

1. General Information

ID 26896-20-8

Date March 21, 2005

1.0 SUBSTANCE INFORMATION

Generic Name :
Chemical Name : Neodecanoic acid
CAS Registry No. : 26896-20-8
Component CAS Nos. :
EINECS No. : 248-093-9
Molecular Formula : C₁₀H₂₀O₂
Molecular Weight : 172.27
Synonyms and Tradenames : 2,2-dimethyloctanoic acid; Topper 5E; Wiltz 65
References : IUCLID Dataset, February 2000; TOXNET (<http://chem.sis.nlm.nih.gov>)

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2. Physico-Chemical Data

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2.1 MELTING POINT

Type :
Guideline/method : MPBWIN v1.41 (EPWIN v3.11)
Value : 57.13°C
Decomposition : at °C
Sublimation :
Year :
GLP :
Test substance : Neodecanoic acid
Method :
Method detail : Melting point 92.32°C (Joback method); 39.54°C (Gold and Ogle method);
mean 65.93°; weighted value (selected) 57.13°C
Result :
Remark :
Reliability : (1) Reliable without restriction; Calculated using scientifically acceptable
method
Reference :

2.2 BOILING POINT

Type :
Guideline/method : Directive 84/449/EEC, A.2 "Boiling point/boiling range"
Value : Approx. 243 - 253°C
Decomposition :
Year :
GLP : No data
Test substance : Neodecanoic acid
Method :
Method detail :
Result :
Remark : Calculated value of 262.37°C (adapted Stein and Brown method), MPBWIN
v1.41 (EPIWIN v3.11)
Reliability : (1) Reliable without restriction; reported experimental result and calculated
result in agreement
Reference : IUCLID dataset, 2000

2.3 DENSITY

Type :
Guideline/method :
Value : Approx. 0.91 g/cm³ at 20°C
Year :
GLP : No data
Test substance :
Method : ASTM D4052
Method detail :
Result :
Remark :
Reliability :
Reference : IUCLID dataset, 2000

2.4 VAPOR PRESSURE

Type :
Guideline/method :

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Value : Approx. 0.29 hPa at 50°C
Decomposition :
Year :
GLP :
Test substance : Neodecanoic acid
Method : Calculated (not specified)
Method detail :
Result :
Remark : Calculated value of 0.0071 mm Hg (modified Grain method), MPBWIN v1.41, EPIWIN v3.11
Reliability :
Reference : IUCLID dataset, 2000

2.5 PARTITION COEFFICIENT

Type :
Guideline/method : WSKOW v1.41 (EPIWIN v3.11)
Partition coefficient :
Log Kow : 3.90
pH value :
Year :
GLP :
Test substance : Neodecanoic acid
Method :
Method detail :
Result :
Remark :
Reliability : (1) Reliable without restriction; Calculated using scientifically acceptable method
Reference :

2.6.1 SOLUBILITY IN WATER

Type :
Guideline/method : WSKOW v1.41 (EPIWIN v3.11)
Value : 68.97 mg/L at 25°C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
PKa : at °C
Description :
Stable :
Deg. product :
Year :
GLP :
Test substance :
Deg. products CAS# :
Method :
Method detail :
Result :
Remark : Reported water solubility < 0.1% by volume at 25°C (IUCLID dataset, 2000)
Reliability : (1) Reliable without restriction; Calculated using scientifically acceptable method
Reference :

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2.7 FLASH POINT

Type	:	
Guideline/method	:	ASTM D92
Value	:	Approx. 122°C
Year	:	
GLP	:	No data
Test substance	:	
Method	:	Open cup
Method detail	:	
Result	:	
Remark	:	
Reliability	:	
Reference	:	IUCLID dataset, 2000

3. Environmental Fate & Transport

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3.2.1 MONITORING DATA

Type of measurement :
Media :
Concentration :
Substance measured :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

3.3.1 TRANSPORT (FUGACITY)

Type :
Media : Air-water-soil-sediment
Year :
Test substance : Neodecanoic acid
Method : EPWIN v.3.11 - Calculation according to Mackay, Level III
Method detail :
Result : Level III Fugacity Model (Full-Output):

=====
Chem Name : Neodecanoic acid
Molecular Wt: 172.27
Henry's LC : 5.6e-006 atm-m3/mole (Henrywin program)
Vapor Press : 0.00708 mm Hg (Mpbpwin program)
Liquid VP : 0.0147 mm Hg (super-cooled)
Melting Pt : 57.1 deg C (Mpbpwin program)
Log Kow : 3.9 (Kowwin program)
Soil Koc : 3.26e+003 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	3.55	34.1	1000
Water	37	360	1000
Soil	57.5	360	1000
Sediment	1.96	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	4.61e-011	662	325	22.1	10.8
Water	5.48e-011	652	339	21.7	11.3
Soil	1.21e-011	1.01e+003	0	33.7	0
Sediment	1.84e-011	8.64	0.359	0.288	0.012

Persistence Time: 305 hr
Reaction Time: 392 hr
Advection Time: 1.38e+003 hr
Percent Reacted: 77.8
Percent Advected: 22.2

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 34.06
Water: 360
Soil: 360
Sediment: 1440

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Biowin estimate: 2.971 (weeks)

Advection Times (hr):

Air: 100

Water: 1000

Sediment: 5e+004

Remark :
Reliability : (1) Reliable without restriction. Calculated using scientifically acceptable method
Reference :

3.5 BIODEGRADATION

Type : Manometric respirometry test
Guideline/method : OECD 301F
Inoculum : Domestic activated sludge
Concentration : 31 – 50 mg/L
related to
Contact time : 28 days
Degradation : 11.0% (Mean) after 28 day(s)
Result :
Kinetic of test subst. : % (specify time and % degradation)
%
%
%
%
Control substance : Sodium benzoate, 44 mg/L
Kinetic : %
%
Deg. product :
Year : 1996
GLP : Yes
Test substance : Neodecanoic acid
Deg. products CAS# :
Method :
Method detail : As described in Appendix D (Robust summaries prepared by ExxonMobil Chemical Company)
Result : The test substance is considered not readily biodegradable
Remark :
Reliability : (1) Reliable without restrictions (as assessed in Appendix D)
Reference : EG&G Bionomics, Wareham, MA. BW-78-1-005. As cited in Appendix D.

3.7 BIOCONCENTRATION

Type :
Guideline/method :
Species :
Exposure period : at °C
Concentration :
BCF :
Elimination :
Year :
GLP :

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Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

4.1 ACUTE TOXICITY TO FISH

Type	: Acute static renewal
Guideline/method	: OECD 203, Fish acute toxicity test
Species	: Rainbow trout (<i>Oncorhynchus mykiss</i>)
Exposure period	: 96 hours
NOEC	:
LC0	:
LC50	: 37.2 mg/L (confidence interval 26.3 – 52.5 mg/L), based upon measured concentrations of mean of “old” and “new” samples
LC100	:
Other	:
Other	:
Other	:
Limit test	:
Analytical monitoring	: Yes, using GC-FID
Year	: 1996
GLP	: Yes
Test substance	: Neodecanoic acid
Method	:
Method detail	: Individual Water Accomodated Fractions (WAFs) were prepared for each treatment, by mixing test substance for 24 hours. Tests were conducted in sealed aspirator bottles (no headspace). Other details described in Appendix D. (Robust Summaries prepared by ExxonMobil Chemical Company)
Result	:
Remark	: Results (96-h LC50) for other species include: Bluegill (<i>Lepomis macrochirus</i>): 32 and 60 mg/L under static conditions; Goldfish (<i>Carassius auratus</i>): 56 mg/L under static conditions. Sheepshead minnow (<i>Cyprinodon variegatus</i>): 181 mg/L under static conditions. (See Appendix C, IUCLID dataset, 2000)
Reliability	: (1) Reliable without restrictions (as assessed in Appendix D)
Reference	: Exxon Biomedical Sciences, Inc. Fish Acute Toxicity Test, 118358. (As cited in Appendix D, Robust Summaries prepared by ExxonMobil Chemical Company).

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	: Static acute
Guideline/method	: US EPA, Methods for acute toxicity with fish, macroinvertebrates and amphibians, EPA-660/3-75-009, 1975
Species	: <i>Daphnia magna</i>
Exposure period	: 48 hours
NOEC	:
EC0	:
EC50	: LL50 (lethal limit for 50%) = 47.1 mg/L (95% confidence interval 33.6 – 57.8 mg/L)
EC100	:
Other	:
Other	:
Other	:
Limit test	:
Analytical monitoring	: No
Year	: 1977
GLP	: No
Test substance	: Neodecanoic acid
Method	:

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Method detail : Test substance was dissolved in triethylene glycol. Study design included control and solvent control. Details described in Appendix D (Robust summaries prepared by ExxonMobil Chemical Company)

Result :

Remark : The 48-h EC50 for *Daphnia magna* has been reported as 47.1 mg/L. For the copepod, *Acartia tonsa*, the 96-h LC50 has been reported as 25 mg/L. (See Appendix C, IUCLID dataset, 2000)

Reliability : (2) Reliable with restrictions (as assessed in Appendix D)

Reference : EG&G Bionomics, Wareham, MA. BW-78-1-005. (As cited in Appendix D, Robust Summaries prepared by ExxonMobil Chemical Company)

4.3 TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

Type :

Guideline/method :

Species :

Endpoint :

Exposure period :

NOEC :

LOEC :

EC0 :

EC10 :

EC50 :

Other :

Other :

Other :

Limit test :

Analytical monitoring :

Year :

GLP :

Test substance :

Method :

Method detail :

Result :

Remark :

Reliability :

Reference :

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In vitro/in vivo	:	
Type	:	
Guideline/method	:	
Species	:	
Number of animals	:	
Males	:	
Females	:	
Doses	:	
Males	:	
Females	:	
Vehicle	:	
Route of administration	:	
Exposure time	:	
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1 st . 2 nd . 3 rd .
Toxic behavior	:	
Deg. product	:	
Deg. products CAS#	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	Neodecanoic acid is relatively resistant to biotransformation and does not readily form bioactive metabolites (ExxonMobil Chemical Company, 2002). Thus it would be primarily eliminated in the urine as glucuronic acid conjugates or by deacylation (Katz and Guest, 1994).
Reliability	:	
Reference	:	

5.1.1 ACUTE ORAL TOXICITY

Type	:	Acute oral toxicity
Guideline/Method	:	
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	males
Number of animals	:	5 per dose
Vehicle	:	Corn oil for four lowest doses; two highest doses administered undiluted
Doses	:	34.6, 120, 417, 1450, 5000 and 10,000 mg/kg
LD50	:	2000 mg/kg (CL: 670 – 5980 mg/kg)
Year	:	1964
GLP	:	Pre-GLP
Test substance	:	Neodecanoic acid
Method	:	
Method detail	:	A single dose was given via gastric intubation. Animals were observed at 1, 4 and 24 hours and once daily thereafter for 14 days, with subsequent

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- Result** : necropsy. Other details described in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company)
- Remark** : There were no principal toxic effects or necropsy findings at the three lowest doses. All animals died at the three highest doses. At 5000 and 10,000 mg/kg, depression, dyspnea, ataxia and sprawling of the limbs were observed, as well as congestion of the lungs, liver, spleen, kidneys and adrenals. See Appendix D for detailed results
- Reliability** : The acute oral LD50 for the rat has been reported as 2700 – 3450 mg/kg bw (Appendix C, IUCLID dataset, 2000)
- Reference** : (2) Reliable with restrictions (as assessed in Appendix D)
- Reference** : Esso Research and Engineering Company, 1964. Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report. As cited in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company).

5.1.2 ACUTE INHALATION TOXICITY

- Type** : Acute inhalation toxicity
- Guideline/method** :
- Species** : Rats, mice and Guinea pigs
- Strain** : Wistar rats, Swiss albino mice, and Harley Guinea pigs
- Sex** : Males and females
- Number of animals** : 10/sex/species
- Vehicle** : none
- Doses** : Liquid aerosol with a mean analytical concentration of 511 mg/m³
- Exposure time** : Single 6-hour exposure
- LC50** : > 511 mg/m³; mean particle size 2.99 ± 1.76 um
- Year** : 1982
- GLP** : No
- Test substance** : Neodecanoic acid
- Method** :
- Method detail** : Groups of animals were exposed to either air only or to aerosolized test material. Exposure concentrations were determined on both a nominal and actual (gravimetric) basis. Animals were observed for mortality and toxic effects at 15 minute intervals during the first hour and hourly thereafter during exposure; and daily for signs of toxicity for 14 days post-exposure. Necropsy was performed on half the animals from each group on the first day post-exposure, with terminal necropsies on the remaining animals. Details are described in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company).
- Result** : No mortality occurred during the study. Animals exposed to the test material exhibited some signs of labored breathing, salivation and eye irritation during exposure. During the two-week post-exposure period, all guinea pigs appeared normal; however some mice appeared ungroomed and some rats exhibited anogenital staining and soft stool. At terminal sacrifice, exposed male mice exhibited a statistically significant decrease in the liver to body weight ratio; no other significant differences were observed.
- Remark** : The acute inhalation LC50 for rats and mice was reported as > 3.0 mg/L (Esso Research and Engineering Company, 1964; see Appendix D). The acute inhalation LC50 for rats, mice, and guinea pigs in the rat has been reported as >73 ppm for an exposure period of 6 hours (Appendix C, IUCLID dataset, 2000). The acute inhalation LC50 for neodecanoic acid chloride in the rat has been reported as approximately 0.40 mg/L for an exposure period of 4 hours (BASF Corp., 1993. Support: Letter from BASF Corp to USEPA re: results of the study on the acute inhalation toxicity LC50 of neodecanoic acid chloride as a vapor in rats w/cover letter dated 113093. Available in microfiche OTS0539604-1 from the National Technical Information Service).

Reliability : (1) Reliable without restrictions (as assessed in Appendix D)
Reference : Bio/dynamics, Inc., 1982. Evaluation of the acute inhalation toxicity in rats, mice, and guinea pigs. Unpublished report. As cited in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company).

5.1.3 ACUTE DERMAL TOXICITY

Type : Acute dermal toxicity
Guideline/method :
Species : Rabbits
Strain : Albino
Sex : Males and females
Number of animals : 4 per dose
Vehicle : none
Doses : 50, 200, 794, 3160 mg/kg
LD50 : > 3160 mg/kg
Year : 1964
GLP : Pre-GLP
Test substance : Neodecanoic acid
Method :
Method detail : A single dosing was conducted by applying undiluted test material to clipped, intact abdominal skin under a dental dam binder. After a 24-hour exposure period, animals were observed for mortality or toxic effects at 1, 4, and 24 hours and daily thereafter for 14 days, followed by necropsy. Details are described in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company).
Result : No deaths, abnormal appearance, behavior, or weight gain or signs of pathology were observed. No dermal irritation was observed at the low dose; minimal irritation was seen at 200 mg/kg. At the 794 and 3160 mg/kg levels, a dose-dependent increase in the degree of irritation was observed, consisting of slight to moderate erythema and slight to moderate atonia and desquamation, subsiding over the course of the study. Additional details are described in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company).
Remark : The acute dermal LD50 for neodecanoic acid in the rat has been reported as >3640 mg/kg (Appendix C, IUCLID dataset, 2000).
Reliability : (2) Reliable with restrictions (as assessed in Appendix D)
Reference : Esso Research and Engineering Company, 1964. Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report. As cited in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company).

5.2.1 SKIN IRRITATION

Type :
Guideline/method : OECD 404, Acute Dermal Irritation/Corrosion
Species : Rabbit
Strain :
Sex :
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
Classification : Not irritating
Year :
GLP : yes
Test substance : Neodecanoic acid

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Method :
Method detail :
Result :
Remark :
Reliability : (4) Not assignable (secondary reference)
Reference : Appendix C, IUCLID dataset, 2000

5.2.2 EYE IRRITATION

Type :
Guideline/method : Draize test
Species : rabbit
Strain :
Sex :
Concentration :
Dose :
Exposure time :
Number of animals :
Vehicle :
Classification :
Year :
GLP : no
Test substance :
Method :
Method detail :
Result : irritating
Remark :
Reliability : (4) Not assignable (secondary reference)
Reference : Appendix C, IUCLID dataset 2000

5.4 REPEATED DOSE TOXICITY

Type :
Guideline/method :
Species : Rat
Strain : Albino
Sex : Males and females
Number of animals :
Route of admin. : Oral feed
Exposure period : 3 months
Frequency of treatment : daily
Post exposure period :
Doses : 500, 1500, 5000 and 15,000 ppm
Control group : Yes
NOAEL : 500 ppm
LOAEL : 1500 ppm
Other :
Year :
GLP : No data
Test substance : 30% preparation of neodecanoic acid
Method :
Method detail :
Result : The LOAEL was 1500 ppm and included changes in the renal tubules of both male and female rats. Morphological changes in the thyroid, including hyperplasia, were also seen in male rats at the feeding level of 1500 ppm.
Remark : Albino rabbits receiving 10 dermal applications of neodecanoic acid (0.4 g/kg and 2.28 g/kg) over a 14 day period showed no systemic effects,

resulting in a NOAEL of 2.26 g/kg (Appendix D, Robust Summaries prepared by ExxonMobil Chemical Company).
 Beagle dogs receiving oral capsules containing neodecanoic acid daily for a period of 13 weeks did not show adverse effects at dosing levels of approximately 30 mg/kg and below. Effects on body weight and declines in hematocrit, hemoglobin and erythrocyte values were seen at doses of 94.8 mg/kg and above. (Appendix C, IUCLID dataset, 2000).

Reliability : (4) Not assignable (secondary reference)
Reference : Hazleton Laboratories, 1964. Final report: Three month dietary administration – Rats. Performed by Hazleton Laboratories for Esso Research and Engineering, July 17, 1964. Exxon unpublished report #64MRL 21. As cited in IUCLID dataset, 2000 (Appendix C).

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
Guideline/method : OECD 471, "Genetic Toxicology: *Salmonella typhimurium* Reverse Mutation Assay"
System of testing :
Species : *Salmonella typhimurium*
Strain : TA 1535, TA 1537, TA 98, TA 100
Test concentrations : 6.1 – 1000 ug/plate without activation; 18.5 – 1500 ug/plate with activation
Cytotoxic concentr. :
Metabolic activation : With and without (S9)
Year :
GLP : yes
Test substance : Neodecanoic acid
Method :
Method detail :
Result : Negative
Remark : Neodecanoic acid produced negative results in a cytogenetic assay (OECD Method 473; "Genetic toxicology: In-vitro mammalian cytogenetic test") with cultured human lymphocytes when tested both with and without metabolic activation at levels up to 800 µg/ml (Shell, 1995. Versatic 10: Chromosome aberration in cultured human lymphocytes, Unpublished Shell Report HSE.95.1079, as cited in IUCLID dataset, 2000)

Reliability : (4) Not assignable (secondary reference)
Reference : Shell, 1995. Versatic 10: Bacterial mutagenicity (Ames test). Unpublished Shell Report HSE 95.1078 (1995). As cited in IUCLID dataset, 2000 (Appendix C).

5.6 GENETIC TOXICITY 'IN VIVO'

Type :
Guideline/method :
Species :
Strain :
Sex :
Route of admin. :
Exposure period :
Doses :
Year :
GLP :
Test substance :
Method :
Method detail :

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Result :
Remark :
Reliability :
Reference :

5.8.2 DEVELOPMENTAL TOXICITY

Type :
Guideline/method :
Species :
Strain :
Sex :
Route of admin. :
Exposure period :
Frequency of treatment :
Duration of test :
Doses :
Control group :
NOAEL maternal tox. :
NOAEL teratogen. :
Other :
Other :
Other :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

5.8.3 TOXICITY TO REPRODUCTION

Type :
Guideline/method :
In vitro/in vivo :
Species : Rat
Strain : Sprague-Dawley
Sex : Males and females
Route of admin. : Dietary
Exposure period :
Frequency of treatment : Continuous
Duration of test : 3 generations
Doses : 0, 100, 500, 1500 ppm in diet (0, 5, 25, and 75 mg/kg/day)
Control group : Purina lab chow, 0 ppm of test substance
Year : 1968
GLP : Pre-GLP
Test substance : Neodecanoic acid
Method :
Method detail : Details described in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company)
Result : No adverse effects were observed in the parental generation or the F₁ and F₂ generations at feeding levels up to 1500 ppm in the diet. Details described in Appendix D (Robust Summaries prepared by ExxonMobil Chemical Company)
Remark :

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Reliability : (2) Reliable with restrictions (as assigned in Appendix D)
Reference : Hazleton Labs, Inc., 1968. Modified three-generation reproduction study – rats. Unpublished report. As cited in Robust Summaries prepared by ExxonMobil Chemical Company (Appendix D).

6.0 OTHER INFORMATION

6.1 Skin Sensitization

Neodecanoic acid was not found to be sensitizing when tested on the guinea pig using the Magnusson and Kligman maximization test. (Shell Research, 1997. Acute toxicity, skin and eye irritancy and skin sensitization potential of Versatic 10. Unpublished report, Shell Research TLGR.0024.77. As cited in IUCLID dataset, 2000).

1. General Information

ID 10043-35-3

Date March 22, 2005

1.0 SUBSTANCE INFORMATION

Generic Name : Boric acid
Chemical Name : Boric acid
CAS Registry No. : 10043-35-3
Component CAS Nos. : Boron, CAS No. 7440-42-8
EINECS No. :
Structural Formula : H_3BO_3
Molecular Weight : 61.83 for boric acid. Boron comprises 17.48%
Synonyms and Tradenames :
References : U.S. EPA, 2004. Toxicological Review of Boron and Boron Compounds, In support of summary information on the Integrated Risk Information System (IRIS), June 2004. (This reference is subsequently listed in this document as EPA, 2004).

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2. Physico-Chemical Data

ID 10043-35-3

Date March 22, 2005

2.1 MELTING POINT

Type :
Guideline/method :
Value : 169 ± 1 °C
Decomposition : at °C
Sublimation :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability : (2) Reliable with restrictions: Source is well established data compendium.
Reference : Weast. R.C. (ed.). 1988-1989. Handbook of Chemistry and Physics. 69th Ed. CRC Press Inc., Boca Raton, FL., p. B-77.

2.2 BOILING POINT

Type :
Guideline/method :
Value : 300 °C (loses 1½ water)
Decomposition :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability : (2) Reliable with restrictions: Source is well established data compendium.
Reference : Weast. R.C. (ed.). 1988-1989. Handbook of Chemistry and Physics. 69th Ed. CRC Press Inc., Boca Raton, FL., p. B-77.

2.3 DENSITY

Type :
Guideline/method :
Value : 1.435 at 15 °C
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability : (2) Reliable with restrictions: Source is well established data compendium.
Reference : Weast. R.C. (ed.). 1988-1989. Handbook of Chemistry and Physics. 69th Ed. CRC Press Inc., Boca Raton, FL., p. B-77.

2.4 VAPOR PRESSURE

Type :
Guideline/method :
Value : hPa at °C

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Decomposition :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

2.5 PARTITION COEFFICIENT

Type :
Guideline/method :
Partition coefficient :
Log Pow : at °C
pH value :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

2.6.1 SOLUBILITY IN WATER

Type :
Guideline/method :
Value : 63.5 g/L at 30 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
PKa : at °C
Description :
Stable :
Deg. product :
Year :
GLP :
Test substance :
Deg. products CAS# :
Method :
Method detail :
Result :
Remark : Value of 50,000 mg/L at 25 °C reported by Shiu, W. Y., et al., 1990, Rev. Environ. Contam. Toxicol. 116:15-187.
Reliability : (2) Reliable with restrictions: Source is well established data compendium
Reference : Weast, R.C. (ed.). 1988-1989. Handbook of Chemistry and Physics. 69th Ed. CRC Press Inc., Boca Raton, FL., p. B-77.

2.7 FLASH POINT

Type :

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Guideline/method	:	
Value	:	°C
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	
Reliability	:	
Reference	:	

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3.5 BIODEGRADATION

Type :
Guideline/method :
Inoculum :
Concentration : related to
related to
Contact time :
Degradation : (±) % after day(s)
Result :
Kinetic of test subst. : % (specify time and % degradation)
%
%
%
%
Control substance :
Kinetic : %
%
Deg. product :
Year :
GLP :
Test substance :
Deg. products CAS# :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

3.7 BIOCONCENTRATION

Type :
Guideline/method :
Species :
Exposure period : at °C
Concentration :
BCF :
Elimination :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

4.1 ACUTE TOXICITY TO FISH

Type	:	Acute									
Guideline/method	:	Static									
Species	:	Fry of chinook salmon (<i>Onchorhynchus tshawytscha</i>) and coho salmon (<i>Oncorhynchus kisutch</i>)									
Exposure period	:	96 hr									
NOEC	:										
LC0	:										
LC50	:	For chinook salmon: 127 mg B/L for swim-up fry; 105 mg B/L for advanced fry. For coho salmon: 78.2 mg B/L for swim-up fry; 105 mg B/L for advanced fry									
LC100	:										
Other	:										
Limit test	:										
Analytical monitoring	:	No									
Year	:	1990									
GLP	:	No									
Test substance	:	Boric acid									
Method	:	American Society for Testing and Materials, 1980, ASTM E-729, Standard practice for conducting acute toxicity tests with fishes, macroinvertebrates and amphibians.									
Method detail	:	Tests were conducted with two life stages of each species. Swim-up fry (8-12 weeks old) were exposed in fresh water and advanced fry (15-21 weeks old) were exposed in brackish water. The fresh water had a conductivity of 721 ± 9 umhos/cm, pH of 7.82 ± 0.35 and hardness of 211 ± 1 mg/L as CaCO_3 . The brackish water had a conductivity of 2887 ± 88 umhos/cm, pH of 7.79 ± 0.16 and hardness of 333 ± 9 mg/L as CaCO_3 . Exposures were conducted in 19.6-L glass jars containing 15 L of test solution and maintained at $12 \pm 1^\circ\text{C}$. Test solutions were prepared by either pipetting aliquots of a stock solution prepared in deionized water into the test vessels or adding the compound directly to the test vessel. In each test, group of 10 fish were exposed to a series of test concentrations that differed by a factor of 60%. Loading density was ≤ 0.8 g/L. Mortality and abnormal behavior was noted every 24 hours. LC50 values were determined according to the graphical method of Litchfield and Wilcoxon (1949). In additional tests, eyed eggs, alevins and swim-up fry of chinook salmon were tested in soft water.									
Result	:	For chinook salmon, the 96 h LC50 was 726 mg/L boric acid (95% confidence interval 590 – 890 mg/L) for swim-up fry (mean weight 1.1 g) and 600 (511 – 706) mg/L boric acid for advanced fry (mean weight 1.6 g). For coho salmon, the 96-h LC50 was 447 (356-561) mg/L boric acid for swim-up fry (mean weight 0.5 g) and 600 (511 – 705) mg/L boric acid for advanced fry (mean weight 1.7). Expressed as boron, the 96-h LC50 values (with 95% confidence intervals) are: <table border="0" style="margin-left: 40px;"> <thead> <tr> <th></th> <th style="text-align: center;"><u>Chinook salmon</u></th> <th style="text-align: center;"><u>Coho salmon</u></th> </tr> </thead> <tbody> <tr> <td>Swim-up fry:</td> <td style="text-align: center;">127 mg B/L (103-156)</td> <td style="text-align: center;">78.2 mg B/L (62.3 – 98.2)</td> </tr> <tr> <td>Advanced fry:</td> <td style="text-align: center;">105 mg B/L (89.4-124)</td> <td style="text-align: center;">105 mg B/L (89.4-124)</td> </tr> </tbody> </table>		<u>Chinook salmon</u>	<u>Coho salmon</u>	Swim-up fry:	127 mg B/L (103-156)	78.2 mg B/L (62.3 – 98.2)	Advanced fry:	105 mg B/L (89.4-124)	105 mg B/L (89.4-124)
	<u>Chinook salmon</u>	<u>Coho salmon</u>									
Swim-up fry:	127 mg B/L (103-156)	78.2 mg B/L (62.3 – 98.2)									
Advanced fry:	105 mg B/L (89.4-124)	105 mg B/L (89.4-124)									
Remark	:	In tests in soft water with chinook salmon, the 96-h LC50 values were > 175 mg B/L for eyed eggs and alevins, and 99 mg B/L (84.3 – 116) for swim-up fry. Reported 96-h LC50 values for boron in fish range from 14.2 mg B/L in zebrafish to 978 mg B/L in mosquito fish (Lowengart, G., 2001. Toxicity of boron to rainbow trout: a weight of evidence assessment. Environ. Toxicol. Chem. 20(4): 796-803). An early study by Birge and Black indicated particular sensitivity of early life stages of rainbow trout (LOECs of 0.001 – 0.0008 mg B/L); later studies, however, resulted in LOEC values of 0.1 –									

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- 1.0 mg B/L. (Birge, W.J. and J.A. Black, 1977. Sensitivity of vertebrate embryos to boron compounds. EPA 560/1-76-008; Black, J.A., Barnum, J.B. and Birge, W.J., 1993. An integrated assessment of the biological effects of boron to the rainbow trout. Chemosphere 26: 1383 – 1413).
- Reliability** : (2) Reliable with restrictions: performed according to accepted method, with sufficient documentation
- Reference** : Hamilton, S.J. and K.J. Buhl, 1990. Acute toxicity of boron, molybdenum, and selenium to fry of chinook salmon and coho salmon. Arch. Environ. Contam. Toxicol. 19:366 - 373.

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

- Type** : Acute
- Guideline/method** : Static, freshwater
- Species** : *Daphnia magna* (water flea)
- Exposure period** : 48 hr
- NOEC** : < 54 mg B/L
- EC0** :
- EC50** : 133 mg B/L (95% C.I. = 115 - 153 mg B/L)
- EC100** : 420 mg B/L
- Other** :
- Limit test** :
- Analytical monitoring** : No
- Year** : 1983
- GLP** : No
- Test substance** : Boric acid
- Method** : American Society for Testing and Materials, 1980. ASTM E 729, Standard practice for conducting acute toxicity tests with fishes, macroinvertebrates and amphibians.
- Method detail** : Brood stock was fed a diet of green algae at 1.25 mg/L dry weight and kept at 20 ± 1°C. Neonates ≤ 24 hours old were isolated for use in testing. Tests were conducted in carbon filtered and UV-irradiated Lake Huron water. The mean hardness was 148 mg CaCO₃/L, alkalinity 58 mg CaCO₃/L, pH 8.1, and conductivity 290 µmhos/cm. Boron content in the dilution water was 0.4 mg/L. Three replicates of 10 neonates each were exposed to six nominal concentrations (54, 91, 151, 252, 420 and 720 mg/L as boron) and a control. Tests were conducted in 200 mL of test solution in 250 mL beakers, at 20 ± 1°C and using a photoperiod of 16 hours light: 8 hours dark. Solutions were not renewed during the test. Daphnids were not fed nor were solutions aerated during the test. Mortality, dissolved oxygen, pH and temperature were recorded at 24 and 48 hours.
- Result** : During the test, dissolved oxygen concentrations were above 60% saturation, the pH ranged from 6.7 to 8.1, and temperature ranged from 20.1 to 20.7°C. There was 7% control mortality. The no observed effect concentration was < 54 mg B/L while 100% effects were observed at 420 mg B/L. The 48 h EC50 was 133 mg B/L (95% confidence interval 115-153 mg/L).
- Remark** : Another study with *Daphnia magna* reported the 48-h LC50 for boric acid as 226 mg B/L (95% confidence interval 200 – 246 mg B/L). (Lewis, M.A. and L.C. Valentine, 1981. Acute and chronic toxicities of boric acid to *Daphnia magna* Straus. Bull. Environ. Contam. Toxicol. 27:309-315).
- Reliability** : (2) Reliable with restrictions: performed according to accepted method, with sufficient documentation
- Reference** : Gersich, F.M., 1984. Evaluation of a static renewal chronic toxicity test method for *Daphnia magna* Straus using boric acid. Environ. Toxicol. Chem. (3): 89-94.

4.3 TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

Type	:	Algal growth assay
Guideline/method	:	Static, freshwater
Species	:	<i>Chlorella pyrenoidosa</i> (green algae)
Endpoint	:	Population growth
Exposure period	:	14 d
NOEC	:	0.4 mg B/L
LOEC	:	0.8 mg B/L
EC0	:	
EC10	:	
EC50	:	
Other	:	
Limit test	:	
Analytical monitoring	:	No
Year	:	1990
GLP	:	no
Test substance	:	Boric acid
Method	:	
Method detail	:	<i>Chlorella pyrenoidosa</i> (University of Texas Culture Collection 251) was grown in a modified complete medium (MCM) at pH 6.8. Toxicity tests were conducted in 250 mL Erlenmeyer flasks containing 95 mL of MCM and 5 mL of late log phase algal culture. A stock solution of boron was prepared by dissolving boric acid in distilled water, and sterilized by autoclaving. Test concentrations were 0.1, 0.2, 0.4, 0.8 and 1.6 mg/L boron. Flasks were incubated at 25 ± 2°C under cool white fluorescent lighting (6000 lux) on a photoperiod of 16 h light: 8 h dark. All controls and test concentrations were in triplicate. Algal growth was monitored by absorbance (625 nm) at 2-day intervals for 14 days. Results were expressed in terms of growth rate and area under the growth curve.
Result	:	Boron at 0.8 mg/L or higher resulted in significant inhibition of algal growth. Based both upon growth rate and area under the growth curve, the NOEC was identified as 0.4 mg B/L and the LOEC as 0.8 mg B/L.
Remark	:	Boron is an essential micronutrient for the healthy growth of algae and other plants, but at high concentrations (> 20 mg/L) can inhibit growth. For the green alga <i>Scenedesmus subspicatus</i> , the reported 72 h EC50 was 34 mg B/L (WHO, 1998, Environmental Health Criteria, Boron). The 96-h EC50 for boron for the floating aquatic vascular plant <i>Lemna gibba</i> was > 60 mg/L (U.S. EPA, ECOTOX data base)
Reliability	:	(2) Reliable with restrictions: Study does not conform to a specific guideline but provides adequate data and is scientifically acceptable.
Reference	:	Wong, P.K. and Wong, C.K., 1990. Toxicity of nickel and nickel electroplating water to <i>Chlorella pyrenoidosa</i> , Bull. Environ. Contam. Toxicol. 45(5): 752-759

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In vitro/in vivo	:	
Type	:	
Guideline/method	:	
Species	:	
Number of animals	:	
Males	:	
Females	:	
Doses	:	
Males	:	
Females	:	
Vehicle	:	
Route of administration	:	
Exposure time	:	
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1 st . 2 nd . 3 rd .
Toxic behavior	:	
Deg. product	:	
Deg. products CAS#	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	Boron is readily adsorbed following oral exposure in both humans and animals. There is no evidence that boron compounds are metabolized in the body. Greater than 90% of an orally administered dose of boron as boric acid is excreted in a short time in both humans and animals. Clearance is primarily through urine. Boron is also absorbed during inhalation exposure but is not absorbed across intact skin in humans or animals. Examinations in rats have revealed a fairly uniform distribution of boron outside the blood compartment across various tissues, except for consistently lower concentrations in fat and consistently higher concentrations in bone. Available data for humans indicates comparable patterns are likely (EPA, 2004).
Reliability	:	
Reference	:	

5.1.1 ACUTE ORAL TOXICITY

Type	:	Oral
Guideline/Method	:	Not specified
Species	:	Rat
Strain	:	Sprague-Dawley and Long-Evans
Sex	:	Male and female for Sprague-Dawley rats; males only for Long-Evans rats
Number of animals	:	6 groups of five rats each
Vehicle	:	0.5% aqueous methyl cellulose (for Sprague-Dawley rats) or distilled water suspension (for Long-Evans rats).
Doses	:	Not reported

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LD50 : 550 – 710 mg B/kg bw
Year : 1972
GLP : No
Test substance : Boric acid
Method :
Method detail : Rats were fasted and dosed by stomach intubation with a single dose of boric acid (50% w/v in 0.5% aqueous methyl cellulose or distilled water suspension). Rats were observed for 14 days post-dosing.
Result : For Sprague-Dawley rats, the LD50 for males was 600 mg B/kg bw and 710 mg B/kg bw for females. For male Long-Evans rats, the LD50 was 550 mg B/kg bw.
Remark : For mice, the reported LD50 for boric acid was 603 mg B/kg bw. (Pfeiffer et al., 1945, cited in WHO, 1998).
Reliability : (2) Reliable with restrictions.
Reference : Weir, R.J. and Fisher, R.S., 1972. Toxicologic studies on borax and boric acid. Toxicol. Appl. Pharmacol. 23:351-364.

5.1.2 ACUTE INHALATION TOXICITY

Type : Inhalation
Guideline/method :
Species : Mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses : 72 mg/m³
Exposure time : 7 h/day, 5 days/week, for 6 weeks
LC50 :
Year :
GLP :
Test substance : Amorphous elemental boron
Method :
Method detail :
Result : No toxic effects observed
Remark :
Reliability : (1) Not assignable; secondary reference
Reference : Stokinger and Spiegl, 1953, cited in WHO, 1998.

5.1.3 ACUTE DERMAL TOXICITY

Type :
Guideline/method :
Species :
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
LD50 :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :

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Reliability :
Reference :

5.2.1 SKIN IRRITATION

Type :
Guideline/method :
Species : Guinea pig and rabbit
Strain :
Sex : Male guinea pigs, male and female rabbits
Concentration : 5 mL of boric acid, 10% in water (w/v)
Exposure :
Exposure time : 72 hours
Number of animals : 6 rabbits with intact skin, 6 rabbits with abraded skin, 6 guinea pigs with intact skin and 6 guinea pigs with abraded skin.
Vehicle :
Classification :
Year : 1964
GLP : No
Test substance : Boric acid
Method :
Method detail : The hair was removed from the test area of all animals by clipping. The guinea pigs had the hair stubble removed with barium sulfide depilatory which was allowed to remain on the skin for only a few minutes. After this the skin was washed in running water and allowed to dry for several hours before application of the test material. For the abraded skin tests, abrasions were made longitudinally every 2-3 cm by drawing a harpoon-shaped needle over the skin with sufficient pressure to penetrate only the stratum corneum. For the rabbits, the procedure was as described in Federal Hazardous Substances Labeling Act, 21 CFR 191, except that the rabbits were not immobilized and a 1-inch square cellulose pad was used rather than surgical gauze. Test material was applied to 6 rabbits with intact skin and 6 rabbits with abraded skin. For guinea pigs, test material was applied on cellulose pads held in contact with skin under a sleeve. Six guinea pigs with clipped, depilated, intact abdomens and 6 with clipped, depilated, abraded backs were used.
Result : Mild to moderate irritant after 24 and 72 h
Remark :
Reliability : (2) Reliable with restrictions.
Reference : Roudebush, R.L., et al., 1965. Comparative acute effects of some chemicals on the skin of rabbits and guinea pigs. Toxicol. Appl. Pharmacol. (7):559-565.

5.2.2 EYE IRRITATION

Type :
Guideline/method :
Species :
Strain :
Sex :
Concentration :
Dose :
Exposure time :
Number of animals :
Vehicle :
Classification :
Year :

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GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Guideline/method : Oral
Species : Mouse
Strain : B6C3F1
Sex : Male and female
Number of animals : 10 per sex per dose
Route of admin. : Diet
Exposure period : 13 – 16 weeks
Frequency of treatment : 5 days/week for 13 weeks for control and highest dose group; other groups up to 16 weeks

Post exposure period :
Doses : 0, 1200, 2500, 5000, 10000 or 20000 ppm boric acid. This is equivalent to 0, 34, 70, 141, 281 and 563 mg B/kg-day for males and 0, 47, 97, 194, 388 and 766 mg B/kg-day for females, based on reported average values for feed consumption by controls in week 4 of the experiment.

Control group : Yes
NOAEL : At or below 34 mg B/kg-day for males and 47 mg/kg-day for females
LOAEL : 34 mg B/kg-day
Other :
Year : 1980
GLP :
Test substance : Boric acid
Method :
Method detail : Mice were observed twice daily and weighed weekly. Necropsy and histologic examination performed on all animals, with the following tissues examined: gross lesions and tissue masses, mandibular lymph nodes, mammary gland, skin, salivary glands, sternbrae, thyroid gland, parathyroids, small intestine, colon, liver, prostate/testes or ovaries/uterus, lungs and bronchi, heart, pancreas, esophagus, stomach, brain, thymus, trachea, spleen, kidneys, adrenal glands, urinary bladder, pituitary gland, spinal cord (if neurologic signs present), eyes (if grossly abnormal) and gall bladder.

Result : At the highest dose, hyperkeratosis and acanthosis of the stomach, as well as >60% mortality, were observed. At the second highest dose, 10% mortality was observed among the males. At 5000 ppm and higher, degeneration or atrophy of the seminiferous tubules was seen in males, and weight gain was suppressed in animals of both sexes. Minimal to mild extramedullary hematopoiesis of the spleen was observed in all dosed groups.

Remark : This subchronic study was preceded by two 14-day feeding studies using 5 male and 5 female mice per group, at dose levels of 0, 600, 1200, 2400, 4900 and 9800 boric acid (first study) and 0, 6200, 12500, 25000, 50000, and 100,000 ppm boric acid (second study). Mortality occurred at 25000 ppm and higher doses, as did hyperplasia and/or dysplasia of the forestomach. No compound-related gross pathologic or histopathologic effects were seen in mice at concentrations up to 12500 ppm.

A 90-day feeding study with rats (Weir, R.J. and Fisher, R.S., 1972, Toxicol. Appl. Pharmacol. 23:351-364). found testicular atrophy at doses of 26.3 mg B/kg-day and above, identifying this value as the LOAEL and 8.8 mg B/kg-day as the NOAEL for systemic toxicity in rats. These same authors also conducted 90-day dietary exposures in beagle dogs in which the NOAEL was identified as 3.9 mg B/kg-day for males and 2.5 mg B/kg-day for females (Weir and Fisher, 1972; EPA, 2004)

Reliability : (1) Reliable without restrictions
Reference : NTP (National Toxicology Program), 1987. Toxicology and carcinogenesis studies of boric acid (CAS No. 10043-35-3) in B6C3F1 mice (feed studies). ; Dieter, M.P., 1994. Toxicity and carcinogenicity studies of boric acid in male and female B6C3F1 mice, Environ. Health Perspect. 102(Suppl 7):93-97; EPA, 2004.

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Mutagenicity
Guideline/method : Ames Assay
System of testing : Bacteria *in vitro*
Species : *Salmonella typhimurium*
Strains : TA100, TA1535, TA1537, TA98
Test concentrations : 33, 100, 333, 1000 and 1820 ug/plate
Cytotoxic concentr. :
Metabolic activation : Conducted with and without activation
Year : 1987
GLP :
Test substance : Boric acid
Method : Haworth et al., 1983. Environ. Mutagen Suppl. 1:3-142
Method detail : The S-9 fractions were prepared from the liver of Aroclor 1254-induced male Sprague-Dawley rats and male Syrian hamsters. Cells and boric acid or solvent (dimethylsulfoxide) were incubated for 20 minutes at 37°C in the presence of either S9 or buffer. After the addition of soft agar, the contents of each tube were poured onto minimal medium, and the plates were incubated at 37°C for 48 hours. The experiment was performed twice, each in triplicate

Result : Negative
Remark : Results of most short-term mutagenicity studies indicate that boron is not genotoxic. Boric acid was negative for mutagenicity in the *Salmonella* preincubation assay using strains TA98 and TA 100 in both the presence and absence of rat liver metabolic activation (Benson, W.H., W.J. Birge, and H.W. Dorough, 1984, Envir. Tox. Chem. (3):209-214). In the streptomycin-dependent *E. coli* Sd-4 assay, boric acid was either not mutagenic or produced equivocal results (EPA, 2004). An isolated positive result for induction of β -galactosidase synthesis was found in *E.coli* PQ37 using the SOS chromotest (EPA, 2004).

Reliability : (1) Reliable without restrictions
Reference : National Toxicology Program, 1987. Toxicology and Carcinogenesis Studies of Boric Acid (CAS NO. 10043-35-3) in B6C3F1 Mice (Feed Studies), Public Health Service, U.S. Dept. of Health and Human Services, NTP TR-324. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr324.pdf

Type : In Vitro Cytogenetics: Chromosome aberrations
Guideline/method : Cell culture
System of testing : Chinese Hamster Ovary Cells
Test concentrations : 500 – 2000 ug/mL
Cytotoxic concentr. :

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Metabolic activation : Conducted with and without activation with S-9 (prepared from the liver of Aroclor 1254-induced male Sprague-Dawley rats)

Year : 1987

GLP :

Test substance : Boric acid

Method : Galloway, S.M., et al., 1985. Environ. Mutagen. 7:1-51.

Method detail : In the absence of S-9, cells were incubated with study compound or solvent for 8-10 hours at 37°C. Cells were then washed, and fresh medium containing colcemid (0.1 ug/mL) was added. After an additional 2-3 hours of incubation, cells were harvested by mitotic shake-off, fixed and stained in 6% Giesma. In the presence of S-9, cells were incubated with study compound or solvent for 2 hours at 37°C. Cells were then washed, medium was added, and incubation continued for 8-10 hours. Colcemid (0.1 ug/mL) was added for the last 2-3 hours of incubation, then cells were harvested by mitotic shake-off, fixed and stained in 6% Giesma. Negative controls included medium and solvent (dimethylsulfoxide) controls; positive controls included mitomycin C in the absence of S9 and cyclophosphamide in the presence of S9.

Result : Negative

Remark :

Reliability : (1) Reliable without restrictions

Reference : National Toxicology Program, 1987. Toxicology and Carcinogenesis Studies of Boric Acid (CAS NO. 10043-35-3) in B6C3F1 Mice (Feed Studies), Public Health Service, U.S. Dept. of Health and Human Services, NTP TR-324. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr324.pdf

Type : In Vitro Cytogenetics: Sister chromatid exchanges

Guideline/method : Cell culture

System of testing : Chinese Hamster Ovary Cells

Test concentrations : 200 – 500 ug/mL

Cytotoxic concentr. :

Metabolic activation : Conducted with and without activation with S-9 (prepared from the liver of Aroclor 1254-induced male Sprague-Dawley rats)

Year : 1987

GLP :

Test substance : Boric acid

Method : Galloway, S.M., et al., 1985. Environ. Mutagen. 7:1-51.

Method detail : In the absence of S-9, cells were incubated with study compound or solvent for 2 hours at 37°C, then 10 uM BrdU was added and incubation continued for an additional 22-24 hours. Cells were then washed, and fresh medium containing BrdU (10 uM) and colcemid (0.1 ug/mL) was added and incubation continued for 2-3 hours. In the presence of S-9, cells were incubated with study compound or solvent for 2 hours at 37°C. Cells were then washed, medium containing 10 uM BrdU was added, and incubation continued for 26 hours with colcemid (0.1 ug/mL) present for the last 2-3 hours. Negative controls included medium and solvent (dimethylsulfoxide) controls; positive controls included mitomycin C in the absence of S9 and cyclophosphamide in the presence of S9.

Result : Negative

Remark :

Reliability : (1) Reliable without restrictions

Reference : National Toxicology Program, 1987. Toxicology and Carcinogenesis Studies of Boric Acid (CAS NO. 10043-35-3) in B6C3F1 Mice (Feed Studies), Public Health Service, U.S. Dept. of Health and Human Services, NTP TR-324. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr324.pdf

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Type : Mouse Lymphoma
Guideline/method : Cell culture
System of testing : Mouse lymphoma L5178Y cells
Test concentrations : 1000 – 5000 ug/mL
Cytotoxic concentr. :
Metabolic activation : Conducted with and without activation with S-9 (prepared from the liver of Aroclor 1254-induced male F344 rats).
Year : 1987
GLP :
Test substance : Boric acid
Method : Clive, D. et al., 1979. Br.J. Cancer 20:184-189
Method detail : Cells (6×10^5 /mL) were treated for 4 hours at 37°C in medium, washed, resuspended in medium and incubated for 48 hours at 37°C. After expression, 2×10^6 cells/mL were plated in medium supplemented with trifluorothymidine for selection of cells that were mutant at the thymidine kinase (TK) locus, and 600 cells were plated in nonselective medium to determine the percentage of viable cells. The control was FOP-Fischer medium, while methyl methanesulfonate was the positive control in the assay without activation and methylcholanthrene served as the positive control in the assay with activation. Experiments were performed twice and all doses were tested in duplicate or quadruplicate.
Result : Negative
Remark :
Reliability : (1) Reliable without restrictions
Reference : National Toxicology Program, 1987. Toxicology and Carcinogenesis Studies of Boric Acid (CAS NO. 10043-35-3) in B6C3F1 Mice (Feed Studies), Public Health Service, U.S. Dept. of Health and Human Services, NTP TR-324. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr324.pdf

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus Test
Guideline/method : In vivo
Species : Mouse
Strain : Swiss-Webster
Sex : Male and female, 10 animals/sex/dose
Route of admin. : Oral, in deionized water
Exposure period : 2 days
Doses : 900, 1800 or 3500 mg/kg b.w.
Year : 1991
GLP :
Test substance : Boric acid
Method :
Method detail : Five mice/sex/dose were sacrificed 24 hours after the final dose, and 5/sex/dose were sacrificed at 48 hours after the final dose. A deionized water vehicle control (10/sex) and a urethane positive control (10 males) were also tested.
Result : Boric acid did not induce chromosomal or mitotic spindle abnormalities in bone marrow erythrocytes
Remark :
Reliability : (1) Not assignable: Secondary reference
Reference : O'Loughlin, K.G., 1991. Bone marrow erythrocyte micronucleus assay of boric acid in Swiss-Webster mice (Unpublished study). Submitted by U.S. Borax Co., MRID No. 42038904 (referenced in EPA, 2004).

5.8.2 DEVELOPMENTAL TOXICITY

Type	:	Teratogenicity and developmental
Guideline/method	:	Not specified
Species	:	Rat
Strain	:	Sprague-Dawley CD
Sex	:	Female
Route of admin.	:	Dietary
Exposure period	:	Day 6 to 15 of gestation
Frequency of treatment	:	Daily
Duration of test	:	To day 20 of gestation (for Phase I, teratology evaluation); To postnatal day 21 for Phase II
Doses	:	0, 3.3, 6.3, 9.6, 13.3 and 25 mg B/kg-day for Phase I; 0, 3.2, 6.5, 9.7, 12.9 and 25.3 mg B/kg-day for Phase II
Control group	:	Yes
NOAEL maternal tox.	:	
NOAEL teratogen.	:	9.6 mg B/kg-day in Phase I
Other	:	NOAEL for Phase II (which examined whether skeletal defects changed during the first 21 postnatal days) was 12.9 mg B/kg-day.
Other	:	
Year	:	1994
GLP	:	
Test substance	:	Boric acid
Method	:	
Method detail	:	Timed-mated CD rats (20 per group) were administered boric acid in the diet from gd 0-20. The experiment was conducted in two phases, and in both phases offspring were evaluated for post-implantation mortality, body weight, and morphology (external, visceral, and skeletal). Phase I was considered the teratology evaluation and was terminated on gd 20, when the uterine contents were evaluated. In Phase II, dams were allowed to deliver and rear their litters until pnd 21. This allowed determination of whether the incidence of skeletal defects in control and exposed pups changed during the first 21 days.
Result	:	During Phase I, no maternal deaths occurred and no clinical symptoms were associated with boric acid exposure. In the high dose group there was a statistically significant reduction in gravid uterine weight; corrected for this, overall maternal weight gain was not affected. Offspring body weights were significantly decreased in the two highest dose groups on gd 20. There was no treatment-related increase in external or visceral malformations. On gd 20, skeletal malformations and variations showed a significant increase in the two highest dose groups. The NOAEL and LOAEL for Phase I were considered to be 9.6 mg B/kg-day and 13.3 mg B/kg-day, respectively. Fetal body weight deficits did not continue into Phase II. The percentage of pups per litter with the skeletal malformation short rib XIII was still elevated on pnd 21 in the highest dose group. The NOAEL and LOAEL for this phase of the study were 12.9 and 25.3 mg B/kg-day, respectively.
Remark	:	
Reliability	:	(1) Reliable without restriction
Reference	:	Price, C.J., Marr, M.C., and Myers, C.B., 1994. Determination of the no-observable adverse effect level (NOAEL) for developmental toxicity in Sprague-Dawley (CD) rats exposed to boric acid in feed on gestational days 0 to 20, and evaluation of postnatal recovery through postnatal day 21. Final report. Research Triangle Institute, Center for Life Science Research, Research Triangle Park, NC. RTI Identification no. 65C-5657-200; Price, C.J., et al., 1996, Developmental toxicity NOAEL and postnatal recovery in rats fed boric acid during gestation, Fund. Appl. Toxicol. 32:179-193; EPA, 2004.

5. Toxicity

ID 10043-35-3

Date March 22, 2005

Type : Developmental toxicity
Guideline/method : Not specified
Species : Rat
Strain : Sprague-Dawley derived
Sex : Female
Route of admin. : Diet
Exposure period : Gestation day (gd) 0 through 20 (for 0, 0.1, 0.2 and 0.4% boric acid), with additional groups (0 and 0.8%) treated on gd 6 through 15 only (restricted to period of major organogenesis in order to eliminate early embryolethality)
Frequency of treatment : Continuous
Duration of test :
Doses : 0, 0.1, 0.2, 0.4 and 0.8% (equivalent to 0, 13.6, 28.5, 57.7, and 94.2 mg B/kg-day)
Control group : Yes
NOAEL maternal tox. : No maternal toxicity. Maternal effects related to treatment included a significant and dose-related increase in relative liver and kidney weights at 0.2% and above (this was the most sensitive effect). NOAEL = 0.1%, LOAEL = 0.2%
NOAEL teratogen. :
Other :
Other :
Other :
Year : 1994
GLP :
Test substance : Boric acid
Method :
Method detail : Timed-mated Sprague-Dawley rats (29/group) were fed a diet containing boric acid from gestation day 0 -20, with additional groups of 14 rats each receiving 0 or 0.8% on gd 6 through 15 only.
Result : Prenatal mortality, as seen in increases in both resorptions and late fetal deaths, was increased only at the highest dose. The number of live fetuses per litter was also decreased at 0.8%. The incidence of fetal malformations was significantly increased at 0.2% and higher doses. The most frequently observed malformations were enlarged lateral ventricles in the brain, and agenesis or shortening of rib XIII. Average fetal body weight per litter was reduced at all doses in a dose-dependent manner. Based upon fetal body weight, the LOAEL was 0.1%; a NOAEL was not defined.
Remark :
Reliability : (1) Reliable without restriction
Reference : Price, C.J., Field, E.A., Marr, M.C., et al., 1990. Developmental toxicity of boric acid (CAS No. 10043-35-3) in Sprague-Dawley rats. National Toxicology Program, Public Health Service, U.S. Department of Health and Human Services, Research Triangle Park, NC. NTP Report No. 90-105 (and Report Supplement No. 90-105A); Heindel, J.J. et al., 1992. Developmental toxicity of boric acid in mice and rats. Fund. Appl. Toxicol. (18):266-277.

Type : Developmental toxicity
Guideline/method :
Species : Mouse
Strain : CD-1 Swiss
Sex : Female
Route of admin. : Diet
Exposure period : Gestation days 0 through 17
Frequency of treatment :

5. Toxicity

ID 10043-35-3

Date March 22, 2005

Duration of test :
Doses : 0, 0.1, 0.2 and 0.4% boric acid (equivalent to 0, 43.4, 79.0 and 175.3 mg B/kg-day).
Control group : Yes
NOAEL maternal tox. : The low exposure (43.4 mg B/kg-day) approached the maternal NOAEL with mild renal lesions in only 2 of 10 females.
NOAEL teratogen. : 43.4 mg B/kg-day
Other :
Other :
Other :
Year : 1989
GLP :
Test substance : Boric acid
Method :
Method detail :
Result : Neither survival rates nor pregnancy rates were affected by boric acid. Dams exposed to the highest dose exhibited decreased weight gain even though food and water consumption were not reduced. Gestational weight gain corrected for gravid uterine weight was not affected. The highest dose caused increased water consumption during late gestation (gd 15-17) and increased relative kidney weight. A dose-related incidence of renal tubule dilatation/regeneration was observed, but this was not significant at the 43.4 mg B/kg-day level. Reduction in fetal body weight was dose-dependent but statistically significant only at the two highest doses. The high dose group had an increased percentage of resorptions (19% vs. 6% for controls) and malformed fetuses/litter (9% vs. 3% for controls). The most apparent treatment-related morphological changes involved deficient rib development at the thoracic-lumbar junction, i.e. an increased incidence of short rib XIII (a malformation) and a decreased incidence of rudimentary or full rib(s) at Lumbar I (a variation).
Remark :
Reliability : (1) Reliable without restriction
Reference : Field, E.A., Price, C.J., Marr, M.C. et al., 1989. Final report of the developmental toxicity of boric acid (CAS No. 10043-35-3) in CD-1-Swiss Mice. National Toxicology Program, Public Health Service, U.S. Dept. of Health and Human Services, Research Triangle Park, NC, NTP Final Report No. 89-250, NTP Study TER89029; EPA, 2004

Type : Developmental toxicity
Guideline/method :
Species : Rabbit
Strain : New Zealand White
Sex : Female
Route of admin. : Gavage
Exposure period : Gestation days 6 through 19
Frequency of treatment :
Duration of test :
Doses : 0, 10.9, 21.9 and 43.7 mg B/kg-day
Control group : Yes
NOAEL maternal tox. : 21.9 mg B/kg-day
NOAEL teratogen. : 21.9 mg B/kg-day
Other :
Other :
Other :
Year : 1991
GLP :

5. Toxicity

ID 10043-35-3

Date March 22, 2005

Test substance	:	Boric acid
Method	:	
Method detail	:	Artificially-inseminated rabbits (30/group) were administered boric acid in aqueous solution by gavage from gd 6-19. Food consumption, body weight, and clinical signs were monitored throughout. At gd 30, the animals were sacrificed and the following endpoints examined: pregnancy status, number of resorptions, fetal body weight, viability, and external, visceral and skeletal malformations.
Result	:	No treatment-related clinical signs of toxicity were observed during the study, except for vaginal bleeding noted on 2-11 does/day on gd 19-30 at the high dose; these does had no live fetuses on day 30. Vaginal bleeding was not observed in any control does and in only one female/group at the other two dosage groups. Two maternal deaths were observed but were not treatment related. Maternal food consumption decreased during most of the treatment period (gd 6-15) at the high dose, and was increased at the two highest doses after treatment (gd 25-30). Maternal body weight (gd 9-30), weight gain during treatment, gravid uterine weight and number of corpora lutea per dam were each decreased at the highest dose. Corrected maternal weight gain was increased at the two highest doses. Maternal liver weight was unaffected. Relative maternal kidney weight was increased at the highest dose, but absolute kidney weight was not. Microscopic evaluation of maternal kidney sections did not indicate any pathology associated with boric acid exposure. The maternal NOAEL was 21.9 mg B/kg-day and the LOAEL was 43.7 mg B/kg-day. No definitive evidence of developmental toxicity was observed following exposure at the two lowest doses during the period of major organogenesis (gd 6-19). At 43.7 mg B/kg-day, developmental toxicity included a high rate of mortality (90% of implants/litter resorbed vs. 6% for controls). Prenatal mortality was also expressed as an increased proportion of pregnant females with no live fetuses and as a reduction in the number of live fetuses/live litter on gd 30. The incidence of malformed live fetuses/litter was also increased at the highest dose (81% vs. 26% for controls), primarily due to the incidence of cardiovascular defects. The NOAEL for developmental toxicity was 21.9 mg B/kg-day and the LOAEL was 43.7 mg B/kg-day.
Remark	:	
Reliability	:	(1) Reliable without restriction
Reference	:	Price, C.J., Marr, M.C., Myers, C.B., et al., 1991. Developmental toxicity of boric acid (CAS No. 10043-35-3) in New Zealand White rabbits. National Toxicology Program, Public Health Service, U.S. Dept. of Health and Human Services, Research Triangle Park, NC, NTP Study TER90003 (and Laboratory Supplement No. TER 90003); EPA, 2004

5.8.3 TOXICITY TO REPRODUCTION

Type	:	Male and female reproduction
Guideline/method	:	Continuous breeding protocol
In vitro/in vivo	:	In vivo
Species	:	Mouse
Strain	:	Swiss CD-1
Sex	:	Male and female
Route of admin.	:	Diet
Exposure period	:	27 weeks
Frequency of treatment	:	Continuous
Duration of test	:	

5. Toxicity

ID 10043-35-3

Date March 22, 2005

- Doses** : 0, 1000, 4500, or 9000 ppm (equivalent to a daily intake of 0, 26.6, 111, or 220 mg B/kg-day for males and 0, 31.8, 152, or 257 mg B/kg-day for females)
- Control group** : Yes
- Year** : 1990
- GLP** :
- Test substance** : Boric acid
- Method** :
- Method detail** : Male and female F0 mice (11 weeks old) were fed a diet containing boric acid for up to 27 weeks. There were 40 pairs in the control group and 20 pairs per treatment group. Following 1 week of treatment, the F0 mice were caged as breeding pairs for 14 weeks. Subsequently, to determine the affected sex, the control and 4500 ppm mice were assigned to three crossover mating groups: control male x control female, 4500 ppm male x control female, and control male x 4500 ppm female. Each group was composed of 19-20 pairs that were mated for 7 days or until a copulatory plug was detected. Mice were on control feed for this week, followed by resumption of the original diet. After completion of the crossover trial (total of 27 weeks), necropsy was performed on control and 4500 ppm F0 males and females and on 1000 and 9000 ppm F0 males that had been maintained on their respective diets to compare semen parameters and testicular histology. The final F1 litters (exposed during gestation and lactation) were fed the same dosage of boric acid as their parents had received. The F1 mice were cohabited in nonsibling pairs (40 pairs for the control and 20 pairs for 1000 ppm, which was the only dose with sufficient F1 animals) for 7 days or until a copulatory plug was observed. They were maintained on their respective diets during mating and until the F2 litters were delivered, then necropsied.
- Result** : During weeks 2-18, body weight gain of high dose males and females was significantly reduced. Mortality rates were not affected by boric acid but fertility was significantly impaired. None of the 9000 ppm pairs were fertile. The number of litters per pair, number of live pups per litter, proportion of pups born alive, live put weight and adjusted (for litter size) pup weight were significantly decreased at 4500 ppm. The initial fertility index was not affected in the 1000 and 4500 ppm groups but the progressive fertility index was decreased in the 4500 ppm group. In the crossover mating study, mating and fertility indices were significantly depressed in the 4500 ppm male x control female group, and only one pair in that group produced a live litter; these indices were not affected in the control male x 4500 ppm female group. Dosed females mated to control males had a lower body weight on pnd 0, longer gestational period, and gave birth to lower weight pups. Necropsy indicated that males treated with 9000 ppm had significantly reduced body, testis and epididymal weights. In the 4500 ppm group, testis, epididymal and prostate weight were reduced; these parameters were not affected at 1000 ppm. Significant reductions in sperm motility were observed at 1000 and 4500 ppm and in sperm concentration at 4500 and 9000 ppm. The percentage of abnormal sperm was increased at 4500 ppm and could not be evaluated in the 9000 ppm group due to the absence or severe reduction in sperm. Dose-related seminiferous tubular atrophy occurred at the two highest doses. Tissues of low dose males exhibited no significant changes. Necropsy of 4500 ppm females indicated a reduction in relative and absolute liver weight and absolute kidney plus adrenal weights. Females at 1000 and 9000 ppm were not necropsied. For the F1 generation, fertility was not affected at 1000 ppm, but the litter-adjusted body weights of the F2 pups were significantly decreased. Effects in 1000 ppm F1 females included significant increases in uterine and kidney plus adrenal weights, shorter estrous cycles, and fewer ambiguous vaginal

5. Toxicity

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smears. A reduction in epididymal sperm concentration in the F1 males approached statistical significance; sperm motility and morphology were not affected. Histopathology was unremarkable.

The lowest dose, 1000 ppm, decreased sperm motility in F0 males, marginally decreased epididymal sperm concentration in F1 males, increased uterine and kidney/adrenal weights and shorted estrous cycles in F1 females, and reduced litter-adjusted birth weights in F2 pups. Thus, the LOAEL for this study is 1000 ppm (26.6 and 31.8 mg B/kg-day for males and females, respectively). A NOAEL was not identified.

Remark :
Reliability : (1) Reliable without restriction
Reference : Fail, P.A., George, J.D., Grizzle, T.B., et al., 1990. Final report on the reproductive toxicity of boric acid (CAS No. 100453-35-3) in CD-1 Swiss mice. National Toxicology Program, Public Health Service, U.S. Dept. of Health and Human Services, Research Triangle Park, NC, NTP report 90-105; Fail, P.A. et al., 1991, Fund Appl. Toxicol. 17:225-239; EPA, 2004.

Type : Multigeneration
Guideline/method :
In vitro/in vivo : In vivo
Species : Rat
Strain : Sprague-Dawley
Sex : 8 Male and 16 female per group
Route of admin. : Diet
Exposure period :
Frequency of treatment :
Duration of test :
Doses : 0, 5.9, 17.5 or 58.5 mg B/kg-day
Control group : Yes
Year : 1972
GLP :
Test substance : Boric acid
Method :
Method detail :
Result : No adverse effects on reproduction or gross pathology were observed in rats dosed at 5.9 or 17.5 mg B/kg-day that were examined to the F3 generation. Litter size, weights of progeny, and appearance were normal. Animals receiving 58.5 mg B/kg-day were sterile. In these groups, males showed lack of spermatozoa in atrophied testes, and females showed decreased ovulation in the majority of ovaries examined. An attempt to obtain litters by mating the treated females with control males. A LOAEL of 58.5 mg B/kg-day and NOAEL of 17.5 mg B/kg-day were identified from this study.

Remark :
Reliability : (2) Reliable with restrictions
Reference : Weir, R.J. and R.S. Fisher, 1972. Toxicologic studies on borax and boric acid. Toxicol. Appl. Pharmacol. 23:351-364; EPA, 2004.

6.0 OTHER INFORMATION

6.1 CARCINOGENICITY

Type : Chronic
Guideline/method : Not specified
Species : Mouse
Strain : B6C3F1

5. Toxicity

ID 10043-35-3

Date March 22, 2005

Sex	:	Male and female
Number of animals	:	50 per sex per group
Route of admin.	:	Diet
Exposure period	:	103 weeks
Frequency of treatment	:	
Post exposure period	:	
Doses	:	0, 2500, and 3000 mg/kg-day (0, 48 and 96 mg B/kg-day)
Control group	:	Yes
NOAEL	:	
LOAEL	:	
Other	:	
Year	:	1981 - 1983
GLP	:	
Test substance	:	Boric acid
Method	:	
Method detail	:	Mice were observed twice daily and weighed weekly for 12 weeks then weighed once every 4 weeks. Necropsy performed on all animals. The following tissues were examined histologically for all control and high dose animals and for low dose animals dying before the end of the study: tissue masses, abnormal regional lymph nodes, skin, mandibular and mesenteric lymph nodes, mammary gland, salivary glands, vertebrae, bone marrow, costochondral junction, thymus, larynx, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, duodenum, jejunum, ileum, colon, liver, gallbladder, pancreas, spleen, kidneys, adrenal glands, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, pituitary gland. The following tissues were examined histologically for low dose mice: lung, liver, stomach, kidney, salivary glands, testis, pancreas, and brain for males and lung, liver, ovary and brain for females.
Result	:	No treatment-related clinical signs were observed throughout the study. Survival of male mice was significantly lower than that of controls after week 63 in the low-dose group and after week 64 in the high-dose group. Survival was not affected in females. Body weight gain was reduced in each sex after week 30; mean final body weights were 7% and 13% below control values for exposed male mice and 7% and 20% below those of controls for exposed female mice. Testicular atrophy and interstitial cell hyperplasia were observed in male mice at the high dose. There were also dose-related increased incidences of splenic lymphoid depletion in males. There was an increase in hepatocellular tumors in the low dose male mice but this was judged by the NTP to be unrelated to the administration of boric acid. Overall, NTP concluded that this study produced no evidence of carcinogenicity of boric acid in male or female mice, although the low number of surviving males may have reduced the sensitivity of the study (NTP, 1987)
Remarks	:	
Reliability	:	(1) Reliable without restriction
Reference	:	NTP (National Toxicology Program), 1987. Toxicology and carcinogenesis studies of boric acid (CAS No. 10043-35-3) in B6C3F1 mice (feed studies). ; Dieter, M.P., 1994. Toxicity and carcinogenicity studies of boric acid in male and female B6C3F1 mice, Environ. Health Perspect. 102(Suppl 7):93-97.
Type	:	Chronic
Guideline/method	:	Oral
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	Male and female
Number of animals	:	35 rats per sex in treatment groups
Route of admin.	:	Diet

5. Toxicity

ID 10043-35-3

Date March 22, 2005

Exposure period	:	2 years
Frequency of treatment	:	
Post exposure period	:	
Doses	:	0, 5.9, 17.5 and 58.5 mg B/kg-day
Control group	:	Yes, 70 rats per sex
NOAEL	:	17.5 mg B/kg-day based on testicular effects
LOAEL	:	58.5 mg B/kg-day based on testicular effects
Other	:	
Year	:	1971
GLP	:	
Test substance	:	Boric acid
Method	:	
Method detail	:	The study was designed to assess systemic toxicity; only tissues from the brain, pituitary, thyroid, lung, heart, liver, spleen, kidney, adrenal, pancreas, small and large intestine, urinary bladder, tests, ovary, bone, and bone marrow were examined histopathologically. Tumors were not mentioned in the report. NTP (1987) concluded that this study provided adequate data on lack of carcinogenic effects of boric acid in rats in deciding to conduct carcinogenicity studies only on mice.
Result	:	At the highest dose, rats had decreased food consumption during the first 13 weeks and suppressed growth throughout the study. Signs of toxicity at this exposure level included swelling and desquamation of the paws, scaly tails, inflammation of the eyelids, and bloody discharge from the eyes. Testicular atrophy was observed in all high-dose males at 6, 12 and 24 months. Testes weights and testes:body weight ratios were significantly decreased, while brain and thyroid:body weight ratios were significantly increased. No treatment-related effects were observed in rats receiving 5.9 or 17.5 mg B/kg-day.
Remark	:	These authors also reported a 90-day study in which rats were fed 0, 2.6, 8.8, 26.3, 87.5 and 262.5 mg B/kg bw/day (as boric acid). Mortality was 100% at the highest dose, and testicular atrophy was observed at 87.5 and 26.3 mg B/kg bw-day. These authors also conducted chronic (104 weeks) and subchronic (90 days) dietary exposures of beagle dogs. In the chronic study, the authors concluded there were no definitive effects observed (dose levels were 0, 1.4, 2.9 and 8.8 mg B/kg-day). The subchronic study (dose levels 0, 0.33, 3.9 and 30.4 mg B/kg-day for males and 0, 0.24, 2.5 and 21.8 mg B/kg-day for females) identified the highest dose level as the LOAEL for both sexes, while the NOAEL was 3.9 mg B/kg-day for males and 2.5 mg B/kg-day for females.
Reliability	:	(2) Reliable with restrictions
Reference	:	Weir, R.J. and Fisher, R.S., 1972. Toxicologic studies on borax and boric acid. Toxicol. Appl. Pharmacol. 23:351-364.

1. General Information

ID 68457-13-6

Date July 22, 2008

1.0 SUBSTANCE INFORMATION

201-16738D

Generic Name :
Chemical Name : Cobalt Borate Neodecanoate Complexes
CAS Registry No. : 68457-13-6
Component CAS Nos. :
EINECS No. :
Structural Formula :
Molecular Weight :
Synonyms and Tradenames : Comend® A Pastilles
Cobalt boro acylate
Cobalt boro-neodecanoate
References :

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2. Physico-Chemical Data

ID 68457-13-6

Date July 22, 2008

2.1 MELTING POINT

Type	:	Melting Point/Melting Range Determination
Guideline/method	:	OECD 102; EEC Directive 92/69, A.1
Value	:	Could not be determined
Decomposition	:	Above about 103°C
Sublimation	:	
Year	:	2003
GLP	:	Yes
Test substance	:	Cobalt borate neodecanoate complexes, batch T297, 21.9% cobalt (w/w), soft purple solid
Method	:	OECD 102 Melting Point/Melting Range, July 1995, capillary method
Method detail	:	Finely ground test substance was packed tightly in triplicate capillary tubes and heated in a BUCHI Melting Point tester, B-545. A beam of light directed through the test item at a photocell detected changes in transparency attributable to melting. A transmission of 40% was defined as the end point of melting. The samples were heated from 25°C to 400°C; the rate of heating was 20 K/min in the preliminary test and 10 K/min in the main study.
Result	:	In this test method, the temperature at the final stage of melting is usually taken as the melting temperature; this usually corresponds with 40% light transmission. In both the preliminary test and the main test, melting began at about 78 -92°C and the color of the test substance changed from dark purple to black violet. Foaming of the test substance was observed at about 103°C, indicating degradation and the formation of gaseous degradation products. The apparatus turned off automatically at 175°C. No clear melting point could be deduced.
Remark	:	Supporting data for dissociation products: Acid: The calculated melting point for neodecanoic acid is 57.13°C (Appendix B). The reported melting point for boric acid is 169°C (Appendix E). Metal: The reported melting point for cobalt chloride is 735°C (Appendix F)
Reliability	:	[1] Reliable without restriction
Reference	:	Tognucci, A., 2003. Determination of the melting point/melting range of cobalt borate neodecanoate complexes. RCC Study No. 849109, conducted for the Metal Carboxylates Coalition by RCC Ltd., Switzerland.

2.2 BOILING POINT

Type	:	Boiling Point/Boiling Range Determination
Guideline/method	:	OECD 103; EPA OPPTS 830.7220
Value	:	Does not boil under atmospheric pressure
Decomposition	:	Above about 125°C
Year	:	2003
GLP	:	Yes
Test substance	:	Cobalt borate neodecanoate complexes, batch T297, 21.9% cobalt (w/w), soft purple solid
Method	:	OECD 103, Boiling Point, 1995 (visual test with capillary tester); EPA Product Properties Test Guidelines OPPTS 830.7220, Boiling point/Boiling Range, August 1996.
Method detail	:	Ground test substance was packed into two small tubes and boiling capillaries inserted. Samples were heated from 25°C to 400°C in a BUCHI Melting Point tester, B-545. The rate of heating was 20 K/min in the preliminary test and 10 K/min in the main study. Samples were observed visually through a lens, with a current stream of bubbles from the capillary indicative of boiling. The temperature at which this occurs is the boiling point. Atmospheric pressure during the main test was 98.0 kPa. No

2. Physico-Chemical Data

ID 68457-13-6

Date July 22, 2008

Result : correction for normalized pressure was made.
: During the preliminary test, the test substance darkened in color starting at about 42°C; foaming was observed at about 105°C and evaporation began at about 309°C. Reduced heating rates were used in the main test but similar results were obtained, with darkening at about 80°C and foaming at about 125°C, which is indicative of degradation. It was concluded that the test substance does not boil under atmospheric pressure.

Remark : **Supporting data for dissociation products:**
Acid:
The reported melting point for neodecanoic acid is 243 - 253°C (Appendix B).
The reported boiling point for boric acid is 300 °C (loses 1½ water) (Appendix E).
Metal: The reported boiling point for cobalt chloride is 1,049°C (Appendix F).

Reliability : [1] Reliable without restriction

Reference : Tognucci, A., 2003. Determination of the boiling point/boiling range of cobalt borate neodecanoate complexes, RCC Study No. 849110, conducted for the Metal Carboxylates Coalition by RCC Ltd., Switzerland.

2.3 DENSITY

Type : Specific gravity

Guideline/method :

Value : 1.32 at 25°C

Year :

GLP :

Test substance :

Method :

Method detail :

Result :

Remark : **Supporting data for dissociation products:**
Acid:
The reported density for neodecanoic acid is 0.91 g/cm³ at 20°C (Appendix B).
The reported density for boric acid is 1.435 at 15 °C (Appendix E).
Metal: The reported density for cobalt chloride is 3.367 at 25°C (Appendix F).

Reliability :

Reference : Material Safety Data Sheet for Comend® A Pastilles, Shepherd Chemical Co.

2.4 VAPOR PRESSURE

Type :

Guideline/method :

Value : hPa at °C

Decomposition :

Year :

GLP :

Test substance :

Method :

Method detail :

Result :

Remark : **Supporting data for dissociation products:**
Acid: The reported vapor pressure for neodecanoic acid is approx. 0.29 hPa at 50°C (Appendix B).

2. Physico-Chemical Data

ID 68457-13-6

Date July 22, 2008

Reliability :
Reference :

2.5 PARTITION COEFFICIENT

Type :
Guideline/method :
Partition coefficient :
Log Pow : at 25°C
pH value :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : **Supporting data for dissociation products:**
Acid: The calculated Log Kow for neodecanoic acid is 3.90 (Appendix B).
Kow not applicable for boric acid (dissociates in water).
Metal: Not applicable. Cobalt chloride dissociates in water.

Reliability :
Reference :

2.6.1 SOLUBILITY IN WATER

Type : Water Solubility Determination
Guideline/method : OECD 105; EPA OPPTS 830.7840
Value : 51.2 mg/L at 20°C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
PKa : at °C
Description :
Stable :
Deg. product :
Year : 2003
GLP : Yes
Test substance : Cobalt borate neodecanoate complexes, batch T297, 21.9% cobalt (w/w), soft purple solid

Deg. products CAS# :
Method : OECD 105, Water Solubility, 1995; EPA Product Properties Test Guidelines, OPPTS 830.7840, Water Solubility: Column Elution Method, Shake Flask Method, 1998.

Method detail : The results of a preliminary test using a simplified flask method indicated the estimated solubility was below 10 mg/L; therefore the column elution method was used in the main test. The column was prepared by adding 6.16933 g of glass beads into a flask, adding 0.12131 g of test material, and mixing for about 5 minutes. This was then poured into the elution column which was subsequently filled with water and equilibrated for approximately 2 hours. A circulation pump was used to elute the cobalt borate neodecanoate from the carrier material. Temperature was 20°C. The flow rate was 0.52 mL/min during the first part of the test (about 94 hours), and was reduced to 0.26 mL/min for the second part of the test (about 28 hours). The apparatus was run until equilibration of the saturation column was obtained, defined by at least five successive samples whose concentrations do not differ more than 30%. The column eluate was

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Result : sampled at intervals of at least 1 hour to determine the concentration of cobalt, using atomic absorption spectroscopy.
: Based upon the results of 12 samples, the cobalt solubility was 11.2 mg/L (SD \pm 0.5 mg/L) which corresponds to a water solubility of cobalt borate neodecanoate of 51.2 mg/L (calculated based on cobalt content of 21.9%).
The pH during the test ranged from 7.78 to 8.36.

Remark : **Supporting data for dissociation products:**
Acid:
The calculated water solubility for neodecanoic acid is 68.97 mg/L at 25°C (Appendix B).
The reported water solubility for boric acid is 63.5 g/L at 30 °C (Appendix E).
Metal: The reported water solubility for cobalt chloride is 450 g/L at 7°C.

Reliability :
Reference :

2.7 FLASH POINT

Type :
Guideline/method :
Value : >231 °C
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :

Supporting data for dissociation products:
Acid: The reported flash point for neodecanoic acid is approx. 122°C (Appendix B).
Reliability :
Reference : Material Safety Data Sheet for Comend® A Pastilles, Shepherd Chemical Co.

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Result Remark Mean (N = 3) pKa value was 6.41 (SD = 0.0411) at 20°C
The results indicate that dissociation of the test substance will occur at environmentally-relevant pH values (approximately neutral) and at physiologically-relevant pH values (approximately 1.2).

Reliability Reference [1] Reliable without restriction.
Lezotte, F.J. and W.B. Nixon, 2002. Determination of the dissociation constant of cobalt, borate neodecanoate complexes, Wildlife International, Ltd. Study No. 534C-118, conducted for the Metal Carboxylates Coalition.

3.2.1 MONITORING DATA

Type of measurement :
Media :
Concentration :
Substance measured :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

3.3.1 TRANSPORT (FUGACITY)

Type :
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Year :
Test substance :
Method :
Method detail :
Result :
Remark : **Supporting data for dissociation products:**
Acid: Fugacity Model, Level III calculations for neodecanoic acid predict 3.55% in air, 37% in water, 57.5% in soil, and 1.96% in sediment when emitted in equal amounts to air, water and soil (Appendix B).

Reliability :
Reference :

3.5 BIODEGRADATION

Type : CO₂ Evolution Test (Ready Biodegradability)
Guideline/method : OECD 301B
Inoculum : Activated Sludge
Concentration : 30 mg/L related to activated sludge concentration
3.0 mL related to fresh soil filtrate
Contact time : 28 Days
Degradation : 4.45 (±) % after 28 day(s)
Result :
Kinetic of test subst. : % (specify time and % degradation)
%
%

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Control substance :
Kinetic :
Deg. product :
Year :
GLP :
Test substance :
Deg. products CAS# :
Method :
Method detail :
Result :

%
%

73.62 % by day 10
91.98 % by day 28

The mean cumulative net CO₂ evolved (amount of biodegradation) from the aqueous medium fortified with Co B Neodecanoate, procedural control, toxicity control and blank control test vessels was 30.41, 62.51, 63.14, and 28.78 mg/L at day 28. The cumulative net percent CO₂ production (blank control values subtracted), or percent ultimate biodegradation, for Co B neodecanoate, procedural control, and toxicity control was calculated to be 4.45, 91.98 and 46.85%, respectively.

The cumulative net CO₂ evolved from the sodium benzoate procedural control was 73.62% of theoretical by day 10 and 91.98% of theoretical by day 28, thus exceeding the "pass" criteria of the test (reaching 60% or greater CO₂ evolution within 28 days and within a 10-day window of reaching 10% biodegradation). This rapid biodegradation of sodium benzoate confirmed the presence of an active microbial population and system integrity.

Based on the CO₂ analysis results from this study, Co B neodecanoate, was not "readily biodegradable" according to the OECD 301B guideline. The rapid degradation of the reference substance confirmed the presence of an acceptable microbial community and confirmed system integrity. The cobalt salt did not inhibit microbial degradation of the reference compound sodium benzoate.

Remark : **Supporting data for dissociation products:**
Acid: Neodecanoic acid is not readily biodegradable, with 11% degradation after 28 days using the manometric respirometry test (Appendix B).
Metal:
Reliability : [1]Reliable without restriction
Reference : Cobalt Borate Neodecanoate (Co B neodecanoate) - Determination of the Biodegradability of a Test Substance Based on OECD Method 301B (CO₂ Evolution Test). (2006) Conducted by Springborn Smithers Laboratories for the Metal Carboxylates Coalition. Study No. 13865.6104

3.7 BIOCONCENTRATION

Type :
Guideline/method :
Species :
Exposure period : at °C

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Concentration :
BCF :
Elimination :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

4.1 ACUTE TOXICITY TO FISH

Type	:	Fish Acute
Guideline/method	:	OECD #203
Species	:	<i>Onchorhynchus mykiss</i>
Exposure period	:	96h
NOEC	:	2.2 mg Co B neodecanoate/L (0.48 mg Co/L)
LC0	:	
LC50	:	4.9 mg Co B neodecanoate/L (1.1 mg Co/L)
LC100	:	
Other	:	
Other	:	
Other	:	
Limit test	:	
Analytical monitoring	:	Nominal concentrations: 6.3, 13, 25, 50 and 100 mg cobalt borate neodecanoate/L (equivalent to 1.4, 2.8, 5.5, 11 and 22 mg Co/L) Measured concentrations: 0.93, 2.2, 3.6, 8.0 and 16 mg cobalt borate neodecanoate/L (equivalent to 0.21, 0.48, 0.80, 1.8 and 3.6 mg Co/L) ¹
Year	:	2008
GLP	:	yes
Test substance	:	Cobalt borate neodecanoate, Batch No. A469, CAS No. 68457-13-6, reported to have a purity of >94% (22.15% cobalt), was received from OM Group on 11 May 2006.
Method	:	OECD #203
Method detail	:	
Result	:	The 96-hour LC50 value for cobalt borate neodecanoate and <i>Oncorhynchus mykiss</i> was estimated by moving average analysis to be 4.9 mg cobalt borate neodecanoate/L (1.1 mg Co/L), with 95% confidence intervals of 3.4 to 7.6 mg cobalt borate neodecanoate/L (0.75 to 1.7 mg Co/L). The No-Observed-Effect Concentration (NOEC) was determined to be 2.2 mg cobalt borate neodecanoate/L (0.48 mg Co/L).
Remark	:	Supporting data for dissociation products: Acid: For neodecanoic acid, the 96-h LC50 for the rainbow trout (<i>Oncorhynchus mykiss</i>) was reported as 37.2 mg/L. Other reported LC50 values range from 32 – 181 mg/L (Appendix B). For boric acid, the 96-h LC50 for fry of chinook salmon (<i>Oncorhynchus tshawytscha</i>) and coho salmon (<i>Oncorhynchus kisutch</i>) ranged from 78.2 – 127 mg B/L. Other reported 96-h LC50 values for boron in fish range from 14.2 mg B/L in zebrafish to 978 mg B/L in mosquito fish. (Appendix E). Metal: For cobalt chloride, the 96-h LC50 was 1.41 mg Co/L for the highly sensitive rainbow trout, <i>Oncorhynchus mykiss</i> . Other fish species are less sensitive with 96-h LC50 values ranging from 22.0 to 333 mg Co/L (Appendix F).
Reliability	:	[1] without restriction
Reference	:	Cobalt Borate Neodecanoate Complex- Acute Toxicity to rainbow trout (<i>Oncorhynchus mykiss</i>) (2008). Conducted by Springborn Smithers Laboratories for the Metal Carboxylates Coalition. Study No. 13865.6122

¹ The concentrations of cobalt borate neodecanoate were calculated from the measured cobalt concentrations.

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	
Guideline/method	:	OECD #202
Species	:	<i>Daphnia</i>
Exposure period	:	48h
NOEC	:	2.3 mg/L
EC0	:	
EC50	:	9.2 mg/L
EC100	:	
Other	:	
Other	:	
Limit test	:	
Analytical monitoring	:	Nominal: 6.3, 13, 25, 50 and 100 mg cobalt borate neodecanoate/L (equivalent to 1.4, 2.8, 5.5, 11 and 22 mg Co/L); Measured: 1.0, 2.3, 4.9, 9.8 and 21 mg cobalt borate neodecanoate/L (equivalent to 0.23, 0.50, 1.1, 2.2, and 4.6 mg Co/L)
Year	:	2007
GLP	:	Yes
Test substance	:	Cobalt borate neodecanoate, Batch No. A469, CAS No. 68457-13-6, reported to have a purity of >94% (22.15% cobalt), was received from OM Group on 11 May 2006.
Method	:	OECD #202
Method detail	:	
Result	:	The 48-hour EC50 value for cobalt borate neodecanoate and <i>Daphnia magna</i> was determined by binomial analysis to be 9.2 mg cobalt borate neodecanoate/L (2.6 mg Co/L) with 95% confidence intervals of 7.0 to 13 cobalt borate neodecanoate/L (1.1 to 4.6 mg Co/L). The No-Observed-Effect Concentration (NOEC) was determined to be 2.3 mg cobalt borate neodecanoate/L (0.50 mg Co/L).
Remark	:	<p>Supporting data for dissociation products:</p> <p>Acid: For neodecanoic acid, the 48-h LL50 for <i>Daphnia magna</i> has been reported as 47.1 mg/L. For the copepod, <i>Acartia tonsa</i>, the 96-h LC50 for neodecanoic acid has been reported as 25 mg/L. (Appendix B)</p> <p>For boric acid, the 48-h EC50 for <i>Daphnia magna</i> has been reported as 133 mg B/L and as 226 mg B/L (Appendix E).</p> <p>Metal: For cobalt chloride, the 48-h EC50 values for <i>Daphnia magna</i> have been reported as 1.52 mg Co/L and as 5.5 mg Co/L. For <i>Ceriodaphnia dubia</i>, 48-h LC50 values ranged from 2.35 to 4.60 mg Co/L (Appendix F).</p>
Reliability	:	[1] without restriction
Reference	:	Cobalt Borate Neodecanoate Complex- Acute Toxicity to Water Fleas (2007).

Conducted by Springborn Smithers Laboratories for the Metal Carboxylates Coalition. Study No. 13865.6105

4.3 TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

Type	:	
Guideline/method	:	OECD #201
Species	:	<i>Pseudokirchneriella subcapitata</i>
Endpoint	:	
Exposure period	:	72h EC50
NOEC	:	
LOEC	:	
EC0	:	
EC10	:	
EC50	:	Growth: Yield: 0.41 mg/L (0.09 mg Co/L)
Other	:	
Other	:	
Other	:	
Limit test	:	
Analytical monitoring	:	Nominal: 0.063, 0.13, 0.25, 0.50 and 1.0 mg cobalt borate neodecanoate/L (equivalent to 0.014, 0.029, 0.055, 0.11 and 0.22 mg Co/L); Measured: 0.042, 0.085, 0.16, 0.31 and 0.56 mg cobalt borate neodecanoate/L (equivalent to 0.0093, 0.019, 0.035, 0.070 and 0.12 mg Co/L)
Year	:	2007
GLP	:	Yes
Test substance	:	Cobalt borate neodecanoate complex, Batch No. A469, CAS No. 68457-13-6, 22.15% cobalt, was received from OM Group on 11 May 2006.
Method	:	OECD #201
Method detail	:	
Result	:	0- to 72-hour average growth rate (μ_{ave}) and biomass expressed as yield relative to the performance of the control data. Based on growth rate the EC10, EC50 and NOEC were 0.33, 0.56, and 0.31 mg cobalt borate neodecanoate/L, respectively. Based on yield the EC10, EC50 and NOEC were 0.16, 0.41, and 0.31, mg cobalt borate neodecanoate/L, respectively.
Remark	:	<p>Supporting data for dissociation products:</p> <p>Acid: For boric acid, a 14-day exposure of <i>Chlorella pyrenoidosa</i> resulted in a NOEC of 0.4 mg B/L and a LOEC of 0.8 mg B/L. The 72-h EC50 for <i>Scenedesmus subspicatus</i> was 34 mg B/L and the 96-h EC50 for the floating aquatic vascular plant <i>Lemna gibba</i> was > 60 mg/L (Appendix E).</p> <p>Metal: For cobalt chloride, the 96-h EC50 for <i>Chorella vulgaris</i> was 0.52 mg Co/L. For the duckweed <i>Lemna minor</i>, the 7-d IC50 was 16.9 mg Co/L, while for the blue-green alga <i>Spirulina platensis</i> the 96-h EC50 was 23.8 mg Co/L (Appendix F).</p>
Reliability	:	[1] without restriction
Reference	:	Cobalt Borate Neodecanoate Complex - Acute Toxicity to the Freshwater

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Green Algae, *Pseudokirchneriella subcapitata*. (2007). Conducted by Springborn Smithers Laboratories for the Metal Carboxylates Coalition. Study No. 13865.6106

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In vitro/in vivo	:	
Type	:	
Guideline/method	:	
Species	:	
Number of animals	:	
Males	:	
Females	:	
Doses	:	
Males	:	
Females	:	
Vehicle	:	
Route of administration	:	
Exposure time	:	
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1 st . 2 nd . 3 rd .
Toxic behavior	:	
Deg. product	:	
Deg. products CAS#	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	<p>Supporting data for dissociation products:</p> <p>Acid: Neodecanoic acid is relatively resistant to biotransformation and does not readily form bioactive metabolites (Appendix D). Thus it would be primarily eliminated in the urine as glucuronic acid conjugates or by deacylation (Katz, G.V., and D. Guest, 1994. "Aliphatic Carboxylic Acids," in <u>Patty's Industrial Hygiene and Toxicology</u>, 4th ed., Vol. 2, Part E. Clayton, G.D., and F.E. Clayton, eds., John Wiley and Sons).</p> <p>Boron is readily adsorbed following oral exposure in both humans and animals. There is no evidence that boron compounds are metabolized in the body. Greater than 90% of an orally administered dose of boron as boric acid is excreted in a short time in both humans and animals. Clearance is primarily through urine. Boron is also absorbed during inhalation exposure but is not absorbed across intact skin in humans or animals. Examinations in rats have revealed a fairly uniform distribution of boron outside the blood compartment across various tissues, except for consistently lower concentrations in fat and consistently higher concentrations in bone. Available data for humans indicates comparable patterns are likely (Appendix E).</p> <p>Metal: Absorption of cobalt in the digestive tract is influenced by the chemical form of the metal, with increasing solubility resulting in increasing absorption.</p>

Approximately 13-34% of cobalt chloride, a soluble form, is absorbed in the gut of rats, but absorption in the gut may be increased in iron deficient individuals. Following oral exposure, cobalt is eliminated primarily in feces and secondarily in urine. For the more soluble forms of cobalt, e.g., cobalt chloride, 70 – 80% of the administered dose is eliminated in the feces. For absorbed cobalt, elimination is rapid primarily in the urine. Elimination is biphasic or triphasic. The terminal phase involves a very small residual level of cobalt and has a half-life in years (Appendix F).

Reliability :
Reference :

5.1.1 ACUTE ORAL TOXICITY

Type :
Guideline/Method : OECD #425
Species : rat
Strain : CrI:CD(SD)
Sex : females
Number of animals : 7
Vehicle : Corn oil
Doses : 175, 550, and 2000 mg/kg
LD50 : 1098 mg/kg
Year : 2007
GLP : Yes
Test substance : Cobalt Borate Neodecanoate Complex 68457-13-6 (CAS Number)

The test substance, was supplied by the sponsor. The test substance appeared to be stable under the conditions of the study. No evidence of instability, such as a change in color or physical state, was observed. The density for cobalt borate neodecanoate is reported as 1.32 g/cm³ at 25°C, the water solubility was estimated to be 51.2 mg/L at 20°C, and the equilibrium constant is reported as pKa was 6.41 at 20°C.

Method : OECD Guideline for the Testing of Chemicals
Section 4 (Part 425) (2001)

Method detail : AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Result : The oral LD₅₀ for cobalt borate neodecanoate was 1098 mg/kg for female rats. The approximate 95% confidence interval is 550 to 2000 mg/kg. No clinical signs of toxicity were observed in the rat dosed at 175 mg/kg. All rats dosed at 550 mg/kg or 2000 mg/kg exhibited clinical signs including various staining, wet fur, high carriage, diarrhea, lethargy, ataxia, clear ocular discharge, labored breathing, brown discharge from the vulva, prostrate posture, and/or decreased muscle tone.

Remark : **Supporting data for dissociation products:**
Acid:
The acute oral LD50 of neodecanoic acid in the rat has been reported as 2000 mg/kg or as 2700 – 3450 mg/kg (Appendix B).

For boric acid, the oral LD50 in rats was 550 – 710 mg B/kg bw. For mice, the reported LD50 for boric acid was 603 mg B/kg bw. (Appendix E).

Metal:

For cobalt chloride hexahydrate, the oral LD50 in rats was 766 mg/kg (equivalent to 190 mg Co/kg). Other reported LD50s range from 19.8 to 85.5 mg Co/mg bw in rats. In mice, values of 40.2 and 55.4 mg Co/kg bw were reported (Appendix F).

Reliability : [1] without retrictions
Reference : Cobalt Borate Neodecanoate Complex: Acute Oral Toxicity Study in Rats - Up-and-Down Procedure (2007). Conducted by DuPonts Haskell Laboratories for the Metal Carboxylates Coalition. Study No. 16637

5.1.2 ACUTE INHALATION TOXICITY

Type :
Guideline/method :
Species :
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time :
LC50 :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :

Supporting data for dissociation products:**Acid:**

The acute inhalation LC50 for neodecanoic acid in the rat has been reported as >511 mg/m³ for an exposure period of 6 hours. Other reported data include LC50 values > 3.0 mg/L for rats and mice, and LC50 values of > 73 ppm for rats, mice and guinea pigs. The acute inhalation LC50 for neodecanoic acid chloride in the rat has been reported as approximately 0.40 mg/L for an exposure period of 4 hours. (Appendix B).

In a 6-week inhalation exposure of mice to 72 mg/m³ amorphous elemental boron, no toxic effects were observed. (Appendix E).

Metal:

No acute inhalation toxicity studies were located for cobaltous chloride (Appendix F).

Reliability :
Reference :

5.1.3 ACUTE DERMAL TOXICITY

Type :
Guideline/method :
Species :
Strain :
Sex :
Number of animals :

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Vehicle :
Doses :
LD50 :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : **Supporting data for dissociation products:**
Acid:
The acute dermal LD50 for neodecanoic acid in the rabbit has been reported as >3160 mg/kg. For rats this value was >3640 mg/kg. (Appendix B).
Metal: Increased proliferation of lymphatic cells was seen in rats, mice and guinea pigs dermally exposed to cobalt chloride, with LOAEL values ranging from 9.6 to 14.7 mg Co/kg/day. (Appendix F).
Reliability :
Reference :

5.2.1 SKIN IRRITATION

Type :
Guideline/method :
Species :
Strain :
Sex :
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
Classification :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : **Supporting data for dissociation products:**
Acid:
Neodecanoic acid was found to be non-irritating to skin when tested on the rabbit (Appendix B).
Boric acid was found to be a mild to moderate irritant to the skin of rabbits and guinea pigs (Appendix E).
Metal:
Dermatitis is a common result of dermal exposure to cobalt in humans and is probably caused by an allergic reaction (Appendix F).
Reliability :
Reference :

5.2.2 EYE IRRITATION

Type :

5. Toxicity

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Date July 22, 2008

Guideline/method :
Species :
Strain :
Sex :
Concentration :
Dose :
Exposure time :
Number of animals :
Vehicle :
Classification :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : **Supporting data for dissociation products:**
Acid: Neodecanoic acid was found to cause eye irritation when tested on the rabbit using the Draize test. (Appendix B).
Reliability :
Reference :

5.4 REPEATED DOSE TOXICITY

Type : See Reproduction
Guideline/method :
Species :
Strain :
Sex :
Number of animals :
Route of admin. :
Exposure period :
Frequency of treatment :
Post exposure period :
Doses :
Control group :
NOAEL :
LOAEL :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : **Supporting data for dissociation products:**
Acid:
When administered to rats in their feed for 3 months, the NOAEL for a 30% preparation of neodecanoic acid was 500 ppm. The LOAEL was 1500 ppm and included changes in the renal tubules of both male and female rats. Morphological changes in the thyroid, including hyperplasia, were also seen in male rats at the feeding level of 1500 ppm. Albino rabbits receiving 10 dermal applications of neodecanoic acid over a 14 day period showed no systemic effects, resulting in a NOAEL of 2.26 g/kg. Beagle dogs receiving oral capsules containing neodecanoic acid daily for a period of 13 weeks did not show adverse effects at dosing levels of approximately 30 mg/kg and below. Effects on body weight and declines in hematocrit, hemoglobin and erythrocyte values were seen at doses of 94.8 mg/kg and above.

(Appendix B).

In a subchronic (13-16 week) feeding study of boric acid to mice, the NOAEL was at or below 34 mg B/kg-day for males and 47 mg/kg-day for females; the LOAEL was 34 mg B/kg-day. This was based upon the observation of minimal to mild extramedullary hematopoiesis of the spleen in all dosed groups. A 90-day feeding study with rats found testicular atrophy at doses of 26.3 mg B/kg-day and above, identifying this value as the LOAEL and 8.8 mg B/kg-day as the NOAEL for systemic toxicity in rats. In 90-day dietary exposures in beagle dogs the NOAEL was identified as 3.9 mg B/kg-day for males and 2.5 mg B/kg-day for females (Appendix E).

Metal:

Repeated oral dosing of rats with cobalt chloride hexahydrate for 8 weeks indicated the NOAEL was 0.6 mg Co/kg and the LOAEL was 2.5 mg Co/kg, based upon changes in hemoglobin content and numbers of erythrocytes. Another study reported oral doses of 0.5 and 2.5 mg Co/kg for 7 months stimulated hematopoiesis and decreased immunological reactivity in rats, while doses of 0.05 mg Co/kg had no effects. (Appendix F).

Reliability :
Reference :

5.5 GENETIC TOXICITY 'IN VITRO'

Type :
Guideline/method : OECD #473
System of testing :
Species : Chinese Hamster Ovary Cells
Strain : CHO-K1 cell line.
Test concentrations :
Cytotoxic concentr. : 100 ug/mL in the 4 h and 30 ug/mL in the 20 h
Metabolic activation : Yes
Year : 2007
GLP : Yes
Test substance : Neodecanoic Acid, Cobalt Salt, (CAS Number 27253-31-2)

Method : OECD 473
Method detail :
Result :

Under the conditions of this study, cobalt borate neodecanoate was found to induce structural chromosome aberrations in the in vitro mammalian chromosome aberration test in Chinese hamster ovary cells in both the non-activated and S9 activated test systems. It was not found to induce numerical chromosome aberrations in any test condition. It was concluded that the test substance was positive in this in vitro test. The concentrations chosen for the chromosome aberration assay were 5, 10, 25, 50, and 100 µg/mL for all three test conditions. The osmolality of the highest test substance concentration in medium was similar to the vehicle control. The pH of the highest test substance concentration in medium was also similar to the vehicle control and did not change throughout Cobalt Borate Neodecanoate Complex: In Vitro Mammalian Chromosome Aberration Test in Chinese Hamster Ovary Cells DuPont-20901the test. No visible precipitate was observed in the treatment medium at the beginning or end of the treatment period at any

concentration tested. Substantial toxicity (greater than a 50% reduction in cell growth relative to the vehicle control) was observed at concentrations ≥ 50 $\mu\text{g}/\text{mL}$ in the 20-hour non-activated test condition (55.2% reduction at 50 $\mu\text{g}/\text{mL}$). In the 4-hour non-activated and activated test conditions, there was a depression in growth of 42.9% and 49.4%, respectively at the highest dose level tested, 100 $\mu\text{g}/\text{mL}$. Additionally, there was a reduction in mitotic index at this dose level of 75.5% for the 4-hour non-activated test condition and 63.2% for the 4-hour activated test condition. Although the reduction in growth was less than 50% in these two test conditions, this dose level was the highest dose level scored for chromosomal aberrations since the reduction in mitotic index was so significant. Selection of doses for microscopic analysis was therefore based on these dose concentration levels.

Cytogenetic evaluations were conducted at 25, 50, and 100 $\mu\text{g}/\text{mL}$ for the 4-hour non-activated and 4-hour S9-activated test conditions and at 5, 10, and 25 $\mu\text{g}/\text{mL}$ for the 20-hour non-activated test condition. These concentrations were chosen based on the scorability of the slides (i.e., metaphase quality, chromosome morphology, and a sufficient amount of metaphases present). The percentage of cells with structural aberrations in the 4-hour non-activated and 4-hour S9 activated test substance-treated groups was significantly increased above that of the vehicle control at 50 and 100 $\mu\text{g}/\text{mL}$ ($p < 0.05$, Fisher's exact test and Cochran-Armitage trend test). The percentage of cells with structural aberrations in the 20-hour non-activated test substance-treated group was significantly increased above that of the vehicle control at 10 and 25 $\mu\text{g}/\text{mL}$ ($p < 0.05$, Fisher's exact test and Cochran-Armitage trend test). These observed changes were dose-dependent, outside the historical control range of 0-5% (non-activated) and 0-6% (S9-activated) for structural aberrations, and are considered biologically significant.

Remark**: Supporting data for dissociation products:****Acid:**

Neodecanoic acid produced negative results in the Ames *Salmonella* assay (OECD Method 471) against four strains of bacteria when tested without metabolic activation at levels up to 1500 $\mu\text{g}/\text{plate}$ and without activation at levels up to 1000 $\mu\text{g}/\text{plate}$. Neodecanoic acid produced negative results in a cytogenetic assay (OECD Method 473) with cultured human lymphocytes when tested both with and without metabolic activation at levels up to 800 $\mu\text{g}/\text{ml}$. (Appendix B).

Results of most short-term mutagenicity studies indicate that boron is not genotoxic. In two different studies, encompassing a total of four bacterial strains, boric acid was negative for mutagenicity in the *Salmonella* assay in both the presence and absence of metabolic activation. In the streptomycin-dependent *E. coli* Sd-4 assay, boric acid was either not mutagenic or produced equivocal results. An isolated positive result for induction of β -galactosidase synthesis was found in *E. coli* PQ37 using the SOS chromotest. Chromosomal aberrations and sister chromatid exchanges did not occur in Chinese hamster ovary cells exposed to boric acid, either with

or without activation, and negative results were obtained in mouse lymphoma cell cultures (with and without activation) as well. (Appendix E).

Metal:

Cobalt compounds with a valence state of II, the form of cobalt released by dissociation of cobalt chloride, are generally non-mutagenic in bacterial assays, including plate incorporation and fluctuation assays with *Salmonella typhimurium* TA strains and *Escherichia coli* WP2. However, a weak positive mutagenic response has been found in the rec assay with *Bacillus subtilis* and in Chinese hamster V9 cells. DNA damage in isolated human lymphocytes was observed at 6.0 mg Co/L in the alkaline comet assay, and an increase in sister chromatid exchanges has been observed in human lymphocytes and macrophages (Appendix F).

Reliability : [1] without restrictions
Reference : Cobalt Borate Neodecanoate Complex: In Vitro Mammalian Chromosome Aberration Test in Chinese Hamster Ovary Cells (2007). Conducted by DuPonts Haskell Laboratories for the Metal Carboxylates Coalition. Study No. 16637

5.6 GENETIC TOXICITY 'IN VIVO'

Type : See Reproduction
Guideline/method :
Species :
Strain :
Sex :
Route of admin. :
Exposure period :
Doses :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :

Supporting data for dissociation products:**Acid:**

In the mouse micronucleus test, boric acid did not induce chromosomal or mitotic spindle abnormalities in bone marrow erythrocytes. (Appendix E).

Metal:

Oral administration of cobalt chloride hexahydrate to mice (20 – 80 mg.kg bw) produced a concentration-dependent increase in chromosomal aberrations. A dose-dependent increase in the incidence of micronucleated polychromatic erythrocytes was observed in mice subsequent to i.p. injection of CoCl₂.6H₂O, at doses of 25 – 90 mg Co/kg bw. Increased micronucleus formation was observed following i.p. injection of 12.4 and 22.3 mg Co/kg (as cobalt chloride), but not after injection of 6.19 mg Co/kg (NOEL). (Appendix F).

Remark :
Reliability :
Reference :

5.8.2 DEVELOPMENTAL TOXICITY

5. Toxicity

ID 68457-13-6

Date July 22, 2008

Type :
Guideline/method :
Species :
Strain :
Sex :
Route of admin. :
Exposure period :
Frequency of treatment :
Duration of test :
Doses :
Control group :
NOAEL maternal tox. :
NOAEL teratogen. :
Other :
Other :
Other :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :

Supporting data for dissociation products:

Acid:

The developmental toxicity of boron has been studied in rats, mice and rabbits. Dietary exposure in rats from gd 6-15 identified a NOAEL of 9.6 mg B/kg-day and a LOAEL of 13.3 mg B/kg-day based upon reduced body weight and skeletal malformations/variations in offspring, as observed at 20 days of gestation. When this study was continued to postnatal day 21, these effects were less severe, resulting in a NOAEL of 12.9 mg B/kg-day and a LOAEL of 25.3 mg B/kg-day, respectively. In another developmental toxicity study with rats exposed to boric acid in the diet, a LOAEL of 13.6 mg B/kg-day was identified based upon fetal body weight. Mice exposed to boric acid in the diet from gd 0 – 17 produced offspring with malformations and variations, with a NOAEL of 43.4 mg B/kg-day. Mortality and malformations were observed in rabbits exposed to boric acid from gd 6 – 19, with a NOAEL of 21.9 mg B/kg-day and LOAEL of 43.7 mg B/kg-day. (Appendix E).

Metal:

In a developmental toxicity study with cobalt chloride exposure (5.4 to 21.8 mg Co/kg/day) in rats from gestation day 14 to lactation day 21 the LOAEL was based on stunted pup growth. However, maternal toxicity was observed in conjunction with effects on the offspring. This growth effect was considered to be a secondary or indirect effect rather than a direct effect of cobalt on the fetus. No teratogenic effects were observed. Another study in rats provided a NOAEL of 24.8 mg Co/kg/day for cobalt chloride exposure from gestation days 6-15. No effects were observed on fetal growth or survival in mice exposed to 81.7 mg Co/kg/day as cobalt chloride during gestation days 8-12 (Appendix F).

Remark :
Reliability :
Reference :

5.8.3 TOXICITY TO REPRODUCTION

Type	:	Combined Repeated Dose Toxicity Study with Reproduction/Developmental Screening Test in Rats
Guideline/method	:	OECD 422
In vitro/in vivo	:	In vivo
Species	:	Rat
Strain	:	CrI:CD(SD)
Sex	:	M/F
Route of admin.	:	Oral gavage
Exposure period	:	42 days
Frequency of treatment	:	daily
Duration of test	:	56 days
Doses	:	0, 5, 15, 40 (males only) and 100 (Females only) mg/kg/day
Control group	:	yes
Year	:	2007
GLP	:	yes
Test substance	:	Cobalt stearate
Method	:	OECD 422
Method detail	:	A combined repeated dose toxicity study with reproduction/developmental toxicity screening test was conducted with Cobalt Borate Neodecanoate. CrI:CD(SD) rats (12/sex/dose level) were dosed with Cobalt Borate Neodecanoate in Mazola® corn oil (5 mL/kg) once daily by gavage at dose levels of 0, 0.5, 1.5, or 5.0 mg/kg/day. Following a 2-week pre-mating period, P ₁ males and females were co-housed for up to 2 weeks within their respective treatment groups to produce F ₁ litters. Dams were allowed to deliver and rear their offspring until postpartum day 4. Careful clinical observations were recorded once daily during dosing; detailed clinical observations were recorded once during pretest and weekly thereafter. Body weights and food consumption were recorded weekly for P ₁ males and females (pre-mating), on days 0, 7, 14, and 21 of gestation and on days 0 and 4 of lactation; food consumption was not measured during cohabitation or thereafter for males, or for females with no evidence of copulation. An abbreviated neurobehavioral evaluation consisting of a functional observational battery and motor activity was conducted in P ₁ rats (12/sex/group) once during pretest and on test days 12 or 13 (prior to cohabitation). Clinical pathology parameters were measured in P ₁ rats (5/sex/group) at the end of the pre-mating period (hematology, clinical chemistry) and at terminal sacrifice (coagulation). F ₁ litter examinations (pup viability, individual pup weights, clinical observations) were performed at birth and on lactation day 4.

All P₁ rats were given a gross pathological examination on test days 33-34 (males), postpartum day 4 (lactating females), and 22 days after the end of cohabitation for females that did not deliver a litter. The following tissues were weighed from all adult rats: liver, kidneys, adrenal glands, thymus, brain, spleen and heart. The following tissues were weighed from all males: testes, epididymides, prostate and seminal vesicles (with coagulating glands and their fluids). The following tissues were weighed from all females: Uterus (with cervix) and ovaries (with oviducts). Organ weight ratios (% final body weight, % brain weight) and group mean values were calculated. Small and large intestines, stomach, bladder, lungs, trachea, heart, spleen, thymus, lymph nodes, bone marrow, thyroid, adrenals, brain, kidneys, liver, spinal cord, sciatic nerve, and sternum were saved from all P₁ rats. Gross observations and reproductive organs were also saved from all P₁ rats. Uterine implantation sites and ovarian *corpora lutea* were counted

in P₁ females. A histological examination of reproductive organs was conducted for all animals in the control and 5.0 mg/kg/day group. Histologic examination of all other tissues saved was conducted for 5/sex/group in the high-dose and control groups. Examination of tissues from the remaining groups was limited to relevant gross lesions.

Result

: There was a compound related effect at the high dose level (5.0 mg/kg/day):

- The sex ratio of F₁ litters was significantly increased at the high dose level, but this was not considered an adverse effect.

There were no other effects considered to be related to treatment on the following parameters at any dose level:

- Mortality and clinical signs of toxicity in P₁ males and females
- Body weight, body weight gain, food consumption and food efficiency in P₁ males and females during pre-mating, post-cohabitation, gestation or lactation
- Abbreviated functional observational battery or motor activity in P₁ males and females
- Hematology, coagulation, and clinical chemistry parameters in P₁ males and females
- Mating, fertility, gestation length, numbers of *corpora lutea*, number of implantation sites, and implantation efficiency in the P₁ generation
- Number of pups born, born alive, alive on day 4, sex ratio, and survival indices during the lactation period in F₁ litters
- Clinical observations and mean pup weights on days 0-4 of lactation in F₁ litters
- Gross pathology and organ weights in P₁ males and females
- Microscopic pathology in P₁ males and females

Under the conditions of this study, the no-observed-effect level (NOEL)² for systemic and reproductive toxicity was considered 5.0 mg/kg/day; the highest level tested.

² The NOEL for this study is defined as the highest dose at which toxicologically important effects attributable to the test substance were not detected. Thus, for this study, the NOEL is equivalent to the NOEL as defined by the United States Environmental Protection Agency (1985) and to the no-observed-adverse-effect level (NOAEL) as defined by the European Union (1994).

Remark : **Supporting data for dissociation studies:**
Acid: In an oral (feeding) multi-generation rat reproduction study with neodecanoic acid, no adverse effects were observed in the parental generation or the F₁ and F₂ generations at feeding levels up to 1500 ppm in the diet. (Appendix B).

The reproductive toxicity of boric acid was studied in mice using a continuous breeding protocol. The lowest dose, 1000 ppm, decreased sperm motility in F₀ males, marginally decreased epididymal sperm concentration in F₁ males, increased uterine and kidney/adrenal weights and shortened estrous cycles in F₁ females, and reduced litter-adjusted birth weights in F₂ pups. Thus, the LOAEL was 1000 ppm (26.6 mg B/kg-day for males and 31.8 mg B/kg-day for females). In a multi-generation study with rats, a NOAEL of 17.5 mg B/kg-day and LOAEL of 58.5 mg B/kg-day were identified based upon sterility of males and decreased ovulation in females. (Appendix E).

Metal:

Cobalt exposure (as cobalt chloride hexahydrate in drinking water for 12 -13 weeks) affected male reproductive parameters for mice in a time- and dose-dependent manner. All dose levels (23.0 – 72.1 mg Co/kg-day) caused decreases in testicular weight and epididymal sperm concentration. Testicular degeneration and atrophy have been reported in rats exposed to 13.2 to 30.2 mg Co/kg/day as cobalt chloride for 2-3 months in the diet or drinking water. (Appendix F).

Reliability : [1] Without restriction
Reference :

6.0 OTHER INFORMATION**6.1 Carcinogenicity****Supporting data for dissociation products:****Acid:**

The U.S. National Toxicology Program (NTP) concluded from a 2-year dietary study in mice that boric acid produced no evidence of carcinogenicity, although the low number of surviving males may have reduced the sensitivity of the study. Based upon a 2-year dietary study in rats, the NTP concluded that there were adequate data to conclude that boric acid was not carcinogenic in rats. (Appendix E).

Metal:

The US National Toxicology Program does not recognize cobalt as a human carcinogen, but IARC has classified cobalt and cobalt compounds as possibly carcinogenic to humans (Class 2B) based on sufficient evidence that cobalt metal powder and cobaltous oxide are carcinogenic in animals. "No studies were located regarding carcinogenic effects in animals after oral exposure to stable [non-radioactive] cobalt." (ATSDR Sept 2001 Draft; see Appendix F).

6.2 Skin Sensitization**Supporting data for dissociation products:**

Acid: Neodecanoic acid was not found to be sensitizing when tested on the guinea pig using the Magnusson and Kligman maximization test. (Appendix B).

1. General Information

ID 7646-79-9
Date January 31, 2005

201-16738E

1.0 SUBSTANCE INFORMATION

Generic Name : Cobalt chloride
Chemical Name : Cobaltous chloride
CAS Registry No. : 7646-79-9
Component CAS Nos. :
EINECS No. :
Structural Formula : CoCl_2
Molecular Weight : 129.84
Synonyms and Tradenames : Cobalt(II) chloride; Cobalt dichloride
References : ATSDR, 2001. Draft Toxicological Profile for Cobalt, U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry (ATSDR), September 2001. (This reference is subsequently listed in this document as ATSDR Sept 2001 Draft).

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2. Physico-Chemical Data

ID 7646-79-9

Date January 31, 2005

2.1 MELTING POINT

Type :
Guideline/method :
Value : 735 °C
Decomposition : at °C
Sublimation :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : Decomposes at 400 °C on long heating in air
Reliability : 2 (reliable with restrictions): Source is well established data compendium.
Reference : O'Neil, M.J., Smith, A., Heckelman, P.E., and J.R. Obenchain (eds.). 2002.
The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals.
13th Ed. Merck & Co., Inc., Whitehouse Station, NJ

2.2 BOILING POINT

Type :
Guideline/method :
Value : 1,049 °C
Decomposition :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability : 2 (reliable with restrictions): Source is well established data compendium.
Reference : O'Neil, M.J., Smith, A., Heckelman, P.E., and J.R. Obenchain (eds.). 2002.
The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals.
13th Ed. Merck & Co., Inc., Whitehouse Station, NJ

2.3 DENSITY

Type :
Guideline/method :
Value : 3.367 at 25 °C
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability : 2 (reliable with restrictions): Source is well established data compendium.
Reference : O'Neil, M.J., Smith, A., Heckelman, P.E., and J.R. Obenchain (eds.). 2002.
The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals.
13th Ed. Merck & Co., Inc., Whitehouse Station, NJ

2. Physico-Chemical Data

ID 7646-79-9

Date January 31, 2005

2.4 VAPOR PRESSURE

Type :
Guideline/method :
Value : hPa at °C
Decomposition :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

2.5 PARTITION COEFFICIENT

Type :
Guideline/method :
Partition coefficient :
Log Pow : at °C
pH value :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : Not applicable – metal dissociates (ionizes) in water
Reliability :
Reference :

2.6.1 SOLUBILITY IN WATER

Type :
Guideline/method :
Value : 450 g/L at 7 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
PKa : at °C
Description :
Stable :
Deg. product :
Year :
GLP :
Test substance :
Deg. products CAS# :
Method :
Method detail :
Result :
Remark : 544 g/L in ethanol; 86 g/L in acetone
Reliability : 2 (reliable with restrictions): Source is well established data compendium
Reference : Weast. R.C. (ed.). 1988-1989. Handbook of Chemistry and Physics. 69th Ed. CRC Press Inc., Boca Raton, FL., p. B-86.

2. Physico-Chemical Data

ID 7646-79-9

Date January 31, 2005

2.7 FLASH POINT

Type	:	
Guideline/method	:	
Value	:	°C
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	
Reliability	:	
Reference	:	

3. Environmental Fate & Transport

ID 7646-79-9

Date January 31, 2005

Method detail :
Result :
Remark :
Reliability :
Reference :

3.5 BIODEGRADATION

Type :
Guideline/method :
Inoculum :
Concentration : related to
related to
Contact time :
Degradation : (±) % after day(s)
Result :
Kinetic of test subst. : % (specify time and % degradation)
%
%
%
%
%
Control substance :
Kinetic : %
%
Deg. product :
Year :
GLP :
Test substance :
Deg. products CAS# :
Method :
Method detail :
Result :
Remark : Not applicable – the metal will not degrade
Reliability :
Reference :

3.7 BIOCONCENTRATION

Type :
Guideline/method :
Species :
Exposure period : at °C
Concentration :
BCF :
Elimination :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

4. Ecotoxicity

ID 7646-79-9

Date January 31, 2005

4.1 ACUTE TOXICITY TO FISH

Type	: Acute
Guideline/method	: Flow-through, freshwater
Species	: Rainbow trout (<i>Onchorhynchus mykiss</i>)
Exposure period	: 96 hr
NOEC	:
LC0	:
LC50	: 1.41 mg Co/L (95% C.I. = 0.57 – 3.47 mg Co/L)
LC100	:
Other	: LC20 = 0.53 mg Co/L (95% C.I. = 0.24 – 1.20 mg Co/L)
Other	: Incipient lethal level for 50% mortality (time independent) = 0.35 mg Co/L
Other	: 144-hr LC50 = 0.52 mg Co/L (95% C.I. = 0.29 – 0.95 mg Co/L)
Limit test	:
Analytical monitoring	: Yes (results based on measured concentrations)
Year	: 1998
GLP	: No
Test substance	: Cobalt chloride dihydrate (CoCl ₂ ·2H ₂ O)
Method	:
Method detail	: Tests were conducted with trout fry in water with an alkalinity and hardness of approximately 25 mg CaCO ₃ /L. Exposure concentrations ranged from 0.125 to 2.0 mg Co/L. Exposures were continued for up to 14 days, with mortality assessed every 2 hr for the first 48 hr, and every 6 h thereafter.
Result	: The onset of mortality was slow (48 hr or greater), generally not reaching a plateau for 200 hr or more.
Remark	: Study data indicate that the rainbow trout is highly sensitive to the toxic effects of cobalt. For comparison, reported 96-h LC50 values for other fish species include 22.0 mg Co/L for the fathead minnow (<i>Pimephales promelas</i>), 333 mg Co/L for the carp (<i>Cyprinus carpio</i>), and 275 mg Co/L for the mummichog (<i>Fundulus heteroclitus</i>) (U.S. EPA, ECOTOX data base, 2003). Available data suggest that toxicity to fish is reduced with increasing hardness up to a hardness of approximately 400 mg CaCO ₃ /L (Diamond, J. et al., 1992. Aquat. Toxicol., 22:163-180).
Reliability	: 2 (Reliable with restrictions): comparable to guideline study
Reference	: Marr, J.C.A., J.A. Hansen, J.S. Meyer, D. Cacela, T. Podrabsky, J. Lipton, and H.L. Bergman. 1998. Toxicity of cobalt and copper to rainbow trout: application of a mechanistic model for predicting survival. Aquat. Toxicol., 43(4):225-238.

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	: Acute
Guideline/method	: Static, freshwater
Species	: <i>Daphnia magna</i> (water flea)
Exposure period	: 48 hr
NOEC	:
EC0	:
EC50	: 1.52 mg Co/L (95% C.I. = 1.01 - 2.28 mg Co/L)
EC100	:
Other	: 24 hr LC50 = 2.11 mg Co/L (95% C.I. = 1.49 - 3.05 mg Co/L)
Other	:
Other	:
Limit test	:
Analytical monitoring	: No
Year	: 1987
GLP	: No
Test substance	: Cobalt chloride hexahydrate (CoCl ₂ ·6H ₂ O)

4. Ecotoxicity

ID 7646-79-9

Date January 31, 2005

Method	:	American Public Health Association (APHA), 1976, Standard Methods for the Examination of Water and Wastewater.
Method detail	:	Tests were conducted in well water with a total hardness of 240 mg CaCO ₃ /L and a total alkalinity of 400 mg CaCO ₃ /L. Solutions were not renewed during the test. Daphnids were not fed during the test.
Result	:	
Remark	:	In an older study, the 48-hr LC50 for <i>Daphnia magna</i> has been reported as 5.5 mg Co/L (Cabejszek and Stasiak, 1960 as cited in the U.S. EPA ECOTOX database, 2003). The 48-hr LC50 for another daphnid, <i>Daphnia hyaline</i> , has been reported as 1.52 mg Co/L (Baudouin and Scoppa, 1974 as cited in the U.S. EPA ECOTOX database, 2003). Others have found 48-hr LC50 values for <i>Ceriodaphnia dubia</i> of 2.35, 4.60, and 4.20 mg Co/L for tests conducted with water hardness of 50, 200, and 400 mg CaCO ₃ /L, respectively (Diamond, J. et al., 1992. Aquat. Toxicol., 22:163-180).
Reliability	:	2 (Reliable with restrictions): comparable to guideline study
Reference	:	Khangarot, B.S., P.K. Ray, and H. Chandra. 1987. <i>Daphnia magna</i> as a model to assess heavy metal toxicity: comparative assessment with mouse system. Acta. Hydrochim. Hydrobiol., 15(4): 427-432.

4.3 TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

Type	:	Algal growth assay
Guideline/method	:	Static, freshwater
Species	:	<i>Chlorella vulgaris</i> (green algae)
Endpoint	:	Population growth
Exposure period	:	96 hr
NOEC	:	
LOEC	:	
EC0	:	
EC10	:	
EC50	:	0.52 mg Co/L (95% C.I. = 0.48 – 0.56 mg Co/L)
Other	:	
Other	:	
Other	:	
Limit test	:	
Analytical monitoring	:	No
Year	:	1993
GLP	:	
Test substance	:	Cobalt chloride
Method	:	
Method detail	:	Tests conducted in modified Bristol's medium (pH 6.5) with a 16:8 day/night photoperiod (280 foot candles). Cultures were incubated at 19°C ± 1°C. Results were based on experiments run in triplicate.
Result	:	Growth was 63.8% and 28.4% of controls at concentrations of 0.32 and 1.00 mg Co/L, respectively.
Remark	:	Other aquatic plants are much less sensitive to cobalt. The reported 96-h EC50 for <i>Spirulina platensis</i> (blue-green algae) is 23.8 mg Co/L (Sharma et al., 1987 as cited in the U.S. EPA ECOTOX database, 2003). The 7-d IC50 for <i>Lemna minor</i> (duckweed) is 16.9 mg Co/L (Dirilgen and Inel, 1994 as cited in the U.S. EPA ECOTOX database, 2003).
Reliability	:	2 (reliable with restrictions); comparable to guideline study
Reference	:	Rachlin, J.W. and A. Grosso. 1993. The growth response of the green alga <i>Chlorella vulgaris</i> to combined divalent cation exposure. Arch. Environ. Contam. Toxicol., 24: 16-20.

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In vitro/in vivo	:	
Type	:	
Guideline/method	:	
Species	:	
Number of animals	:	
Males	:	
Females	:	
Doses	:	
Males	:	
Females	:	
Vehicle	:	
Route of administration	:	
Exposure time	:	
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1 st . 2 nd . 3 rd .
Toxic behavior	:	
Deg. product	:	
Deg. products CAS#	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	Absorption of cobalt in the digestive tract is influenced by the chemical form of the metal, with increasing solubility resulting in increasing absorption (ATSDR Sept 2001 Draft). Approximately 13-34% of cobalt chloride, a soluble form, is absorbed in the gut of rats, but absorption in the gut may be increased in iron deficient individuals. Following oral exposure, cobalt is eliminated primarily in feces and secondarily in urine. For the more soluble forms of cobalt, e.g., cobalt chloride, 70 – 80% of the administered dose is eliminated in the feces. For absorbed cobalt, elimination is rapid primarily in the urine (Barceloux, D.G. 1999. Cobalt. Clin. Tox. 37:201-206). Elimination is biphasic or triphasic. The terminal phase involves a very small residual level of cobalt and has a half-life in years (ATSDR Sept 2001 Draft).
Reliability	:	
Reference	:	

5.1.1 ACUTE ORAL TOXICITY

Type	:	Oral
Guideline/Method	:	Not specified
Species	:	Rat
Strain	:	Wistar
Sex	:	Male and female
Number of animals	:	5 per sex per dose level
Vehicle	:	Distilled water
Doses	:	50, 600, 720, 864, and 1137 mg/kg

5. Toxicity

ID 7646-79-9

Date January 31, 2005

LD50 : 766 mg/kg as compound (hexahydrate); 95% C.I. = 677 – 867 mg/kg)
190 mg/kg as cobalt

Year : 1982

GLP : No

Test substance : Cobalt(II) chloride hexahydrate (CoCl₂·6H₂O)

Method : Single dose administered by gastric incubation

Method detail : Mortality assessed after a 10-d observation period.

Result :

Remark : Reported LD50s of cobalt chloride to rats range from 42.4 to 190 mg Co/mg bw (ATSDR Sept 2001 Draft). Toxicity of cobalt sulfate is reported to be similar to that of the chloride with oral LD50s for rats ranging from 123 to 161 mg Co/kg bw (ATSDR Sept 2001 Draft). For the mouse, LD50 values are 89.3 and 123 mg Co/kg for cobalt chloride and cobalt sulfate, respectively, which are equivalent to 40.2 and 46.7 mg Co/kg b.w. when expressed as the metal only (ATSDR Sept 2001 Draft).

Reliability : 2 (Reliable with restrictions): comparable to guideline study with adequate documentation.

Reference : Speijers, G.J.A., E.I. Krajnc, J.M. Berkvens, and M.J. van Logten. 1982. Acute oral toxicity of inorganic cobalt compounds in rats. Food Chem. Toxicol., 20:311-314.

5.1.2 ACUTE INHALATION TOXICITY

Type :

Guideline/method :

Species :

Strain :

Sex :

Number of animals :

Vehicle :

Doses :

Exposure time :

LC50 :

Year :

GLP :

Test substance :

Method :

Method detail :

Result :

Remark : No acute toxicity studies have been located for this compound.

Reliability :

Reference :

5.1.3 ACUTE DERMAL TOXICITY

Type :

Guideline/method :

Species :

Strain :

Sex :

Number of animals :

Vehicle :

Doses :

LD50 :

Year :

GLP :

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Test substance :
Method :
Method detail :
Result :
Remark : Increased proliferation of lymphatic cells was seen in rats, mice and guinea pigs dermally exposed to cobalt chloride in DMSO once per day for 3 consecutive days, with LOAEL values ranging from 9.6 to 14.7 mg Co/kg/day (Ikarashi, Y., et al., 1992. Toxicology, 76:283-292). Stimulation indices of 3 or greater (indicative of a significant response by the authors), were reported for mice exposed to 1, 2.5 or 5% CoCl₂ (equivalent to 10.8, 27, or 54.1 mg Co/kg/day), rats exposed to 2.5 or 5% CoCl₂ (equivalent to 9.6 or 19.2 mg Co/kg/day), and guinea pigs exposed to 5% CoCl₂ (equivalent to 14.7 mg Co/kg/day).
Reliability :
Reference :

5.2.1 SKIN IRRITATION

Type :
Guideline/method :
Species :
Strain :
Sex :
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
Classification :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : Dermatitis is a common result of dermal exposure to cobalt in humans and has been verified in a large number of studies (ATSDR Sept 2001 Draft). The dermatitis is probably caused by an allergic reaction to cobalt.
Reliability :
Reference :

5.2.2 EYE IRRITATION

Type :
Guideline/method :
Species :
Strain :
Sex :
Concentration :
Dose :
Exposure time :
Number of animals :
Vehicle :
Classification :
Year :
GLP :
Test substance :

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Method :
Method detail :
Result :
Remark :
Reliability :
Reference :

5.4 REPEATED DOSE TOXICITY

Type : Repeated dose
Guideline/method : Oral
Species : Rat
Strain : Not specified
Sex : Male
Number of animals : 30
Route of admin. : Oral via stomach tube
Exposure period : 150 to 210 days
Frequency of treatment : Five days per week
Post exposure period : 0 to 30 days
Doses : 4 or 10 mg Co/kg
Control group : Yes
NOAEL :
LOAEL : 4 mg Co/kg (organ weights increased)
Other :
Year : 1959
GLP : No
Test substance : Cobalt chloride
Method :
Method detail : The erythrocyte count, hemoglobin and hematocrit determinations were performed at frequent intervals for animals receiving 10 mg Co/kg. At study termination, all rats were sacrificed, organs examined and weighed, and sections made histological examination.
Result : The average weights of kidneys, livers, and spleens of the cobalt-treated groups were slightly heavier than the controls. Cobalt exposure at 10 mg/kg produced significant polycythemia. Histological examination of the kidneys revealed necrosis of the linings of the tubules of the tubules in rats treated with 10 mg Co/kg, but not in those of the 4 mg Co/kg group. The effects was reversible, however, as examination of kidneys of rats autopsied 30 days after cobalt administration was discontinued showed no necrosis and were normal compared to the kidneys from control rats.
Remark : Results are highly consistent with those reported by others. Repeated oral dosing of rats with cobalt chloride at levels ranging from 0.5 to 30.2 mg Co/kg/day (as cobalt chloride) for periods ranging from 12-16 days up to 7 months resulted in the following observations associated with LOAELs: reduced weight gain, increases in some organ weights (heart, liver and lungs); increased hematocrit, hemoglobin, and red blood cells; renal tubular necrosis; and various changes on cardiac physiology (left ventricular hypertrophy, impaired ventricular function, and degeneration of myofibrils) (ATSDR Sept 2001 Draft). Cardiac effects were observed in rats at LOAEL's ranging from 8.4 to 12.4 mg Co/kg/day, for cobalt sulfate or cobalt chloride, with exposure periods of 3 weeks to 6 months (ATSDR Sept 2001 Draft).
Reliability : 2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
Reference : Murdock, H.R. 1959. Studies on the pharmacology of cobalt chloride. J. Amer. Pharm. Assoc., 48:140-142.

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Type	:	Repeated dose
Guideline/method	:	Not specified
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	Male
Number of animals	:	4
Route of admin.	:	Oral
Exposure period	:	8 weeks
Frequency of treatment	:	Daily
Post exposure period	:	None
Doses	:	2.5, 10, or 40 mg/kg (equivalent to 0.6, 2.5, or 10 mg Co/kg)
Control group	:	Yes
NOAEL	:	0.6 mg Co/kg
LOAEL	:	2.5 mg Co/kg (hemoglobin, red blood cell count)
Other	:	
Year	:	1947
GLP	:	No
Test substance	:	Cobalt chloride hexahydrate (CoCl ₂ ·6H ₂ O)
Method	:	
Method detail	:	Cobalt was administered orally in a gelatin capsule (mixed in equal part of wheat flour and powdered sugar). Blood counts and hemoglobin determinations were made at the start of the test and at two week intervals.
Result	:	Hemoglobin content and numbers of erythrocytes were increased in rats receiving either 2.5 or 10 mg Co/kg/day, but not in those receiving 0.6 mg Co/kg/day.
Remarks	:	Other researchers have reported similar results in long-term studies with rats although many study details are lacking in the published report (Krasovskii, G.N. and S.A. Fridlyand. 1971. Hyg. Sanit., 26:277-279). They found that oral doses of 0.5 and 2.5 mg Co/kg six days per week for seven months stimulated hemopoiesis and decreased immunological reactivity (reduced the phagocytic index). Daily doses of 0.5 mg Co/kg and greater also produced mild to moderate increases in conditioned flexes. However, daily doses of 0.05 mg Co/kg had no effects on the indices investigated. Others have also reported the neurotoxic and behavior effects of cobalt on rats after chronic dietary exposures (Nation, J.R. et al., 1983. Neurobehav. Toxicol. Teratol., 5:9-15).
Reliability	:	2 (reliable with restrictions): Documentation was incomplete; however, the results are highly consistent with others in the scientific literature.
Reference	:	Stanley, A.J., H.C. Hopps, and A.M. Shideler. 1947. Cobalt polycythemia. II. Relative effects of oral and subcutaneous administration of cobaltous chloride. Proc. Soc. Exp. Biol. Med., 66:19-20.

5.5 GENETIC TOXICITY - MUTAGENICITY

Type	:	Mutagenicity
Guideline/method	:	Ames Assay
System of testing	:	Bacteria <i>in vitro</i>
Species	:	<i>Salmonella typhimurium</i> LT2
Strains	:	TA100
Test concentrations	:	10 ⁻⁴ to 10 ⁻¹ M
Cytotoxic concentr.	:	10 ⁻² M
Metabolic activation	:	No
Year	:	1981
GLP	:	No
Test substance	:	Cobalt chloride hexahydrate (CoCl ₂ ·6H ₂ O)
Method	:	Ames, B.N., J. McCann, and E. Yamasaki. 1975. Mutat. Res., 31:347-364.

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Method detail	:	
Result	:	Negative both above and below the cytotoxic concentration
Remark	:	Cobalt compounds with a valence state of II, the form of cobalt released by dissociation of cobalt chloride, are generally nonmutagenic in <i>in vitro</i> bacterial assays (ATSDR Sept 2001 Draft). For example, cobalt chloride was not mutagenic in plate incorporation and fluctuation assays with <i>Salmonella</i> TA strains or a <i>Escherichia coli</i> WP2 strain (Arlauskas, A., et al., 1985. Environ. Res., 36:379-388). However, a weak positive mutagenic response has been found in the rec assay with <i>Bacillus subtilis</i> at a concentration of 0.05 M (Kanematsu, N. et al., 1980. Mutat. Res., 77:109-116). A very weak positive response has also been found in Chinese hamster V79 cells, but only at a highly cytotoxic concentration (Miyaki, M. et al. 1979. Mutat. Res., 68: 259-263).
Reliability	:	2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
Reference	:	Tso, W-W. and W-P Fung. 1981. Mutagenicity of metallic cations. Toxicolog. Lett., 8:195-200.
Type	:	Mutagenicity
Guideline/method	:	Ames Assay
System of testing	:	Bacteria <i>in vitro</i>
Species	:	<i>Salmonella typhimurium</i> LT2
Strains	:	TA98, TA100, TA1537, and TA2637
Test concentrations	:	0.1 to 1,000 µM/plate
Cytotoxic conc.	:	Not specified
Metabolic activation	:	No
Year	:	1986
GLP	:	No
Test substance	:	Cobalt chloride
Method	:	Ames, B.N., J. McCann, and E. Yamasaki. 1975. Mutat. Res., 31:347-364.
Method detail	:	A modified Tris-HCl minimal medium with low phosphate content was used to prevent formation of insoluble metal phosphates in the test system.
Result	:	Negative
Remark	:	Although cobalt chloride alone did not produce mutants in this test system, it was mutagenic when it was added as a mixture with one of several heteroaromatic compounds (e.g., 4-aminoquinoline, 9-aminoacridine). The enhanced mutagenicity was attributed by the authors to the formation of weak to moderate complexes between these chemicals and the Co(II) cation, which may have enhanced transmembrane permeation or intercellular binding.
Reliability	:	2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
Reference	:	Ogawa, H.I., K. Sakata, T. Inouye, S. Jyosui, Y. Niyitani, K. Kamimoto, M. Morishita, S. Tsuruta, and Y. Kato. 1986. Combined mutagenicity of cobalt(II) salt and heteroaromatic compounds in <i>Salmonella typhimurium</i> . Mutat. Res., 172: 97-104.

5.6 GENETIC TOXICITY - CLASTOGENICITY

Type	:	Chromosomal aberrations in bone marrow cells
Guideline/method	:	<i>In vivo</i>
Species	:	Mouse (<i>Mus musculus</i>)
Strain	:	Swiss albino
Sex	:	Male
Route of admin.	:	Oral (single dose)
Exposure period	:	6, 12, 18, or 24 hr.
Dose	:	20, 40 , or 80 mg/kg b.w.
Year	:	1991
GLP	:	No
Test substance	:	Cobalt chloride hexahydrate (CoCl ₂ ·6H ₂ O)
Method	:	Preston, R.J. et al., 1987. <i>Mutat. Res.</i> , 189:157.
Method detail	:	Test compound was administered orally to five animals per dose group. Mice were 6-8 weeks old at that time. Colchicine (0.04%) was injected i.p. at 90 min prior to sacrifice. Bone marrow cells were removed from femurs by flushing with 0.8% sodium citrate. From each animal, 50 well-scattered metaphase plate were scored for chromosomal aberrations. Abnormalities were scored separately as total aberrations (with and without gaps) and as breaks per cell.
Result	:	Administration of cobalt chloride produced a concentration-dependent increase in total chromosomal aberrations.
Remark	:	Cobalt compounds, including soluble salts, are observed to be clastogenic (cause chromosomal aberrations) in a range of mammalian assay systems. For example, increased micronucleus formation was observed following i.p. injection of 12.4 and 22.3 mg Co/kg (as cobalt chloride), but not after injection of 6.19 mg Co/kg (NOEL) (ATSDR Sept 2001 Draft). There is evidence that soluble cobalt(II) cations exert a genotoxic activity in vitro and in vivo in experimental systems, but evidence in humans is lacking (Lison, D. et al., 2001. <i>Occup. Environ. Med.</i> , 58: 619-625).
Reliability	:	2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
Reference	:	Palit, S., A. Sharma, and G. Talukder. 1991. Chromosomal aberrations induced by cobaltous chloride in mice in vivo. <i>Biol. Trace Elem. Res.</i> , 29:139-145.
Type	:	Micronucleus Test
Guideline/method	:	<i>In vivo</i>
Species	:	Mouse
Strain	:	BALB/c AnNCRj
Sex	:	Male
Route of admin.	:	Intraperitoneally
Exposure period	:	30 hr
Doses	:	25, 50, or 90 mg Co/kg b.w.
Year	:	1993
GLP	:	No
Test substance	:	Cobalt chloride hexahydrate (CoCl ₂ ·6H ₂ O)
Method	:	Von Ledbur, M. and W. Schmid. 1973. <i>Mutat. Res.</i> , 19:109-117.
Method detail	:	Mice were injected once ip and sacrificed after 30 hr. Bone marrow smears were prepared and stained. The incidence of micronucleated polychromatic erythrocytes (MPCE) was determined in 1,000 cells. In addition, the ratio of polychromatic erythrocytes (P) to normochromatic erythrocytes (N) was determined in 2,000 erythrocytes.
Result	:	Treatment with cobalt induced a dose-dependent increase in the frequency of MPCE. The P/N ratio was significantly reduced (P<0.05) in mice dosed at 90 mg/kg b.w.

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- Remark** : This study also included an *in vitro* micronucleus test with mouse bone marrow cells, both with and without metabolic activation with an S9 fraction. In contrast to the *in vivo* test, the *in vitro* test did not produce any significant changes in frequency of MPCE or the P/N ratio at dose levels of cobalt chloride hexahydrate up to 50 mg/L in the cell suspension.
- Reliability** : 2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
- Reference** : Suzuki, Y., H. Shimizu, Y. Nagae, M. Fukumoto, H. Okonogi, and M. Kadokura. 1993. Micronucleus test and erythropoiesis: effect of cobalt on the induction of micronuclei by mutagens. *Environ. Mol. Mutagen.*, 22:101-106.
- Type** : DNA damage in isolated human lymphocytes
- Guideline/method** : Alkaline Comet Assay (*in vitro*)
- Species** : Human
- Strain** :
- Sex** : Female
- Route of admin.** : In vitro
- Exposure period** : 15 min
- Doses** : 0.3, 0.6, 1.2, 1.5, 2.0, 2.5, 3.0, and 6.0 mg Co/L
- Year** : 1998
- GLP** : No
- Test substance** : Cobalt chloride hexahydrate (CoCl₂·6H₂O)
- Method** : The alkaline comet assay performed using a modification of the method of Singh et al. 1988. *Exp. Cell. Res.*, 175:184-191.
- Method detail** : Tests were conducted on lymphocytes taken from two healthy female donors. Cells were for 15 min exposed after 24 of stimulation by phytohaemagglutinin. After treatment, the cells were centrifuged for 10 min at 400 g. The supernatant was removed and the cell pellet was resuspended and processed for the alkaline comet assay (single cell electrophoresis assay). Fifty or 100 randomly selected slides were analyzed, with tail length, tail DNA, and tail movement recorded.
- Result** : There was considerable interexperimental and interdonor variability in data; however, at the highest dose level (6.0 mg Co/L) there was a statistically significant increase in tail movement in all experiments, indicating DNA damage (single strand breaks and alkali labile sites). Tail movement was also increased at lower doses, but did not show a clear dose-dependent trend.
- Remark** : Using human lymphocytes and macrophages (P388D₁ cells), an increase in sister chromatid exchanges (SCE) after exposure to cobalt chloride at 10⁻⁴ to 10⁻⁵ M has been also demonstrated (Andersen, O. 1983. *Environ. Health Perspect.*, 47: 239-253). Others have also found that cobalt chloride increases DNA strand breaks in human diploid fibroblasts and Chinese hamster ovary cells after *in vitro* exposures, although only when determined by alkaline sediment sucrose velocity sedimentation and not when measured by nucleoid sedimentation or nick translation assays (Hamilton-Koch, W. et al., 1986. *Chem.-Biol. Interactions*, 59:17-28).
- Reliability** : 2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
- Reference** : De Beck, M., D. Lison, and M. Kirsch-Volders. 1998. Evaluation of the *in vitro* direct and indirect genotoxic effects of cobalt compounds using the alkaline comet assay. Influence of interdonor and interexperimental variability. *Carcinogenesis*, 19:2021-2029.

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5.8.2 DEVELOPMENTAL TOXICITY

Type	:	Developmental toxicity
Guideline/method	:	Not specified
Species	:	Rat
Strain	:	Wistar
Sex	:	Female
Route of admin.	:	Gastric intubation
Exposure period	:	Gestation day 14 through 21 days of lactation
Frequency of treatment	:	Daily
Duration of test	:	Through lactation day 21
Doses	:	12, 24, and 48 mg/kg b.w. (equivalent to 5.4, 10.8, or 21.8 mg Co/kg b.w.)
Control group	:	Yes
NOAEL maternal tox.	:	Not determined (no maternal data reported)
NOAEL teratogen.	:	Malformations not observed
Other	:	
Other	:	
Other	:	
Year	:	1985
GLP	:	No
Test substance	:	Cobalt chloride
Method	:	
Method detail	:	Cobalt chloride was administered to three groups of 15 pregnant rats from gestation day 14 through the 21 st day of lactation. Pups were weighed and examined for signs of toxicity on days 1, 4, and 21 of lactation, and were sacrificed on day 21. Macroscopic examinations were made of the heart, lungs, spleen, liver, and kidneys following sacrifice. Clinical chemistry parameters were also measured.
Result	:	There was significant mortality of pups in the highest dose group and fewer litters produced at all dose levels. In addition, pups showed stunted growth (weight and length) at all dose levels. Relative weights of the liver (males and females) and spleen (females only) were reduced by cobalt exposure, but did not show a dose-related trend. Blood analysis and clinical chemistry showed no treatment related differences. No external malformations were observed in pups. Data from previous studies by the authors suggests that the upper two doses levels were maternally toxic, therefore, the results observed may have been indirectly due, at least in part, to effects on the mothers, rather than direct effects on the fetuses.
Remark	:	
Reliability	:	2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
Reference	:	Domingo, J.L., J.L. Paternain, J.M. Llobet, and J. Corbella. 1985. Effects of cobalt on postnatal development and late gestation in rats upon oral administration. <i>Rev. Esp. Fisiol.</i> , 41:293-298.

Type	:	Teratogenicity
Guideline/method	:	Not specified
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	Female
Route of admin.	:	Oral gavage
Exposure period	:	Day 6 to 15 of gestation
Frequency of treatment	:	Daily
Duration of test	:	To day 20 of gestation
Doses	:	25, 50, or 100 mg/kg (equivalent to 6.2, 12.4, and 24.8 mg Co/kg b.w.)
Control group	:	Yes

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NOAEL maternal tox.	:	Not determined (effects on weight gain seen at lowest dose)
NOAEL teratogen.	:	24.8 mg Co/kg b.w.
Other	:	NOAEL for maternal hematology was 12.4 mg Co/kg b.w.
Other	:	
Other	:	
Year	:	1998
GLP	:	
Test substance	:	Cobalt chloride hexahydrate (CoCl ₂ ·6H ₂ O)
Method	:	
Method detail	:	Pregnant females (20 per group) were dosed daily with cobalt chloride hexahydrate in distilled water during gestation days 6 to 15. Maternal body weights were recorded on days 0, 6, 9, 12, 16, and 19 of gestation. Individual food consumption was recorded for the following intervals: days 0-6, 6-9, 9-12, 12-16 and 16-19. Detailed physical examinations for signs of toxicity were performed at the same time that weights were recorded. On day 20 of gestation, dams were weighed, then sacrificed. Blood samples were collected for hematological analyses. After exsanguinations, the uterine horns were opened, examinations made and the following recorded: number of corpora lutea, total implantations, number of live and dead fetuses number of resorptions, average fetus body weight, number of stunted fetuses, fetal body length, and fetal tail length. Fetuses were also fixed, stained and examined for skeletal abnormalities.
Result	:	Maternal effects included significant reductions in weight gain and food consumption, particularly at the 24.8 mg Co/kg dose level, although effects on weight gain were found at all dose levels. Hematological parameters (e.g., hematocrit, hemoglobin content) were significantly increased in the highest dose group. No treatment-related changes were observed in the number of corpora lutea, total implants, resorptions, number of live and dead fetuses per litter, fetal size parameters, or fetal sex distribution data. Increased incidences of stunted fetuses per litter (those under two-thirds of the average fetus body weight) were seen in the two highest dose groups; however, the increases were not statistically significant. Examination of fetuses for gross external abnormalities, skeletal malformations, and ossification variations produced negative findings, indicating that cobalt doses as high as 24.8 mg Co/kg do not produce teratogenicity or significant fetotoxicity in the rat.
Remark	:	A lack of teratogenicity in the golden hamster has also been reported (Ferm, V.H. 1972. Adv. Teratol., 6:51-75.
Reliability	:	2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
Reference	:	Paternain, J.L., J.L. Domingo, and J. Corbella. 1988. Developmental toxicity of cobalt in the rat. J. Toxicol. Environ. Health, 24:193-200.
Type	:	Developmental toxicity
Guideline/method	:	Chernoff/Kavlock developmental toxicity screen
Species	:	Mouse
Strain	:	ICR/SIM
Sex	:	Female
Route of admin.	:	Oral intubation
Exposure period	:	Gestation days 8 through 12
Frequency of treatment	:	Daily
Duration of test	:	Through postnatal day 3
Dose	:	180 mg/kg/day (equivalent to 81.7 mg Co/kg)
Control group	:	Yes
NOAEL maternal tox.	:	Not determined
NOAEL teratogen.	:	180 mg/kg/day (equivalent to 81.7 mg Co/kg)
Other	:	

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Other	:	
Other	:	
Year	:	1986
GLP	:	
Test substance	:	Cobalt chloride
Method	:	Chernoff, N. and R.J. Kavlock. 1982. J. Toxicol. Environ. Health, 10:541-550.
Method detail	:	The screening test was carried out with a single minimally dose that was expected to result in significant maternal weight reduction, up to 10% mortality, or other clinical sings of overt toxicity. Treatment was by oral intubation on days 8 through 12 of gestation. Mice were allowed to deliver, and neonates examined, counted, and weighed on the day of birth (day 1) and day 3. Dead neonates were recovered from the nest and examined for abnormalities.
Result	:	The average maternal weight gain was significantly affected by cobalt treatment as desired in the protocol. Despite this, there was no effect of cobalt on litter size, percent survival of neonates on days 1-3, or average neonatal weight.
Remark	:	Results are in agreement with those seen in the rat, although another researcher has reported that injections of cobalt chloride to pregnant mice can lead to interference of skeletal ossification in fetuses (Wide, M. 1984. Environ. Res., 33:47-53).
Reliability	:	2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
Reference	:	Seidenberg, J.M. D.G. Anderson, and R.A. Becker. 1986. Validation of an in vivo developmental toxicity screen in the mouse. Teratog. Carcinog. Mutagen., 6:361-374.

5.8.3 TOXICITY TO REPRODUCTION

Type	:	Male reproduction
Guideline/method	:	Not specified
In vitro/in vivo	:	In vivo
Species	:	Mouse
Strain	:	CD-1
Sex	:	Male
Route of admin.	:	Drinking water
Exposure period	:	12 weeks (dose-response study); 13 weeks (time course study)
Frequency of treatment	:	Continuous
Duration of test	:	12 weeks (dose-response study); 33 weeks (time course study)
Doses	:	10, 200, or 400 ppm in the dose-response study (equivalent to a daily intake of 23.0, 42.0, or 72.1 mg Co/kg b.w.); 400 ppm in the time course study (equivalent to a daily intake of 58.9 mg Co/kg b.w.)
Control group	:	Yes
Year	:	1988
GLP	:	No
Test substance	:	Cobalt chloride hexahydrate (CoCl ₂ ·6H ₂ O)
Method	:	
Method detail	:	In the dose-response study, males (5 per dose) were evaluated after 12 weeks of exposure for testicular weight, epididymal sperm concentration, sperm motility, sperm fertilizing ability (fertility), prostatic weight, seminal vesicle weight, and serum levels of testosterone. In the time course study, males (5 per dose and time point) were evaluated after 7, 9, 11, or 13 weeks of exposure for most of these same parameters. In addition, fertility of the males was evaluated at regular intervals up to 20 weeks after cessation of cobalt treatment in the drinking water.
Result	:	Cobalt exposure affected male reproductive parameters in a time- and

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- dose-dependent manner. There was a significant decrease in testicular weight and epididymal sperm concentration after 11-13 weeks of exposure at all dose levels. Sperm motility and fertility were significantly depressed in the highest exposure groups. After cessation of exposure, some recovery was seen in fertility over time; however, indices remained significantly depressed through study termination (20 weeks after cessation). Parallel studies with acute cobalt chloride exposures (i.p injections of 200 µmoles/kg for 3 consecutive days) did not result in significant changes in male reproductive parameters, although transient affects on fertility were observed.
- Remark** : Histopathology studies of testes from mice treated with the same general exposure regimen as in this study (i.e., 400 ppm in drinking water for 13 weeks) showed a reproducible, sequential pattern of seminiferous tubule degeneration (Anderson, M.B. et al., 1992. *Reprod. Toxicol.*, 6:41-50). Results of this study are highly consistent with others in which testicular degeneration and atrophy have been reported in rats exposed to 13.2 to 30.2 mg Co/kg/day as cobalt chloride for 2-3 months in the diet or drinking water (ATSDR Sept 2001 Draft).
- Reliability** : 2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
- Reference** : Pedigo, N.G., W.J. George, and M.B. Anderson. 1988. Effects of acute and chronic exposure to cobalt on male reproduction in mice. *Reprod. Toxicol.*, 2:45-53.
- Type** : Male reproduction
- Guideline/method** : Not specified
- In vitro/in vivo** : In vivo
- Species** : Rat
- Strain** : Sprague-Dawley
- Sex** : Male
- Route of admin.** : Diet
- Exposure period** : 98 d
- Frequency of treatment** : Continuous in diet
- Duration of test** : Up to 98 d
- Doses** : 265 ppm in diet (equivalent to 20 mg Co/kg b.w. at test initiation)
- Control group** : Yes
- Year** : 1985
- GLP** : No
- Test substance** : Cobalt chloride hexahydrate (CoCl₂·6H₂O)
- Method** :
- Method detail** : Three rats from the control and treatment groups were sacrificed on days 1, 2, 7, 14, 21, 28, 35, 42, 56, 63, 70, 84, and 98. Tissue specimens from the testes, cauda epididymus, and seminal vesicles were fixed and later examined.
- Result** : Dietary cobalt exposure induced consistent degenerative and necrotic lesions in the seminiferous tubules of rats. Cyanosis and engorgement of testicular vasculature on day 35 and thereafter was followed on day 70 by degenerative and necrotic changes in the germinal epithelium and Sertoli cells. Findings indicate that cobalt readily crosses the blood-testes barrier.
- Remark** : Results are consistent with those of Nation et al. (1983), who found significant testicular atrophy in rats exposed chronically to 20 mg Co/kg in the diet (Nation, J.R. et al., 1983. *Neurobehav. Toxicol. Teratol.*, 5:9-15).
- Reliability** : 2 (Reliable with restrictions): comparable to guideline study with adequate documentation.
- Reference** : Corrier, D.E., H.H. Mollenhauer, D.E. Clark, M.F. Hare, and M.H. Elissalde. 1985. Testicular degeneration and necrosis induced by dietary cobalt. *Vet. Pathol.*, 22:610-616.

6.0 OTHER INFORMATION

6.1 CARCINOGENICITY

The US National Toxicology Program does not recognize cobalt as a human carcinogen, but IARC has classified cobalt and cobalt compounds as possibly carcinogenic to humans (Class 2B) based on sufficient evidence that cobalt metal powder and cobaltous oxide are carcinogenic in animals (Barceloux 1999, ATSDR Sept 2001 Draft). "No studies were located regarding carcinogenic effects in animals after oral exposure to stable [non-radioactive] cobalt." (ATSDR Sept 2001 Draft).

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HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For The

NEOACIDS C5-C28 CATEGORY

CAS# 75-98-9: Propanoic acid, 2,2-dimethyl-
CAS# 598-98-1: Propanoic acid, 2,2-dimethyl-, methyl ester
CAS# 95823-36-2: Carboxylic acid, C6-8 neo
CAS# 26896-20-8: Neodecanoic acid
CAS# 68938-07-8: Fatty acids, C9-C13 neo
CAS# 72480-45-6: Fatty acids, C9-C28 neo

Prepared by:

ExxonMobil Chemical Company

November 15, 2001
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EXECUTIVE SUMMARY

Under EPA's High Production Volume (HPV) Challenge Program ExxonMobil Chemical Company has committed to voluntarily compile a Screening Information Data Set (SIDS) on a category of chemicals defined as Neoacids C5-C28. This category is supported by the basic screening data needed for an initial assessment of the physicochemical properties, environmental fate, and human and environmental effects of chemicals as defined by the Organization for Economic Cooperation and Development (OECD). The information used to complete the HPV SIDS endpoints comes from existing data.

ExxonMobil Chemical Company believes a category of Neoacids C5-C28 is scientifically justifiable because their physicochemical and toxicological properties are very similar and follow a regular pattern as a result of the synthesis process. The structural similarities create a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. The similarities are based on the following:

- A common structure represented by R3CCOH,
- An incremental and constant change in carbon number across the category where the total number of carbons represented by R ranges from 3 to 26, and
- A likelihood of common precursors and breakdown products that can result in structurally similar metabolites (e.g. carboxylic acid).

This test plan is based on the observation that the toxicological properties are similar or vary in an incremental and predictable fashion within the category.

The test data compiled for the category anchor studies proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 75-98-9, 598-98-2, 95823-36-2, 26896-20-8, 68938-07-8, and 72480-45-6). The untested endpoints can be assessed by interpolation between data from the category anchor studies.

To complete the hazard assessment of the category, algal toxicity studies will be completed on both low and high molecular weight members of the category (75-98-9 and 72480-45-6 or 68938-07-8). Also, a fish acute and invertebrate toxicity study will be conducted on a high molecular weight member (68938-07-8).

Evaluation of the Neoacids C5-C28 as a category has several advantages. The category can be evaluated by using a matrix of completed anchor studies for various members of the category. By using this approach, the safety of the category can be determined without having to conduct tests for every end-point with every chemical. Not only will this inform the public earlier about any hazards of Neoacids C5-C28, but it will also reduce the number of animals that would be required to evaluate the toxicity of individual members of the Neoacids C5-C28 category.

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TEST PLAN FOR NEOACIDS C₅-C₂₈

I. INTRODUCTION

Under EPA's High Production Volume (HPV) Chemical Challenge Program ExxonMobil Chemical Company has committed to voluntarily compile a Screening Information Data Set (SIDS) on a category of chemicals defined as Neoacids C5-C28. This category is supported by the basic screening data needed for an initial assessment of the physicochemical properties, environmental fate, and human and environmental effects of chemicals as defined by the Organization for Economic Cooperation and Development (OECD). The information used to complete the HPV SIDS endpoints comes from existing data and fulfills an ExxonMobil obligation to the HPV Challenge Program.

ExxonMobil Chemical Company believes a category of Neoacids C5-C28 is scientifically justifiable because their physicochemical and toxicological properties are very similar and follow a regular pattern as a result of the synthesis process. The structural similarity of the component chemicals from these products creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. The similarities are based on the following:

- A common structure represented by R3CCOH,
- An incremental and constant change in carbon number across the category where the total number of carbons represented by R ranges from 3 to 26, and
- A likelihood of common precursors and breakdown products that can result in structurally similar metabolites (e.g. carboxylic acid).

This test plan is based on the observation that the toxicological properties are similar or vary in an incremental, predictable fashion within the category.

The test data compiled for the category proves adequate to support a hazard assessment for the category and its members (CAS numbers, 75-98-9, 598-98-2, 95823-36-2, 26896-20-8, 68938-07-8, and 72480-45-6) with the exception of few studies that have been identified as necessary to complete a thorough hazard dataset. Once all data are available, the untested endpoints can be assessed by interpolation between data from the category anchor studies. The existing data suggest that products in the Neoacids (C₅-C₂₈) Category exhibit relatively low toxicity for human health endpoints and moderate toxicity for the environmental health endpoints.

To complete the hazard assessment of the category, algal toxicity studies will be completed on the low and high molecular weight members of the category (75-98-9 and 72480-45-6 or 68938-07-8). Also, a fish acute and invertebrate toxicity study will be conducted on a high molecular weight member (68938-07-8).

The data from this category will be used to inform the public about the potential hazards of the Neoacids C5-C28. Developing a data matrix of anchor studies and applying justifiable read across practices will provide a sufficiently robust data set to characterize each endpoint in the HPV Chemical Challenge Program without having to conduct a test

for each endpoint and product. This resourceful use of existing data will result in fewer animals needed for testing purposes while adequately assessing the potential hazards of products in the Neoacids C5-C28 Category.

II. CHEMICAL PROCESS AND DESCRIPTION

The Neoacids C5-C28 Category contains a group of neoacid products whose physicochemical and toxicological properties are very similar and follow a regular pattern as a result of synthesis and structural similarity (Table 1). The production of neoacid products involves the reaction between a branched olefin with carbon monoxide and water at elevated temperatures and pressures in the presence of an acid catalyst.

The category also contains propanoic acid, 2,2-dimethyl-, methyl ester (CAS#: 598-98-1). This material is an ester that is rapidly hydrolyzed to the parent neoacid - propanoic acid, 2,2-dimethyl- (CAS#: 75-98-9). Because of this rapid hydrolysis, propanoic acid, 2,2-dimethyl-, methyl ester has properties for health effects, aquatic toxicity, and environmental fate that are consistent with the neoacids.

The structural similarity of chemicals in this category creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. Neoacids are trialkylacetic acids in which each hydrogen on the non carboxyl carbon of acetic acid has been replaced by an alkyl group. The structural features of members of the category are as follows:

- A common structure - a quaternary carbon with the general structure R_3CCOOH ,
- An incremental and constant change across the category where R can be a branched alkyl group ranging from CH_3 to C_6H_{13} as the main constituent,
- A likelihood of common precursors and breakdown products which result in structurally similar chemicals.

Table 1. CAS Numbers and Descriptions

CAS Number	Chemical Name
75-98-9	Propanoic acid, 2,2-dimethyl-
598-98-1	Propanoic acid, 2,2-dimethyl-, methyl ester
95823-36-2	Carboxylic acid, C6-8 neo*
26896-20-8	Neodecanoic acid
68938-07-8	Fatty acids, C9-13 neo
72480-45-6	Fatty acids, C9-28 neo

* = Not currently HPV but included to facilitate category evaluation

The Neoacids C5-C28 category accomplishes the goal of the Challenge Program - to obtain screening level hazard information through the strategic selection of products to be tested within the category. The testing strategy is based on the principle that:

- These products behave in a similar or predictable manner, and
- Interpolation of data can be used to assess the neoacid products for which data are not available.

Procedures to assess the reliability of selected data for inclusion in this test plan are based on the guidelines described by Klimisch et al, 1997.

III. TEST PLAN RATIONALE

A. Physicochemical Data

Physicochemical Data (i.e., melting point, boiling point, vapor pressure, water solubility, and Kow) for selected chemical components in the Neo Acid C5 - C28 Category were calculated using EPIWIN© model (EPIWIN, 1999), as discussed in the EPA document entitled "The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program." These data will be presented as ranges, based on the chemical components selected to represent each neoacid product. In addition, measured data for some of these endpoints will also be provided for selected neoacid products where readily available. Where possible, measured and calculated data will be presented together for comparison purposes.

Table 2 lists selected measured physicochemical data (melting point, boiling point, and vapor pressure) as they appear on the material safety data sheets for products in this category. These data are provided with this test plan to further justify these products as a distinct category under the HPV Chemical Challenge Program. Also included are calculated values for water solubility and K_{ow}. As shown by the data in Table 2, the structural similarity of the neoacid products results in a predictable and incrementally increasing pattern of physiochemical properties from the C5 to C9-28 products.

Table 2. Selected Physical Properties of Neoacids (C₅-C₂₈)

CAS NUMBER	CHEMICAL NAME	MELTING POINT (° C)	BOILING POINT (° C)	WATER SOLUBILITY mg/L	VAPOR PRESSURE (mm Hg @ 25° C)	Log Kow
75-98-9	Propanoic acid, 2,2-dimethyl- (C5)	35 ^a	163.8 ^a	15,590	1.54	1.5 ^a
598-98-1	Propanoic acid, 2,2,-dimethyl-, methyl ester (C6)	-62.5	101 ^a	2,835	35.7	1.8 ^a
95823-36-2	Carboxylic acid, C6-8 neo (C7)	24.6	207.8	1912	0.244	2.4
26896-20-8	Neodecanoic acid (C10)	57.1	262.4	69	0.0071	3.9
68938-07-8	Fatty acids, C9-13 neo	37 - 76	234 - 291	3.1 - 243	0.001 - 0.046	3.3 - 5.2
72480-45-6	Fatty acids, C9-28 neo	37 - 204	234 - 504	<1 - 243	<1.7 E ⁻¹² - 0.046	3.3 - 6.0

^a Measured values supplied by experimental database in EPIWIN

B. Human Health Effects

The structural similarity of the Neoacids C5-C28 influences both their physicochemical (Table 2) and their toxicological properties (Sections C and D). As a chemical category, the Neoacids C5-C28 have predictable, low-level environmental and health hazards.

ExxonMobil Chemical Company believes the category of Neoacids C5-C28 is scientifically justifiable and that the test data compiled for the category proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 75-98-9, 598-98-2, 95823-36-2, 26896-20-8, 68938-07-8, and 72480-45-6). One can assess the untested endpoints by extrapolation between and among the category members. The proposed category assessment plan is shown in Table 3.

Metabolism

Propanoic acid, 2,2-dimethyl-, methyl ester is rapidly cleaved to Propanoic acid, 2,2-dimethyl-. Due to the stability conferred by the quaternary carbon, Neoacids C5-C28 are relatively resistant to biotransformation and do not readily form bioactive metabolites. Enzymatic removal of the alkyl groups at the quaternary carbon would allow for other metabolic processes to occur. These would likely be mitochondrial beta-oxidation or by cytochrome P450 mediated omega and omega-minus-one oxidation (may be followed by beta-oxidation) to produce acetate. However, since Neoacids C5-C28 are not readily metabolized, they would primarily be eliminated in the urine as glucuronic acid conjugates or by dealkylation (Katz and Guest, 1994).

C. Presentation of Neoacids C5-C28 Category Health Effects Data Associated with the Anchor Studies under the HPV Challenge Program

Acute Oral Toxicity

TEST	Propanoic acid, 2,2-dimethyl-(C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
ACUTE ORAL - RAT	= 2000 mg/kg	RA	1860 mg/kg	= 2000 mg/kg	RA	RA

All of the Neoacids C5-C28 have a low order of toxicity to rats via the oral route of exposure (EBSI, 1964). The LD₅₀ values for Propanoic acid, 2,2-dimethyl- and Neodecanoic acid were 2000 mg/kg. In addition, the LD₅₀ for Carboxylic acid, C6-8 neo was 1860 mg/kg. These results demonstrate that members of the Neoacids C5-C28 Category have a consistent, low order of acute oral toxicity.

Acute Dermal Toxicity

TEST	Propanoic acid, 2,2-dimethyl-(C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
ACUTE DERMAL - RABBIT	= 3160 mg/kg	RA	> 3160 mg/kg	> 3160 mg/kg	RA	RA

The Neoacids C5-C28 have a low order of toxicity via the dermal route of exposure (EBSI, 1964). The rabbit dermal LD₅₀ for all members of the category was equal to or greater than 3160 mg/kg. This indicates that the members of this category have a consistent pattern of acute toxicity via the dermal route of exposure.

Genotoxicity

TEST	Propanoic acid, 2,2-dimethyl-(C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
AMES - S. typhimurium; TA98, 100, 1535, 1537, 1538 ± Activation	D	RA	RA	D	D	RA
Chromosomal Aberration - In Vitro or In Vivo	D	RA	RA	D	D	RA

RA Read Across

D Data available from another source, robust summaries will be submitted when they become available

There are no structural alerts to suggest that Neoacids C5-C28 are likely to be genotoxic. In addition, it has come to our attention that another producer of these materials has genetic toxicology data available. These data include both mutagenicity and chromosomal aberration studies on several members of the category. Pending our receipt and review of these studies, we will re-evaluate the need to do genetic toxicology testing. However, we do not anticipate that any additional genotoxicity testing will be required. We will submit additional robust summaries once this information is available to us.

Subchronic Toxicity

TEST	Propanoic acid, 2,2-dimethyl-(C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
RAT DERMAL	NOAEL (dermal) = 300 mg/kg	RA	NOAEL (dermal) = 553.7 mg/kg	NOAEL (dermal) = 2280 mg/kg	RA	RA

The subchronic toxicity of Neoacids C5-C28 has been assessed by conducting repeat dermal exposure studies. Dermal exposure is the primary route of exposure for Neoacids C5-C28, particularly in an industrial setting. An evaluation of the repeated dose studies indicates that Neoacids C5-C28 have a low order of subchronic toxicity. Propanoic acid, 2,2-dimethyl-, in isopropyl alcohol solution, was repeatedly applied to the shaved intact skin of albino rabbits 5 days/week for two weeks (for a total of 10 applications) at doses of 30 or 300 mg/kg/day (Hazleton, 1964a). Slight to moderate irritation at the low dose and moderate to marked irritation at the high dose was observed. Slight or moderate erythema, atonia, and desquamation were seen at the low dose. At the high dose, skin irritation consisted of moderate erythema, slight to marked edema, moderate or marked atonia and desquamation. Some dermal necrosis at the site of application was seen in three rabbits and persisted throughout the study. Control animals that received only the solvent (isopropyl alcohol) showed slight irritation. There were no signs of systemic toxicity attributable to dermal absorption of propanoic acid, 2,2-dimethyl-. The NOAEL for systemic toxicity in this study was 300 mg/kg.

In a similar study, carboxylic acid, C6-8 neo was applied at 55.4 mg/kg and 553.7 mg/kg for 10 applications (Hazleton, 1964b). No treatment related effects were observed on behavior of clinical signs during the in-life phase of the study. Gross pathology of the animals in all dose groups did not reveal any abnormalities. Repeated application of carboxylic acid C6-8 neo did produce marked skin irritation with some dermal necrosis at the site of application in the high dose group. Since no systemic effects were observed in this study, the NOAEL for systemic effects following subchronic dermal application of carboxylic acid, C6-8 neo was 553.7 mg/kg.

Repeated dermal application (400 or 2800 mg/kg daily for a total of 10 applications) of undiluted Neodecanoic acid generally produced irritation at the low dose and fissuring at the high dose (Hazleton, 1964c). Slight to moderate erythema, atonia and desquamation were seen at the low dose. At the high dose, skin irritation consisted of moderate erythema, moderate to severe atonia, and desquamation with fissuring. No signs of systemic toxicity were attributed to Neodecanoic acid. Therefore, the NOAEL for systemic toxicity following subchronic dermal application of Neodecanoic acid was 2280 mg/kg.

In summary, Neoacids C5-C28 have a low order of subchronic toxicity. In addition, they display a consistent pattern of subchronic toxicity in that the NOAEL for systemic toxicity increases in a predictable pattern from the low to the high molecular weight end of the category. Therefore, Neoacids C5-C28 do not require further testing to assess subchronic toxicity.

Developmental Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
DEVELOPMENTAL ORAL - RAT	RA	RA	NOAEL maternal = 250 mg/kg NOAEL fetal = 250 mg/kg NOAEL (isooctanoic) maternal = 400 mg/kg NOAEL fetal = 800 mg/kg NOAEL (isooctanoic acid) = 7500 ppm in diet	NOAEL parental = 1500 ppm in diet NOAEL F1 = 1500 ppm NOAEL F2 = 1500 ppm	NOAEL (isononanoic acid) = 1200 ppm in diet	RA

The potential for developmental toxicity of Neoacids C5-C28 can be assessed by evaluating the available data on neoacids as well as by comparison to the data on isoacids and structure-teratogenicity relationships. The available developmental toxicity data on neoacids indicate that they are not selective developmental toxicants. A developmental toxicity study conducted on Carboxylic acid, C6-8 neo produced a NOAEL of 250 mg/kg for both maternal and fetal effects (EBSI, 1986). Carboxylic acid, C6-8 neo was not a selective developmental toxicant in this study. In a 3-generation reproduction study with Neodecanoic acid, developmental effects were not observed in either the F1 or F2 offspring (Hazleton, 1968). This study produced a NOAEL of 1500 ppm (in diet) for the maternal, F1, and F2 generations.

Additional developmental toxicology data are available for isoacids, which are isomers of the neoacids. The isoacids are aliphatic carboxylic acids that have saturated branching structures. Isooctanoic acid was tested for developmental toxicity in female rats at doses of 0, 200, 400, and 800 mg/kg/day during gestation days 6 - 15 (EBSI, 1995). At 800 mg/kg/day, maternal toxicity was observed; however, there were no effects at 400 mg/kg/day. There were no biologically significant developmental effects in this study. The no-observable-adverse-effect level (NOAEL) for maternal toxicity was 400 mg/kg/day and for developmental toxicity was 800 mg/kg/day.

In a one-generation reproductive toxicity range-finding study, rats were exposed to isooctanoic acid at dietary levels of 1000, 5000, 75000, or 10,000 ppm (EBSI, 1999). In the parental generation, there were no treatment-related effects on survival, organ weights, or reproductive function. In the offspring, there were no treatment-related effects on survival, developmental landmarks, or any significant findings in postmortem evaluations. Statistically significant decreases in the mean offspring body weights of males and females were observed at 10,000 ppm. The high dose also resulted in a

suppression of body weight gain in the adult females. Thus, the NOAEL for both parental and offspring effects was 7500 ppm.

A one-generation reproduction study was conducted on isononanoic acid (EBSI, 1998). Rats were administered the test material in the diet at doses of 0, 600, 1200, 2500, and 5000 ppm. There were no treatment-related effects observed on mating, fertility, fecundity, or gestation indices or during sperm analysis. Evidence of maternal toxicity included decreased body weights and increased liver weights in the 2500 and 5000 ppm dose groups. In the offspring, reduced survival indices were noted in the 5000 ppm dose group, and reduced body weights were noted in the 2500 and 5000 ppm dose groups. The NOAEL for both maternal and offspring effects in this study was 1200 ppm.

Further support for the evaluation of the potential of neoacids to be developmental toxicants comes from an analysis of the structure activity relationships that affect teratogenicity. A structure-teratogenicity analysis of carboxylic acids concluded that aliphatic acids, which have a dimethyl substitution at the C-2 position, are not developmental toxicants (Di Carlo, 1990). Furthermore, the structural requirements for carboxylic acid teratogenicity require an alpha hydrogen and a free carboxylic group. Since the neoacids are defined by their trialkyl substitution at the alpha carbon, there is no alpha hydrogen. In addition, steric hindrance of the carbonyl group by the quaternary center of the alpha carbon inhibits reactions.

In conclusion, the available test data on neoacids and their isomers, as well as the structure-teratogenicity relationship for aliphatic acids, provide sufficient information for a screening-level assessment of the developmental toxicity of neoacids. Based on these analyses, neoacids are not considered to be selective developmental toxicants and no further testing is proposed.

Reproductive Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C6)	Carboxylic acid, C6-8 neo (C7)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
REPRODUCTIVE ORAL - RAT	RA	RA	NOAEL (isooctanoic acid) = 7500 ppm in diet	NOAEL parental = 1500 ppm in diet NOAEL F1 = 1500 ppm NOAEL F2 = 1500 ppm	NOAEL (isononanoic acid) = 1200 ppm in diet	RA

The available reproductive toxicity studies and developmental toxicity studies prove adequate to support a screening-level hazard assessment for the reproductive toxicity potential of Neoacids C5-C28. These data support the conclusion that the Neoacids C5-C28 are not selective reproductive toxicants.

In a modified three-generation reproduction study, rats were exposed to 100, 500, or 1500 ppm Neodecanoic acid in the diet (approximately 5, 25 and 75 mg/kg/day, respectively) (Hazleton, 1968). No significant effects were observed in survival, appearance, behavior, or reproductive performance of the parents. No adverse effects were demonstrated in offspring on growth, appearance, or behavior. No treatment related effects were observed at gross or microscopic pathology. The NOAEL in this study was greater than 1500 ppm. The data indicate that Neodecanoic acid is not a reproductive toxicant.

In a one-generation reproductive toxicity range-finding study, rats were exposed to isooctanoic acid at dietary levels of 1000, 5000, 75000, or 10,000 ppm (EBSI, 1999). In the parental generation, there were no treatment-related effects on survival, organ weights, reproductive function, or sperm indices. In the offspring, there were no treatment-related effects on survival, developmental landmarks, or any significant findings in postmortem evaluations. Statistically significant decreases in the mean offspring body weights of males and females were observed at 10,000 ppm. The high dose also resulted in a suppression of body weight gain in the adult females. Thus, the NOAEL for both parental and offspring effects was 7500 ppm.

A one-generation reproduction study was also conducted on isononanoic acid (EBSI, 1998). Rats were administered the test material in the diet at doses of 0, 600, 1200, 2500, and 5000 ppm. There were no treatment-related effects observed on mating, fertility, fecundity, or gestation indices or during sperm analysis. Evidence of maternal toxicity included decreased body weights and increased liver weights in the 2500 and 5000 ppm dose groups. In the offspring, reduced survival indices were noted in the 5000 ppm dose group, and reduced body weights were noted in the 2500 and 5000 ppm dose groups. The NOAEL for both maternal and offspring effects in this study was 1200 ppm.

In summary, these data prove adequate to support a screening level assessment of the reproductive toxicity of Neoacids C5-C28. Furthermore, these data indicate that Neoacids C5-C28 have a low order of reproductive toxicity.

D. Aquatic Toxicity

The neoacid products ranging from Propanoic acid, 2,2-dimethyl- to fatty acids, C9-13 neo, have been shown to produce an expected increasing level of acute toxicity to freshwater fish and invertebrates. This is based on data from the literature that are used to read across to selected neoacid products in this test plan and company data specifically for products in this category. Although there are insufficient data to confirm that a similar pattern of alga toxicity exists, based on the fish and invertebrate data, a similar increasing level of toxicity is expected from the lower to higher carbon numbered products. Proposed testing will develop the data needed to confirm this expectation. Based on the existing data, products in the Neoacids (C₅-C₂₈) Category demonstrate a low to moderate degree of aquatic toxicity from the low to high carbon numbered products, respectively.

Fish Acute Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C7)	Carboxylic acid, C6-8 neo (C6-8)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
FISH ACUTE TOXICITY (96-hour, mg/L)	380	RA	630*	37.2	TESTING PROPOSED	RA

RA read across

* Data are for a C7 branched and linear aliphatic acid product that does not contain a quaternary carbon, but is used to read across to a C6-8 neoacid product

Acute experimental fish toxicity tests are reported for Rainbow Trout (*Oncorhynchus mykiss*) and Goldfish (*Carassius auratus*). The results show that a C5 neo acid, C7 linear and branched aliphatic acid (used as read across to the C6-8 neo acid), and C10 neo acid products demonstrate that these products have a potential to cause acute fish toxicity (96-hour LC50) in the range of 630 to 37.2 mg/L. (Bridie 1979, EBSI 1993c, EBSI 1996b). The C9-13 neoacid, and the C9-28 neoacid products are not characterized. Therefore, to adequately assess the potential toxicity of the Neoacids (C₅-C₂₈) Category to fish, an acute toxicity test with the fatty acids, C9-13, neo, product will be conducted. The data from this study will be used to read across to the fatty acids, C9-28, neo, product. Comparable toxicity is expected for these two products because the higher molecular weight fatty acid components in the C9-28 neo acid product have extremely low water solubilities and do not have the potential to be in solution at effect causing levels, unlike the lower molecular weight components whose water solubilities are sufficient to cause an effect as demonstrated by the C10 neoacid product.

Invertebrate Acute Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C7)	Carboxylic acid, C6-8 neo (C6-8)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
DAPHNID ACUTE TOXICITY (48-hour, mg/L)	203	RA	138*	47.1	TESTING PROPOSED	RA

RA read across

*Data are for a C7 branched and linear aliphatic acid product that does not contain a quaternary carbon, but is used to read across to a C6-8 neoacid product

Acute experimental toxicity studies are reported for the Daphnid (*Daphnia magna*). The results show that a C5 neo acid, C7 linear and branched aliphatic acid (used as read across to the C6-8 neo acid), and C10 neo acid product have the potential to cause

acute toxicity (48 hour EL50 or EC50) in the range of 203 to 47.1 mg/L (EG&G 1977a, EG&G 1977b, EBSI 1993a). The C9-13 neoacid, and the C9-28 neoacid products are not characterized. Therefore, to adequately assess the potential toxicity of the Neoacids (C₅-C₂₈) Category to the Daphnid, an acute toxicity test with the fatty acids, C9-13, neo, product will be conducted. The data from this study will be used to read across to the fatty acids, C9-28, neo, product. Comparable toxicity is expected for these two products because the higher molecular weight fatty acid components in the C9-28 neo acid product have extremely low water solubilities and do not have the potential to be in solution at effect causing levels, unlike the lower molecular weight components whose water solubilities are sufficient to cause an effect as demonstrated by fish and invertebrate toxicity data for the C10 neoacid product.

Alga Toxicity

TEST	Propanoic acid, 2,2-dimethyl- (C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C7)	Carboxylic acid, C6-8 neo (C6-8)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
ALGA TOXICITY (96-hour, mg/L)	TESTING PROPOSED	RA	6.5 (2)*	RA	TESTING PROPOSED	RA

(1) biomass

(2) growth rate

RA read across

*Data are for a C7 branched and linear aliphatic acid product that does not contain a quaternary carbon, but is used to read across to a C6-8 neoacid product

An acute experimental toxicity value is reported for the freshwater alga (*Selenastrum capricornutum*) for a C7 linear and branched aliphatic acid product that is used as read across data to the C7 neoacid. This result shows that a C7 acid product has the potential to cause toxicity (72 hour EC50) at a concentration of 6.5 mg/L, based on alga growth rate (EBSI 1993b). Although there are no data for the remaining neoacid and neoacid ester products, overall, they are expected to exhibit a range of toxicity that falls above and below the value for the C7 aliphatic acid product. To adequately assess the potential toxicity of the Neoacids (C₅-C₂₈) Category to an alga, toxicity tests with a C5 neoacid and fatty acids, C9-13, neo, product will be conducted. The data from the fatty acids, C9-13, neo, product will be used to read across to the fatty acids, C9-28, neo, product. Comparable toxicity is expected for these two products because the higher molecular weight fatty acid components in the C9-28 neo acid product have extremely low water solubilities and do not have the potential to be in solution at effect causing levels, unlike the lower molecular weight components whose water solubilities are sufficient to cause an effect as demonstrated by the C10 neoacid product.

E. Environmental Fate

Biodegradation data are available for three neoacid products. They show that neoacid products do not have the potential to biodegrade to a great extent within a standard 28-day test duration.

Although there is some information on photodegradation and fugacity, a complete data set to adequately characterize the neoacid products does not exist. Chemical equilibrium models are used to calculate fugacity, which describes the potential of a chemical to partition in the environment. These data can only be calculated.

Preliminary information for selected component chemicals of products in the Neoacids (C₅-C₂₈) Category suggests that these products are expected to partition primarily to water and soil. However, their fate in air is of environmental interest (this is discussed below under photodegradation). In addition, the majority of the component chemicals in these products have relatively low K_{ow} values, which suggests that they will not tend to partition to suspended organic matter in air and precipitate to aquatic and terrestrial environmental compartments to a significant extent.

Biodegradation

TEST	Propanoic acid, 2,2-dimethyl-(C5)	Propanoic acid, 2,2-dimethyl-, methyl ester (C7)	Carboxylic acid, C6-8 neo (C6-8)	Neodecanoic acid (C10)	Fatty acids, C9-13 neo (C9-13)	Fatty acids, C9-28 neo (C9-28)
28-Day Aerobic Biodegradation Test	24.1 %ThOD	RA	44.0 %ThOD	11 % ThOD	2.3 % ThOD	RA

RA read across

The existing biodegradation data for the neoacids products suggest that these products will not degrade rapidly in the environment. Four products have been tested and they exhibited an extent of biodegradation that ranged from approximately 2 to 44% after 28 days incubation (EBSI 1996a). These data were generated using a closed system with non-acclimated inocula. The test systems were continuously stirred, which is recommended when evaluating mixtures with several components, some of which have minimal water solubility.

Photodegradation – Photolysis

Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. Simple chemical structures can be examined to determine whether a chemical has the potential for direct photolysis in

water. First order reaction rates can be calculated for some chemicals that have a potential for direct photolysis using the procedures of Zepp and Cline (Zepp, 1977). UV light absorption of the chemical components in this category will be evaluated to identify those having the potential to degrade in solution. For those compounds with a potential for direct photolysis in water, first order reaction rates will be calculated. A technical document will be prepared that summarizes the results of information developed for this endpoint.

Photodegradation – Atmospheric Oxidation

Photodegradation can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 113 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b). An estimation method accepted by the EPA includes the calculation of atmospheric oxidation potential (AOP).

Atmospheric oxidation as a result of hydroxyl radical attack (OH⁻) is not direct photochemical degradation, but rather indirect degradation. AOPs can be calculated using a computer model. Neoacid products, such as those in the Neoacid (C₅-C₂₈) Category, have a lower potential to volatilize to air. In air, these chemicals may undergo reaction with photosensitized oxygen in the form of ozone and hydroxyl radicals.

The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPIWIN, 1999) is used by OPPTS (Office of Pollution Prevention and Toxic Substances). This program calculates a chemical half-life based on an overall OH⁻ reaction rate constant, a 12-hr day, and a given OH⁻ concentration. This calculation will be performed for the representative chemical components in the Neoacids (C₅-C₂₈) Category and summarized in robust summaries for this group of products.

Stability in Water (Hydrolysis)

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Neely, 1985). Stability in water can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 111 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b).

All of the chemical structures included in this category are neoacids with the exception of propanoic acid, 2,2-dimethyl-, methyl ester (C₆ neoacid methyl ester), which is a carboxylic acid ester. The neoacid products are not expected to hydrolyze at a measurable rate. A technical document will be prepared that discusses the nature of the chemical bonds present and the potential reactivity of this group of chemicals with water. The computer model Hydrowin version 1.67 (EPIWIN 1999) will be used to calculate the potential hydrolysis rate for the C₆ neoacid methyl ester. This information will be summarized in robust summaries for this group of products.

Chemical Transport and Distribution In The Environment (Fugacity Modeling)

Fugacity based multimedia modeling can provide basic information on the relative distribution of chemicals between selected environmental compartments (i.e., air, soil, sediment, suspended sediment, water, biota). The US EPA has acknowledged that computer modeling techniques are an appropriate approach to estimating chemical partitioning (fugacity is a calculated endpoint and is not measured). A widely used fugacity model is the EQC (Equilibrium Criterion) model (Mackay, 1996). EPA cites the use of this model in its document titled *Determining the Adequacy of Existing Data* (US EPA, 1999a), which was prepared as guidance for the HPV Program.

In its document, EPA states that it accepts Level I fugacity data as an estimate of chemical distribution values. The input data required to run a Level I model include basic physicochemical parameters; distribution is calculated as percent of chemical partitioned to 6 compartments (air, soil, water, suspended sediment, sediment, biota) within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. This model will be used to calculate distribution values for representative chemical components identified in products in this category. A computer model, EPIWIN – version 3.02 (EPIWIN, 1999), will be used to calculate the properties needed to run the Level I EQC model. This information will be summarized in robust summaries for this group of products.

IV. TEST PLAN SUMMARY

ExxonMobil Chemical Company believes that the Neoacids C5-C28 Category of chemicals should be further examined in the following manner:

- Conduct Ames assays on Propanoic acid, 2-2-dimethyl- (CAS# 75-98-9) and Neodecanoic acid (CAS# 26898-20-8) to evaluate the mutagenic potential of Neoacids C5-C28.
- Conduct mouse micronucleus assays Propanoic acid, 2-2-dimethyl- (CAS# 75-98-9) and Neodecanoic acid (CAS# 26898-20-8) to evaluate the clastogenic potential of Neoacids C5-C28.
- Calculate physicochemical data as described in the EPA document titled, *The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program* for selected chemical components of the neo acid products in this category. Provide measured data for selected products where readily available.

- Prepare a technical discussion on the potential of neo acid products in this category to photodegrade. Calculate AOP values for selected chemical components of neoacid products in this category.
- Prepare a technical discussion on the potential of neo acid products in this category to hydrolyze. Calculate the hydrolysis rate of Propanoic acid, 2,2-dimethyl-, methyl ester (CAS# 598-98-1).
- Calculate fugacity data for selected chemical components of neo acid products in this category.
- Conduct a fish acute toxicity test with Fatty acids, C9-13 neo (CAS# 68938-07-8).
- Conduct a Daphnid acute toxicity test with Fatty acids, C9-13 neo (CAS# 68938-07-8).
- Conduct algal toxicity tests with Propanoic acid, 2-2-dimethyl- (CAS# 75-98-9) and Neodecanoic acid (CAS# 26898-20-8).

ExxonMobil Chemical Company believes the thorough evaluation of the strategic anchor studies, the development of selected information and data, and the overall robustness of the final screening data set for the Neoacids C5-C28 Category complies with the objectives of the HPV volunteer testing program.

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**Table 3. Assessment Plan for the Neoacids C5-C28 Category Under the Program.
(Robust summaries for existing studies are submitted separately.)**

Stream Description	Human Health Effects						Ecotoxicity			Physical Chem. ¹	Environmental Fate			
	Acute Toxicity	Genetic Point Mut.	Genetic Chrom.	Sub-chronic	Developmental	Reproduction	Acute Fish	Acute Invert.	Algal Toxicity		Photo-deg.	Hydrolysis	Fugacity	Biodeg.
Propanoic acid, 2,2-dimethyl-	A	D	D	A	RA	RA	A	A	T	CM/M	CM	CM	CM	A
Propanoic acid, 2,2-dimethyl-, methyl ester	RA	RA	RA	RA	RA	RA	RA	RA	RA	CM/M	CM	CM	CM	RA
Carboxylic acid, C6-8 neo	A	RA	RA	A	A	RA isooctanoic	A	A	A	CM/M	CM	CM	CM	A
Neodecanoic acid	A	D	D	A	RA	A	A	A	RA	CM/M	CM	CM	CM	A
Fatty acids, C9-13 neo	RA	D	D	RA	RA	RA isononanoic	T	T	T	CM/M	CM	CM	CM	A
Fatty acids, C9-28 neo	RA	RA	RA	RA	RA	RA	RA	RA	RA	CM/M	CM	CM	CM	RA

¹ Measured data for selected physicochemical endpoints will be identified in conjunction with calculated data to characterize this category.

A Adequate existing data available

TD Technical Discussion proposed

RA Read Across (see Sec. III.B)

CM Computer Modeling proposed

T Testing proposed

M Measured data where available

NA Not Applicable

D Data available from another supplier; robust summaries will be provided

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Neoacids (C₅-C₂₈) Category

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**Robust Summaries
(Mammalian Toxicity)**

CAS# 75-98-9: Propanoic acid, 2,2-dimethyl-
CAS# 598-98-1: Propanoic acid, 2,2-dimethyl-, methyl ester
CAS# 95823-36-2: Carboxylic acid, C6-8 neo
CAS# 26896-20-8: Neodecanoic acid
CAS# 68938-07-8: Fatty acids, C9-C13 neo
CAS# 72480-45-6: Fatty acids, C9-C28 neo

Prepared by:

ExxonMobil Chemical Company

November 15, 2001

(Revised December 17, 2002)

Table of Contents

CAS # 75-98-9; Propanoic acid, 2,2-dimethyl-

Acute Oral
Acute Dermal
Acute Inhalation
Repeat Dose - Dermal

CAS # 95823-36-2; Carboxylic acid, C6-8 neo

Acute Oral
Acute Dermal
Acute Inhalation
Repeat Dose - Dermal
Developmental Toxicity

CAS #26896-20-8; Neodecanoic acid

Acute Oral
Acute Dermal
Acute Inhalation (vapor)
Acute Inhalation (aerosol)
Repeat Dose - Dermal
Reproductive Toxicity

CAS # 25103-52-0; Isooctanoic acid (read-across)

Developmental Toxicity
Reproductive Toxicity

CAS #3302-10-1; Isononanoic acid (read-across)

Reproductive Toxicity

Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p>	<p>Propanoic acid, 2,2-dimethyl- 75-98-9</p> <p>Other Acute oral toxicity Pre-GLP 1964 Sprague-Dawley Rats Males 5/dose Gastric Intubation None Single Dose 34.6, 120, 417, 1450, 5000, and 10000 mg/kg None</p>
<p>Remarks on Test Conditions</p>	<p>The animals were fasted for a period of three to four hours prior to treatment. The animals were observed for toxic effects and mortality at one, four and 24 hours; and once daily thereafter for 14 days. A necropsy was performed on any animal that died. All surviving animals were weighed, sacrificed and necropsied.</p>
<p>Results</p>	<p>LD₅₀= 2000 mg/kg (CL: 830-4820 mg/kg) Number of animals dead per number tested: 34.6, 120 and 417 mg/kg: 0/5 1450 mg/kg: 2/5 5000 mg/kg: 5/5 10,000 mg/kg: 5/5</p>
<p>Remarks</p>	<p>There were no deaths and no findings at necropsy in animals treated with 34.6, 120 and 417 mg/kg. At the 1450 mg/kg level, 2 of 5 animals died by day 2 and the remaining animals survived until the end of the study. These animals showed depression, severe dyspnea, depressed reflexes, sprawling, and lack of coordination. All animals in the 5000 and 10,000 mg/kg dose groups died within 48 hours of treatment. Severe depression, dyspnea, and prostration preceded death in all of the animals that died. Necropsy findings in high dose animals indicated congestion of lungs, liver, kidneys, and adrenals.</p>
<p>Conclusions</p>	<p>Under conditions of this study, Propanoic acid, 2,2-dimethyl- acid has a low order of acute oral toxicity in rats.</p>
<p>Data Quality</p>	<p>2 - Valid with restrictions (Pre-GLP)</p>
<p>Reference</p>	<p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p>
<p>Date last changed</p>	<p>October, 2000</p>

Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p>	<p>Propanoic acid, 2,2-dimethyl- 75-98-9</p> <p>Other Acute dermal toxicity Pre-GLP 1964 Rabbits/Albino Males and Females 2/sex/dose Dermal None Single Dose 50, 200, 794, 3160 mg/kg None</p>
<p>Remarks on Test Conditions</p>	<p>Undiluted test sample was applied to clipped, intact abdominal skin under a dental dam binder. The trunk was subsequently wrapped with gauze and adhesive tape. Following a 24-hour exposure period, binders were removed and the abdominal area was sponged with corn oil to remove sample residue. Following exposure, animals were observed for mortality or toxic effects at 1, 4, and 24 hours, and once daily thereafter for a total of 14 days. A necropsy was performed on any animal that died during the study. At the end of the 14-day observation period, all surviving animals were weighed, sacrificed, and necropsied.</p>
<p>Results</p>	<p>LD50 = 3160 mg/kg</p>
<p>Remarks</p>	<p>In the highest dose group, two deaths occurred at 24 and 48 hours after exposure to the test substance. Death was preceded by marked depression, severe, dyspnea, prostration, excessive urination, and coma. Necropsy revealed congestion of the lungs, adrenals, kidneys, and blanched areas on the liver and spleen. In addition, inflammation of the bladder and gastrointestinal tract were noted. In the 794 mg/kg group, three of the four animals exhibited slight depression, dyspnea, unsteady gait with slight sprawling of the limbs at 24 hours after exposure to the test substance. However, by the third day post-exposure, all of the animals appeared normal. At the termination of the study, necrotic tissue was seen in the abdominal skin at the site of application of the test substance. Otherwise, no gross pathology was observed. In animals exposed to 50 and 200 mg/kg of the test substance, no signs of systemic toxicity were observed. These animals exhibited normal weight gain, appearance, and behavior.</p> <p>Dermal irritation was noted at all dose levels and was characterized by slight, transient erythema, edema, atonia, and desquamation at the lowest level. There was a dose-dependent increase in the intensity and persistence with pronounced irritation at the highest dose levels characterized by blanching, eschar formation, and necrosis.</p>
<p>Conclusions</p>	<p>Under conditions of this study, Propanoic acid, 2,2-dimethyl- has a low order of acute dermal toxicity in rabbits.</p>
<p>Data Quality</p>	<p>2 - Valid with restrictions (Pre-GLP)</p>
<p>Reference</p>	<p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p>
<p>Date last changed</p>	<p>January, 2001</p>

Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p>	<p>Propanoic acid, 2,2-dimethyl- 75-98-9</p> <p>Other Acute inhalation toxicity Pre-GLP 1964 Rats Wistar, Mice/Swiss albino Males 10/species Inhalation Other Single 6-hour exposure Saturated vapors - the mean nominal concentration was 4.0 mg/L. A group of mice and rats that served as a common control for the substances tested in this study were sacrificed and examined grossly.</p>
<p>Remarks on Test Conditions</p>	<p>An atmosphere of saturated vapors was produced by forcing air through a bubbler system that contained the test substance. 29 ml of liquid was vaporized at a flow rate of 23 L/min. Animals were caged in wire mesh compartments within the exposure chamber. Animals were observed for mortality and toxic effects at 30-minute intervals during exposure and daily thereafter. The animals were observed for two weeks following exposure, at which point animals were sacrificed and necropsied. Any animals that died during the exposure or observation periods were necropsied.</p>
<p>Results</p>	<p>Mouse LC50 < 4.0 mg/L Rat > 4.0 mg/L</p>
<p>Remarks</p>	<p>No deaths occurred among any of the animals during the inhalation exposure. Hyperactivity followed by prostration was observed in mice. All 10 mice died within the 24 hours following exposure. Two rats died on the second and fifth days. Rats displayed piloerection, epistaxis, and dyspnea following exposure. Due to advanced autolysis, necropsy of the animals that died did not reveal any meaningful findings. Necropsy of the animals that survived until termination of the study did not reveal any significant gross pathology.</p>
<p>Conclusions</p>	<p>Propanoic acid, 2,2-dimethyl- has a moderate order of inhalation toxicity in rodents.</p>
<p>Data Quality</p>	<p>2 - Valid with restrictions - No vapor concentration verification (analytical)</p>
<p>Reference</p>	<p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p>
<p>Date last changed</p>	<p>January, 2001</p>

Repeat Dose Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p> <p>Statistical method</p> <p>Remarks on Test Conditions</p> <p>Results</p> <p>Remarks</p>	<p>Propanoic acid, 2,2-dimethyl- 75-98-9</p> <p>Other Repeat dermal application Pre-GLP 1964 Albino Rabbits Male 4/dose Dermal Isopropyl Alcohol (IPA) 10 applications with a two-day rest between the 5th and 6th applications. 30mg/kg and 300mg/kg weight/volume solution in isopropyl alcohol Isopropyl Alcohol (IPA) was administered to 8 animals at a level of 2.5 ml/kg body weight per application. Not reported</p> <p>The test material was applied to clipped abdominal skin. A loose gauze binder or a collar was used to prevent ingestion of the test substance. Animals were housed individually and allowed free access to food and water. Each animal was weighed, sacrificed, and necropsied 24 hours after the final application of test material. At the beginning of the study and prior to the final application, the following clinical parameters were evaluated: total erythrocyte count, total and differential leukocyte count, hematocrit, and urinalysis. Histological analysis was performed on sections of liver and kidney. Sections of brain, thyroid, lungs, heart, liver, kidneys, adrenals, skin, and bone marrow were preserved for possible future analysis.</p> <p>For systemic effects: NOAEL = 300 mg/kg Propanoic acid, 2,2-dimethyl- produced moderate to severe skin irritation.</p> <p>The control animals exhibited normal appearance and behavior throughout the study with the exception of nasal discharge in one animal and diarrhea in another. Slight body weight loss was observed during the first week, but the animals regained the weight and most animals showed overall weight gains by the end of the study. No treatment-related effects were observed at gross necropsy. Repeat applications did not cause any histopathological alterations to the liver or kidney of the rabbits.</p> <p>Control animals exhibited slight erythema throughout the study and slight atonia and desquamation following the fifth application. Animals that received the test substance exhibited normal appearance and behavior throughout the study. Animals in the low dose group showed a net body weight gain by the end of the study and animals in the high dose group showed a slight weight loss by the end of the study. Gross pathological findings revealed parasitic infection of the liver and pitted kidneys in one rabbit, congested lungs in another, and congestion in the pancreas and kidney of a third rabbit. Slight to moderate erythema was observed in the low dose animals. Animals in the high dose group displayed moderate erythema, moderate edema, and moderate to marked atonia and desquamation. Three of the animals in the high dose group had areas of necrosis that persisted through the study.</p>
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Conclusions	Under the conditions of this study, Propanoic acid, 2,2-dimethyl- has a low order of systemic toxicity following repeated dermal exposure.
Data Quality	2 - Valid with restrictions (Pre-GLP)
Reference	Hazleton Laboratories, Inc. (1964) "Repeated Dermal Application - Rabbits," Unpublished report.
Date last changed	January 2001

Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels (mg/kg Control group and Treatment</p>	<p>Carboxylic acid, C6-8 neo 95823-36-2</p> <p>Other Acute oral toxicity Pre-GLP 1964 Sprague-Dawley Rats Males 5/dose Gastric Intubation Corn oil for 34.6, 120, 417, 1450 mg/kg doses Single Dose 34.6 (1%v/v), 120(1%v/v), 417(10%v/v), 1450(10%v/v), 5000 (undiluted), and 10000 (undiluted) mg/kg None</p>
<p>Remarks on Test Conditions</p>	<p>The animals were fasted for a period of three to four hours prior to treatment. The animals were observed for toxic effects and mortality at one, four and 24 hours; and once daily thereafter for 14 days. Necropsy was performed on any animal that died. All surviving animals were weighed, sacrificed and necropsied.</p>
<p>Results</p>	<p>LD₅₀= 1860 mg/kg (No CL - all or none response)</p>
<p>Remarks</p>	<p>There were no principal toxic effects at 34.6, 120 and 417 mg/kg. In addition there were no findings at necropsy in these animals. At 1450 mg/kg, although there were no findings at necropsy, clinical signs were observed after dosing which included depression, dyspnea and slight to marked ataxia. At the two highest dose levels, all animals were dead within 24 hours. Prior to death, animals exhibited marked depression, sprawling of the limbs and depressed reflexes. Congestion of the lungs, kidneys and adrenals were observed in these animals.</p>
<p>Conclusions</p>	<p>Under conditions of this study, Carboxylic acid, C6-8 neo acid has a low order of acute oral toxicity in rats.</p>
<p>Data Quality</p>	<p>2 - Valid with restrictions (Pre-GLP)</p>
<p>Reference</p>	<p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p>
<p>Date last changed</p>	<p>January, 2001</p>

Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p>	<p>Carboxylic acid, C6-8 neo 95823-36-2</p> <p>Other Acute dermal toxicity Pre-GLP 1964 Albino Rabbits Males and Females 2/sex/dose Dermal None Single Dose 50, 200, 794, 3160 mg/kg None</p>
<p>Remarks on Test Conditions</p>	<p>Undiluted test sample was applied to clipped, intact abdominal skin under a dental dam binder. The trunk was subsequently wrapped with gauze and adhesive tape. Following a 24-hour exposure period, binders were removed and the abdominal area was sponged with corn oil to remove sample residue. Following exposure, animals were observed for mortality or toxic effects at 1, 4, and 24 hours, and once daily thereafter for a total of 14 days. A necropsy was performed on any animal that died during the study. At the end of the 14-day observation period, all surviving animals were weighed, sacrificed, and necropsied.</p>
<p>Results</p>	<p>LD50 > 3160 mg/kg</p>
<p>Remarks</p>	<p>One death occurred in the 200 mg/kg group at 48 hours post-exposure, but this was not considered to be treatment-related, since no deaths occurred in any of the other treatment groups. Upon necropsy, cecal obstruction and a large amount of fluid in the abdominal cavity were found. No signs of systemic toxicity were seen in any of the animals exposed to 50, 200, or 794 mg/kg. In the highest dose group, marked depression, dyspnea, ataxia, and sprawling of the limbs were observed 1 to 4 hours after application. However, the animals had completely recovered by 24 hours following exposure and exhibited normal appearance and behavior for the remainder of the 14-day post-exposure period. Necropsy revealed no significant signs of gross pathology in these animals.</p> <p>Dose-dependent dermal irritation occurred at all of the doses tested. This ranged from slight to moderate erythema, atonia, and desquamation at the lower dose levels to moderate erythema and edema with atonia and desquamation at the two higher dose levels.</p>
<p>Conclusions</p>	<p>Under conditions of this study, Carboxylic acid, C6-8 neo acid has a low order of acute dermal toxicity in rabbits.</p>
<p>Data Quality</p>	<p>2 - Valid with restrictions (Pre-GLP)</p>
<p>Reference</p>	<p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p>
<p>Date last changed</p>	<p>January, 2001</p>

Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p>	<p>Carboxylic acid, C6-8 neo 95823-36-2</p> <p>NA Acute inhalation toxicity Pre-GLP 1964 Rats/Albino, Mice/Albino Males 10/species Inhalation None Single 6-hour exposure Saturated vapors - the mean nominal concentration was 3.0 mg/L. Groups of mice and rats that served as common controls for the substances tested in this study were sacrificed and examined grossly.</p>
<p>Remarks on Test Conditions</p>	<p>An atmosphere of saturated vapors was produced by forcing air through a bubbler system that contained the test substance. 31 ml of liquid was vaporized at a flow rate of 27 L/min. Animals were caged in wire mesh compartments within the exposure chamber. Animals were observed for mortality and toxic effects at 30-minute intervals during exposure and daily thereafter. The animals were observed for two weeks following exposure, at which point animals were sacrificed and necropsied. Any animals that died during the exposure or observation periods were necropsied.</p>
<p>Results</p>	<p>LD50 > 3.0 mg/L</p>
<p>Remarks</p>	<p>No significant toxic signs were observed during the 6-hour exposure period. All mice and rats appeared normal up to 5 days following exposure, when the mice developed urticaria. No deaths occurred in mice or rats throughout the study and no significant observations were made at necropsy.</p>
<p>Conclusions</p>	<p>Under conditions of this study, Carboxylic acid, C6-8 neo has a low order of acute inhalation toxicity in mice and rats.</p>
<p>Data Quality</p>	<p>2 - Valid with restrictions - No vapor concentration verification (analytical)</p>
<p>Reference</p>	<p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p>
<p>Date last changed</p>	<p>January, 2001</p>

Repeat Dose Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p> <p>Statistical method</p> <p>Remarks on Test Conditions</p> <p>Results</p> <p>Remarks</p>	<p>Carboxylic acid, C6-8 neo 95823-36-2</p> <p>Other Repeat dermal application Pre-GLP 1964 Albino Rabbits Male 4/dose Dermal None 10 applications with a two-day rest between the 5th and 6th applications. 55.4 mg/kg, 553.7 mg/kg Isopropyl Alcohol (IPA) was administered to 8 animals at a level of 2.5 ml/kg body weight per application. Not reported</p> <p>The test material was applied to clipped abdominal skin. A loose gauze binder or a collar was used to prevent ingestion of the test substance. Animals were housed individually and allowed free access to food and water. Each animal was weighed, sacrificed, and necropsied 24 hours after the final application of test material. At the beginning of the study and prior to the final application, the following clinical parameters were evaluated: total erythrocyte count, total and differential leukocyte count, hematocrit, and urinalysis. Histological analysis was performed on sections of liver and kidney. Sections of brain, thyroid, lungs, heart, liver, kidneys, adrenals, skin, and bone marrow were preserved for possible future analysis.</p> <p>For systemic effects: NOAEL = 553.7 mg/kg Carboxylic acid, C6-8 neo produced moderate to severe skin irritation.</p> <p>Animals in the low dose group showed normal appearance behavior throughout the study. With the exception of one animal that showed a slight weight loss, the animals in the low dose group showed an overall body weight gain. In the high dose group, 3 of the 4 animals displayed normal appearance and behavior and either maintained their weight or had a slight weight loss. From the fifth through the ninth application, the fourth animal had labored breathing, weight loss, and was found dead 24 hours after the final application. Upon necropsy, this animal had congested and emphysematous lungs in addition to hemorrhagic areas in the renal medulla. The death of this animal was deemed to be unrelated to the treatment. Gross pathology of the remaining animals of the high dose group did not reveal any abnormalities other than a slight parasitic infection in the liver of one of the rabbits. Repeat applications did not cause any histopathological alterations to the liver or kidney of the rabbits.</p> <p>In the low dose animals, slight erythema was observed during the first week, with slight to moderate atonia and desquamation that followed the third application and lasted through the study. At the highest dose, slight to moderate erythema was observed and slight to moderate edema was present from the second through the fifth applications. After the fourth application, moderate to marked atonia, desquamation, and slight fissuring was observed through the remainder of the study. All animals showed areas of necrosis at the application site and in two animals, the skin was hypersensitive to touch.</p>
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<p>Conclusions</p> <p>Data Quality</p> <p>Reference</p> <p>Date last changed</p>	<p>Under the conditions of this study, Carboxylic acid, C6-8 neo has a low order or systemic toxicity following repeated dermal exposure.</p> <p>2 - Valid with restrictions (Pre-GLP)</p> <p>Hazleton Laboratories, Inc. (1964) "Repeated Dermal Application - Rabbits," Unpublished report.</p> <p>January 2001</p>
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Developmental Toxicity

<p>Test Substance CAS No.</p> <p>Method Type of Study GLP Year Species/Strain Sex Number/sex/dose Route of administration Exposure Period Concentrations Controls Statistical methods</p>	<p>Carboxylic acid, C6-8 neo 95823-36-2</p> <p>OECD 414 Developmental toxicity Yes 1986 Sprague-Dawley Rats Pregnant Females 22/dose Oral gavage Days 6-15 of gestation 0, 50, 250, 600, or 800 mg/kg Controls received 800 mg/kg of distilled water ANOVA, Kruskal-Wallis, Fisher's exact test</p>
<p>Remarks on Test Conditions</p>	<p>Test material was assumed to be 100% pure for purposes of dosing. Physical examinations were performed and body weight and food consumption were measured throughout gestation. Mated females were sacrificed on gestational day 20 and a gross necropsy was performed. Uteri and ovaries were weighed and corpora lutea were counted. The number of implantation sites, early and late resorptions, and live and dead fetuses were determined. Full term fetuses were examined for abnormalities, weight, and crown-rump distance. From each litter, the heads of half of the fetuses were preserved and examined, while the other half of the fetuses were examined for skeletal malformations and ossification variations.</p>
<p>Results</p>	<p>NOAEL fetal: 250 mg/kg NOAEL maternal: 250 mg/kg</p>
<p>Remarks for Results</p>	<p>Maternal: The high dose of 800 mg/kg produced morbidity and mortality in 4 of the 22 mated females. This group displayed lethargy, abnormal breathing, rales, and staining around the muzzle and anogenital areas. Animals in the 600 mg/kg group had a significant incidence of rales. In the high dose group, group mean maternal body weight gain (800 mg/kg: 306.1± 26.3g vs. CON: 391.9 ±29.7g) and uterine weight at term (800 mg/kg: 17.6 ±18.3g vs. CON: 76 ±18g) were significantly reduced. In the 600 mg/kg group, there was a significant reduction in body weight gain during the intervals of gd6-9 and gd0-20, although there was no statistically significant difference in body weight at term. Maternal food consumption was significantly reduced during gestational intervals gd6-9 and gd9-12 for both the 600 and 800 mg/kg groups and during gd12-16 in the 800 mg/kg group.</p> <p>Fetus: In the high dose group, there was a significant increase in early embryonic resorptions with a corresponding decrease in the mean number of live fetuses. The remaining fetuses in the high dose group had significantly reduced fetal body weight (800 mg/kgmales: 2.52±0.48g, 800 mg/kg/ females: 2.33±0.39g; CON males: 3.49±0.33g, Con females: 3.33±0.34g) and crown-rump distance. Microphthalmia and anophthalmia were observed in 14% of the fetuses from the high dose group. In addition, fused cervical vertebrae and misaligned thoracic vertebra were observed in the high dose group. Significant incidences of hydrocephalus and structural malformation of thoracic ribs occurred in both the 600 and 800 mg/kg groups. The fraction of malformed fetuses/live fetuses was significantly increased in the 600 and 800 mg/kg groups. In the 250 mg/kg group, there was an increase in the fraction of implants affected, however, this was not significantly different from the control group.</p>

Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels (mg/kg) Control group and Treatment</p>	<p>Neodecanoic acid 26896-20-8</p> <p>Other Acute oral toxicity Pre-GLP 1964 Rats/Sprague-Dawley Males 5/dose Gastric Intubation Corn oil for 34.6, 120, 417, 1450 mg/kg Single Dose 34.6 (1%v/v), 120(1%v/v), 417(10%v/v), 1450(10%v/v), 5000 (undiluted), and 10000 (undiluted) mg/kg None</p>
<p>Remarks on Test Conditions</p>	<p>Test material was assumed to be 100% pure for purposes of dosing. The animals were fasted for a period of three to four hours prior to treatment. The animals were observed for toxic effects and mortality at one, four and 24 hours; and once daily thereafter for 14 days. Necropsy was performed on any animal that died. All surviving animals were weighed, sacrificed and necropsied.</p>
<p>Results</p>	<p>LD50= 2000 mg/kg (CL: 670-5980 mg/kg)</p>
<p>Remarks</p>	<p>There were no principal toxic effects or necropsy findings for animals in the 34.6, 120 and 417 mg/kg treatment groups. At 1450 mg/kg, 1 animal died within 24 hours of exposure and one animal died each day thereafter until all 5 animals were dead by day 5 of the study. Prior to death, slight to marked CNS depression, dyspnea, and ataxia was observed. In addition, congestion of the lungs, kidneys and adrenals were observed at necropsy. In the 5,000 mg/kg dose group, 2/5 animals died by 4 hours and 5/5 animals were dead by 24 hours following exposure. In the highest dose group, 4/5 animals died by 4 hours and all animals were dead by 24 hours post-treatment. Animals in the 5,000 and 10,000 mg/kg groups appeared to have depression, dyspnea, ataxia and sprawling of the limbs. Also at these two dose levels, necropsy findings indicated congestion of the lungs, liver, spleen, kidneys and adrenals.</p>
<p>Conclusions</p>	<p>Neodecanoic acid has a low order of acute oral toxicity in rodents.</p>
<p>Data Quality</p>	<p>2 - Valid with restrictions (Pre-GLP)</p>
<p>Reference</p>	<p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p>
<p>Date last changed</p>	<p>October, 2000</p>

Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p> <p>Remarks on Test Conditions</p> <p>Results</p> <p>Remarks</p> <p>Conclusions</p> <p>Data Quality</p> <p>Reference</p> <p>Date last changed</p>	<p>Neodecanoic acid 26896-20-8</p> <p>NA Acute dermal toxicity Pre-GLP 1964 Albino Rabbits Males and Females 4/dose Dermal None Single Dose 50, 200, 794, 3160 mg/kg None</p> <p>Test material was assumed to be 100% pure for purposes of dosing. Undiluted test sample was applied to clipped, intact abdominal skin under a dental dam binder. The trunk was subsequently wrapped with gauze and adhesive tape. Following a 24-hour exposure period, binders were removed and the abdominal area was sponged with corn oil to remove sample residue. Following exposure, animals were observed for mortality or toxic effects at 1, 4, and 24 hours, and once daily thereafter for a total of 14 days. A necropsy was performed on any animal that died during the study. At the end of the 14-day observation period, all surviving animals were weighed, sacrificed, and necropsied.</p> <p>LD50 > 3160 mg/kg</p> <p>No deaths occurred with any of the doses tested. The animals appeared normal in appearance and behavior throughout the study. All of the animals exhibited a normal pattern of weight gain. No signs of gross pathology were observed at necropsy.</p> <p>No dermal irritation was observed at the 50 mg/kg dose level and minimal irritation characterized by slight erythema, atonia, and desquamation that subsided in 10 days was noted at the 200 mg/kg level. At the 794 and 3160 mg/kg levels, a dose-dependent increase in the degree of irritation was observed. This consisted of slight to moderate erythema, which subsided after the fourth and eighth days, and slight to moderate atonia and desquamation that diminished in severity through the 14-day period.</p> <p>Under conditions of this study, Neodecanoic acid has a low order of acute dermal toxicity in rabbits.</p> <p>2 - Valid with restrictions (Pre-GLP)</p> <p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p> <p>January, 2001</p>
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Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment: Dose/Concentration Levels: Control group and Treatment:</p> <p>Remarks on Test Conditions</p> <p>Results</p> <p>Remarks</p> <p>Conclusions</p> <p>Data Quality</p> <p>Reference</p> <p>Date last changed</p>	<p>Neodecanoic acid 26896-20-8</p> <p>Other Acute inhalation toxicity Pre-GLP 1964 Rats/Wistar, Mice/Swiss albino Males 10/species Inhalation None Single 6-hour exposure Saturated vapors - the mean nominal concentration was 3.0 mg/L. A group of mice and rats that served as a common control for the substances tested in this study were sacrificed and examined grossly.</p> <p>Test material was assumed to be 100% pure for purposes of dosing. An atmosphere of saturated vapors was produced by forcing air through a bubbler system that contained the test substance. 20 ml of liquid was vaporized at a flow rate of 21 L/min. Animals were caged in wire mesh compartments within the exposure chamber. Animals were observed for mortality and toxic effects at 30-minute intervals during exposure and daily thereafter. The animals were observed for two weeks following exposure, at which point animals were sacrificed and necropsied. Any animals that died during the exposure or observation periods were also necropsied.</p> <p>LD50 > 3.0 mg/L</p> <p>No mortality or significant signs of toxicity were observed during the 6-hour exposure period. No deaths occurred in mice or rats throughout the study and no significant observations were made at necropsy.</p> <p>Under conditions of this study, Neodecanoic acid has a low order of acute inhalation toxicity in mice and rats.</p> <p>2 - Valid with restrictions - No vapor concentration verification (analytical)</p> <p>Esso Research and Engineering Company (1964). Acute Oral, Dermal, Eye Irritation and Inhalation Toxicity. Unpublished report.</p> <p>January, 2001</p>
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Acute Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle Frequency of Treatment Dose/Concentration Levels Control group and Treatment</p> <p>Remarks on Test Conditions</p>	<p>Neodecanoic acid 26896-20-8</p> <p>Other Acute inhalation toxicity No 1982 Rats/Wistar, Mice/Swiss albino, Guinea Pigs/Harley Males and Females 10/sex/species Inhalation None Single 6-hour exposure Liquid aerosol with a mean analytical concentration of 511 mg/m³ 10/sex/species</p> <p>Test material was assumed to be 100% pure for purposes of dosing. Groups of animals (10/sex/species) were exposed to either air only or to aerosolized test material. Aerosol was generated by pumping the test material into an atomizer at 15.0 psi. The resulting aerosol was sprayed into a glass aerosol diffuser, where it was mixed with incoming room air before entering the chamber. Exposure concentrations were determined on both a nominal and actual (gravimetric) basis. Particle size determinations were conducted twice during exposure. During the exposure, control and treated animals were observed every 15 minutes for the first hour and hourly thereafter. On the first day post-exposure, one half of the animals from each group were randomly selected and sacrificed, and an interim necropsy was performed. The remaining animals were observed daily for signs of toxicity for 14 days post-exposure. Body weights were recorded at the beginning of the study, and at 1, 2, 3, 4, 7, and 14 days post-exposure. A necropsy was performed on all animals that died or were sacrificed during the study. Major organs were examined for macroscopic abnormalities and lungs plus trachea, liver, kidneys, whole head, and any abnormal tissues were preserved. Organ weights were recorded at necropsy for lungs plus trachea, liver, and kidneys.</p>
<p>Results</p>	<p>LD50 > 511 mg/m³; Mean Particle size: 2.99±1.76µm</p>
<p>Remarks</p>	<p>No animals died during the study. The control animals appeared normal throughout the exposure. During the two-week post-exposure period, incidences of ungroomed appearance, soft stool, and anogenital staining were observed in some of the control animals. One female guinea pig in the control group died on the fifth day of the post-exposure observation period.</p> <p>Animals exposed to the test material exhibited some signs of labored breathing, salivation, and eye irritation during the exposure. Upon removal from the chamber, exposed mice and guinea pigs had material-covered fur and exposed rats had some red staining around the nasal area, anogenital staining, soft stool, salivation, and lacrimation. During the two-week post-exposure observation period, all guinea pigs appeared normal. However, some of the mice appeared ungroomed and some rats exhibited anogenital staining and soft stool. Throughout the study, body weights remained normal except for a slight weight loss on the first and second post-exposure days in both the control and treated groups (all species). However, there was no statistically significant difference between control and treated groups.</p>

<p>Results, continued</p> <p>Conclusions</p> <p>Data Quality</p> <p>Reference</p> <p>Date last changed</p>	<p>At terminal sacrifice, male mice exposed to the aerosolized test substance exhibited a statistically significant decrease in the liver to body weight ratio versus control animals. No other statistically significant differences were observed for group mean organ weight to body weight ratios. Minor macroscopic abnormalities were observed in both control and treated groups at the interim and terminal necropsies, but were not considered to be related to exposure to the test substance.</p> <p>Under conditions of this study, aerosolized Neodecanoic acid has a low order of acute inhalation toxicity in mice, rats, and guinea pigs.</p> <p>1 - Valid without restrictions</p> <p>Bio/dynamics, Inc. (1982) "Evaluation of the Acute inhalation Toxicity in Rats, Mice, and Guinea Pigs". Unpublished report.</p> <p>January, 2001</p>
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Repeat Dose Toxicity

<p>Test Substance CAS No.</p> <p>Method Type of Study GLP Year Species/Strain</p> <p>Sex Number/sex/dose Route of administration Vehicle Exposure Period Concentrations Controls</p> <p>Statistical method</p> <p>Remarks on Test Conditions</p> <p>Results</p> <p>Remarks for Results</p>	<p>Neodecanoic acid 26896-20-8</p> <p>Other Repeat dermal application Pre-GLP 1964 Albino Rabbits</p> <p>Male 4/dose Dermal None 10 applications with a two-day rest between the 5th and 6th applications. 0.4 g/kg and 2.28 g/kg Isopropyl Alcohol (IPA) was administered to 8 animals at a level of 2.5 ml/kg body weight per application. Not reported</p> <p>Test material was assumed to be 100% pure for purposes of dosing. The test material was applied to clipped abdominal skin. A loose gauze binder or a collar was used to prevent ingestion of the test substance. Animals were housed individually and allowed free access to food and water. Each animal was weighed, sacrificed, and necropsied 24 hours after the final application of test material. At the beginning of the study and prior to the final application, the following clinical parameters were evaluated: total erythrocyte count, total and differential leukocyte count, hematocrit, and urinalysis. Histological analysis was performed on sections of liver and kidney. Sections of brain, thyroid, lungs, heart, liver, kidneys, adrenals, skin, and bone marrow were preserved for possible future analysis.</p> <p>For systemic effects: NOAEL = 2.28 g/kg Neodecanoic acid produced moderate skin irritation.</p> <p>Wheezing was noted in one animal of the low dose group. However, the rest of the animals appeared normal in behavior and appearance throughout the study. Animals in the low dose group showed overall body weight gain while animals in the high dose group had a slight reduction in weight at the end of the study. Necropsy revealed parasitic areas on the liver and/or mesentery of three animals, emphysema in three animals, and fluid in the cranial cavity and sinuses of one animal. These findings, however, did not correlate with the dose of test material received and were not attributed to exposure to the test substance. Animals in both the low and high dose groups displayed a decrease in terminal total leukocyte count. However, these values were within the normal limit value for rabbits. Repeat applications did not cause any histopathological alterations to the liver or kidney of the rabbits.</p> <p>Animals in the low dose group displayed slight erythema and moderate atonia and desquamation starting on the first or fourth application and persisting through the remainder of the study. All animals in the high dose group had moderate erythema, moderate to marked atonia and desquamation, and slight edema after the fifth application. After seven applications, slight fissures were observed in some of the animals and the exposed skin became hypersensitive to touch.</p>
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<p>Conclusions</p> <p>Data Quality</p> <p>Reference</p> <p>Date last changed</p>	<p>Under the conditions of this study, Neodecanoic acid has a low order of systemic toxicity following subchronic dermal exposure.</p> <p>2 - Valid with restrictions (Pre-GLP)</p> <p>Hazleton Laboratories, Inc. (1964) "Repeated Dermal Application - Rabbits," Unpublished report.</p> <p>January 2001</p>
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Reproductive Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Frequency of Treatment Dose/Concentration Levels Control group and Treatment Duration of Test Pre-mating Exposure Period</p>	<p>Neodecanoic acid 26896-20-8</p> <p>Other Reproductive Toxicity Pre-GLP 1968 Rats/Sprague-Dawley Males and Females P₁: 80 females and 40 males Dietary Continuous 0, 100, 500, 1500 ppm in diet (5, 25, and 75 mg/kg/day) Purina Lab Chow, 0 ppm of test substance 3 generations P1: 9 weeks for both males and females</p>
<p>Remarks on Test Conditions</p>	<p>Test material was assumed to be 100% pure for purposes of dosing. Pre-mating Period: For each dose level, 10 males and 20 females comprised the P₁ generation. The parental generation animals were maintained in individual cages and fed the corresponding diet for 9 weeks prior to mating. Individual body weights, food consumption, and observations of the physical appearance and behavior of the animals were recorded initially, at 5 weeks, and 9 weeks (P₁), or at 8 weeks, and 12 weeks (P₂). The F2B weanlings (P3) were fed the appropriate diets for 9 weeks and the same observations were recorded at 0, 8, and 9 weeks of exposure.</p> <p>Reproduction Period: Following 9 weeks of exposure, two females and 1 male from each group were housed together and allowed a 3-week mating period, during which time, males were rotated among the females on a weekly basis. 24 hours following birth of the F1A generation, litters were arbitrarily reduced to a maximum of 8 pups (4/sex) to be nursed. The number of conceptions, litters, live births, stillbirths, the size of natural and nursing litters, deaths during the period of lactation, and number of pups weaned were all recorded. The weights of the pups by sex were recorded at 24 hours and at weaning and all pups were observed for gross signs of abnormalities. Following the 21-day nursing period, representative pups from each litter were sacrificed and gross necropsies were performed. The remaining pups were discarded.</p> <p>One week following the weaning of the F1A litters, the P1 parents were re-mated in the same fashion to produce the F1B pups. Following the 21-day nursing period, 20 female and 10 male weanlings from each of the test groups were randomly designated as the P2 generation. The remaining F1B pups were sacrificed and necropsied. The P2 generation was fed the appropriate diet until 100 days of age and then mated in the same fashion to produce the F2A and F2B litters. The same procedures were followed as during the first reproductive phase. After the second litter, F2B, 20 females and 10 males were selected at random to be the P3 generation. Following 9 weeks of dietary administration to this generation, the study was terminated and gross necropsies were performed. The following tissues were preserved: brain, pituitary, eye, thyroid, lung, heart, liver, spleen, kidney, adrenal, stomach, pancreas, small and large intestine, urinary bladder, gonad, bone, bone marrow, and trachea. Tissues from 5 females and 5 males of the control and high dose groups underwent histological examination. In addition, sections of thyroid, lung, liver, kidney, adrenal and trachea from 5 females and 5 males of the low level and intermediate level groups were examined microscopically.</p>

<p>Results</p>	<p>NOAEL Parental: 1500 ppm NOAEL F1 Offspring: 1500 ppm NOAEL F2 Offspring: 1500 ppm</p>
<p>Remarks</p>	<p>For all of the concentrations tested, no adverse effects were observed on survival, appearance, behavior, body weight gain, and food consumption in either the parental generation or either the F1 or F2 generations. In addition, the reproductive performance of the parents was not affected. No treatment-related gross or microscopic pathological findings were observed at any of the dietary levels.</p> <p>All of the P1 and P2 animals survived the pre-mating periods and all of the P3 animals survived the 9-week post-weaning period of exposure. The body weight gain, food consumption, appearance, and behavior of the rats in these test groups were comparable with that of the control rats. In the F1A and F1B litters, litter size, pup body weights, appearance, and behavior were comparable between the treated groups and the control group. There were a variety of incidental findings in pups of the F1A and F1B litters, however, pups of these litters did not display any signs of treatment-related toxicity. At necropsy, there were no gross alterations that could be attributed to exposure to the test substance. The F2A and F2B litters, similar to the F1 litters had incidental findings, but did not show any treatment-related signs of toxicity, or effects on litter size, pup body weights, appearance, or behavior. Examination of the F2B weanling pups also (P3) did not reveal any treatment-related abnormalities.</p>
<p>Conclusions</p>	<p>Under the conditions of this study, dietary exposure to Neodecanoic acid has a low order of reproductive toxicity in rats.</p>
<p>Data Quality</p>	<p>2 - Valid with restrictions (Pre-GLP)</p>
<p>Reference</p>	<p>Hazleton Labs, Inc. (1968) "Modified Three-Generation Reproduction Study - Rats," Unpublished report.</p>
<p>Date last changed</p>	<p>January 2001</p>

Developmental Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Vehicle: Dose/Concentration Levels Control group and Treatment Statistical methods</p>	<p>Isooctanoic Acid 25103-52-0</p> <p>Other Developmental Toxicity Yes 1995 Rat/Sprague-Dawley Female 25/dose Oral gavage Corn oil 0, 50, 200, 400, 800, and 1000 mg/kg/day Vehicle control: corn oil Statistical evaluation of equality of means was done by appropriate one way analysis of variance. Also, a standard regression analysis for linear response in the dose groups was performed.</p>
<p>Remarks on Test Conditions</p>	<p>Test material was assumed to be 100% pure for purposes of dosing. Males and females were housed together until confirmation of mating. The presence of a sperm plug was set as gestational day (GD) 0. Mated females were dosed once daily from GD 6-15. Dosing volumes were 5 ml/kg for all groups and were based on the most recent body weight. Clinical observations were made daily during gestation. Food consumption and body weight measurements were made on every three days through GD21. On GD21, animals were euthanized and cesarean sections were performed. Gross necropsies were performed, uterine weights with ovaries were measured, uterine contents were examined, and uterine implantation data were recorded. All live fetuses were weighed, examined externally to determine sex and for gross malformations.</p>
<p>Results</p>	<p>Maternal NOAEL = 400 mg/kg/day Fetal NOAEL = 800 mg/kg/day</p>
<p>Remarks</p>	<p>Maternal: There were no treatment-related deaths during the study. However, there were some deaths in the different dose groups that were attributed to intubation errors. Animals in the 800 and 1000 mg/kg/day groups displayed clinical signs that included rales, stool abnormalities, and anogenital/abdominal staining following dose initiation on GD6. Animals in the remaining dose groups were free of clinical signs for the entire gestation period. Overall, there were no statistically significant differences in mean body weight gain for the entire gestation interval or the entire gestation interval corrected for uterine weight between treated and control animals. However, in the 800 and 1000 mg/kg/day groups, there were statistically significant decreases in body weight gain early during gestation (GD 6-15). This correlated with decreased mean food consumption in these groups during this time frame. In the 400 mg/kg/day group, there was evidence of slight body weight gain suppression during the interval following dosing. However, these animals recovered quickly and in the absence of a consistent response, this finding was considered the result of slight dosing trauma. There were no significant findings at necropsy other than some trauma that was indicative of dosing errors.</p>

Reproductive Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Dose/Concentration Levels Control group and Treatment Statistics</p>	<p>Isooctanoic Acid 25103-52-0</p> <p>Other One-Generation Reproductive Toxicity Yes 1999 Rat/Sprague-Dawley Males and Females 10/sex/dose Dietary 0, 1000, 5000, 7500, and 10,000 ppm in diet 10/sex For the statistical analysis the percent of normal sperm were transformed by Bloom’s transformation. All variables were analyzed by standard one-way analysis of variance (ANOVA). Residuals from the model were tested for normality by the Shapiro-Wilk. When there were differences in-group means based on the ANOVA, differences in means were tested using Duncan’s multiple range test.</p>
<p>Remarks on Test Conditions</p>	<p>Test material was assumed to be 100% pure for purposes of dosing. P1 males and females (10 animals/sex) were exposed to the test substance for 10 weeks prior to mating. One male and one female were paired for up to 2 weeks. Beginning on GD 21, mated females were examined at least twice daily for signs of parturition. On PND 0, 1, 4, 7, 14 and 21 the offspring were counted, sexed and each live pup was weighed. Pups were counted and examined externally on a daily basis during the postnatal period. All animals were weighed and examined on PND 28, 35, 42, and 49 (males only were weighed and examined on PND Day 49). On PND 4, after counting, weighing, and examining the pups, the size of each litter was adjusted by eliminating extra pups by random selection to yield as nearly as possible, 4 males and 4 females per liter. Pups from each litter were examined daily for developmental landmarks. Sperm analyses were conducted at necropsy. Surviving F1 females were sacrificed on PND 42 and surviving F1 males were sacrificed on PND 49 unless they had not met criteria for vaginal patency or preputial separation, respectively.</p>
<p>Results</p>	<p>Maternal and Offspring NOAEL = 7500 ppm</p>
<p>Remarks</p>	<p>There were signs of a slight palatability problem with the 7500 ppm and 10,000 ppm diets with the males and the 10,000 ppm diet with the females as indicated by decreases in mean food consumption during the early part of the first week of the study. This problem resolved itself by the second week of the study. However, during the first week of gestation and for the entire postpartum period, mean food consumption was significantly decreased in the 10,000 ppm group females. There were no treatment-related clinical in-life observations, gross postmortem observations, or organ weight effect in the parental animals during this study. In addition, there were no statistically significant effects on reproductive indices or sperm parameters. The offspring displayed no treatment-related effects on survival, clinical observations, time to developmental landmarks, or offspring postmortem observations. Statistically significant suppression of body weight gain was observed in the 10,000 ppm adult females on PPD 4 and 14 when compared with controls. There were statistically significant decreases in the 10,000 ppm group’s male mean offspring body weights on PND 14, 21, and 28. There also was a statistically significant decrease in the 10,000 ppm females’ mean offspring body weight on PND 14 and 28. These decreases in body weight in dams and offspring were transient and were thought to be related to decreased maternal food consumption.</p>

<p>Conclusions</p> <p>Data Quality</p> <p>Reference</p> <p>Date last changed</p>	<p>Under the conditions of this study Isooctanoic acid did not adversely affect reproductive parameters at doses that were nontoxic to the dams or their offspring.</p> <p>1 - Reliable without restrictions</p> <p>Exxon Biomedical Sciences, Inc. (1999) "One generation reproduction toxicity range-finding study in rats," Unpublished report.</p> <p>August, 2001</p>
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Reproductive Toxicity

<p>Test Substance CAS No.</p> <p>Method/Guideline Type of Study GLP Year Species/strain Sex No. of animals/sex/dose Route of administration Dose/Concentration Levels Control group and Treatment</p> <p>Statistics</p> <p>Remarks on Test Conditions</p> <p>Results</p> <p>Remarks</p>	<p>Isononanoic Acid 3302-10-1</p> <p>Other One-Generation Reproductive Toxicity Yes 1998 Rat/Sprague-Dawley Males and Females 10/sex/dose Dietary 0, 600, 1200, 2500, 5000 ppm in diet 10/sex</p> <p>For the statistical analysis the percent of normal sperm were transformed by Bloom's transformation. All variables were analyzed by standard one-way analysis of variance (ANOVA). Residuals from the model were tested for normality by the Shapiro-Wilk. When there were differences in-group means based on the ANOVA, differences in means were tested using Duncan's multiple range test.</p> <p>Test material was assumed to be 100% pure for purposes of dosing. P1 males and females (10 animals/sex) were exposed to the test substance for 10 weeks prior to mating. One male and one female were paired for up to 2 weeks. Beginning on GD 21, mated females were examined at least twice daily for signs of parturition. On PND 0, 1, 4, 7, 14, 21 and 28 the offspring were counted, sexed and each live pup was weighed. Pups were counted and examined externally on a daily basis during the postnatal period. On PND 4, after counting, weighing, and examining the pups, the size of each litter was adjusted by eliminating extra pups by random selection to yield as nearly as possible, 4 males and 4 females per litter. Pups from each litter were examined daily for developmental landmarks. Sperm analyses were conducted at necropsy. Surviving F1 females were sacrificed on PND 42 and surviving F1 males were sacrificed on PND 49 unless they had not met criteria for vaginal patency or preputial separation, respectively.</p> <p>Maternal and Offspring NOAEL = 1200 ppm</p> <p>There were no treatment-related deaths or clinical signs noted in the parental animals during this study. There also were no treatment-related clinical signs noted for the offspring. There were no treatment-related effects noted for the male reproductive parameters such as sperm motility, total cauda sperm count, homogenization resistant spermatid count, sperm morphology, or the reproduction indices of mean male fertility, male mating, female fertility, fecundity, or gestational indices. In addition, there were no treatment-related effects on absolute or relative reproductive organ weights.</p> <p>In the 5000 ppm dose group, statistically significant decreases in parental food consumption were attributed to reduced palatability of the diet. Decreases in body weights were noted in the 5000 ppm females at Gestation Days (GD) 7 and 21 and at Postpartum Days (PPD) 4, 7, and 14. Mean absolute and mean relative liver weights were increased in both sexes of the 5000 ppm group.</p> <p>The offspring of the 5000 ppm group had reduced Live Birth Index and reduced survival indices on Day 1 and Day 4. Also, offspring body weights of both sexes were reduced during the postnatal period. Offspring body weight was also reduced in males and female of the 2500 ppm group.</p>
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<p>Conclusions</p> <p>Data Quality</p> <p>Reference</p> <p>Date last changed</p>	<p>Under the conditions of this study the test substance did not adversely affect reproductive parameters at doses that were nontoxic to the dams or their offspring.</p> <p>1 - Reliable without restrictions</p> <p>Exxon Biomedical Sciences, Inc. (1998) "One generation reproduction toxicity range-finding study in rats," Unpublished report.</p> <p>August, 2001</p>
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Neoacids C5-C28 Category

Robust Summaries (Environmental Fate and Effects)

Prepared by:

ExxonMobil Chemical Company

November 15th, 2001

(updated December 19, 2002)

Robust Summaries - Neoacids C5-C28

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Biodegradation -Manometric Respirometry

Robust Summaries - Neoacids C5-C28

Invertebrate Acute Toxicity

Test Substance:	Propanoic acid, 2,2-dimethyl (C5)																													
Method/Guideline:	USEPA -660/3-75-009 Methods for Acute Toxicity with Fish and Macroinvertebrates, and Amphibians, 1975																													
Type (test type):	Daphnid Acute Toxicity Test																													
GLP:	Unknown																													
Year (study performed):	1977																													
Species:	Water Flea (Daphnia magna)																													
Analytical Monitoring:	No																													
Exposure Period:	48 hour																													
Statistical Method:	Moving Average-Angle Method, (Harris 1959)																													
Test Conditions:	<p>For each test concentration, the appropriate amount of test substance was dissolved in ethanol and pipetted into 500ml of dilution water. This solution was mixed with a magnetic stirrer and divided into three 150ml replicates for testing. The remaining 50ml was used for pH and dissolved oxygen measurements. A positive control (with ethanol) and a negative control (dilution water) were also tested. Test vessels were 250ml beakers containing five daphnids each. Dilution water was reconstituted deionized water with a hardness of 180mg/L as CaCO₃, with a pH of 8.0. The test was performed under static conditions with no aeration.</p> <p>Nominal test concentrations were 36, 60, 100, 170, 280, and 460 mg/L</p> <p>Test temperature was 22+/- 1 Deg C. Dissolved oxygen ranged from 8.6 to 8.8 mg/L during the study. The pH of the test solutions varied from Control - 8.3; 36 mg/L - 8.2; 170 mg/L - 7.6; and 460 mg/L - 5.2.</p> <p>Organisms were supplied by in-house cultures. Age = <24 hours old</p>																													
<ul style="list-style-type: none">Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.																														
Results:	LC50 = 202.94 mg/L (95% CI 241.23 to 168.21) based upon nominal test concentrations.																													
Units/Value:																														
<ul style="list-style-type: none">Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.	<table><thead><tr><th rowspan="2">Test Concentration</th><th colspan="2">Mean % Mortality</th></tr><tr><th>24 hr.</th><th>48 hr.</th></tr></thead><tbody><tr><td>Positive Control</td><td>0</td><td>0</td></tr><tr><td>Negative Control</td><td>0</td><td>0</td></tr><tr><td>36 mg/L</td><td>0</td><td>0</td></tr><tr><td>60 mg/L</td><td>0</td><td>0</td></tr><tr><td>100 mg/L</td><td>0</td><td>7</td></tr><tr><td>170 mg/L</td><td>7</td><td>13</td></tr><tr><td>280 mg/L</td><td>20</td><td>93</td></tr><tr><td>460 mg/L</td><td>100</td><td>100</td></tr></tbody></table>	Test Concentration	Mean % Mortality		24 hr.	48 hr.	Positive Control	0	0	Negative Control	0	0	36 mg/L	0	0	60 mg/L	0	0	100 mg/L	0	7	170 mg/L	7	13	280 mg/L	20	93	460 mg/L	100	100
Test Concentration	Mean % Mortality																													
	24 hr.	48 hr.																												
Positive Control	0	0																												
Negative Control	0	0																												
36 mg/L	0	0																												
60 mg/L	0	0																												
100 mg/L	0	7																												
170 mg/L	7	13																												
280 mg/L	20	93																												
460 mg/L	100	100																												
Conclusion:	Test substance is considered to be of low toxicity																													
Reliability:	Code 2, Reliable with Restriction																													

Robust Summaries - Neoacids C5-C28

Lack of analytical verification, concentration of ethanol unknown, missing pH value of 280mg/L concentration, quality assurance unknown.

Reference: EG&G Bionomics, Wareham, Mass.

Other (source): ExxonMobil Biomedical Sciences, Inc.

Fish Acute Toxicity

Test Substance:	Propanoic acid, 2,2-dimethyl (C5)
Method/Guideline:	Standard Methods for the Examination of Water and Wastewater Method #231, 1971
Type (test type):	Fish Static Acute Toxicity Test
GLP:	No
Year (study performed):	1979
Species:	Gold Fish (Crassius auratus)
Analytical Monitoring:	Yes
Exposure Period:	96 hour
Statistical Method:	Interpolation of graph of log of concentration (APHA 1971)
Test Conditions:	<p>The test material was added to ~30 L glass tank containing laboratory dilution water. Each chemical was tested in a series of concentrations in 25 L of solution. All tanks contained 10 fish. All test solutions were aerated unless it was a volatile compound.</p> <p>Test temperature was 20 +/- 1 Deg C., Lighting was not reported Dissolved Oxygen = test solutions aerated during study, dissolved oxygen content remained above 4 mg/L. The pH was 5.4.</p> <p>Laboratory dilution water was local tap water: 100 mg/L Ca²⁺, 8 mg/L Mg²⁺, 0.05 mg/L Fe, and 0 mg/L Mn. Although not reported, this equates to a total hardness of 283 mg/L as carbonate.</p> <p>Fish Mean Wt.= 3.3 +/- 1.0g. Mean Total length = 6.2 +/-cm, Test Loading = 1.3 g of fish/L.</p>
<ul style="list-style-type: none">Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.	
Results:	
Units/Value:	LC50 = 380mg/L
<ul style="list-style-type: none">Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.	Analytical method used was Total Organic Carbon or by extraction and subsequent GC analysis. Analytical results not reported.
Conclusion:	Test substance is considered to have low toxicity
Reliability:	Code 2, Reliable with Restriction
	Minimal data presented (i.e. lacking conc. series, analytical measurements, Dissolved Oxygen measurements).

Robust Summaries - Neoacids C5-C28

Reference: Bridie, A.L. et al., The Acute Toxicity Test of some Petrochemicals to Goldfish. Water Research Vol. 13. 1979

Other (source): ExxonMobil Biomedical Sciences, Inc.

Biodegradation

Test Substance: Propanoic acid 2,2-dimethyl (C5)

Method/Guideline: OECD 301F, 1992

Type (test type): Manometric Respirometry Test

GLP: Yes

Year (study performed): 1996

Inoculum: Domestic activated sludge

Exposure Period: 28 days

Test Conditions:

- Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.**

Non acclimated activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).

Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption.

Test material was tested in triplicate, controls and blanks were tested in duplicate.

Test material concentration was between 31 and 50 mg/L. Sodium benzoate (positive control) concentration was 44mg/L.

Test temperature was 22 +/- 1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Results:

Units/Value:

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Test material was not readily biodegradable. Half-life was not reached. By day 28, 24% degradation of the test material was observed. 10% biodegradation was achieved on day 20

By day 14, >60% biodegradation of positive control was observed, which meets the guideline requirement. No excursions from the protocol were noted.

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

<u>Sample</u>	<u>% Degradation*</u> <u>(day 28)</u>	<u>Mean % Degradation</u> <u>(day 28)</u>
Test Material	18.9, 42.7, 10.7	24.1
Na Benzoate	98.9, 95.5	97.2

* replicate data

Robust Summaries - Neoacids C5-C28

Conclusion:	Test substance is considered not readily biodegradable.
Reliability:	Code 1, Reliable without Restrictions
Reference:	Exxon Biomedical Sciences Inc., Ready Biodegradability : OECD 301F Manometric Respirometry Test. 136894A..
Other (source):	ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Biodegradation

Test Substance: Carboxylic acid, C6-8 neo
Method/Guideline: OECD 301F, 1992
Type (test type): Manometric Respirometry Test
GLP: Yes
Year (study performed): 1996
Inoculum: Domestic activated sludge
Exposure Period: 28 days

Test Conditions:

- **Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.**

Non acclimated activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).

Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption.

Test material was tested in triplicate, controls and blanks were tested in duplicate.

Test material concentration was between 31 and 50 mg/L. Sodium benzoate (positive control) concentration was 44mg/L.

Test temperature was 22 +/- 1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Results:

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Test material was not readily biodegradable. Half-life was not reached. By day 28, 44% degradation of the test material was observed. 10% biodegradation was achieved on day 19

By day 14, >60% biodegradation of positive control was observed, which met the guideline requirement. No excursions from the protocol were noted.

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

<u>Sample</u>	<u>% Degradation*</u> <u>(day 28)</u>	<u>Mean % Degradation</u> <u>(day 28)</u>
Test Material	62.8, 24.6, 44.6	44.0
Na Benzoate	98.9, 95.5	97.2

* replicate data

Conclusion: Test substance is considered not readily biodegradable.

Reliability: Code 1, Reliable without Restrictions

Reference: Exxon Biomedical Sciences Inc., Ready Biodegradability : OECD 301F Manometric Respirometry Test. 136894A..

Other (source): ExxonMobil Biomedical Sciences, Inc.

Fish Acute Toxicity

Test Substance: Carboxylic acid, C6-8 neo

Method/Guideline: US EPA TSCA 797.1400

Type (test type): Fish Acute Flow-through Toxicity Test

GLP: Yes

Year (study performed): 1993

Species: Fathead Minnow (*Pimephales promelas*)

Analytical Monitoring: Yes

Exposure Period: 96 hour

Statistical Method: Graphical (EPA-600/4-90-027)

Test Conditions: A stock solution of 900mg/L was prepared daily and administered via a stainless steel and glass proportional diluter to achieve the desired study concentrations. The stock solution was mixed for 30 minutes and adjusted to a pH of 7.5 +/- 0.1 as needed. All test material went into solution. The test chambers were duplicate 1L glass dishes located within 19L glass aquaria with a flow rate of 6 dish volumes per day. Each dish contained 10 fish.

- **Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**

Test temperature was 22.8 Deg C., Lighting was 16 hours light : 8 hours dark with 51.8 to 52.9 ft-candles during full daylight periods. Dissolved Oxygen at initiation ranged from 8.4 to 8.5 mg/L and from 6.6 to 8.0 mg/L at termination. The pH was ranged from 7.6 to 7.2 during the study. Water hardness was 84 mg/L as CaCO₃.

Fish Mean Wt.= 0.065g. Mean Total length = 1.6cm, Test Loading = 0.11 g of fish/L.

Results: LC50 = 630mg/L, based upon measured concentrations.

Units/Value:

Analytical method used was GC-FID

Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.	<u>Nominal Conc.</u>	<u>Measured Conc.</u>	<u>% Mortality @ 96 hr.</u>
	Control	<0.79 mg/L	0
	56.25 mg/L	51.4 mg/L	0
	112.5 mg/L	124 mg/L	0
	225 mg/L	200 mg/L	0
	450 mg/L	436 mg/L	0
	900 mg/L	882 mg/L	0

Robust Summaries - Neoacids C5-C28

Conclusion:	Test substance is considered low toxicity
Reliability:	Code 1, Reliable without Restrictions
Reference:	Exxon Biomedical Sciences, Inc. Fish Acute Flow-through Toxicity Test, 148641.
Other (source):	ExxonMobil Biomedical Sciences, Inc.

Algal Toxicity

Test Substance: Carboxylic acid, C6-8 neo

Method/Guideline: US EPA TSCA 40 CFR792.1989

Type (test type): Algal Toxicity Test

GLP: Yes

Year (study performed): 1993

Species/Strain: Fresh water Green Algae (Selenastrum capricornutum)

Analytical Monitoring: Yes

Exposure Period: 72 hour

Statistical Method: Linear Interpolation

Test Conditions:

- Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organism culture, age.**

A 500mg/L stock solution was prepared by adding the appropriate amount of test substance to algal nutrient media in an aspirator bottle. The stock solution was mixed for 15 minutes at <10% vortex on a magnetic stir plate. After mixing the solution was drawn out the bottom port. The pH was adjusted to 7.5 +/- 0.1 as necessary. The stock was diluted with algal nutrient media to prepared test solutions. Three replicates and a media/toxicant blank were prepared for each concentration. Replicate vessels were 125ml autoclaved Erlenmeyer flasks sealed with gauze stoppers. Test flasks (except blanks) were inoculated with ~1.0E⁴ cells/ml of algae. All test vessels were placed on a shaker table at ~100 rpm during the study.

Nominal treatment levels were 8.0, 31.0, 62, 125, and 250mg/L

Test temperature was 23.9 Deg. C. Lighting was continuous at 399.8 to 411.65 ft candles. The pH was 7.5 at test initiation and ranged from 7.4 to 7.6 at test termination.

Results: 96 hour EC50 = 6.49mg/L (95% CI 5.64 to 7.54) based upon initial measured values (day 0).

Units/Value:

Measurement (cells/growth)

Analytical method used was Headspace Gas Chromatography with Flame Ionization Detection (GC-FID).

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

<u>Nominal Conc.</u> (mg/L)	<u>Measured Conc.</u> Day 0 (mg/L)	<u>Mean Cells</u> at 96 hr	<u>% Inhibition</u> at 96 hr
Control	0	2.3 E6	-
3.12	3.03	2.3 E6	0
6.25	6.20	1.2 E6	47.8
12.5	12.24	4.8 E5	79.1
25.0	23.55	4.2 E5	81.7
50.0	52.15	3.6 E5	84.3

Conclusion: Test substance is considered moderately toxic

Robust Summaries - Neoacids C5-C28

Reliability: Code 1, Reliable without Restrictions

Reference: Exxon Biomedical Sciences Inc., Algal Acute Toxicity Test, 148667

Other (source): ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Biodegradation

Test Substance: Neodecanoic Acid (C10)
Method/Guideline: OECD 301F, 1992
Type (test type): Manometric Respirometry Test
GLP: Yes
Year (study performed): 1996
Inoculum: Domestic activated sludge
Exposure Period: 28 days

Test Conditions:

- Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.**

Non acclimated activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).

Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption.

Test material was tested in triplicate, controls and blanks were tested in duplicate.

Test material concentration was between 31 and 50 mg/L. Sodium benzoate (positive control) concentration was 44mg/L.

Test temperature was 22 +/- 1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Results:

Units/Value:

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Test material was not readily biodegradable. Half-life was not reached. By day 28, 11% degradation of the test material was observed. 10% biodegradation was achieved on day 27

By day 14, >60% biodegradation of positive control was observed, which met the guideline requirement. No excursions from the protocol were noted.

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

<u>Sample</u>	<u>% Degradation*</u> <u>(day 28)</u>	<u>Mean % Degradation</u> <u>(day 28)</u>
Test Material	20.5, 3.60, 8.90	11.0
Na Benzoate	98.9, 95.5	97.2

* replicate data

Conclusion: Test substance is considered not readily biodegradable.

Reliability: Code 1, Reliable without Restrictions

Reference: Exxon Biomedical Sciences Inc., Ready Biodegradability : OECD 301F Manometric Respirometry Test. 136894A..

Other (source): ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Invertebrate Acute Toxicity

Test Substance:	Neodecanoic Acid (C10)																																
Method/Guideline:	USEPA -660/3-75-009 Methods for Acute Toxicity with Fish and Macroinvertebrates, and Amphibians, 1975																																
Type (test type):	Daphnid Acute Toxicity Test																																
GLP:	No																																
Year (study performed):	1977																																
Species:	Water Flea (Daphnia magna)																																
Analytical Monitoring:	No																																
Exposure Period:	48 hour																																
Statistical Method:	Moving Average-Angle Method, (Harris 1959)																																
Test Conditions:	<p>For each test concentration, the appropriate amount of test substance was dissolved in triethylene glycol (TEG) and pipetted into 500ml of dilution water. This solution was mixed with a magnetic stirrer and divided into three 150ml replicates for testing. The remaining 50ml was used for pH and dissolved oxygen measurements. A positive control (with TEG) and a negative control (dilution water) were also tested. Test vessels were 250ml beakers containing five daphnids each. Dilution water was reconstituted deionized well water with a hardness of 180mg/L as CaCO₃, with a pH of 8.0. The test was performed under static conditions with no aeration.</p> <p>Nominal test concentrations were 13, 22, 36, 60, 100, 170, and 280 mg/L</p> <p>Test temperature was 22+/- 1 Deg C. Dissolved oxygen ranged from 8.6 to 8.8 mg/L during the study. The pH of the test solutions ranged from 7.1 to 8.2.</p> <p>Organisms were <24 hrs old, supplied by in-house cultures</p>																																
Results:	LL50 = 47.1 mg/L (95% CI 33.6 to 57.8) based upon nominal test concentrations.																																
Units/Value:																																	
Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.	<table><thead><tr><th rowspan="2"><u>Test Concentration</u></th><th colspan="2"><u>Mean % Mortality</u></th></tr><tr><th><u>24 hr.</u></th><th><u>48 hr.</u></th></tr></thead><tbody><tr><td>Positive Control</td><td>0</td><td>0</td></tr><tr><td>Negative Control</td><td>0</td><td>0</td></tr><tr><td>13 mg/L</td><td>0</td><td>13</td></tr><tr><td>22 mg/L</td><td>0</td><td>13</td></tr><tr><td>36 mg/L</td><td>0</td><td>20</td></tr><tr><td>60 mg/L</td><td>20</td><td>67</td></tr><tr><td>100 mg/L</td><td>53</td><td>100</td></tr><tr><td>170 mg/L</td><td>87</td><td>100</td></tr><tr><td>280 mg/L</td><td>73</td><td>100</td></tr></tbody></table>	<u>Test Concentration</u>	<u>Mean % Mortality</u>		<u>24 hr.</u>	<u>48 hr.</u>	Positive Control	0	0	Negative Control	0	0	13 mg/L	0	13	22 mg/L	0	13	36 mg/L	0	20	60 mg/L	20	67	100 mg/L	53	100	170 mg/L	87	100	280 mg/L	73	100
<u>Test Concentration</u>	<u>Mean % Mortality</u>																																
	<u>24 hr.</u>	<u>48 hr.</u>																															
Positive Control	0	0																															
Negative Control	0	0																															
13 mg/L	0	13																															
22 mg/L	0	13																															
36 mg/L	0	20																															
60 mg/L	20	67																															
100 mg/L	53	100																															
170 mg/L	87	100																															
280 mg/L	73	100																															
Conclusion:	Test substance is considered to be of moderate toxicity																																

Robust Summaries - Neoacids C5-C28

Reliability:	Code 2, Reliable with Restrictions Lack of measured concentrations, no documentation of pH adjustment of treatments.
Reference:	EG&G Bionomics, Wareham, Mass. BW-78-1-005
Other (source):	ExxonMobil Biomedical Sciences, Inc.

Fish Acute Toxicity

Test Substance:	Neodecanoic Acid (C10)
Method/Guideline:	OECD 203 Fish Acute Toxicity Test
Type (test type):	Fish Acute Toxicity Test
GLP:	Yes
Year (study performed):	1996
Species:	Rainbow Trout (<i>Oncorhynchus mykiss</i>)
Analytical Monitoring:	Yes
Exposure Period:	96 hour
Statistical Method:	Bionomial Method
Test Conditions:	<p>Individual Water Accomodated Fractions (WAF's) were prepared for each test treatment. The test substance was added volumetrically, via a syringe, to 19L of dilution water in a 20L glass carboy. The solution was mixed for 24 hours at a vortex of \leq 10% of the total depth. After mixing the mixtures were adjust for pH to that of the dilution water using 1.0m NaOH. The test solutions were pumped from each mixing vessel into three replicates of 4.5L in 4.0L glass aspirator bottles (no headspace). Five fish were added to each test replicate and the replicates sealed. Daily renewals were performed by removing ~80% of the test solution through the port at the bottom and refilling with fresh solution.</p> <p>Test temperature was 15.0 Deg C., Lighting was 19 hours light : 5 hours dark with 528 to 538 Lux during full daylight periods. Dissolved Oxygen at initiation ranged from 8.5 to 9.0 mg/L and from 5.9 to 7.4 mg/L in "old" solutions prior to renewals. The pH was ranged from 7.0 to 7.6 during the study. Fish were not fed during the study.</p> <p>Dilution water hardness = 160 to 174 mg/L as CaCO₃.</p> <p>Fish Mean Wt.= 0.260g. Mean Total length = 3.3cm, Test Loading = 0.29 g of fish/L.</p>
<ul style="list-style-type: none">Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.	
Results:	LC50 = 37.2mg/L (CI 26.3 to 52.5), based upon measured concentrations of mean of old and new samples.
Units/Value:	
<ul style="list-style-type: none">Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.	Analytical method used was GC-FID
	LL50 = 35.4 mg/L (CI 25.0 to 50.0), based upon nominal loading levels.

Robust Summaries - Neoacids C5-C28

Results continued	<u>Nominal Conc.</u>	<u>Measured Conc.</u>	<u>% Mortality @ 96 hr.</u>
	Control	Below detection	0
	6.25 mg/L	10.3 mg/L	0
	12.5 mg/L	13.6 mg/L	0
	25 mg/L	26.3 mg/L	0
	50 mg/L	52.5 mg/L	100
	100 mg/L	102 mg/L	100

Conclusion: Test substance is considered moderate toxicity

Reliability: Code 1, Reliable without Restrictions

Reference: Exxon Biomedical Sciences, Inc. Fish Acute Toxicity Test, 118358.

Other (source): ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

Biodegradation

Test Substance: Fatty Acids C9-13, Neo 913 Acid

Method/Guideline: OECD 301F, 1992

Type (test type): Manometric Respirometry Test

GLP: Yes

Year (study performed): 1996

Inoculum: Domestic activated sludge

Exposure Period: 28 days

Test Conditions:

- Note: Concentration prep. vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, loading.**

Non acclimated activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride).

Test vessels were 1L glass flasks placed in a waterbath and electronically monitored for oxygen consumption.

Test material was tested in triplicate, controls and blanks were tested in duplicate.

Test material concentration was between 31 and 50 mg/L. Sodium benzoate (positive control) concentration was 44mg/L.

Test temperature was 22 +/- 1 Deg C.

All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Results:

Units/Value:

- Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Test material was not readily biodegradable. Half-life was not reached. By day 28, 2.3% degradation of the test material was observed. 10% biodegradation was not achieved by day 28.

By day 14, >60% biodegradation of positive control was observed, which met the guideline requirement. No excursions from the protocol were noted.

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

<u>Sample</u>	<u>% Degradation*</u> <u>(day 28)</u>	<u>Mean % Degradation</u> <u>(day 28)</u>
Test Material	4.50, 0.00, 2.50	2.33
Na Benzoate	98.9, 95.5	97.2

* replicate data

Conclusion: Test substance is considered not readily biodegradable.

Reliability: Code 1, Reliable without Restrictions

Reference: Exxon Biomedical Sciences Inc., Ready Biodegradability : OECD 301F Manometric Respirometry Test. 136894A..

Other (source): ExxonMobil Biomedical Sciences, Inc.

Robust Summaries - Neoacids C5-C28

201-16738H

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I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 26896-20-8
CAS No.	26896-20-8
EINECS Name	neodecanoic acid
EINECS No.	248-093-9
Molecular Weight	173
Molecular Formula	C10H20O2

Dataset created by: EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEdSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

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European Chemicals Bureau

1.0.1 OECD and Company Information

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

Name: Deutsche Exxon Chemical G.m.b.H
Street: Neusser Landstrasse, 16
Town: 5000 Koeln
Country: Germany
Phone: 0221.7703.1
Telefax: 0021.7703.355
Telex: 8885260

Name: Exxon Chemical France
Street: 31 Place des Corolles
Town: F-92098 PARIS La Defense 2
Country: France
Phone: (331) 49 03 50 00
Telefax: 47 73 55 11
Telex: 611191 F
Cedex: 31

Name: EXXON CHEMICAL HOLLAND BV
Street: Botlekweg 121
Town: 3197 KA Botlek Rt.
Country: Netherlands
Phone: 31.1819.55971
Telefax: 31.1819.55983

Name: Shell Nederland Chemie B.V.
Street: Vondelingenweg 601
Town: 3196 KK Rotterdam
Country: Netherlands

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: liquid

Substance type: organic
Physical status:

1.1.1 Spectra

-

1.2 Synonyms

2,2-dimethyloctanoic acid

Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

Neo Acids C10

Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

Neo decanoic acid prime

Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

Neodecanoic acid (8CI, 9CI)

Source: BASF AG Ludwigshafen

Topper 5E

Source: BASF AG Ludwigshafen

Wiltz 65

Source: BASF AG Ludwigshafen

1.3 Impurities

-

1.4 Additives

-

1.5 Quantity

Quantity 50 000 - 100 000 tonnes

1.6.1 Labelling

-

1.6.2 Classification

-

1.7 Use Pattern

Type: type
Category: Non dispersive use

1. General Information

date: 18-FEB-2000
Substance ID: 26896-20-8

Type: type
Category: Use in closed system

Type: industrial
Category: Chemical industry: used in synthesis

Type: use
Category: Intermediates

1.7.1 Technology Production/Use

-

1.8 Occupational Exposure Limit Values

Type of limit: other: Exxon Internal Occupational Exposure Limit
Limit value: 25 mg/m3
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

(1)

Type of limit:
Limit value:
Remark: None established
Source: Shell Nederland Chemie B.V. Rotterdam

1.9 Source of Exposure

-

1.10.1 Recommendations/Precautionary Measures

-

1.10.2 Emergency Measures

-

1.11 Packaging

-

1.12 Possib. of Rendering Subst. Harmless

-

1.13 Statements Concerning Waste

-

1.14.1 Water Pollution

-

1.14.2 Major Accident Hazards

-

1.14.3 Air Pollution

-

1.15 Additional Remarks

Remark: DIPOSAL OPTIONS

Dispose to licensed disposal contractor.
Recover or recycle if possible; otherwise incinerate in
licensed waste incineration plant.

TRANSPORT INFORMATION

Not dangerous for conveyance under UN, IMO, ADR/RID and
IATA/ICAO codes.

Source: Shell Nederland Chemie B.V. Rotterdam

1.16 Last Literature Search

-

1.17 Reviews

-

1.18 Listings e.g. Chemical Inventories

-

2.1 Melting Point

Value: ca. -39 degree C
Decomposition: no
Method: other: ASTM D97
GLP: no
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

2.2 Boiling Point

Value: ca. 243 - 253 degree C at 1013.25 hPa
Decomposition: no
Method: Directive 84/449/EEC, A.2 "Boiling point/boiling range"
GLP: no data
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(2)

Value: ca. 243 - 253 degree C at 1013.25 hPa
Decomposition: no
Method: Directive 84/449/EEC, A.2 "Boiling point/boiling range"
GLP: no data
Source: Exxon Chemical France PARIS La Defense 2

(3)

2.3 Density

Type: density
Value: ca. .91 g/cm3 at 20 degree C
Method: other: ASTM D4052
GLP: no data
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(2)

Type: density
Value: ca. .91 g/cm3 at 20 degree C
Method: other: ASTM D4052
GLP: no data
Source: Exxon Chemical France PARIS La Defense 2

(3)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: ca. .29 hPa at 50 degree C
Method: other (calculated): not specified
GLP: no data
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(2)

Value: ca. .29 hPa at 50 degree C
Method: other (calculated): not specified
GLP: no data
Source: Exxon Chemical France PARIS La Defense 2

(3)

2.5 Partition Coefficient

log Pow: ca. 3.6
Method: other (calculated)
Year:
GLP: no data
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

2.6.1 Water Solubility

Value: < .1 vol% at 25 degree C
Qualitative: not soluble
Method: other: not specified
GLP: no data
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(2)

Value: < .1 vol% at 25 degree C
Qualitative: not soluble
Method: other: not specified
GLP: no data
Source: Exxon Chemical France PARIS La Defense 2

(3)

2.6.2 Surface Tension

-

2.7 Flash Point

Value: ca. 122 degree C
Type: open cup
Method: other: ASTM D92
Year:
GLP: no data
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(2)

Value: ca. 122 degree C
Type: open cup
Method: other: ASTM D92
Year:
GLP: no data
Source: Exxon Chemical France PARIS La Defense 2

(3)

2.8 Auto Flammability

-

2.9 Flammability

-

2.10 Explosive Properties

-

2.11 Oxidizing Properties

-

2.12 Additional Remarks

-

3.1.1 Photodegradation

-

3.1.2 Stability in Water

-

3.1.3 Stability in Soil

-

3.2 Monitoring Data (Environment)

-

3.3.1 Transport between Environmental Compartments

-

3.3.2 Distribution

-

3.4 Mode of Degradation in Actual Use

-

3.5 Biodegradation

Type:

Inoculum:

Method:

Year:

GLP:

Test substance:

Remark: ThOD = 2.6 g/g. COD = 0.3 g/l (estimated). BOD5 < 4% COD.

Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.

Exxon Chemical France PARIS La Defense 2

Deutsche Exxon Chemical G.m.b.H Koeln

(4)

3.6 BOD5, COD or BOD5/COD Ratio

-

3.7 Bioaccumulation

-

3.8 Additional Remarks

-

AQUATIC ORGANISMS**4.1 Acute/Prolonged Toxicity to Fish**

Type: static
Species: Carassius auratus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 2.6
Method: other: not specified
Year: **GLP:** no data
Test substance: other TS: 30% preparation of neodecanoic acid.
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

(5)

Type: static
Species: Carassius auratus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
NOEC: = 56
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

(6)

Type: static
Species: Cyprinodon variegatus (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = 100
LC50: = 181
LC100: > 320
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

(7)

4. Ecotoxicity

date: 18-FEB-2000
Substance ID: 26896-20-8

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 4.9
Method: other: not specified
Year: **GLP:** no data
Test substance: other TS: 30% preparation of neodecanoic acid.
Remark: 48 hr static LC50 = 5.6 mg/l.
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

(8)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 60
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: 24 hr static LC50 > 280 mg/l. 48 hr. static LC50 = 94 mg/l.
72hr static LC50 = 77 mg/l.
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(9)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 60
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: 24 hr static LC50 > 280 mg/l. 48 hr. static LC50 = 94 mg/l.
72hr static LC50 = 77 mg/l.
Source: Exxon Chemical France PARIS La Defense 2

(10)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
NOEC: = 32
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

(11)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
NOEC: < 13
EC50: = 47.11
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
 Deutsche Exxon Chemical G.m.b.H Koeln (12)

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
NOEC: < 13
EC50: = 47.11
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Exxon Chemical France PARIS La Defense 2 (13)

Species: other: Acartia tonsa (copepod)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50 : = 25
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: 24 hr. LC50 > 100 mg/l. 48 hr LC50 = 65 mg/l. 72 hr. LC50
 = 43 mg/l.
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
 Deutsche Exxon Chemical G.m.b.H Koeln (14)

Species: other: Acartia tonsa (copepod)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50 : = 25
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: 24 hr. LC50 > 100 mg/l. 48 hr LC50 = 65 mg/l. 72 hr. LC50
 = 43 mg/l.
Source: Exxon Chemical France PARIS La Defense 2 (14)

4.3 Toxicity to Aquatic Plants e.g. Algae

-

4.4 Toxicity to Microorganisms e.g. Bacteria

-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

-

4.6.2 Toxicity to Terrestrial Plants

-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

Species: other avian: bobwhite quail
Endpoint: mortality
Expos. period:
Unit: other: ppm
LC50: > 5620
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

(15)

4.7 Biological Effects Monitoring

-

4.8 Biotransformation and Kinetics

-

4.9 Additional Remarks

-

5.1 Acute Toxicity**5.1.1 Acute Oral Toxicity**

Type: LD50
Species: rat
Sex:
Number of
Animals:
Vehicle:
Value: 2700 - 3450 mg/kg bw
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

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5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: > 73 ppm
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(17)

Type: LC50
Species: rat
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: > 73 ppm
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Exxon Chemical France PARIS La Defense 2

(18)

5. Toxicity

date: 18-FEB-2000
Substance ID: 26896-20-8

Type: LC50
Species: mouse
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: > 73 ppm
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(19)

Type: LC50
Species: mouse
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: > 73 ppm
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Exxon Chemical France PARIS La Defense 2

(18)

Type: LC50
Species: guinea pig
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: > 73 ppm
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(17)

Type: LC50
Species: guinea pig
Sex:
Number of
Animals:
Vehicle:
Exposure time: 6 hour(s)
Value: > 73 ppm
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Exxon Chemical France PARIS La Defense 2

(18)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rat
Sex:
Number of
Animals:
Vehicle:
Value: > 3640 mg/kg bw
Method: other
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(20)

Type: LD50
Species: rat
Sex:
Number of
Animals:
Vehicle:
Value: > 3640 mg/kg bw
Method: other
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Exxon Chemical France PARIS La Defense 2

(21)

5.1.4 Acute Toxicity, other Routes

-

5.2 Corrosiveness and Irritation**5.2.1 Skin Irritation**

Species: rabbit
Concentration:
Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

(22)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.: irritating
Method: Draize Test
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

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5.3 Sensitization

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: other: Magnusson and Kligman maximisation test
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

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5.4 Repeated Dose Toxicity

Species: rat **Sex:** male/female
Strain: other: albino
Route of admin.: oral feed
Exposure period: 3 months
Frequency of treatment: daily
Post. obs. period:
Doses: 500, 1500, 5000 and 15000 ppm
Control Group: yes
NOAEL: = 500 ppm
LOAEL: = 1500 ppm
Method: other: not specified
Year: **GLP:** no data
Test substance: other TS: 30% preparation of neodecanoic acid.
Remark: The 15,000 ppm group showed a DECREASED BODY WEIGHT and a DECREASE IN HEMATOCRIT HEMOGLOBIN and RED BLOOD CELL COUNTS. There were MORPHOLOGICAL CHANGES IN THE THYROID, characterized by HYPERPLASIA of the follicular epithelium, manifested by increased cell height, increased cellularity, vacualization of the follicular epithelium and irregularity of the follicular walls. These changes were seen at the high dose and as low as 1500 ppm in the male rats. The female rats showed this effect at 15,000 and 5000 ppm only. HEPATOTOXIC CHANGES were seen in the male and female rats at 15000 and 5000 ppm. There were RENAL CHANGES affecting the TUBULES of both the male and female rats at 15000, 5000 and 1500 ppm.
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
 Deutsche Exxon Chemical G.m.b.H Koeln

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Species: rat **Sex:** male/female
Strain: other: albino
Route of admin.: oral feed
Exposure period: 3 months
Frequency of treatment: daily
Post. obs. period:
Doses: 500, 1500, 5000 and 15000 ppm
Control Group: yes
NOAEL: = 500 ppm
LOAEL: = 1500 ppm
Method: other: not specified
Year: **GLP:** no data
Test substance: other TS: 30% preparation of neodecanoic acid.
Remark: The 15,000 ppm group showed a DECREASED BODY WEIGHT and a DECREASE IN HEMATOCRIT HEMOGLOBIN and RED BLOOD CELL COUNTS. There were MORPHOLOGICAL CHANGES IN THE THYROID, characterized by HYPERPLASIA of the follicular epithelium, manifested by increased cell height, increased cellularity, vacualization of the follicular epithelium and irregularity of the follicular walls. These changes were seen at the high dose and as low as 1500 ppm in the male rats. The

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female rats showed this effect at 15,000 and 5000 ppm only.
HEPATOTOXIC CHANGES were seen in the male and female rats
at 15000 and 5000 ppm. There were RENAL CHANGES affecting
the TUBULES of both the male and female rats at 15000, 5000
and 1500 ppm.

Source: Exxon Chemical France PARIS La Defense 2 (24)

Species: rabbit Sex: male
Strain: other: albino
Route of admin.: dermal
Exposure period: 14 days
Frequency of
treatment: 10 applications
Post. obs.
period:
Doses: 0.5 and 2.5 ml/kg
Control Group: yes
NOAEL: > 2.5
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(25)

Species: rabbit Sex: male
Strain: other: albino
Route of admin.: dermal
Exposure period: 14 days
Frequency of
treatment: 10 applications
Post. obs.
period:
Doses: 0.5 and 2.5 ml/kg
Control Group: yes
NOAEL: > 2.5
Method: other: not specified
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Exxon Chemical France PARIS La Defense 2

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5. Toxicity

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Substance ID: 26896-20-8

Species: dog **Sex:** male/female
Strain: other: beagle
Route of admin.: other: oral capsule
Exposure period: 13 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 9.48, 30, 94.8 or 300 mg/kg/day
Control Group: yes
NOAEL: ca. 30 mg/kg
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Frequent EMESIS and/or DIARRHEA was seen in the 94.8 and 300 mg/kg dose groups. WEIGHT SUPPRESSION was also seen at these doses. DECLINES IN HEMATOCRIT, HEMOGLOBIN and ERYTHROCYTE VALUES were seen at 94.8 and 300 mg/kg groups. No characteristic or consistent compound-related organ alterations were noted at terminal necropsy. Significant LIVER/BODY WEIGHT RATIO INCREASES were seen in the high dose group.
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

(27)

Species: dog **Sex:** male/female
Strain: other: beagle
Route of admin.: other: oral capsule
Exposure period: 13 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 9.48, 30, 94.8 or 300 mg/kg/day
Control Group: yes
NOAEL: ca. 30 mg/kg
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Frequent EMESIS and/or DIARRHEA was seen in the 94.8 and 300 mg/kg dose groups. WEIGHT SUPPRESSION was also seen at these doses. DECLINES IN HEMATOCRIT, HEMOGLOBIN and ERYTHROCYTE VALUES were seen at 94.8 and 300 mg/kg groups. No characteristic or consistent compound-related organ alterations were noted at terminal necropsy. Significant LIVER/BODY WEIGHT RATIO INCREASES were seen in the high dose group.
Source: Exxon Chemical France PARIS La Defense 2

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5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: TA 1535, TA 1537, TA 98, TA 100
Concentration: 6.1 - 1500 ug/plate (-S9:6.1 - 1000; +S9:18.5 - 1500)
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

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Type: Cytogenetic assay
System of testing: cultured human lymphocytes
Concentration: 100 - 800 ug/ml (-S9: 100 - 400; +S9: 250 - 800)
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 473 "Genetic Toxicology: In vitro Mammalian Cytogenetic Test"
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Exxon Chemical France PARIS La Defense 2
Deutsche Exxon Chemical G.m.b.H Koeln

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5.6 Genetic Toxicity 'in Vivo'

-

5.7 Carcinogenicity

-

5.8 Toxicity to Reproduction

Type: other: modified 3 generation
Species: rat **Sex:** male/female
Strain: other: albino
Route of admin.: oral feed
Exposure Period: 3 generations
Frequency of treatment: daily
Premating Exposure Period
male: 9 weeks
female: 9 weeks
Duration of test: 3 generations
Doses: 100, 500 and 1500 ppm
Control Group: yes
NOAEL Parental: > 1500 ppm
NOAEL F1 Offspr.: > 1500 ppm
NOAEL F2 Offspr.: > 1500 ppm
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: There was no evidence at any test level of an adverse effect on the survival, appearance, behavior, body weight gain and food consumption on the parental generation; on the reproductive performance of the parents; or on the growth, appearance and behavior of the offspring. Gross and microscopic pathological findings revealed no evidence of a compound-related effect at any of the dietary levels.
Source: EXXON CHEMICAL HOLLAND BV Botlek Rt.
Deutsche Exxon Chemical G.m.b.H Koeln

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Type: other: modified 3 generation
Species: rat **Sex:** male/female
Strain: other: albino
Route of admin.: oral feed
Exposure Period: 3 generations
Frequency of treatment: daily
Premating Exposure Period
male: 9 weeks
female: 9 weeks
Duration of test: 3 generations
Doses: 100, 500 and 1500 ppm
Control Group: yes
NOAEL Parental: > 1500 ppm
NOAEL F1 Offspr.: > 1500 ppm
NOAEL F2 Offspr.: > 1500 ppm
Method: other: not specified
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: There was no evidence at any test level of an adverse effect on the survival, appearance, behavior, body weight gain and food consumption on the parental generation; on the reproductive performance of the parents; or on the growth, appearance and behavior of the offspring. Gross and microscopic pathological findings revealed no evidence of a

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Source: compound-related effect at any of the dietary levels.
Exxon Chemical France PARIS La Defense 2

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5.9 Developmental Toxicity/Teratogenicity

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5.10 Other Relevant Information

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5.11 Experience with Human Exposure

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6. References

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Substance ID: 26896-20-8

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7.1 Risk Assessment

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