AR201-1378-7B

I U C L I D

Data Set

Existing Chemical : Butanedioic acid, sulfo-1,4-bis(1,3-dimethylbutyl) ester, sodium salt
CAS No. : 2373-38-8

Creation date : 30.04.2001
Revision date : 13.05.2002

1. General Information

Id 2373-38-8
Date 30.04.2001

1.2 SYNONYMS

Succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt

2.1 MELTING POINT

Value	:	>300° C
Method	:	other (calculated)
Year	:	2002
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	:	The melting point of the neat substance was estimated by the EPIWIN (v1.40) to be 349.84 degrees C. Organic salts, which exist in ionic form, generally have high melting points. The commercial product is available as a 78-80% mixture with either isopropyl alcohol (5%) and water or as a 69-73% mixture with ethanol (4%), methyl isobutyl carbinol (CAS No. 108-11-2)(2%) and water. The commercial products are liquids.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

2.2 BOILING POINT

Value	:	> 300° C at 750 mm Hg
Decomposition	:	yes
Method	:	other (calculated)
Year	:	2002
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	:	The neat substance is an organic salt with negligible volatility. It undergoes decomposition before boiling when heated. The boiling point of 623.49° C was derived using the EPIWIN model, based on an adapted Stein and Brown Method. The commercial products, which are sold as mixtures with water and isopropyl alcohol or ethanol will boil at temperatures close to the boiling points of the respective alcohols.
Reliability	:	(3) invalid. Material will decompose before boiling.

03.03.2001

2.4 VAPOUR PRESSURE

Value	:	< .000001 hPa at 25° C
Method	:	other (calculated)
Year	:	2002
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	:	The vapor pressure was estimated from the melting point using the EPIWIN model. The substance is not volatile, since it is an organic salt. The commercial products, which are sold as mixtures of water and alcohol, will exhibit volatility associated with the alcohols present.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

2.5 PARTITION COEFFICIENT

Log Pow	:	ca. 1.8371 at 25° C
Method	:	other (calculated)
Year	:	2002
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	:	The log Pow was calculated using the EPIWIN model, based on molecular structure and functionality.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

2.6.1 WATER SOLUBILITY

Value	:	ca. 300-320 g/lat 25° C
Method	:	no data
Year	:	200l
GLP	:	no data
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	:	Data were supplied by the manufacturer.
Reliability	:	(2) valid with restrictions. Details on how value was obtained are unknown

03.03.2001 (3)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	sun light
Light spect.	:	nm
Rel. intensity	:	based on Intensity of Sunlight
Direct photolysis		
Halflife t1/2	:	ca. 7.3 hour(s)
Method	:	other (calculated)
Year	:	2002
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	:	The half-life and rate constant at 25°C were estimated using the EPIWIN/AOPWIN model that estimates the rate constant for the atmospheric gas-phase reaction between photochemically produced hydroxyl radicals and ozone with organic chemicals. The rate constant estimated by the program was used to calculate the atmospheric half-life based upon the average atmospheric concentration of hydroxyl radicals. It should be noted that due to the negligible volatility of organic salts and negligible presence in the atmosphere, atmospheric photodegradation is not an important degradation path for this substance.
Result	:	The hydroxyl radical photolysis rate constant was calculated to be 17.4 E-12 cm^3/molecule-sec.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.
03.03.2001		

3.1.2 STABILITY IN WATER

Type	:	other:estimation
t1/2 pH7	:	ca. 156 years at 25° C
t1/2 pH 8	:	ca. 15.6 years at 25° C
Deg. Product	:	not determined
Method	:	other (calculated)
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	:	The EPIWIN/HYDROWIN program cannot assess hydrolysis rates for all fragments of this neat substance. The commercial products are sold as water/alcohol mixtures that have demonstrated long-term stability to hydrolysis at neutral pHs and ambient temperatures. The ester groups are subject to base or acid catalyzed hydrolysis.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.
03.03.2001		

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	volatility
Media	:	water – air
Air (level III)	:	0.911
Water (level III)	:	38.7

Soil (level III)	:	60.3 0.101
Method	:	Other
Year	:	2002
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt
Remark	:	Level III Fugacity was estimated using the Mackay model
Result	:	A Henry's Law Constant of 1.62 E -12 atm-m^3/mol was calculated, based on molecular structure and functionality. The Koc was estimated by the EPIWIN model to be 57.6.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge
Contact time	:	28 day
Degradation	:	= 40.3 % after 28 day
Result	:	not readily biodegradable
Kinetic of test substance	:	14 day 50 **%** 21 day 38 **%** 28 day 40.3 **%**
Control substance	:	aniline
Kinetic	:	14 day 90% 21 day 87% 28 day 86.7 **%**
Method	:	OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year	:	1988
GLP	:	yes
Test substance	:	Test material was 80% CAS #2373-38-8, 15% water, 5% ethyl alcohol. It was identified as 68% carbon by analysis.
Result	:	The amount of biodegradation observed occurred within the first seven days of the test and remained constant for the remainder of the study. The reference material yielded a degradation percentage over 80%, so the results of this test are therefore considered valid.
Test condition	:	Testing was conducted in accordance with a modified OECD Screening Test for Ready Biodegradability. Activated sludge bacteria was from Bergen Co., New Jersey. The test compound was dissolved in an organic medium at a concentration of 30.8 mg/ml. The medium was inoculated with a relatively low concentration of micr oorganisms from a mixed population and aerated at a temperature of 20-25° C for a period of 28 days. Biodegradation was followed by dissolved organic carbon (DOC) analysis. Positive control flasks containing aniline (30.8 mg/l) were run parallel to determine the validity of the test. The amount of DOC reduction in blank controls was subtracted from values obtained for the test material and positive control to obtain the final values.
Reliability	:	(1) valid without restriction

03.03.2001 (5)

Type	:	aerobic
Inoculum	:	activated sludge

Contact time	:	28 day
Degradation	:	= 16.2 % after 28 day
Result	:	not readily biodegradable
Kinetic of test substance	:	see result
Control substance	:	aniline
Kinetic	:	15 day 66.7 **%** 28 day 98.1 **%**
Deg. Product	:	not measured
Method	:	OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year	:	1991
GLP	:	yes

Test substance : Test material was 78-80% CAS #2373-38-8, 15% water, 5% ethyl alcohol, less than 1.0% $C_6H_{14}O$, less than 0.5% $C_{16}H_{28}O_4$ and $H_20_4S.2Na$, 0.25% CH_4O, and less than 0.2% $H_2O_3S.Na$. It was verified as containing the same carbon content (68%) as identified by the supplier.

Remark: : The percent degradation listed above is average of two determinations with 2 mg/l material and one determination with 1 mg/l material.

Result : Duplicate tests performed with 2 mg/l test material revealed 0 and 2.9% degradation by day 5, 20.4% and 12.6 degradation by day 15, and 16.7 and 13.3% degradation by day 28. Test material at 1 mg/l degraded by 7.4%, 25.9%, and 18.5% over 5, 15, and 28 days, respectively. Aniline degraded by 18.5%, 66.7% and 98.1% over 5, 15, and 28 days, respectively. The test was therefore considered valid. The test material was not readily biodegradable.

Test condition : Testing was done in accordance with the OECD "Ready Biodegradability: Closed Bottle Test". The stock solution was prepared by adding 2 g of sample to 1 liter of distilled water. This solution was diluted to 100 ppm as carbon after analysis. The diluted stock was added to BOD bottles at 3.33, 6.67 and 16.65 ml to yield test concentrations of 1, 2 and 5 mg/l (as carbon, respectively). Aniline (2 mg/l) was used as a reference. The test and reference solutions were inoculated with microorganisms from a mixed population (activated sludge material from Bergen Co., New Jersey) and kept in closed bottles in the dark at a constant temperature of 20 +/- 1° C. Degradation was followed by oxygen analyses using the YSI Dissolved Oxygen analyzer 54A over a 28-day period. Degradability was based on a comparison between readings of actual oxygen demand to theoretically expected oxygen demand. Results were adjusted for blanks without inoculum.

Test substance : Test material was 78-80% CAS #2373-38-8, 15% water, 5% ethyl alcohol, less than 1.0% $C_6H_{14}O$, less than 0.5% $C_{16}H_{28}O_4$ and $H_20_4S.2Na$, 0.25% CH_4O, and less than 0.2% $H_2O_3S.Na$. It was verified as containing the same carbon content (68%) as identified by the supplier.

Reliability : (1) valid without restriction
03.03.2001 (7)

3.7 BIOACCUMULATION

Species	:	other
BCF	:	ca. 3.16 at 25° C
Method	:	other: calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-1,4-bis(1,3-dimethylbutyl)ester, sodium salt

Remark	:	The bioconcentration factor was estimated based on molecular structure and functionality using the EPIWIN/BCF p rogram.
Reliability 04.03.2001	:	(2) valid with restrictions. Data were obtained by modeling.

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	g/l
Analytical monitoring	:	no data
LC50	:	m = 1200
LC100	:	m = 2000
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1990
GLP	:	no data
Test substance	:	Test material was 80% CAS # 2373-38-8, 15% water, 5% ethyl alcohol
Remark	:	An initial range finding test was performed to determine the optimal concentrations for the test
Result	:	Water conditions: Dissolved oxygen and pH ranged between 8.8-9.6 mg/l and 7.0-7.7 units, respectively. There was no difference between groups. Conductivity increased in a dose-dependent manner, with control values at approximately 200 µmohs and 4000 ppm values at 550 µmohs. Temperature was maintained at 15° C throughout the test. Alkalinity and water hardness were 80 and 90 mg/l $CaCO_3$, respectively. Test Results: None of the fish exposed to 0 (control), 250 or 500 ppm died by 96 hours. The corresponding mortalities at 96 hours for fish exposed to 1000, 2000, and 4000 ppm were 10, 100, and 100%, respectively. Most of the deaths that occurred at these concentrations occurred within 24 hours.
Test condition	:	This 96-hour static, non-renewal bioassay was performed on six groups of 10 Onchorhyncus mykiss (rainbow trout) approximately 74 days old. Trout were housed (5 per tank) in 4L polypropylene vessels containing 3 L of US EPA moderately hard, reconstituted water. The test concentrations were 0 (control), 250, 500, 1000, 2000, and 4000 ppm. Tests were performed in duplicate. Fish were maintained at 15 ± 2 ° C under a 16hr/8hr light/dark cycle and were not fed during tests. Oil-free air was supplied at less than or equal to 100 bubbles per minute to maintain equal to or greater than 60% saturation. Mortality, behavior, physiology, dissolved oxygen, pH, and conductivity were measured initially and daily thereafter. Initial alkalinity and hardness of diluent were also determined. The test was considered valid if greater than 90% of control fish survived 96 hours. Data were analyzed according to the Spearman-Karber method, Probit analysis, or graphical interpolation (where applicable).
Reliability	:	(1) valid without restriction

03.03.2001 (6)

Type	:	static
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
NOEC	:	m = 560
LC50	:	m > 1000
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test'
Year	:	1987
GLP	:	yes

Test substance	:	The test material was 80% CAS # 2373-38-8, 15% H2O, 5% ethanol.
Result	:	None of the fish exposed to concentrations <= 560 mg/l died after 96 hours of exposure. Mortality of those exposed to 1000 mg/l was 10%. Water temperature and pH were maintained within acceptable limits for all tanks. A dose- and time-dependent decrease in dissolved O_2 was noted: it ranged from 6.4 (control) to 3.1 mg/l (560 and 1000 mg/l) at 48 hours and 5.9 (control) to 2.0 mg/l (1000 mg/l) at 96 hours. All solutions containing 100 to 1000 mg/l test material were slightly cloudy at 48, 72 and 96 hours. The NOEC was 560 mg/l based on the lack of mortality and abnormal effects.
Test condition	:	Bluegill sunfish (Lepomis macrochirus) were acclimated for at least 14 days prior to test. They were fed a standard commercial fish food occasionally supplemented with brine shrimp daily until 48-96 hours prior to testing. A 96-hour static bioassay was conducted on the fish at the following nominal test concentrations 0 (control), 100, 180, 320, 560, and 1000 mg/l. Fish weighed an average of 0.30 g and had a mean length of 24 mm. The test material was tested on an as is basis and was not corrected for solids content. Ten fish were exposed per group. The tests were conducted in five-gallon tanks containing 15 l of reconstituted water. The water was prepared to yield a total hardness of 40-48 mg as $CaCO_3$, total alkalinity of 25-35 mg/l as $CaCO_3$ and an initial pH of 7.2 to 7.6. Tanks were maintained at 22 +/- 1° C and were not aerated. Water quality parameters of temperature, dissolved oxygen, and pH were measured throughout the test. Fish were observed every 24 hours for abnormal effects and lethality. Data were analyzed according to a computerized LC_{50} program, which utilized the binomial, moving average and probit tests.
Reliability	:	(2) valid with restrictions. Results at the high concentrations may have been confounded by low dissolved oxygen concentration and insolubility of test material.

03.03.2001 (2)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	other:albino
Sex	:	male
Number of animals	:	20
Vehicle	:	water
Value	:	= 1750 mg/kg bw
Method	:	other
Year	:	1957
GLP	:	pre-GLP
Test substance	:	Test material contained 80 +/- 1% active solids, 6-8% 2B ethanol, 0.4% sodium sulfate, 0.4% unreacted ester and a maximum of 10 ppm heavy metals. Test material was diluted with water to a solution of 5% solids content.
Result	:	All animals died within 24 hours following the 2.5 g/kg dose, but all survived treatment with the lower doses. Animals exposed to 2.5 g/kg exhibited profound depression and severe diarrhea prior to death. Moderate to severe irritation with hemorrhage of the gastrointestinal tract was found on post-mortem examination. At the lower doses, the animals were depressed for 24 to 48 hours, but thereafter regained normal appearance and behavior. Autopsy of these animals revealed a greater than usual distention of the intestines in some instances, but otherwise no significant gross findings.
Test condition	:	Test material was administered in single doses by mouth to 4 groups of 5 young male albino rats (90-116 g) at dosages ranging from 0.31 to 2.5 g/kg in terms of solids. Animals were observed for a period of 7 days, and then were sacrificed and autopsied. Animals that died before 7 days were autopsied upon death. The method of moving averages was used to calculate the LD50 value. A mortality rate of 5/5 of 5 g/kg was assumed.
Reliability	:	(1) valid without restriction

03.03.2001 (1)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	rabbit
Strain	:	other:albino
Sex	:	male
Number of animals	:	12
Value	:	= 4000 mg/kg bw
Method	:	other
Year	:	1957
GLP	:	pre-GLP
Test substance	:	Test material contained 80 +/- 1% active solids, 6-8% 2B ethanol, 0.4% sodium sulfate, 0.4% unreacted ester and a maximum of 10 ppm heavy metals
Result	:	All animals exposed to 10 ml/kg died within one to three days following removal of the dose. Animals exposed to 10 ml/kg exhibited very severe

erythema, edema, and necrosis of the skin and extreme depression prior to death. Post-mortem examination of these animals gave additional evidence of severe injury to the skin and abdominal wall. The mortality rate of rabbits exposed to the two lower doses was 1/4. Erythema and edema were initially quite severe at the lower dosages, but the edema subsided within 24 to 48 hours. Erythema persisted for 4 to 5 days. Autopsy of animals receiving 2.5 or 10 ml/kg revealed no gross internal pathology that could be related to administration of the product. The LD_{50} value and 95% confidence interval for the test material was 5.0 (2.6 - 9.6) ml/ kg or 4 (2.1 - 7.7) g/kg as contained solids.

Test condition : The substance as received (containing 80% solids) was applied to the closely-clipped skin of male albino rabbits (2720 to 4120 g) in single doses that remained in contact with skin for a 24-hour period. Animals were exposed to 2.5 ml/kg (N = 4), 5 ml/kg (N = 4) or 10 ml/kg (N = 6). The dose was retained by placing a cuff of polyethylene film around the trunk of each animal. Animals were observed for a period of 7 days, and then were sacrificed and autopsied. Animals that died before 7 days were autopsied upon death. The LD50 value was calculated by the method of moving averages. A mortality of 4/4 at 20 ml/kg was assumed for purposes of calculation.

Reliability : (1) valid without restriction
03.03.2001 (1)

5.4 REPEATED DOSE TOXICITY

Species : rat
Sex : male
Strain : other: albino
Route of admin. : oral feed
Exposure period : 32 days
Post obs. period : none
Doses : 0.125, 0.25, 0.5%
Control group : yes
NOAEL : > .5 %
Method : other
Year : 1957
GLP : pre-GLP

Test substance : Test material contained 80 +/- 1% active solids, 6-8% 2B ethanol, 0.4% sodium sulfate, 0.4% unreacted ester and a maximum of 10 ppm heavy metals.

Result : Appearance and behavior of the animals over the study period were normal. None of the animals died. Mean daily food intake of animals receiving 0.125 % (18.8 g) was significantly lower than control (19.6 g). Mean weight gain of this group (165 g) also was significantly different from control (177g). There was no difference in food consumption or body weight gain of the other two groups with respect to control. No pathology attributable to ingestion of the material was found

Test condition : The product was added to the diet of three groups of young male albino rats (ten/group), in amounts sufficient to give concentrations of 0, 0.125, 0.25, and 0.5% (solids content). Mean daily dosage of the product is calculated as 0, 0.13, 0.25, and 0.51 g/kg of solids for each percentage, respectively. These dietary levels were fed over a 32-day period. All animals were sacrificed and autopsied at the end of the study.

Reliability : (1) valid without restriction

03.03.2001 (1)

Species	:	rat
Sex	:	male/female
Strain	:	other:Charles River albino
Route of admin.	:	oral feed
Exposure period	:	90 days
Post obs. period	:	none
Doses	:	1.0%
Control group	:	no
NOAEL	:	> 1 %
Method	:	other
Year	:	1969
GLP	:	pre-GLP
Test substance	:	A commercial sample was dried to remove the liquid phase. Dried product was 100% solids or active ingredients.
Result	:	No deaths or abnormal behaviors were noted in the animals. No significant differences were noted in final body weights, food consumption, hematologies, urinalyses, or gross pathology (as compared to controls)
Test condition	:	Design: 20 albino rats / sex were fed test material for 90 days at a dietary concentration of 1.0%, which was prepared by blending the appropriate amount of test material with standard rat ration. Twenty control rats/sex received normal food. Rats were weighed biweekly and food consumption was recorded weekly. Fresh diets were prepared weekly. Standard hematologies and urinalyses were performed on blood and urine samples collected from 5 rats/sex/group on treatment day 84. Endpoints: Animals were sacrificed 90 days after treatment and a complete set of organs and other tissues was examined. At autopsy, the weight of the liver and kidneys of 10 rats/sex/group were recorded. The following tissues from 5 rats/sex/group were examined histologically:esophagus, stomach (cardia, fundus, pyloris), small intestine (duodenum, jejunum, ileum), cecum, colon , liver, kidneys, spleen, pancreas, urinary bladder, pituitary, adrenal, testes, seminal vesicle, ovary, bone marrow, thyroid, parathyroid, salivary gland, prostate, heart, aorta, lung, lymph node (cervical and mesenteric), skeletal muscle, peripheral nerve, bone (femur), spinal cord, uterus, trachea, eye, optic nerve and brain. Statistical Analyses: Data for food consumption, weight, absolute organ weight and organ/body weight ratios were analyzed by analysis of variance (ANOVA). Effects uncovered were further analyzed by t-tests.
Reliability	:	(1) valid without restriction

02.03.2001 (4)

5.8 TOXICITY TO REP RODUCTION

Type	:	other: histological examination of reproductive organs
Species	:	rat
Sex	:	male/female
Strain	:	other:albino
Route of admin.	:	oral feed
Exposure period	:	90 days
Duration of test	:	90 days
Doses	:	1.0%
Control group	:	yes
Method	:	other
Year	:	1969

GLP	:	pre-GLP
Test substance	:	A commercial sample was dried to remove the liquid phase. Dried product was 100% solids or active ingredients.
Remark	:	This study was a component of a 90-day repeated dose oral toxicity study. Additional details about the conduct of this study can be found in section 5.4.
Result	:	No biologically significant changes were observed in any of the reproductive organs that were examined in males or females
Test condition	:	Diet was prepared by blending the appropriate amount of test material with standard rat ration. Twenty albino rats / sex were fed a diet containing 1.0% test material for a period of 90 days. Animals were sacrificed 90 days after treatment and gross pathologies were performed. Ovaries and uteri from female rats and prostate, testes, and seminal vesicles from male rats were examined histopathologically.
Reliability	:	(1) valid without restriction

03.03.2001 (4)

6. References

(1) American Cyanamid Company. 1957. Report on Aerosol MA-80%. Limited Release Toxicity Studies. Report No. 57-15, October 7, 1957

(2) Analytical Biochemistry Laboratories, Inc. 1987. Report No. 36262 to American Cyanamid, October 29, 1987

(3) Cytec Research and Development. 2001. Unpublished information.

(4) Industrial BIO-TEST Laboratories, Inc. 1969. Ninety-day subacute oral toxicity of Aerosol A-196, Aerosol IB, Aerosol AY, Aerosol MA, Aerosol OT and Aerosol TR in albino rats. Report No. B7409 to American Cyanamid.

(5) United States Testing Company, Inc. 1988. OECD Screening test for ready biodegradability. Report No. 07278-4 to American Cyanamid, January 15, 1988

(6) United States Testing Company, Inc. 1990. Aquatic Toxicity tests versus Onchorhyncus mykiss. Report No. 063102-9 to American Cyanamid Co, January 21, 1990

(7) United States Testing Company, Inc. 1991. OECD Screening test for ready biodegradability. Test Report No. 063012-12 to American Cyanamid, February 20, 1991.

I U C L I D

Data Set

Existing Chemical	:	Butanedioic acid, sulfo-, 1,4-dicyclohexyl ester, sodium salt
CAS No.	:	23386-52-9

Creation date	:	09.05.2001
Revision date	:	13.05.2002

1. General Information

Id 23386-52-9
Date 30.04.2001

1.2 SYNONYMS

Succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt

Dicyclohexyl sodium sulfosuccinate

2.1 MELTING POINT

Value	:	203 ° C
Method	:	other
Year	:	2002
GLP	:	no data
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt, 97% pure
Remark	:	Data were supplied by the manufacturer.
Result	:	Melting points of 202 and 204 ° C were obtained in the duplicate tests. The average value is 203 ° C
Reliability	:	(2) valid with restrictions. Details on how data were obtained are unknown.

03.03.2001 (4)

Value	:	ca. 311.3 ° C
Method	:	other: calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt
Remark	:	The melting point was estimated using the EPIWIN model based on molecular structure and functionality.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

03.03.2001

2.2 BOILING POINT

Value	:	> 300° C at 1 hPa
Decomposition	:	yes
Method	:	other: calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt
Remark	:	The substance is a salt with negligible volatility. It decomposes on heating above 300 degrees C. The boiling point was estimated using the EPIWIN model.
Reliability	:	(3) invalid. Material will decompose before boiling.

03.03.2001

2.4 VAPOUR PRESSURE

Value	:	< .00001 hPa at 25° C
Method		other (calculated)
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt
Remark	:	The substance is a salt, and has negligible vapor pressure. The vapor pressure was estimated using the EPIWIN model, based on molecular structure and functionality.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
03.03.2001

2.5 PARTITION COEFFICIENT

Log Pow : ca. 1.76 at 25° C
Method other (calculated)
Year : 2000
GLP : not applicable for estimations
Test substance : succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt

Remark : The partition coefficient was estimated using the EPIWIN/KOWWIN model based on molecular structure and functionality.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
03.03.2001

2.6.1 WATER SOLUBILITY

Value : 12.0 g/ 100 ml at 25 ° C
Method : no data
Year : 2001
GLP : no data
Test substance : succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt

Remark : Data were supplied by the manufacturer.

Reliability : (2) valid with restrictions. Details on how value was obtained are unknown.
03.03.2001 (4)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	other
Rel. intensity	:	based on Intensity of Sunlight
Direct photolysis		
Halflife t1/2	:	ca. 5.2 hour(s) at 25° C
Method	:	other (calculated)
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt
Remark	:	It should be noted that due to the negligible volatility of organic salts and negligible presence in the atmosphere, atmospheric photodegradation is not an important degradation path for this substance.
Result	:	The rate constant of 24.6 E-12 cm^3/molecule-sec at 25°C was estimated using AOPWIN, that estimates the rate constant for the atmospheric gas-phase reaction between photochemically produced hydroxyl radicals and ozone with organic chemicals. The rate constant estimated by the program was used to calculate the atmospheric half-life based upon the average atmospheric concentration of hydroxyl radicals.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.
03.03.2001		

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH7	:	ca. 14.5 years at 25° C
t1/2 pH 8	:	ca. 1.5 years at 25° C
Method	:	other (calculated)
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt
Remark	:	Stability half-lives were estimated using the EPIWIN/HYDROWIN model, based on molecular structure and functionality.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.
03.03.2001		

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	water – soil
Air (level III)	:	.875
Water (level III)	:	40.8
Soil (level III)	:	58.3
Method	:	other
Year	:	2000
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt
Remark	:	Level III Fugacity was estimated using the Mackay model (the currently accepted model for estimation of theoretical distribution) with standard defaults. Of the 58.3% shown for soil, 0.1% is estimated to be in sediment

and the remainder in soil.

Result : The Henry's Law constant is estimated by the EPIWIN model to be 3.14E-13, based on molecular structure and functionality. The Koc is estimated by EPIWIN/PCKOC to be 111. This Koc value indicates moderately low mobility through soil.

Reliability : (2) valid with restrictions. Data were obtained by modeling.
03.03.2001

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge
Degradation : = 35.9 % after 28 day
Kinetic of test substance : 7 day 31.4 **%**
14 day 39.4 **%**
21 day 33.7 **%**
28 day 35.9 **%**
Control substance : aniline
Kinetic : 7 day 84.3 **%**
28 day 86.7 **%**
Deg. Product : not measured
Method : OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year : 1988
GLP : yes
Test substance : succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt

Result : There was no significant difference between the results of both tests. Biodegradation (average of 31.4%) occurred within the first seven days of the test and remained relatively constant throughout the study. The test material is not considered "readily" biodegradable according to OECD guidelines. The results of the test were considered valid because aniline was readily biodegraded.

Test condition : The test compound was dissolved in deionized water to make a stock solution of 14%. Test material was diluted to a concentration of 31.5 mg/l with inorganic nutrient medium and the medium was inoculated with micoorganisms from a mixed population. Aniline (30.0 mg/l) was used as a positive control. Test and positive control flasks were shaken for 28 days at 20-25° C in the dark. Tests were performed in duplicate. Biodegradation was followed by dissolved organic carbon (DOC) analysis. Results are reported as the average of the two tests. Results were corrected for blanks without inoculum (except on day 0).

Test substance : Test substance was 53% carbon by analysis.

Reliability : (1) valid without restriction
03.03.2001 (9)

Type : aerobic
Inoculum : other:predominantly gram negative bacteria
Concentration : 1.25 mmol/l
Contact time : 4 hour(s)
Result : other:not readily biodegradable
Method : other
Year : 1999
GLP : no data

Test substance	:	other TS
Result	:	A biodegradation rate of 11.4 micromoles surfactant/min.g cell protein was calculated for di(2-ethylhexyl) sodium sulfosuccinate
Test condition	:	The bacterial consortium was obtained from a detergent-polluted soil by enrichment cultivation and adaptati on in the presence of Surfactant 9 (mono-n-dodecyl sulfosuccinate). Bacteria were cultivated under aeration at 25° C in a phosphate mineral medium. Surfactant 9 was added to the culture in a crystalline form to a final concentration of 0.5 g/l. Microscopic examination of microorganisms present in the adapted mixed culture revealed predominantly Gram-negative motile bacteria. The rate constants of primary biodegradation of 10 different alkyl sulfosuccinates (including dicyclohexyl sodium sulfosuccinate) at a concentration of 1.25 mmol/l by the adapted mixed culture (cell protein 0.4 g/l) was measured at 25° C over 4 hours. The culture was incubated under stirring and samples were taken (times not noted) to determine the amount of surfactant remaining. The extent of biodegradation was estimated as a loss of methylene blue active substances in a chloroform extract of the media. The rate constants were calculated as maximum rates of primary degradation catalyzed by one gram of biomass protein in the initial phase of the reaction.
Test Substance	:	The test substance was listed as the di-cyclo-hexyl ester of sulfosuccinic acid. Other studies performed by the authors list the supplier as Cytec. Cytec markets this material as the sodium salt. Therefore, it i s likely that the material used was the sodium salt.
Reliability	:	(2) valid with restrictions

27.02.2001 (11)

3.7 BIOACCUMULATION

Species	:	other
BCF	:	ca. 3.16 at 25° C
Method	:	other: calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt
Remark	:	The bioconcentration factor was estimated based on molecular structure and functionality using EPIWIN model.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

04.03.2001

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
NOEC	:	m = 240
LC50	:	m = 470
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1987
GLP	:	yes
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt. Purity was 85%.

Result :

Water condition: Dissolved oxygen concentrations ranged from 1.1 to 8.5 mg/l during the test. They decreased with increasing time of test; dissolved oxygen ranged from 1.1 to 4.0 mg/l (13-48% dissolved oxygen) at 48 and 96 hours. The control chamber remained at above 73% saturation throughout the 96-hour test. At 24 hours, tanks with 1000 mg/l appeared cloudy. After 48 hours and for the remainder of the study, all test tanks were slightly cloudy.

Test Results: None of the controls or fish exposed to 240 or 320 mg/l of test material died. The corresponding mortalities at 48 or 96 hours for fish exposed to 420, 560, 750 and 1000 mg/l were 20%, 90%, 100% and 100% respectively. The majority of these mortalities occurred by 24 hours. Abnormal effects such as surfacing, loss of equilibrium, fish on the bottom of the test chamber, quiescence and/or labored respiration were noted in fish exposed to 320 mg/l or more test compound. The NOEC was 240 mg/l, based on the lack of mortality and abnormal effects.

Test condition :

Fish were acclimated for at least 14 days prior to testing. Fish received a standard commercial fish food occasionally supplemented with brine shrimp daily until 48-96 hours prior to testing. Fish were not fed during testing. A 96-hour static bioassay was conducted on 10 fish per test group at the following concentrations: 0 (Control), 240, 320, 420, 560, 750, and 1000 mg/l. The average weight and length of the fish were 0.23 g and 22 mm, respectively. Tests were performed in 5-gallon glass vessels containing 15 l of reconstituted water. Water was prepared to yield a total hardness of 40-48 mg/l as $CaCO_3$, a total alkalinity of 25-35 mg/l as $CaCO_3$ and an initial pH of 7.2 to 7.6. Test vessels were maintained at 22 +/- 1.0° C and were not aerated. Fish were observed every 24 hours for abnormal effects and lethality.

The LC_{50} values were calculated by a computer program that utilized data from the binomial, moving average and probit tests.

Reliability :

(2) valid with restrictions. Results at the high concentrations may have been confounded by low dissolved oxygen concentration and test material insolubility.

03.03.2001 (3)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l

Analytical monitoring	:	yes
NOEC	:	m = 90
EC50	:	m = 457
EC100	:	m = 1000
Method	:	OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year	:	1993
GLP	:	yes
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt. Purity was 80 – 83%.
Result	:	There was no evidence of insolubility of test material in any of the chambers. Measured concentrations of test material were 80% or greater than nominal concentrations, therefore nominal values were used for the statistical analyses. No immobilization was noted at concentrations lower than 300 mg/l. At 300 mg/l, 15% mobilization was noted at 48 hours. Treatment with 1000 mg/l caused 100% mobilization within 24 hours
Test condition	:	Nominal treatment levels were 8.1, 27, 90, 300 and 1000 mg/l. Individual treatment solutions were prepared by adding the appropriate amount of test material to laboratory dilution water (100 ml) in glass aspirator bottles. Solutions were mixed for approximately 1 hour, after which they appeared clear. The water accommodated fraction (WAF) of each treatment solution was drawn through the outlet at the bottom of the vessels and divided into 4 replicate chambers (25 ml each). Samples were analyzed for test material, dissolved oxygen, temperature and pH. Test chambers were covered with glass to minimize evaporation and/or volatilization. Daphnids were less than 24 hours old when exposure was initiated. Five daphnids were housed in each chamber. The daphnids were exposed to the Water Accommodated Fraction (WAF) of each treatment solution at 20° C in the dark for a 48-hour period. Observations for immobilization, abnormal behavior and appearance were performed at 24 and 48 hours. Water quality measurements (pH, dissolved oxygen and temperature) were performed at study termination. The 48-hour EC50 value was determined using the Spearman-Karber method.
Reliability	:	(1) valid without restriction

03.03.2001 (5)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Analytical monitoring	:	no data
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
NOEC	:	none determined
Year	:	1993
GLP	:	yes
Test substance	:	succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt. Purity was 80 – 83%.
Result	:	In general, the effect of the test material was stimulatory instead of inhibitory. The concentration-response curves for growth rate and growth were bell-shaped. No EC_{50} value or NOEL could be determined. Incubation of Selenastrum capricornutum with 8.1, 90 and 300 mg/l cyclohexyl ester for 72 hours stimulated the growth rate by 35.1, 44.1 and 20.2%, respectively, and growth by 40.2, 130, and 28.3%, respectively Incubation of Selenastrum capricornutum with 8.1, 90 and 300 mg/l cyclohexyl ester for 96 hours stimulated the growth rate by 64.5, 57.8 and 38.2%,

respectively, and growth by 164, 243, and 86.4%, respectively. The maximal effect on growth rate and growth was 90 mg/l. Exposure to 1000 mg/l had no effect on the growth rate or growth. The values for 27 mg/l appeared to be outliers.

Test condition : Treatment solutions (0, 8.1, 27, 90, 300 or 1000 mg/l) were prepared by adding the appropriate amount of test material to algal nutrient media. Solutions were mixed for approximately 1 hour, after which they appeared clear. The Water Accommodated Fraction (WAF) was drawn through an outlet at the bottom or the vessels and analyzed analytically for test material. The pH of each treatment was measured and adjusted to 7.5 +/- 0.1, as necessary. A 50 ml aliquot of each solution was removed to serve as a blank.

Each treatment solution (150 mL) was inoculated with Algae (S. capricornutum; 7500 to 9100 cells/ml) and divided into 3 replicate chambers (50 ml/125 ml flask). Test chambers were closed with cotton-gauze stoppers during the study to minimize evaporation and/or volatilization. Test flasks were shaken (100 rpm) to keep algae in suspension and facilitate transfer of CO_2. Algae were incubated for 96 hours at 23.2 +/- 0.2° C under continuous light.

Cell densities were determined for each replicate chamber at 1, 24, 48, 72 and 96 hours. The pH was measured at Day 0 and at termination.

Data were evaluated using the ANOVA procedure of SAS for NOEC determination. An inverse interpolation method was used for the EC_{50} determination.

Reliability : (1) valid without restriction
03.03.2001 (6)

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species : Other:Tradescantia bicolor
Endpdoint : necrosis
Exposure period : 48 hour(s)
Unit : mmo/l
NOEC : m = 1.25
Method : other
Year : 1999
GLP : no data
Test substance : other TS

Remark : Using a molecular weight of 384.423, the 48 and 24-hour NOECs in mg/l were 480 and 3844, respectively.

Result : At 24 hours, the necrosis scores for all test concentrations except 20 mmol/l were 0. The score for 20 mmol/l was 1. At 48 hours, concentrations of 1.25 mmol/l and lower had no effect. A concentration of 2.5 mmol/ induced a score of 1. Higher concentrations produced scores of 2.

Test condition : Eleven different sulfosuccinate esters were tested. Solutions of the di-cyclo-hexyl ester of sulfosuccinic acid were tested at 0.3125, 0.625, 1.25, 2.5, 5, 10 and 20 mmol/l. Test solutions were infiltrated into leaf sheets of

Tradescantia bicolor plants (approximately an area of 10 x 10 mm). Distilled water was used as a control. Each experiment was run in triplicate. Phytotoxicity was evaluated after 24- and 48- hours and was scored according to the following method (0 = no effect, 1 = no necrosis but infiltrated area appears yellow, 2 = necrosis). A spectral mapping technique was used to analyze the effects of the ester compared to the other esters tested.

Test substance : The test substance was listed as the di-cyclo-hexyl ester of sulfosuccinic acid. Other studies performed by the authors list the supplier as Cytec. Cytec markets this material as the sodium salt. Therefore, it is likely that the material used was the sodium salt.

Reliability : (1) valid without restriction
03.03.2001 (8)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Wistar
Sex	:	male
Number of animals	:	20
Value	:	= 3540 mg/kg bw
Method	:	other
Year	:	1969
GLP	:	pre-GLP
Test substance	:	Material tested was 80% CAS # 23386-52-9, 12% H_20, and 8% ethanol
Result	:	Signs of intoxication included diarrhea, lethargy, prostration, and coma. None of the animals given 1.25 or 2.5 g/kg died or appeared intoxicated. All animals in the 5.0 and 10.0 g/kg groups died.
Test condition	:	Twenty male rats (average weight 150-265 g) were fasted for 24 hours before dosing. Animals (5 per group) were dosed with a 20% w/v aqueous dispersion of the product at 1.25, 2.5, 5.0 or 10.0 g/kg. Animals were observed for behavior and death for 14 days and then autopsied. The method used to calculate the LD50 value was not stated.
Reliability	:	(1) valid without restriction

03.03.2001 (1, 10)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	rabbit
Strain	:	other:albino
Sex	:	male
Number of animals	:	10
Value	:	> 5000 mg/kg bw
Method	:	other
Year	:	1969
GLP	:	pre-GLP
Test substance	:	other TS
Result	:	One out of the 10 animals died. Signs of intoxication included hind leg weakness, skin irritation, severe erythema and severe edema followed by eschar formation. Gross autopsies of all survivors appeared normal. The LD_{LO} value was 5 g/kg.
Test condition	:	An aqueous paste of the product was held under an impervious cuff in continuous 24-hour contact with the shaved skin of 10 male albino rabbits (mean wt 2.84 kg) at a dosage of 5.0 g/kg. Animals were observed for up to 14 days.
Test substance	:	Material tested was 80% CAS # 23386-52-9, 12% H_20, and 8% ethanol
Reliability	:	(1) valid without restriction

03.03.2001 (1,10)

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female

Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	32 days
Doses	:	0.25, 0.5 and 1.0%
Control group	:	yes
NOAEL	:	> 1 %
Method	:	other
Year	:	1969
GLP	:	pre-GLP
Test substance	:	other TS

Result : There were no deaths and the overall appearance and behavior of both the test and control animals were good. No relevant gross lesions were observed in treated animals. There were no significant differences in mean food intake, mean weight gain, or mean adjusted weight gain between the test and control groups.

Test condition : The product was incorporated into the diet to give concentrations of 0.25, 0.5, and 1.0% (mean dose 240, 470 and 960 mg/kg/day). Diets were fed to young rats (5/sex/group) weighing an average of 143 g for 32 days. A control group of 10 rats/sex was included. Behavior, food intake and weight were monitored over the course of the study. Animals were terminated 32 days after study initiation, and autopsies were performed on high-dose animals. Since there was no sex-related effect of treatment, results from males and females were combined for statistical analyses. The method of multiple comparisons was used to evaluate food intake and weight gain data.

Test substance : Material tested was 80% CAS # 23386-52-9, 12% H_20, and 8% ethanol

Reliability : (1) valid without restriction
03.03.2001 (1)

Species	:	rat
Sex	:	male/female
Strain	:	other:Charles River albino
Route of admin.	:	oral feed
Exposure period	:	90 days
Doses	:	1.0%
Control group	:	yes
NOAEL	:	>1 %
Method	:	other
Year	:	1969
GLP	:	pre-GLP
Test substance	:	other TS

Result : No deaths or abnormal behavioral reactions were noted in treated animals. There was no effect of treatment on final body weight, food consumption, hematologies, urinalyses, or gross or histopathology (as compared to controls).

Test condition : Design: 20 albino rats / sex were fed test material for 90 days at a dietary concentration of 1.0%, which was prepared by blending the appropriate amount of test material with standard rat ration. Twenty control rats/sex received normal food. Rats were weighed biweekly and food consumption was recorded weekly. Fresh diets were prepared weekly. Standard hematologies and urinalyses were performed on blood and urine samples collected from 5 rats/sex/group on treatment day 84.

Endpoints: Animals were sacrificed 90 days after treatment and a complete set of organs and other tissues were examined. At autopsy, the weight of

the liver and kidneys of 10 rats/sex/group were recorded. The following tissues from 5 rats/sex/group were examined histologically:esophagus, stomach (cardia, fundus, pyloris), small intestine (duodenum, jejunum, ileum), cecum, colon , liver, kidneys, spleen, pancreas, urinary bladder, pituitary, adrenal, testes, seminal vesicle, ovary, bone marrow, thyroid, parathyroid, salivary gland, prostate, heart, aorta, lung, lymph node (cervical and mesenteric), skeletal muscle, peripheral nerve, bone (femur), spinal cord, uterus, trachea, eye, optic nerve and brain (cerebrum, cerebellum, and pons).

Statistical Analyses: Data for food consumption, weight, absolute organ weights and organ/body weight ratios were analyzed by analysis of variance (ANOVA). Effects uncovered were further analyzed by t-tests.

Test substance : A commercial sample of the material was dried to remove the liquid phase. The dried products were 100% solids or "active ingredients"

Reliability : (1) valid without restriction
02.03.2001 (7)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
Concentration : 1 mg/plate
Metabolic activation : without
Result : negative
Method : other
Year : 1976
GLP : pre-GLP
Test substance : succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt

Test condition : Salmonella typhimurium strainsTA-98, TA-100, TA-1535, WP-2 uvrA-, TA-1530 and TA 1538 (1 x 10E8) were plated with 1000 micrograms test material per disc or plate according to the method of Ames. Plates were incubated at 37 degrees C for 48 hours. Plates were not supplemented with S9. There were no positive controls. The effect of test material on survival of the bacteria was determined from examination of the background lawn. The potential mutagenic effect was determined from the number of colonies present in the plates with selective medium. No further details were listed.

Reliability : (2) valid with restrictions. The methodology was poorly documented. There were no positive controls.
03.03.2001 (2)

Type : Bacterial mutagenicity
Concentration : 1 mg/plate
Metabolic activation : without
Result : negative
Method : other
Year : 1976
GLP : pre-GLP
Test substance : succinic acid, sulfo-,1,4-dicyclohexyl ester, sodium salt

Test condition : A tryptophan-dependent tester strain of E. coli WP-2 uvra$^-$ (1 x 10E8) was plated with 1000 micrograms test material per disc or plate. Plates were incubated at 37 degrees C for 48 hours. Plates were not supplemented with S9. There were no positive controls. The effect of test material on

survival of the bacteria was determined from examination of the background lawn. The potential mutagenic effect was determined from the number of colonies present in the plates with selective medium. No further details were listed.

Reliability : (2) valid with restrictions. The methodology was poorly documented. There were no positive controls.

03.03.2001 (2)

5.8 TOXICITY TO REPRODUCTION

Type	:	other:histopathology of reproductive organs
Species	:	rat
Sex	:	male/female
Strain	:	other:Charles River albino
Route of admin.	:	oral feed
Exposure period	:	90 days
Doses	:	1.0%
Method	:	other
Year	:	1969
GLP	:	pre-GLP
Test substance	:	other TS

Remark : This study was part of a 90-day oral toxicity study described in Section 5.4

Result : There was no effect of treatment on any reproductive organ

Test condition : Twenty albino rats / sex were fed test material for 90 days at a dietary concentration of 1.0%, which was prepared by blending the appropriate amount of test material with standard rat ration. Animals were sacrificed after 90 days of treatment and were subjected to gross pathology. Ovaries and uteri from females and prostate, testes and seminal vesicles from males were examined histologically.

Test substance : A commercial sample of the material was dried to remove the liquid phase. The dried products were 100% solids or "active ingredients"

Reliability : (1) valid without restriction

03.03.2001 (7)

(1) American Cyanamid Company. 1969. Toxicity data report 69-256. December 23, 1969

(2) American Cyanamid Company. 1976. Mutagenicity test report of Aerosol A-196 (extruded). Report Number M76-122

(3) Analytical Biochemistry Laboratories, Inc. 1987. Report No. 36260 to American Cyanamid. October 18, 1987

(4) Cytec Research and Development. Unpublished information (2001 for water solubility and 2002 for melting point).

(5) Exxon Biomedical Sciences, Inc. 1993. Daphnia acute immobilization test. Project No.142842. May 7, 1993

(6) Exxon Biomedical Sciences, Inc. 1993. Alga, growth inhibition test. Project No. 142867. October 13, 1993

(7) Industrial BIO-TEST Laboratories, Inc. 1969. Ninety-day subacute oral toxicity of Aerosol A-196, Aerosol IB, Aerosol AY, Aerosol MA, Aerosol OT and Aerosol TR in albino rats. Report No. B7409 to American Cyanamid.

(8) Oros G, Cserhati T, Forgacs E, Vrbanova A. 1999. Relationship between hydrophobicity parameters and the strength and selectivity of phytotoxicity of sulfosuccinic acid esters. Gen Physiol Biophys. 18:283-292.

(9) United States Testing Company, Inc. 1988. OECD Screening test for ready biodegradability. Report No. 07278-2 to American Cyanamid. January 15, 1988.

(10) Vernon PA, Deskin R, Dulak LM. 1990. Acute toxicologic evaluation of bis-cyclohexyl sodium sulfosuccinate (80%). J Am Coll Toxicol 1(Part B):108.

(11) Vrbanova A, Gregorova D, Cserhati T, Forgacs E. 1999. Relationship between the physiochemical parameters and biodegradation rate of sulfosuccinic acid ester surfactants. Int Biodeter Biodeg 43(4):207-211.

I U C L I D

Data Set

Existing Chemical	**:**	Butanedioic acid, sulfo-, 1,4-bis(2-ethylhexyl) ester, sodium salt
CAS No.	**:**	577-11-7
Creation date	**:**	30.04.2001
Revision date	**:**	13.05.2002

1.2 SYNONYMS

1,4-Bis(2-ethylhexyl) sodium sulfosuccinate

Bis(2-ethylhexyl) sodium sulfosuccinate

Bis(2-ethylhexyl) sulfosuccinate sodium

Di(2-ethylhexyl) sulfosuccinate sodium

Di(2-ethylhexyl) sulfosuccinic acid, sodium salt

Di-2-ethylhexyl sodium sulfosuccinate

Dioctyl sodium sulfosuccinate

Dioctyl sulfosuccinate sodium

Docusate sodique

Docusate sodium

Docusatnatrium

Sodium docusate

Sodium dioctyl sulfosuccinate

Sodium dioctyl sulphosuccinate

Succinic acid, sulfo-,1,4-bis(2-ethylhexyl) ester, sodium salt

Sulfobutanedioic acid 1,4-bis(2-ethylhexyl)ester sodium salt

2.1 MELTING POINT

Value	:	ca. 153 - 157° C
Method	:	other:measured
Year	:	2002
GLP	:	No data
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Remark	:	Test substance purity >97% Cytec Material Safety Data Sheet
Reliability	:	(2) valid with restrictions. Methodology was not provided.

05.03.2001

Value	:	ca. 162.5 - 168.5° C
Method	:	other:calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Remark	:	The melting point is estimated by the EPIWIN/MPBPWIN model, using Joback, and Gold and Ogle methods.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

05.03.2001

2.2 BOILING POINT

Value	:	ca. 683° C at 750 mm Hg
Decomposition	:	Yes
Method	:	other: calculated
Year	:	2002
GLP	:	not applicable for estimations
Test substance	:	bis (2-ethylhexyl) sodium sulfosuccinate
Remark	:	The boiling point of neat substance is estimated using EPIWIN/Stein and Brown Method. In actuality the substance, as a organic salt, which does not boil, but decomposes at high temperatures.
Reliability	:	(3) invalid. The material will decompose before boiling.

05.03.2001

2.4 VAPOUR PRESSURE

Value	:	= .0000000000217 at 20° C
Method	:	other (calculated)
Year	:	1990
GLP	:	no data
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Reliability	:	(2) valid with restrictions. Documentation as to how value was obtained is missing.

05.03.2001 (19)

Value	:	<.00001 hPa @ 25
Method	:	Other (calculated)
Year	:	2002
GLP	:	No
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Reliability	:	(2) valid with restrictions. EPIWIN MPBPWIN (v1.40) was used to estimate vapor pressure. The program is consistent with the negligible vapor pressure exhibited by organic salts as a substance class.

29.04.2002

2.5 PARTITION COEFFICIENT

Log Pow	:	ca. 3.95 at 25° C
Method	:	other (calculated)
Year	:	2002
GLP	:	no
Test substance	:	bis (2-ethylhexyl) sodium sulfosuccinate
Remark	:	The log Kow was estimated using EPIWIN/KOWWIN (v1.66) based on molecular structure and functionality.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

05.03.2001

2.6.1 WATER SOLUBILITY

Value	:	15 g/l at 25° C, 23 g/l at 40° C, 30 g/l at 50° C, 55 g/l at 70° C
Method	:	no data
Year	:	1983
GLP	:	no data
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Reliability	:	(2) valid with restrictions. Details on experimental conditions are not present.

05.03.2001 (28)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	other
Rel. intensity	:	based on Intensity of Sunlight
Conc. of subst.	:	at 25° C
Direct photolysis		
Halflife t1/2	:	= 5.6 hour(s)
Method	:	other: calculated
Year	:	2002
GLP	:	not applicable for estimations
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Remark	:	A rate constant was estimated using the EPIWIN AOP (v1.90) Program that estimates the rate constant for the atmospheric gas-phase reaction between photochemically produced hydroxyl radicals and ozone with organic chemicals. The estimated rate constant was then used to calculate the atmospheric half-life based upon the average atmospheric concentration of hydroxyl radicals. It should be noted that due to the negligible volatility of organic salts and negligible presence in the atmosphere, atmospheric photodegradation is not an important degradation path for this substance.
Result	:	EPIWIN estimates a hydroxyl radical rate constant of 22.9 E-12 cm^3/molecule-sec.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

05.03.2001

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH7	:	ca. 6.7 year at 25° C
t1/2 pH 8	:	ca. 243 day at 25° C
Method	:	other: calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Remark	:	The EPIWIN/HYDROWIN (v1.67) program cannot assess hydrolysis rates for all fragments of this neat substance. The commercial product is sold both as the neat substance as well as a solution in water. The long-term use of the commercial aqueous solution demonstrates that this substance is stable toward hydrolysis at neutral pHs and ambient temperatures. The ester groups are subject to base or acid catalyzed hydrolysis.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.

05.03.2001

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	volatility
Media	:	water – air
Air (level III)	:	1.55
Water (level III)	:	37.3

Soil (level III)	:	59.9
Sediment (level III)	:	1.33
Method	:	other: calculated
Year	:	2002
GLP	:	not applicable for estimations
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Result	:	The EPIWIN model estimates a Henry's Law Constant of 5.00E-12 atm-m^3/mole. The EPIWIN model estimates a Koc of 1040.
Reliability 05.03.2001	:	(2) valid with restrictions. Data were obtained by modeling.

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge
Contact time	:	28 day
Degradation	:	= 66.4 % after 28 day
Result	:	not readily biodegradable
Kinetic of test substance	:	5 day 0 **%** 15 day 42.8 **%** 28 day 66.4 **%**
Control substance	:	aniline
Kinetic	:	5 day 18.5 % 15 day 66.7 % 28 day 98.1 **%**
Method	:	OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year	:	1991
GLP	:	yes
Test substance	:	other TS
Result	:	The sample stock solution fell within the organic content range stated in the formula. The sample containing 1 mg/l degraded by 0%, 40.7% and 77.8% over 5, 15 and 28 days, respectively. The sample containing 2 mg/l degraded by 0%, 38.9% and 66.7% over 5, 15 and 28 days, respectively. The sample containing 5 mg/l degraded by 0%, 48.9% and 54.8% over 5, 15 and 28 days, respectively. The average degradation for the three concentrations was 0%, 42.8% and 66.4% over 5, 15 and 28 days, respectively. Aniline degraded by 18.5, 66.7 and 98.1% over the three time periods. Because a level of 70% was not reached, the test substance is not "Readily Biodegradable" by this test procedure.
Test condition	:	Stock solution was prepared by adding 1 g of sample to 1 liter of distilled water. The stock solution was screened to determine if it had a similar percent carbon content as stated in the formula provided by the supplier. Stock solution was diluted to 100 ppm as carbon after analysis. The diluted stock was then added to BOD bottles at 3.33 ml, 6.67 ml and 16.65 ml to yield test concentrations of 1 mg, 2 mg and 5 mg as carbon, respectively. Test solutions were inoculated with a low concentration of microorganisms from a mixed population and kept in closed bottles in the dark at a constant temperature of 20 ± 1° C. The activated sludge bacteria was from Bergen Co., New Jersey. The degradation was followed by oxygen analyses with the YSI Dissolved Oxygen Analyzer 54A over a 28-day period. Degradability was based on a comparison of readings of actual oxygen demand to the theoretically expected oxygen demand. A parallel control with inoculum, but without test material, was run as a blank correction factor. The procedure was validated by means of a reference substance (aniline, 2 mg/l) of known biodegradability.

Test Substance	:	$C_2OH_{37}0_7NaS$ (>97%), H_2O (< 2%), C_8H_{18} (< 1%), $C_2OH_{36}O_4$ (<0.5%), $H_2O_4S.2Na$ (<0.5%), $H_2O_3S.2Na$ (<0.2%). Carbon content was 53.5%.
Reliability	:	(1) valid without restriction
30.01.2001		(26)

Type	:	aerobic
Inoculum	:	other:predominantly gram negative bacteria
Concentration	:	1.25mmol/l
Contact time	:	4 hour(s)
Result	:	other:biodegradable
Method	:	other
Year	:	1999
GLP	:	no data
Test substance	:	other TS
Result	:	A biodegradation rate of 31.3 micromoles surfactant/min.g cell protein was calculated for bis(2-ethylhexyl) sodium sulfosuccinate
Test condition	:	The bacterial consortium was obtained from a detergent-polluted soil by enrichment cultivation and adaptation in the presence of surfactant 9 (mono-n-dodecyl sulfosuccinate). Bacteria were cultivated under aeration at 25° C in a phosphate mineral medium. Surfactant 9 was added to the culture in a crystalline form to a final concentration of 0.5 g/l. Microscopic examination of microorganisms present in the adapted mixed culture revealed predominantly Gram-negative motile bacteria. The rate constants of primary biodegradation of 10 different alkyl sulfosuccinates (including bis(2-ethylhexyl) sodium sulfosuccinate) at a concentration of 1.25 mmol/l by the adapted mixed culture (cell protein 0.4 g/l) were measured at 25° C over 4 hours. The culture was incubated under stirring and samples were taken (times not noted) to determine the amount of surfactant remaining. The extent of biodegradation was estimated as a loss of methylene blue active substances in a chloroform extract of the media. The rate constants were calculated as maximum rates of primary degradation catalyzed by one gram of biomass protein in the initial phase of the reaction.
Test Substance	:	The test substance was listed as bis(2-ethylhexyl) sulfosuccinate from Sigma. As Sigma markets this chemical as the sodium salt, it is likely that the sodium salt was used in this study.
Reliability	:	(1) valid without restriction
27.02.2001		(27)

3.7 BIOACCUMULATION

BCF	:	ca. 56.2 at 25° C
Method	:	other: calculated
Year	:	2000
GLP	:	not applicable for estimations
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate
Remark	:	The BCF was estimated using EPIWIN/BCF program based on log Kow.
Reliability	:	(2) valid with restrictions. Data were obtained by modeling.
05.03.2001		

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Lepomis sp.
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
NOEC	:	m = 32
LC50	:	m = 37
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1987
GLP	:	yes
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate (100%)
Remark	:	Using the Acute-Toxicity Rating Scale, published by the U.S. Fish and Wildlife Service, this substance is slightly toxic to bluegill sunfish
Result	:	Temperature remained steady throughout the experiment. The pH decreased from 7.6 to 7.1-7.2 by 48 hours. Dissolved oxygen decreased from approximately 8.3 to 6.1-6.5 mg/l by 48 hours, and to 5.9- 6.2 mg/l (70% saturation) by 96 hours. All solutions had a small amount of undissolved compound at 0 hours, which increased slightly with increasing concentration. A small amount of undissolved material was present in chambers containing 56, 75 and 100 mg/l after 24 hours. Chambers containing 42 mg/l were slightly cloudy at 48 and 72 hours. None of the controls or fish exposed to 32 mg/l died. There was 100% mortality by 96 hours in fish exposed to 42 mg/l and by 24 hours in those exposed to 56, 75 or 100 mg/l. The 96-hour LC_{50} was 37 mg/l. The NOEC was 32 mg/l, based on the lack of mortality and abnormal effects.
Test condition	:	A 96-hour static bioassay was conducted on Bluegill Sunfish (average weight 0.27 +/- 0.16 g, average length 22 +/- 3.7 mm). All fish were acclimated for at least 14 hours prior to testing. Fish were fed with commercial fish food occasionally supplemented with brine shrimp daily until 48-96 hours prior to testing. Ten fish were exposed per group to 0 (control), 32, 42, 56, 75, or 100 mg/l test material. Test material purity was specified as 99+% in the protocol. Tests were conducted in 5 gallon vessels containing 15 liters of soft, reconstituted water (total hardness of 4-48 mg/l as $CaCO_3$, total alkalinity of 25-35 mg/l as $CaCO_3$ and initial pH of 7.2 to 7.6) at 22 +/- 1° C. Water quality parameters of temperature, dissolved oxygen, and pH were measured throughout the test. Initial dissolved oxygen and pH were 8.3 mg/l and 7.6, respectively. Tanks were not aerated during the tests. Data were analyzed according to a computerized LC50 program, which utilized the binomial, moving average and probit tests.
Reliability	:	(2) valid with restrictions. High concentrations of test material may have been insoluble.

27.02.2001 (3)

Type	:	static
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
NOEC	:	m = 20
LC50	:	m = 28
Method	:	Other:APHA

Year	:	1985
GLP	:	no data
Test substance	:	sodium docusate (purity 100%)
Result	:	The initial dissolved oxygen and pH of the tanks ranged from 9.8-9.9 ppm and 7.84- 7.97, respectively. At 48 hr, initial dissolved oxygen and pH of the tanks ranged from 9.6-9.8 ppm and 7.69 to 7.76, respectively. Temperature at 48 hours was 11.9 to 12.0° C. Water quality parameters at 96 hours were not listed. None of the controls or fish exposed to 10 or 20 ppm died within 96 hours. All fish exposed to 40 or 80 ppm died within 24 hours. The LC50 was evaluated using probit methods, moving average angle, and Trinned Spearman-Karber. The values were 27.1, 28.3, and 28.3, respectively.
Test condition	:	Rainbow trout fingerlings (average weight 4.8 g) were acclimated (time not noted) in flowing dechlorinated Milwaukee tap water at 12° C. Fish were fed a commercially prepared pelleted feed during acclimation. Tests were performed in 5 gallon aquariums. Each aquarium was filled with 16 liters of dechlorinated Milwaukee tap water (12° C) and supplied with pressurized air via glass pipettes. Sodium docusate was added to 4 of the 5 aquariums used, producing concentrations of 10, 20, 40 and 80 mg/liter. Ten trout were added to each aquarium. They were not fed during the test. Fish were observed for behavior and death every 24 hours, for a total of 96 hours. Temperature and dissolved O_2were measured at each observation, and the pH was measured at the onset, midpoint and end of the test. Test water was replaced 48 hours into the test.
Reliability	:	(1) valid without restriction

30.01.2001 (7, 9)

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
NOEC	:	m = 12.5
LC50	:	m = 28
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1990
GLP	:	yes
Test substance	:	bis(2-ethylhexyl) sodium sulfosuccinate (100%)
Remark	:	Using the Acute-Toxicity Rating Scale published by the U.S. Fish and Wildlife Service, this substance is slightly toxic to rainbow trout
Result	:	Temperature was maintained at 15° C throughout the test. The pH ranged from 6.8 to 7.4, and did not vary significantly according to group or ti me. Dissolved oxygen remained close to 9.8 mg/l in the control group and decreased to a value of 8.0 mg/l at 48 hours in the other groups. None of the controls or fish exposed to 6.25 or 12.5 ppm died. Twenty percent of fish exposed to 25 ppm died. All fish exposed to 50 or 100 ppm died within 1 hour. The NOEC was 12.5 ppm based on the lack of mortality and abnormal effects.
Test condition	:	This 96-hour static, non-renewal bioassay was performed on six groups of 10 Onchorhyncus mykiss (rainbow trout) approximately 70 days old. Trout were housed (5 per tank) in 4L polypropylene vessels containing 3 L of US EPA moderately hard, reconstituted water. The test concentrations were 0 (control), 6.25, 12.5, 25, 50 and 100 ppm. Fish were maintained at 15 ± 2 ° C under a 16hr/8hr light/dark cycle and were not fed during tests. Oil-free air was supplied at less than or equal to 100 bubbles per minute to

maintain equal to or greater than 60% saturation. Mortality, behavior, physiology, dissolved oxygen, pH, and conductivity were measured initially and daily thereafter. Initial alkalinity and hardness of diluent were also determined. The test was considered valid if greater than 90% of control fish survived 96 hours.

Data were analyzed according to the Spearman-Karber method, Probit analysis, or graphical interpolation (where applicable).

Reliability : (2) valid without restriction
30.01.2001 (25)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
NOEC	:	m = 10
LC50	:	m = 36.2
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	sodium docusate (100%)

Result : The average pH and alkalinity values obtained at 0 and 48 hours ranged from 8.42 - 8.47 and 122.1-128.7. Alkalinity increased slightly with increasing concentration. The mean temperature was 20.0 +/- 0.5° C. None of the controls or animals exposed to 5 or 10 ppm died or were found at the bottom of the test vessel. Mortality at 24 hours of those exposed to 20, 40 or 80 ppm was 0, 50, and 90%, respectively. Mortality at 48 hours of those exposed to 20, 40 or 80 ppm was 5, 60, and 100%, respectively. The 48- hour LC50 was evaluated using Spearman Karber, log-probit, and MAA methods. The corresponding LC50 values at 48 hours were 36.0, 36.8, and 35.8 ppm, respectively. The 48-hour NOEC was 10 ppm.

Test condition : Adult Daphnia magna were cultured in a medium containing reconstituted fresh water, Selenastrum capricornutum and trout food suspension. A stock solution was prepared prior to the bioassay at a concentration of 1 mg dioctyl sodium sulfosuccinate (DSS) per ml of solution in reconstituted water. Offspring of the adults were used in the test. Twenty animals per group were exposed to 0 (control), 5, 10, 20, 40 or 80 ppm. Animals were twenty-four hours of age or less. There were four beakers per test group and five Daphnia per test vessel (100 ml). The vessels were filled with 80 ml test water prior to introduction of Daphnia. Daphnia were not fed during the test. The test beakers were placed in constant flow water bath at 20 ± 2 ° C and were covered with glass to reduce evaporation. A photoperiod of 16 hours and a light intensity of 80 foot candles was used. Temperature was measured daily and the pH and alkalinity of the test media were measured prior to and at study termination. Test animals were observed for mortality and abnormal orientation after 24 and 48 hours of exposure.

Reliability : (2) valid with restrictions. Oxygen content is unknown.
30.01.2001 (8)

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	:	other:Tradescantia bicolor
Endpdoint	:	necrosis
Exposure period	:	48 hour(s)
Unit	:	mmo/l
NOEC	:	< 0.3125
Method	:	other
Year	:	1999
GLP	:	no data
Test substance	:	other TS
Remark	:	Using a molecular weight of 444.56, the NOEC at 48 hours was < 138.9 mg/l. The NOEC at 24 hours was 277.85 mg/l.
Result	:	At 24 hours, the necrosis scores for 0.3125 and 0.625 mmol/l were 0. The score for 1.25 mmol/l was 1. Higher concentrations induced scores of 2. At 48 hours, 0.3125 and 0.625 mmol/l induced scores of 1. Higher concentrations produced scores of 2.
Test condition	:	Eleven different sulfosuccinate esters were tested. Solutions of the bis(2-ethyl-hexyl) ester of sulfosuccinic acid were tested at 0.3125, 0.625, 1.25, 2.5, 5, 10 and 20 mmol/l. Test solutions were infiltrated into leaf sheets of Tradescantia bicolor plants (approximately an area of 10 x 10 mm). Distilled water was used as a control. Each experiment was run in triplicate. Phytotoxicity was evaluated after 24- and 48- hours and was scored according to the following method (0 = no effect, 1 = no necrosis but infiltrated area appears yellow, 2 = necrosis). A spectral mapping technique was used to analyze the effects of the ester compared to the other esters tested.
Test substance	:	The test substance was listed as the di-(2-ethyl-hexyl) ester of sulfosuccinic acid. Other studies performed by the authors list the supplier as Sigma. As Sigma markets this chemical as the sodium salt, it is likely that the sodium salt was used in this study. Purity was not listed.
Reliability	:	(1) valid without restriction

03.03.2001 (23)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	mouse
Strain	:	other: ARS/ICR
Sex	:	male
Number of animals	:	80
Value	:	= 2643 mg/kg bw
Method	:	other
Year	:	1977
GLP	:	pre-GLP
Test substance	:	dioctyl sodium sulfosuccinate (purity not listed)
Result	:	Mortality rates for exposure to 2340, 2520, 2690, 2880, 3090, 3310, 3550 or 3825 mg/kg were 3/10, 6/10, 4/10, 7 /10, 5/10, 7/10, 7/10, 9/10, respectively. Deaths at high doses occurred within 4-8 hours of dosing. High lethal doses caused mice to be hypoactive. There was no mention of any clinical signs in survivors . The LD_{50} value was 2643 (2029-3440) mg/kg. Necropsy findings were not listed.
Test condition	:	Mice (10/group) weighing 18-22 g were given 2.5 to 5.0 ml/100 g dioctyl sodium sulfosuccinate (DSS) in 4% acacia by gastric intubation. The doses administered were: 2340, 2520, 2690, 2880, 3090, 3310, 3550, and 3825 mg/kg. Mice were observed for abnormal signs and mortality for 14 days following dosing and then were necropsied. The method of Litchfield and Wilcoxon (J Pharm Exp Ther 96:99, 1949) was used to calculate LD_{50} values.
Reliability	:	(1) valid without restriction

27.02.2001 (5)

Type	:	LD50
Species	:	rat
Strain	:	CF Nelson
Sex	:	male
Number of animals	:	20
Vehicle	:	water
Value	:	= 3080 mg/kg bw
Method	:	other
Year	:	1966
GLP	:	pre-GLP
Test substance	:	dioctyl sodium sulfosuccinate, 100%
Result	:	None of the animals administered 0.625 or 1.25 g/kg died. Mortalities of rats given 2.5 or 5 g/kg were 1/5 and 5/5, respectively. All deaths occurred within 24 hours. Signs of intoxication included depression of varying intensity and diarrhea. No visible lesions were noted in the surviving animals at terminal necropsy.
Test condition	:	Four groups of 5 male rats (average weight 131 g) fasted for 24 hours were dosed with a 5% aqueous dispersion at 0.625, 1.25, 2.5, and 5.0 g/kg. At 5 g/kg, the dose was administered in 2 separate portions ¼ hour apart. Animals were observed over a period of 14 days and then necropsied. The method of calculating the LD_{50} value was not stated.
Reliability	:	(1) valid without restriction

30.01.2001 (1)

Type	:	LD50

Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male
Number of animals	:	20
Vehicle	:	water
Value	:	= 4200 mg/kg bw
Method	:	other
Year	:	1977
GLP	:	pre-GLP
Test substance	:	sodium dioctyl sulfosuccinate (purity not listed)
Remark	:	The LD50 value listed in report was 4.2 ml/kg. This is obviously incorrect. According to the data, it is somewhere between 3.56 and 4.48 g/kg.
Result	:	Mortalities of rats exposed to 14.1, 17.8, 22.4, 25.2 ml/kg (2.82, 3.56, 4.48, and 5.04 g/kg) were 0/5, 1/5, 3/5, and 5/5, respectively. Most deaths occurred within 6-24 hours of dosing. Signs of intoxication included prostration and lethargy. Yellow fluid was observed in the gastrointestinal tract of those found dead. No visible lesions were observed in the surviving animals at terminal necropsy.
Test condition	:	Rats (5 per group, average weight 145-152 g) that had been fasted overnight were dosed with a 20% aqueous solution of the test material in dosages of 14.1, 17.8, 22.4 and 25.2 ml/kg (2.82, 3.56, 4.48, and 5.04 g/kg) by oral gavage. Animals were observed up to 14 days following dosing and then necropsied. The method used to calculate the LD_{50} value was not stated.
Reliability	:	(2) valid with restrictions. Documentation as to how doses were prepared is not present.

27.02.2001 (16)

Type	:	LD50
Species	:	rat
Strain	:	Wistar
Sex	:	female
Value	:	ca. 2000 mg/kg bw
Method	:	other
Year	:	1962
GLP	:	pre-GLP
Test substance	:	dioctyl sodium sulfosuccinate (purity not listed)
Remark	:	The actual doses given and the number of deaths at each dose were not listed. The LD50 value was listed at approximately 2 g/kg, with a range of approximately 0.8 g/kg. No clinical signs or signs of toxicity at necropsy were described.
Test condition	:	Groups of 5 unfasted female rats (135-180 g) were given dioctyl sodium sulfosuccinate (DSS) as a 10% aqueous solution or emulsion in doses ranging in geometric progression from 0.252 to 7.95 g/kg. Mortality was monitored 2 weeks postdosing. Animals were necropsied 14 days after dosing. LD50 values were calculated by the Weil Modification of the Method of Thompson.
Reliability	:	(2) valid with restrictions. Number of deaths at each dose is not listed.

27.02.2001 (22)

Type	:	LD50
Species	:	mouse
Strain	:	other:Harlan
Sex	:	male/female
Value	:	= 4800 mg/kg bw

Method	:	other
Year	:	1949
GLP	:	pre-GLP
Test substance	:	sodium dioctyl sulfosuccinate (purity not listed)
Remark	:	The doses that were given, the number of deaths at each dose, clinical signs, necropsy findings, and time of necropsy were not listed.
Test condition	:	Mice (14-23 g) were given test material so that 0.5 cc of solution was given by gavage for each 20 g of mouse. Groups (5/sex/dose) were given test material with increasing increments between doses of 20% or less. Mice were observed over a 72-hour period. The LD_{50} value was calculated from the death rate at the dosages given.
Reliability	:	(2) valid with restrictions. Doses given and number of deaths at each dose is not listed.

27.02.2001 (15)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	rabbit
Strain	:	New Zealand White
Sex	:	male
Number of animals	:	5
Value	:	> 10 g/kg bw
Method	:	other
Year	:	1977
GLP	:	pre-GLP
Test substance	:	sodium dioctyl sulfosuccinate (purity not stated)
Result	:	None of the animals died. Skin irritation including fissuring, desquamation, and coriaceousness was noted. Rabbits were noted pulling fur out. No gross pathology was observed.
Test condition	:	5 male rabbits (avg. weight 2.29 kg) received a 10ml/kg dose by covered dermal application to clipped unabraded skin for 24 hours. Animals were observed over 14 days and then necropsied
Reliability	:	(1) valid without restriction

30.01.2001 (16)

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	other:Charles River albino
Route of admin.	:	oral feed
Exposure period	:	90 days
Doses	:	1.0%
Control group	:	yes
NOAEL	:	>= 1 %
Method	:	other
Year	:	1969
GLP	:	pre-GLP

Test substance	:	A commercial sample of CAS 577-11-7 was dried to remove the liquid phase. The dried products were 100% solids or "active ingredients"
Result	:	No deaths or abnormal behavioral reactions were noted. There was no effect of treatment on final body weights, food consumption, hematologies, urinalyses, organ weights, or gross or microscopic pathology (as compared to controls).
Test condition	:	Design: 20 albino rats / sex were fed test material for 90 days at a dietary concentration of 1.0%, which was prepared by blending the appropriate amount of test material with standard rat ration. Twenty control rats/sex received normal food. Rats were weighed biweekly, and food consumption was recorded weekly. Fresh diets were prepared weekly. Standard hematologies and urinalyses were performed on blood and urine samples collected from 5 rats/sex/group on treatment day 84. Endpoints: Animals were sacrificed 90 days after treatment and a complete set of organs and other tissues was examined. At autopsy, the weight of the liver and kidneys of 10 rats/sex/group were recorded. The following tissues from 5 rats/sex/group were examined histologically: esophagus, stomach (cardia, fundus, pyloris), small intestine (duodenum, jejunum, ileum), cecum, colon, liver, kidneys, spleen, pancreas, urinary bladder, pituitary, adrenal, testes, seminal vesicle, ovary, bone marrow, thyroid, parathyroid, salivary gland, prostate, heart, aorta, lung, lymph node (cervical and mesenteric), skeletal muscle, peripheral nerve, bone (femur), spinal cord, uterus, trachea, eye, optic nerve and brain (cerebrum, cerebellum, and pons). Statistical Analyses: Data for food consumption, weight, absolute organ weights and organ/body weight ratios were analyzed by analysis of variance (ANOVA). Effects uncovered were further analyzed by t-tests.
Reliability	:	(1) valid without restriction

02.03.2001 (17)

Species	:	dog
Sex	:	male/female
Strain	:	Beagle
Route of admin.	:	other: oral tablet
Exposure period	:	1 year
Frequency of treatment	:	once per day, 7 d/wk
NOAEL	:	>= 30 mg/kg
Method	:	other
Year	:	1977
GLP	:	pre-GLP
Test substance	:	dioctyl sodium sulfosuccinate
Result	:	There were no effects of treatment with DSS on organ or body weights, gross and microscopic tissue observations, or hematological, blood chemistry, or urinalysis parameters. No evidence of gastric irritation was noted
Test condition	:	72 dogs (7-8 months of age) were conditioned for approximately 6 weeks prior to compound administration. They were divided into 9 groups of 8 dogs each (4 of each sex). Groups of dogs were dosed orally with tablets containing danthron (5 or 15 mg/kg), dioctyl sodium sulfosuccinate (DSS; 30 mg/kg), poloxalkol (POL; 120 mg/kg), danthron (5 or 15 mg/kg) + DSS (10 or 30 mg/kg), or danthron (5 or 15 mg/kg) + POL (40 or 120 mg/kg) once a day, seven days/week, for one year. A control group received a daily quantity of tables that contained all materials in the 15 mg danthron

tablets except the active material. All formulations met appropriate analytical specifications. All dogs were weighed at weekly intervals and doses were adjusted accordingly. Physical examinations were conducted pre-dose and at 3, 6, 9 and 12 months post dose. Urinalyses were done on urine samples collected pre-dose and at 6 and 12 months. Standard hematology parameters and serum chemistries were determined on blood collected from the external jugular vein on days -28, -7, 14, 30, 80, 130, 210, 280, and 365. Fundus photographs were taken pre-dose and just prior to termination. Various tissues were weighed and examined microscopically at termination.

Reliability : (1) valid without restriction
27.02.2001 (5)

Species	:	rat
Sex	:	male
Strain	:	Osborne-Mendel
Route of admin.	:	oral feed
Exposure period	:	16 weeks
Doses	:	2, 4, 8 %
Control group	:	yes
NOAEL	:	< 2 %
LOAEL	:	= 2 %
Method	:	other
Year	:	1948
GLP	:	pre-GLP
Test substance	:	dioctyl sodium sulfosuccinate

Result : All animals that received 8% had severe GI symptoms and died within the first week of treatment. Only one animal given 4% lived for 16 weeks and it grew slowly. Rats given 2% gained less weight than controls (220.4 +/- 24.9 g vs. 393.0 +/- 22.6 g) and had evidence of gastrointestinal irritation upon necropsy

Test condition : Groups of 5 male rats (21 days old) received diet (ground commercial rat biscuits) containing 2, 4, or 8% dioctyl sodium sulfosuccinate (DSS) or a control diet containing 1% cod liver oil. Test material was mixed with the diet by means of a rotary batch mixer. Body weights and food consumption were determined at weekly intervals. Surviving animals were sacrificed and subjected to necropsy after 16 weeks. Lung, heart, liver, spleen, pancreas, stomach, small intestine, kidney, adrenal and testes were sectioned in all instances and colon, thyroid, parathyroid, lymph nodes, leg bones, leg muscles, and bone marrow were sectioned in some (number not noted).

Reliability : (2) valid with restrictions. Whether fresh diets were prepared frequently is not documented. It is assumed that the test diet was only prepared at the beginning of the experiment.
27.02.2001 (6)

Species	:	rat
Sex	:	male/female
Route of admin.	:	oral feed
Exposure period	:	26 weeks
Doses	:	0.5, 1.04, 1.5%
Control group	:	yes, concurrent no treatment
NOAEL	:	= .5 %
LOAEL	:	= 1.04 %
Method	:	other
Year	:	1966
GLP	:	pre-GLP

Test substance	:	dioctyl sodium sulfosuccinate
Result	:	Weight gain of females given 1.04 or 1.5% was reduced during the third week. Two controls and 4 test animals given 1.5% died. Two out of the four that died after 1.5% exhibited hemorrhagic gastroenteritis. No other effects were noted.
Test condition	:	Groups of 12 male and female weanling rats were treated with diets containing 0. 0.5, 1.04 and 1.5% dioctyl sodium sulfosuccinate (DSS) for 26 weeks. Body weight and food consumption were monitored over the course of the study. Hematological analysis and urinalyses were performed. The weight of the spleen, liver, adrenal, kidney and gonads was determined at autopsy. Heart, lung, liver, spleen, kidney, adrenal, bladder, thyroid, pancreas, lymph nodes, gut, muscle, bone, marrow, gonads and thymus were examined histologically.
Reliability	:	(2) valid with restrictions. The primary reference was not available.

27.02.2001 (24)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella strains TA98, TA100, TA1535, TA1537 and TA1538
Concentration	:	0, 1, 10, 100 micrograms/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1980
GLP	:	no data
Test substance	:	dioctyl sodium sulfosuccinate
Result	:	Tests with all strains were negative at all concentrations. Results for two strains (TA98 and TA100) were listed. The number of revertants in TA98 incubated with 0, 1, 10 or 100 micrograms without metabolic activation were 22, 31, 32 and 35, respectively, and with metabolic activation were 58, 50, 43, and 55, respectively. The number of revertants in TA100 incubated with 0, 1, 10 or 100 micrograms without metabolic activation were 201, 183, 180 and 185, respectively, and with metabolic activation were 158, 146, 135, and 140, respectively.
Test condition	:	Salmonella strains TA98, TA100, TA1535, TA1537 and TA1538 were cultured according to established procedures. Liver microsomes were prepared from Sprague-Dawley rats 5 days after a single i.p. injection of 500 mg/kg Aroclor 1254. The livers of animals were homogenized, pooled and centrifuged at 9000 g for 10 min and the resulting supernatant (S-9) was stored at -90° C until required. S-9 mix was prepared with NADP, MgCl2, KCl and glucose-6-phosphate as cofactors. Concentrations of test materials (dioctyl sodium sulfosuccinate and 23 other food additives) ranging from 100 micrograms to 10 mg per plate were first tested for cytotoxicity. For each Salmonella strain, duplicate plates were set up with 4 dilutions of test materials in dimethyl sulfoxide in the optimal non-toxic dose range with or without S-9 mix. Bacteria from an overnight stationary-broth culture (10E*8 organisms/ml), test material, and S-9 mix (as required) were mixed in 2 ml of minimal agar at 42° C. This was added to 30 ml of minimal agar in 100 mm Petri plates and incubated at 37° C for 48 hours. The number of His+ revertant colonies was then enumerated. Data were not statistically evaluated.
Reliability	:	(2) valid with restrictions. There was no positive control.

27.02.2001 (4)

Type	:	Ames test
System of testing	:	Salmonella strains TA98, TA100, TA102, TA1535 and TA1537
Concentration	:	micrograms/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Test guideline 471
Year	:	1993
GLP	:	yes
Test substance	:	sodium dioctyl sulphosuccinate

Result : Cytotoxicity (as evidenced by the thinning of the background bacterial lawn) was observed at the highest concentration used in experiments 1 and 2 and the top two concentrations used in experiments 3 and 4. The tests were considered valid since the average number of revertants in the negative controls for TA98, TA100, TA1535, TA1537 and TA102 in the absence (17.4, 101.0, 13.2, 8.8, and 273.8, respectively) or presence of S-9 (23.6, 122.2, 16.2, 10.0, and 331.8, respectively) were within historical ranges and positive controls used in each strain caused significant increases in the number of revertants in TA98, TA100, TA1535, TA1537 and TA102 in the absence (1176.0, 737.3, 399.0, 594.7, and 504.0, respectively) of S-9 and TA98 and TA100 in the presence of S-9 (937.0, and 1689.3). No concentration of sodium dioctyl sulphosuccinate, either in the presence or absence of S-9 resulted in a statistically significant increase in the number of revertants in any of the test strains. The largest increase in revertants induced by test material was a 1.4-fold increase observed in TA98 incubated with 8 micrograms (compared to a 67.6 fold increase in the positive control) and in TA1537 incubated with 40 micrograms of test material (also compared to a 67.6-fold increase in the positive control).

Test condition : Salmonella strains TA98, TA100, TA102, TA1535 andTA1537 were utilized. Liver S-9 that was prepared from male Sprague-Dawley rats induced with Aroclor 1254 (MolTox S-9) was obtained from Molecular Toxicology Incorporated, Anapolis MD. The S-9 was stored at - 80° C until use. Each batch was tested by the manufacturer for sterility, protein content (minimum 32 mg/ml), ability to convert ethidium bromide and cyclophosphamide to bacterial mutagens, and cytochrome p-450-catalyzed enzyme activity.

Test chemical solutions were prepared by dissolving sodium dioctyl sulphosuccinate in analytical grade acetone. Test chemical solutions were protected from light and were used within 24 hours of preparation. A range-finding study was first performed to determine cytotoxic concentrations. Four separate mutagenicity experiments were performed. The concentrations used in the first experiment were 1.6, 8.0, 40, 200 and 1000 micrograms per plate. The concentrations used in the second experiment were 4, 20, 100, 50 and 2500 micrograms per plate. The third experiment used 62.5, 125, 250, 500 and 1000 micrograms per plate, and the fourth used 156.25, 312.5, 625, 1250 and 2500 micrograms per plate. S-9 was used in the second and fourth experiments. The solvent (acetone) was also tested for mutagenicity. The positive control 2-nitrofluorene (50 micrograms per plate) was tested in TA98, sodium azide (2 micrograms per plate) in TA100 and TA1535, 9-aminoacridine (50 micrograms per plate) in TA1537, glutaraldehyde (25 micrograms per plate) in TA102, and 2-aminoanthracene (5 micrograms per plate) in TA98 in TA100 in the presence of S-9 . Bacteria that had been checked for strain characteristics were cultured for 10 hours at 37° C in nutrient broth. Triplicate plates containing 2.5 ml molten agar were prepared for each concentration. For

experiments 2 and 4, 0.5 ml S-9 mix was added to each plate. Bacteria were added at 0.1 ml bacterial culture per plate (number of bacteria not noted) and test agent was added at 0.05 ml per plate. Plates were inverted and incubated at 37° C in the dark for 3 days. Colonies were counted electronically and inspected for signs of toxicity.

The m-statistic was calculated to check that the data were Poisson distributed. Dunnett's test was used to compare the counts at each dose to control. The presence of a dose-response was examined using linear regression. The assay was considered valid if negative controls fell within a historical range, positive controls induced clear increases in revertants, and no more than 5% of the plates were lost due to contamination or error. The test compound was considered to be mutagenic if the assay was valid, Dunnett's test gave a significant response ($p \leq 0.01$), the data set showed a significant dose-correlation and the positive responses were reproducible.

Reliability : (1) valid without restriction
27.02.2001 (11)

Type : Chromosomal aberration
System of testing : Chinese Hamster Ovary (CHO) Cells
Concentration : micrograms/plate
Metabolic activation : with and without
Result : negative
Method : OECD Test guideline 473
Year : 1993
GLP : yes
Test substance : sodium dioctyl sulphosuccinate

Remark : The test personnel concluded that the test material was positive in the assay. However, the results do not conform to the guidelines for a positive test. According to their assessment criteria, the fact that chromosome aberrations were observed in only one test at a dose level close to the toxic threshold is not indicative of a positive result. The authors mention that the fact that chromosome aberrations were only seen at a dose close to the toxic threshold in the presence of S-9 implies that the test material was not directly genotoxic. Another possibility is that the genotoxicity was secondary to cytotoxicity.

According to the criteria of Loveday et al. (Environ Mol Mutagen 16:272-303, 1990), a positive CHO cell result at a single dose is indicative of weak evidence for clastogenicity. If this result cannot be repeated, then the test is considered to be negative. Based on these criteria, the test is negative.

Result : The test was considered valid. Positive controls induced significant increases in the number of cells with aberrations, the proportion of cells with aberrations in negative control cultures were within normal range for all but two of the cultures, and at least 160/200 cells were analyzed at each treatment level. In Experiment 1, approximately 52% and 19% mitotic inhibition was observed following treatment with 55.3 or 112.8 micrograms/ml in the absence or presence of S-9, respectively. Complete toxicity was observed at higher doses. Additional experiments were therefore conducted at dose ranges expected to induce 50-75% mitotic inhibition. Treatment of cultures with sodium dioctyl sulphosuccinate (DSS) in the absence of S-9 resulted in aberration frequencies similar to those of negative controls (a maximum of 8/200 scored cells at 55.29 micrograms/ml vs. 3/200 in the negative control and 22/50 in the positive control). Cultures treated with DSS in the presence of S-9 in Experiment 2 had significantly increased frequencies of cells with aberrations (44/200 vs. 7/200 in negative control) at the highest dose chosen for analysis (120

micrograms/ml). Approximately 62% mitotic inhibition was noted at this concentration. In contrast, cultures treated with this and higher scorable concentrations (up to 130 micrograms/ ml) in other experiments had normal frequencies of aberrations (highest frequency was 7/200). However, mitotic inhibition of at least 50% was not observed at these concentrations in these experiments. In all experiments, treatment with 140 micrograms/ml caused complete toxicity.

Test condition : Liver S-9 that was prepared from male Sprague-Dawley rats induced with Aroclor 1254 (MolTox S-9) was obtained from Molecular Toxicology Incorporated, Annapolis MD. The S-9 was stored at -80° C until use. Each batch was tested by the manufacturer for sterility, protein content (minimum 32 mg/ml), ability to convert ethidium bromide and cyclophosphamide to bacterial mutagens, and cytochrome p-450-catalyzed enzyme activity. As needed, a 0.25 ml aliquot of S-9 was added to each cell culture (4.75 ml).

Sodium dioctyl sulfosuccinate was tested for cytogenicity using duplicate cultures of CHO cells in the presence and absence of S-9. The highest dose used (470 micrograms/ml) was close to the solubility limit in the culture medium. Stock solutions were prepared by dissolving test material in acetone to give 47 mg/ml. Stock solutions were diluted with acetone to make test concentrations ranging from 9.3 to 470 micrograms/ml for Experiment 1, 70 to 160 micrograms/ml for Experiment 2, 10 to 140 micrograms/ml for Experiment 3, 101 to 140 micrograms/ml for Experiment 4, and 90 to 170 mg/ml for Experiment 5. Acetone was also tested as a vehicle control. The positive control chemicals 4-nitroquinoline 1-oxide (0.0625, 0.125, 0.25 micrograms/ml) and cyclophosphamide (12.5 and 25.0 micrograms/ml + S9) were also tested. All test solutions were used within 2.5 hours of preparation.

CHO cells of low confluence were used in the tests (number not indicated). In Experiment 1, cells were incubated in the absence of S-9 for 20 hours, or in the presence of S-9 for two hours, followed by 18-hrs of recovery. In Experiments 2, 3, and 5, the S-9 protocol for experiment 1 was followed. Experiment 3 followed the protocol of experiment 1, plus additional plates were incubated for 44 hours in the absence of S-9. Cultures were prepared in duplicate or quadruplicate. Colchicine was added at 1 microgram/ml approximately 1.5 hours prior to harvest to arrest dividing cells in metaphase. Cells were harvested , fixed, stained with Giemsa, and examined for mitotic index. Twenty-five cells from each of the positive control cultures were analyzed to ensure that the test was valid. Where possible, 100 metaphases from each test and negative control culture were analyzed for chromosome aberrations. Aberrants were categorized as 1) cells with structural aberrations including gaps, 2) cells with structural aberrations excluding gaps, and 3) polyploid, endoreduplicated or hyperdiploid cells. The proportion of cells in category 2 for each test condition was examined with the proportion in negative controls using Fisher's exact test. The proportions of cells in categories 1 and 3 were examined in relation to historical controls. The category 2 totals for negative control cultures were used to determine whether the test was acceptable. The proportion of aberrant cells in each replicate were used to establish acceptable heterogeneity between replicates by means of a binomial dispersion test. Probability values of $p \leq 0.05$ were accepted as significant.

The test was considered to be valid if the binomial dispersion test demonstrated acceptable heterogeneity between replicates, the proportion of cells with structural aberrations (excluding gaps) in negative control cultures fell within the normal range and the percentage of polyploid/endoreduplicated/hyperdiploid cells was < 10%, at least 160 cells

out of an intended 200 were analyzable at each treatment level and the positive control chemicals induced statistically significant increases in the number of cells with structural aberrations.

The test chemical was considered to be clearly positive if 1) statistically significant increases in the proportion of cells with structural aberrations (excluding gaps) occurred at one or more concentrations, 2) the proportion of aberrant cells at such data points exceeded the normal range, 3) and the results could be duplicated. Increases in the numbers of cells with gaps or increases in the proportions of cells with structural aberrations not exceeding the normal range or occurring only at very high or toxic concentrations were considered to be "equivocal". A positive result only at the delayed harvest in Experiment 2 was to be taken as evidence of clastogenicity provided that criteria 1 and 2 were met.

Reliability : (2) valid with restrictions
27.02.2001 (12)

5.7 CARCINOGENICITY

Species	:	rat
Sex	:	male
Strain	:	Osborne-Mendel
Route of admin.	:	oral feed
Exposure period	:	2 years
Doses	:	0.25, 0.5, 1.0 %
Control group	:	yes
NOAEL	:	= .5 %
LOAEL	:	= 1 %
Method	:	other
Year	:	1948
GLP	:	pre-GLP
Test substance	:	dioctyl sodium sulfosuccinate

Result : There was no effect of DSS on food intake. Consumption of 1.0% DSS in the diet was associated with significantly less weight gain (395.8 +/- 11.6 g) than controls (471.9 +/- 13.2 g). There was no other effect of treatment on the animals.

Test condition : Groups of 12 male rats (21 days old) received diet (ground commercial rat biscuits) containing 0.25, 0.5 and 1.0% dioctyl sodium sulfosuccinate (DSS) or a control diet containing 1% cod liver oil. Test material was mixed with the diet by means of a rotary batch mixer. Body weights and food consumption were determined at weekly intervals. Surviving animals were sacrificed and subjected to necropsy after two years. Lung, heart, liver, spleen, pancreas, stomach, small intestine, kidney, adrenal and testes were sectioned in all instances and colon, thyroid, parathyroid, lymph nodes, leg bones, leg muscles, and bone marrow were sectioned in some (number not noted).

Reliability : (2) valid with restrictions. The stability of test material in the diet and when diets were prepared is not documented.
27.02.2001 (6)

5.8 TOXICITY TO REP RODUCTION

Type : other: three generation

Species	:	rat
Sex	:	male/female
Strain	:	other: Crl:CD (SD)BR
Route of admin.	:	oral feed
Premating exposure period		
Male	:	10 weeks
Female	:	2 weeks
Doses	:	0.1, 0.5, 1.0%
Control group	:	yes
NOAEL Parental	:	= .1 %
NOAEL F1 Offspr.	:	= .1 %
NOAEL F2 Offspr.	:	= .1 %
Method	:	other
Year	:	1986
GLP	:	yes
Test substance	:	dioctyl sodium sulfosuccinate (99.4%pure)

Remark : The NOAEL listed is for effect on lactation and pup weight on Day 21

Result : Dietary composition: Average concentrations of DSS in the diets were 0.0984% and 0.972% for the 0.1 and 1.0% dose levels, respectively. DSS did not hydrolyze in the diet to form significant amounts of 2-ethylhexanol. The level of acetone in the diets (< 50 ppm and 50.2 ppm for the 0.1 and 1.0% dose groups, respectively) was not expected to affect the results of the study.

Food consumption and body weight: Food consumption of F0, F1 and F2 males treated with 1.0% DSS was significantly less than controls at week 4, weeks 2, 4, 8, and 10, and weeks 2 and 10, respectively. There was no consistent effect of any dose on food consumption in females. Body weights of F1 males and females treated with 1.0% (131 and 114 g, respectively) were lower than controls (149 and 127 g, respectively) and final weights of F1 (447 g) and F2 (467 g) males and females (255 and 269 g, respectively) treated with 1.0% and F2 males treated with 0.5% (492 g) were lower than their respective controls (510 and 531 g for F1 and F2 males, and 281 and 285 g for F1 and F2 females, respectively). Mean birth weight of male (6.1 g) and female (5.8 g) pups born to animals treated with 1.0% were significantly lower than control (6.7 and 6.4, respectively). All three generations of male and female pups born to animals treated with 0.5% (43, 43 and 49 g for F1, F2 and F3 males and 41, 42 and 46 g for females) or 1.0% (36, 36 and 38 g for F1, F2 and F3 males and 34, 35 and 37 g for females weighed significantly less than controls on Day 21 (47, 49 and 54 g for F1, F2 and F3 males and 45, 46 and 51 g for females, respectively). No milk was found in the abdomens on lactation day 4 in 3 control F2 pups, 7 F2 pups in the 0.1% dose group, 18 F2 pups and 1 F3 pup in the 0.5% dose group, and 10 F2 pups and 17 F3 pups in the 1.0% dose groups.

Reproductive indices: There was no effect of treatment on the total number of pups (ranged from 326 for F3 treated with 0.1% to 416 for F1 control) or litters [ranged from 25 for F3 treated with 0.1% to 30 for four other groups (F1 control, 0.1 and 1.0% F1 and 1.0% F2)], litter size (ranged from 5.9 for F1 males treated with 1.0% to 7.2 for female F2 control) or sex ratio (ranged from 47.2 for F2/1.0% to 51.5 for F2/0.5%). Perinatal pup survival across the three generations was 99% for controls and ranged from 96% (for F3 generation of animals treated with 1.0%; significantly different from control of 99%) to 100% for the treated groups. The pup survivability ranged from 95-100% for controls, from 98-100% for low- and mid-dose groups and from 91-99% for the high dose group (no effect of treatment). There were no treatment-related mortatily and antemortem or microscopic observations in any animals examined (F0, F1 and F2 adults and F3

weanlings).

Test condition : Treatment: Test diets (ground Purina Certified Rodent Chow No. 5002) containing 0.1, 0.5 or 1.0 dioctyl sodium sulfosuccinate (DSS) dissolved in acetone were mixed weekly. Samples of test diets were assayed periodically for DSS to verify homogeneity and stability of DSS after storage. After a 4-week acclimation period, groups of 30 male and 30 female rats (7 weeks of age, guaranteed non littermates) were fed the basal diet or a test for 10 and 2 weeks, respectively. These animals (F0) were then mated to produce an F1 litter. Groups of 30 male and 30 female F1 animals were fed the same dose levels for at least 10 weeks postweaning, and the breeding program was repeated to produce F2 animals. Sibling and half-sibling matings were avoided. Groups of 30 male and 30 female F1 animals were fed the same dose levels for at least 10 weeks postweaning, and the breeding program was repeated to produce F2 animals. The same feeding and mating procedure was repeated with F2 animals to produce F3 offspring. The study was terminated upon weaning of the F3 generation.

Data: Individual pup weights and the number of pups born live or found dead were recorded on lactation Day 0. Intact dead pups were examined and preserved. The number and sex of pups and individual pup weights were recorded on lactation Day 4. Pups were culled from litters to achieve a maximum of 10 (5 of each sex if possible)/ litter. Pups were weighed and examined externally on Days 7, 14 and 21 of lactation. At least one male and female/litter (for a total of 30/sex/group) were selected to continue on the study. Twenty weanlings/sex/group from the F3 litter were necropsied. Weanlings not selected for mating or necropsy were examined externally. All F0, F1 and F2 animals were observed twice daily during the study and subjected to gross necropsy upon study termination. Organs grossly examined at necropsy were colon, duodenum, epididymides, ileum, jejunum, kidneys, liver, mammary gland (with skin), ovaries, prostate, seminal vesicles, stomach, testes, uterus and vagina. Body weights were recorded weekly for males and before mating, Days 0, 7, 14 and 20 of gestation and Days 0, 7, 14 and 21 of lactation for females. Food consumption of males and females was recorded weekly before mating, and twice weekly during gestation and lactation (females only).

Statistical Analyses: Body weight, food consumption, reproductive indices, precoital interval, length of gestation, pup viability and body weight, sex ratios and litter size (alive and dead by sex) were analyzed using a one-way ANOVA. When necessary, data were transformed to achieve homogeneity. Dunnett's t- test was used to compare means of groups analyzed by ANOVA. Data that could not be transformed to homogeneity were analyzed nonparametrically, using a Kruskal-Wallis test. The Nemenyi , Nemenyi-Kruskal-Wallis or Wilcoxon-Mann-Whitney two sample rank test were used compare nonparametric means. Reproductive indices and the total number of live and dead pups were analyzed by the Cochran-Armitage test for trend and the Fisher-Irwin exact test for heterogeneity.

Conclusion : DSS at 0.5 and 1.0% affected lactation. Reduced body weights in animals receiving 0.5 or 1.0% did not interfere with growth and development or normal reproductive performance.

Reliability : (1) valid without restriction
27.02.2001 (10, 20)

Type : other:three generation
Species : rat
Sex : male/female
Strain : other:CFE
Route of admin. : oral feed

Doses	:	0.5, 1.0%
Control group	:	yes
NOAEL Parental	:	< .5 %
NOAEL F1 Offspr.	:	< .5 %
NOAEL F2 Offspr.	:	< .5 %
other: NOEL F3 Offspring	:	< .5 %
Method	:	other
Year	:	1970
GLP	:	pre-GLP
Test substance	:	other TS

Remark : Results are based on the concentration of DSS in the diet, and not the original test material. It is presumed that the test material was dried to remove ethanol. Statistical analyses were not listed.

The lowering of survival rate of the F3b pups was attributed to impairment of nutrition, presumably because of the taste of DSS secreted in the milk of the dams. Skeletal changes were concluded to be unrelated to DSS. The NOAELs listed are for an effect on lactation.

Result : No effects of DSS on fertility and gestation indices were noted in the F0 generation and F2 generation dams that were continuously fed test diet. There was no effect of treatment on the number of live-born litters (ranged from 14 for F3b/1.0% to 16 for F1b/0.5% and F3a/ 0.5% and 1.0%), live-born pups (ranged from 164 for F3a control to 212 for F1b/1.0%). The viability index was slightly depressed for F3b pups from dams given 0.5 or 1.0% (78 and 72 vs. 93 for controls). The lactation index for both F0 and F2 dams that were fed test diet continuously at 0.5 or 1.0% DSS was depressed (46 and 42 for versus control of 64 for F1a pups and 59 and 53 versus control of 71for F3b pups). The mean weanling weight of F1a (37 and 35 g) and F3b pups (45 and 42 g) from dams with reduced lactation indices (0.5 and 1.0%, respectively) were slightly less than controls (39 and 49 g).

With the exception of F1b pups, no effect of DSS on lactation indices was noted in pups from dams that did not receive DSS during lactation (F1b, F2, F3a). Lactation indices for the F1b pups from dams treated with 0.5 or 1.0% were 74 and 66 (compared to 89 for control). The viability index of F1b, F2 and F3a pups was not adversely affected by treatment of dams up to (but not during) lactation.

Autopsy and skeletal studies of the pups indicated no significant changes, with the exception of the occasional presence of an extra sternebra in the sternum between the fifth and sixth sternebra (1/29, 7/30 and 4/29 at 0. 0.5 and 1.0% DSS)

Test condition : Dioctyl sodium sulfosuccinate (DSS) was incorporated on a weight basis into rodent chow at concentrations of 0.5 and 1.0%. Diets were prepared on a weekly basis. Test or control diets (0% DSS) were fed to groups of 40 male (372.0 to 499.7 g) and female (243.0 – 304.9 g) rats. Pairs of rats were mated to produce two litters per generation with the exception of the F1b generation (which was bred once to produce a single F2 generation). The F0 generation was maintained on the test diet until 3-4 months of age before mating. For the first mating of the F0 and F2 generations, dams were continuously fed test diets, and the pups weaned directly onto test diets at 21 days of age. For the other 3 matings (F1b, F2 and F3a pups), DSS was removed from the diet of the dams before they were expected to deliver, and pups were placed on test diets after weaning. Reproductive performance was assessed by determining fertility, gestation, viability and lactation indices. Litter size was reduced to 10 pups at day 5. Pups from

all litters (including those that died before weaning) were examined for gross defects. Autopsies were performed on pups from the first mating of the F2 animals. Portions of all major organs from one female and one male from each litter were examined histologically. Carcasses of the other pups were cleared and skeletons were examined for defects.

Test Substance : A formulation consisting of 50% dioctyl sodium sulfosuccinate in an aqueous beverage grade ethanol solution was the original test material.

Conclusion : Lactation was affected by DSS. No effects other than those due to reduced lactation (eg. reduced lactation index, weight of pups, and survival rate) were observed. Changes in these parameters were not observed if exposure was terminated prior to lactation.

Reliability : (2) valid with restrictions. Ethanol may have been present in test material. Drying of material to remove ethanol is not documented.

27.02.2001 (2)

Type : other: histologic examination of reproductive organs
Species : rat
Sex : male/female
Strain : other:albino
Route of admin. : oral feed
Exposure period : 90 days
Doses : 1.0%
NOAEL Parental : >1 %
Method : other
Year : 1969
GLP : pre-GLP
Test substance : A commercial sample of Aerosol-OT was dried to remove the liquid phase. The dried products were 100% solids or "active ingredients".

Remark : This study was part of a 90 day oral toxicity study described in Section 5.4

Result : There was no effect of treatment on histology of any reproductive organ

Test condition : 20 albino rats / sex were fed test material for 90 days at a dietary concentration of 1.0%, which was prepared by blending the appropriate amount of test material with standard rat ration. Weight and food consumption were monitored biweekly and weekly, respectively. Animals were sacrificed 90 days after treatment and ovaries and the uterus from females and prostate, testes and seminal vesicles from males were examined grossly and histologically.

Reliability : (1) valid without restriction

27.02.2001 (17)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : days 6-15 of gestation
Doses : 1.0 and 2.0%
Control group : yes
NOAEL Teratogen : = 1 %
Method : other
Year : 1976
GLP : pre-GLP
Test substance : dioctyl sodium sulfosuccinate

Result	:	Ingestion of 1% had no effect on reproduction or condition of fetuses. The 2% dietary level produced effects th at included reduced weight gain in dams, a significant increase in fetal resorptions (13.7% vs. 5.6% in controls), and a significant percentage of externally malformed fetuses (20.2% vs. 0% in controls). The abnormalities consisted primarily of exencephaly of varying degrees of severity. This malformation was frequently associated with spina bifida and microphthalmia. Skeletal observations of fetuses from rats treated with 2% showed a significant increase in incomplete ossification of various cranial bones and curved or open vertebral columns.
Test condition	:	Test material was prepared as a 40% solution in USP corn oil. Rats were mated when they were approximately 2 months of age. The first day following mating was counted as Day 1 of gestation. Dietary concentrations of 1.0 and 2.0% were administered to 22 and 20 female rats, respectively, on days 6-15 of gestation. Two groups of control animals received 1.5% or 2.0% corn oil in the diet. Rats were observed each day for clinical condition and signs of illness. Body weight and food consumption were recorded at various times during the test. Mothers were killed on day 21 of gestation, and fetuses were removed by cesarean section. The number of fetal implantations, resorptions, dead and viable fetuses was determined. Fetuses were grossly examined, weighed, and measured. One half of the fetuses were examined for visceral abnormalities, and the other for skeletal abnormalities. Maternal body weight gains, food consumption and weights were analyzed by Dunnett's two-sided, multiple comparison test. Frequencies of resorptions and abnormalities were analyzed by the Mann-Whitney U or the Chi-square test, as appropriate.
Reliability	:	(1) valid without restriction

30.01.2001 (13)

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	days 6-16 of gestation
Doses	:	2%
Control group	:	yes
NOAEL Maternalt.	:	< 2 %
NOAEL Teratogen	:	< 2 %
Method	:	other
Year	:	1979
GLP	:	no data
Test substance	:	other TS
Remark	:	The primary reference (Hoechst-Roussel, 1979) was not available.
Result	:	There was a significant decrease in maternal weight, food consumption and weight gain in dams treated with 2% DSS. Following treatment with control diet, there was a compensatory weight gain among DSS treated animals, so that at term maternal weights of treated animals were similar to controls. There was no effect of treatment on reproduction. Fetuses had decreased weight and crown-rump length. Increased incidences of skeletal abnormalities were observed in the fetuses. The major skeletal abnormality observed was an increase in unossified 5th sternebrae and xiphisternum .
Test condition	:	Rats were treated with 2% corn oil in the diet (controls) or 2% dioctyl

sodium sulfosuccinates on days 6-16 of gestation, and control diet thereafter.

Reliability : (2) valid with restrictions. The primary reference was not consulted.
27.02.2001 (14, 21)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Remark : Although the rate of congenital disorders in the general population was not noted, the authors concluded that there was not a strong association between docusate sodium use and congential defects in offspring

Result : Out of the 6,837 women studied, 473 received docusate sodium during the first trimester. One infant that had been exposed to docusate sodium during this period had a congenital disorder. The estimated prevalence of a disorder in infants of women taking docusate sodium is 2/1000, which was lower than the overall rate in the entire group (12/1000).

Test condition : Records from all liveborn infants born from July 1, 1977 to Dec 31, 1979 to mothers that were members of the Group Health Cooperative of Puget Sound for at least 280 days before delivery were analyzed. Infants with major disorders diagnosed at birth were identified. Disorders diagnosed subsequent to the hospital admission for childbirth (such as pyloric stenosis) were excluded. Some disorders diagnosed at birth (e.g. benign skin conditions, hernia, or functional or positional disorders) were not considered. Clinical records of infants with disorders (excepting those with Down's syndrome, trisomy 18, undescended testicle, cleft lip and/or palate, or rectal atresia) were reviewed to confirm diagnoses. Infants with abnormalities noted at birth that were not confirmed upon follow-up examination were classified as not having disorders. Infants that had minor changes (e.g. syndactly of the second and third toes (n = 1), polydactyly of the postaxial type (n = 2), clinodactyly (n=1), curly or overlapping toes (n = 4), and coronal (first degree) hypospadias (n=10)) were also removed from consideration. All reviews and exclusions were made without prior knowledge of exposure.

The relationship between drugs that were used by at least 200 mothers and defects in their infants was analyzed. Exposure was considered to have occurred during the first month of pregnancy if a mother's prescription had been filled between 365 and 250 days before delivery. Drug use by mothers of children with disorders was tabulated by hand. For the population at large, exposure rates were determined by computer files. Contraceptives, antacids, vitamins and minerals, hormones, and topical preparations were not considered.

Reliability : (2) valid with restrictions. Epidemiology studies can be confounded by variables unrelated to treatment.
27.02.2001 (18)

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