: with and without

Result:

Method: other: according to Hinderer, R.K., B. Myhr, D.R. Jagannath,
S.M. Galloway, S.W. Mann, J.C.Riddle, and D.J. Brusick (1983)
Environ. Mutagen. 5:193-215

Year: 1983 GLP:

Test substance: other TS: Commercial Cure-Rite® 18; purity: Not noted

Remark: Mouse Lymphoma cells (L5178Y TK^{+/-}, clone 3.7.2C derived from the Fischer line from Dr. Donald Clive) were treated with doses of 0, 1.25, 5, 15, and 20 µg/ml. The negative solvent control was prepared by adding 0.1 DMSO per 10 ml of culture. The positive control was 0.5 µl/ml ethyl methanesulfonate under nonactivation conditions and) and 0.3 µl/ml dimethylnitrosamine under activation conditions. The assay procedure was very similar to the method of Clive and Spector (1975). Each treated culture consisted of 3x10⁶ cells suspended in 10 ml final volumes in 15 ml centrifuge tubes. Nonactivation and activation assays were conducted the same except the cell cultures in the activation assay contained the S-9, Aroclor 1254-induced liver preparation with cofactors. The cells were exposed to the test material dose for 4 hours, were washed, and were allowed an expression time of two days in growth medium. At the end of the expression period, 3x10⁶ cells from each treated culture were seeded in the selection medium (1x10⁶ cells per 100 mm dish). Cloning efficiency was determined by serially diluting a portion of the cells and seeding 300 cells in the nonselective cloning medium at 100 cells per 100 mm dish. BrdUrd-resistant colonies (TK^{-/-} mutants) and viable colonies (nonselective medium) were counted after 10 days incubation at 37°C in a humidified atmosphere containing 5% CO₂. The ratio of resistant to viable colonies yielded the mutant frequency in units of 10⁻⁴. The average of the solvent and untreated negative control mutant frequencies was used as the background or spontaneous mutant frequency for each trial. A treated culture was considered to have a significantly elevated mutation frequency if the frequency exceeded 10x10⁻⁶ plus 1.5 times the background frequency. Additional criteria such as a dose or toxicity related response and repeatability between trial were also used to determine the presence of mutagenic activity.

5. Toxicity

The test substance was positive with and without activation but only at doses that were very toxic.

Precipitation conc: >250 ug/ml
Signed QA assurance statement provided.

Result: With metabolic activation: weakly active
Without metabolic activation: negative

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

Reference: (9) (10)

5.6 Genetic Toxicity 'in Vivo'

Type: Dominant lethal assay

Species: rat Sex: male/female

Strain: Sprague-Dawley

Route of admin.: gavage

Exposure period: 56 consecutive days to males

Doses: 0, 6.25, 12.5, or 25 mg/kg. (0.25 mg/kg triethylenemelamine positive control)

Result: negative

Method: other: according to Hinderer, R.K., M. Knickerbocker, and F.J. Koschier (1982) Toxicol. Appl. Pharmacol. 62:335-341.

Year: 1982 GLP: yes

Test substance: other TS: Commercial Cure-Rite® 18; Purity = 95.6%

Result: The test material (0, 6.25, 12.5, or 25 mg/kg) in corn oil was administered by gavage for 56 consecutive days to groups of male Sprague-Dawley rats (10 animals per group). The negative vehicle control group received corn oil while the positive control received a single ip dose of 0.25 mg/kg triethylenemelamine 1 day prior to mating. On the day following the last treatment, each male was cohabited with two sexually mature female rats for 1 week. The females were then removed and replaced with two more females for 1 week. Females were checked for vaginal plugs indicating that matings had occurred. Thirteen days after the midpoint of each cohabitation, all females were sacrificed and subjected to uterine examination. For each female numbers of corpora lutea, implantation sites, live fetuses, and early and late absorptions were recorded. After completion of the mating period, 3 males per treatment group were randomly selected for necropsy. The liver spleen, kidneys, heart, brain, adrenals, and thyroid were weighed and organ-to-body weight ratios were calculated. Data were analyzed for statistical significance.

A significant depression in body weight gain was observed in the males administered the highest dose. Similar pregnancy rates were observed in all test groups compared with the controls. No evidence of dominant lethal mutations were observed in the test groups. In the TEM positive controls, the number of implantation sites and preimplantation losses were significantly decreased, and the number of early fetal deaths per pregnant female were significantly elevated.

5. Toxicity

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented
and acceptable for assessment
Flag: Critical study for SIDS endpoint
Reference: (13)

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure period: 2 years
Frequency of
treatment: continuous daily
Post. obs.
period: none
Doses: 0, 20, 60, 200, or 600 ppm
Result:
Control Group: yes, concurrent no treatment
Method: other: according to Hinderer, R.K., G.R. Lankas, A.L.
Knezevich, and C.S. Auletta (1986). Toxicol. Appl. Pharmacol.
82:521-531
Year: 1986 GLP:
Test substance: other TS: Commercial Cure-Rite® 18; purity = 96.8%
Result: Diets containing 0, 20, 60, or 600 ppm of the test material were administered to
groups (60/sex/group) of Sprague-Dawley rats for 112 weeks. Ten rats/sex/group were
identified for a 12 month interim sacrifice. Animals were checked twice dail for mortality
and gross signs of toxicity. A detailed physical exam palpation for tissue masses was
performed weekly. Body weight and feed consumption were measured weekly through
week 12 and biweekly from week 13 to 26 and monthly thereafter. Hematology, clinical
chemistry, and urinalysis were conducted pretest on 15 animals/sex and at months 6, 12, 18,
and 24. Animals were given a complete gross post mortem examination following
spontaneous death, death *in extremis*, or scheduled sacrifices. A full set of organs were
subjected to gross and histological examination. All tissues from the control and high dose
were processed for pathological examination at 12 months and termination. Tissues in mid
and low dose groups were identified for pathological evaluation based on the pathological
evaluations in the controls and high dose groups. Organs also were weighed. Furthermore,
the testes from 3 of the 10 males at 12 months were processed for electron and light
microscopy examination. Statistical analyses were conducted on the end points.

A compound related increase in tumors of the urinary system was observed in the high dose
group: males (**kidney**: urothelia carcinoma, 2/60; squamous cell carcinoma, 1/60; **ureters**:
urothelial carcinoma 4/6 [2 in one male]; **urinary badder**: urothelial papilloma, 3/59;
urothelial carcinoma, 4/59; squamous cell papilloma, 1/59; squamous cell carcinoma, 2/59;
combined total neoplasms: 17 vs 1 urothelial papilloma in the control); females (**kidney**:
urothelial papilloma, 1/60; urothelia carcinoma, 3/60; squamous cell carcinoma, 3/60;
ureters: urothelial carcinoma 2/8; **urinary badder**: urothelial papilloma, 3/59; urothelial
carcinoma, 2/59; squamous cell papilloma, 2/59; squamous cell carcinoma, 1/59; **combined
total neoplasms**: 15 vs 0 in the control). Tumors of the urinary system were not found in

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the mid and low dose groups. Ureters were not evaluated in the controls, low or mid dose groups.

Kidney weights, non-neoplastic urinary tract abnormalities, and rales was observed in the high dose males and females. Body weights also were significantly lower in the high dose males and females. No compound-related effects on hematology, clinical chemistry, or urinalysis were noted.

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented
and acceptable for assessment
Flag: Critical study for SIDS endpoint
Reference: (8)

5.8 Toxicity to Reproduction

Type: Fertility
Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure Period: 12 weeks
Frequency of
treatment: daily
Premating Exposure Period
male: Males were sacrificed over a 6-7 day period following the 21-day mating period.
Duration of test: 12 weeks
Doses: 0, 60, 200, or 600 ppm.
Control Group: yes, concurrent no treatment
NOAEL Parental: 200 ppm
NOAEL F1 Offspr.: 600 ppm
Method: other: according to Hinderer, R.K., B.Y. Cockrell, S.M.
Debanne, and P.T. Goad. (1987). Fund. Appl. Toxicol.
9:763-772.

The test material (0, 60, 200, or 600 ppm) was administered in the diet to groups of male Sprague-Dawley rats (12 animals per group) for up to 12 weeks. Following 56-days of treatment each male was cohabited nightly with two females until a sign of mating (sperm in a vaginal smear) was observed or for 21-days. During the 21-day period, feeders were removed from the male's cage for nightly cohousing. A similar regimen was used for the control males; control males received the basal diet only. Females received the untreated diet throughout the study. Females were examined each morning for evidence of mating. Estrous cycle data were recorded during the mating period for each female until evidence of gestation was observed (Day 0 of gestation). Following mating the female was removed from the mating unit and housed individually for the remainder of gestation and lactation.

The parents were observed during the course of the study and body weights were recorded weekly and then on days 0 and 20 of gestation and days 0 and 21 of lactation for females. Litters were checked for dead pups twice daily and the numbers of pups per litter was recorded on days 0, 4, 14, and 21. Individual pup weights were recorded on days 0, 4, 14,

5. Toxicity

and 21 of lactation. Each pup was given a gross external examination. Pups found dead during parturition and lactation were given a gross internal and external examination. At necropsy the testes of 12 males from each treatment group were evaluated by electron microscopy; epididymis, seminal vesicles, and prostate were evaluated by light microscopy. Data were analyzed for statistical significance.

Year: 1987 GLP: yes
Test substance: other TS: Commercial Cure-Rite® 18; purity = 98.0%.
Result: NOAEL : 600 ppm

No clear dose-related effect on body weights was observed in either the parents or the pups. However, body weight gain was significantly higher in the low dose parental males. No evidence of compound related effects on mating, fertility, gestation length, number of implantations or live birth, pup growth, or survival was observed.

No morphological changes in the testes from the high dose males was observed by either light or electron microscopy.

Toxicity to offspring: None

Also, no pathological findings in female reproductive tissues following long-term feeding with the test material (see 5.7 above).

Reliability: (1) valid without restriction
GLP study, Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag: Critical study for SIDS endpoint
Reference: (14)

5.9 Developmental Toxicity/Teratogenicity

5.10 Other Relevant Information

5.11 Experience with Human Exposure

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6. References

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- (4) Bio/dynamics Inc., East Millstone, NJ (1980) Project #6216-80.
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- (6) Hill Top Research, Inc., Miamiville, Ohio (1971).
- (7) Biosearch Inc, Philadelphia, PA (1981).
- (8) Hinderer, R.K., G.R. Lankas, A.L. Knezevich, and C.S. Auletta (1986). Toxicol. Appl. Pharmacol. 82:521-531
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- (10) Litton Bionetics, Inc Report Project Number 20988 (1979)
- (11) Litton Bionetics, Inc Report Project Number 20990 (1979)
- (12) Litton Bionetics, Inc Report Project Number 20992 (1980)
- (13) Hinderer, R.K., M. Knickerbocker, and F.J. Koschier (1982). Toxicol. Appl. Pharmacol. 62:335-341.
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7. Risk Assessment

7.1 End Point Summary

7.2 Hazard Summary

7.3 Risk Assessment