201-16473B

IUCLID

Data Set

Existing Chemical	:	ID: 14666-94-5
CAS No.	:	14666-94-5
EINECS Name	:	oleic acid, cobalt salt
EC No.	:	238-709-4
Common name	:	9-Octadecenoic Acid (Z)-Cobalt Salt
Molecular Formula	:	C18H34O2.xCo
Producer related part		
Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	16.10.2006
Substance related part		
Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	16.10.2006
Status	:	
Memo	:	ExxonMobil Chemical Company - HPV
Printing date	:	16.10.2006
Revision date	:	
Date of last update	:	16.10.2006
Number of pages	:	29
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	**:**	
Smiles Code	**:**	[Co](OC(=O)CCCCCCCC=CCCCCCCCC)OC(=O)CCCCCCCC=CCCCCCCCC
Molecular formula	**:**	621.86
Molecular weight	**:**	
Petrol class	**:**	

1.1.1 GENERAL SUBSTANCE INFORMATION

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

cobalt oleate

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

Type of search	:	Internal and External
Chapters covered	:	
Date of search	:	16.10.2006
Remark	:	Search covered all Physical Chemical Properties, Environmental Fate, Aquatic and Mammalian Toxicity endpoints related to the CAS number.

1.13 REVIEWS

2.1 MELTING POINT

Value	:	313.2 °C
Sublimation	:	
Method	:	Other: calculated
Year	:	2006
GLP	:	No
Test substance	:	CAS No. 14666-94-5; cobalt oleate
Method	:	Calculated values using MPBPWIN version 1.41, a subroutine of the computer program EPIWIN version 3.12
Test condition	:	Melting Point estimations performed by MPBPWIN are based on the average result of the calculation methods of K. Joback and Gold and Ogle. Joback's Method is described in Joback, K.G. 1982. A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. In The Properties of Gases and Liquids. Fourth Edition. 1987. R.C. Reid, J.M. Prausnitz and B.E. Poling, Eds. The Gold and Ogle Method simply uses the formula Tm = 0.5839Tb, where Tm is the melting point in Kelvin and Tb is the boiling point in Kelvin.
Reliability	:	(2) valid with restrictions The result is a calculated value based on the chemical structure and represents a potential melting point for the substance with the CAS number listed under test substance.

15.11.2006 EPI Suite (2004)

2.2 BOILING POINT

Value	:	
Decomposition	:	
Method	:	Other: calculated
Year	:	2006
GLP	:	No
Test condition	:	Boiling point calculated by MPBPWIN subroutine, which is based on the method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. 34: 581-587.
Test substance	:	
Reliability	:	(2) valid with restrictions The result is a calculated value based on the chemical structure and represents a potential boiling point for the substance with the CAS number listed under test substance.
Flag	:	Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004).

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= 1.7 x 10^{-13} Pa
Decomposition	:	
Method	:	other (calculated)
Year	:	2006
GLP	:	No

Test substance	:	CAS No. 14666-94-5; cobalt oleate
Method	:	Vapor pressure calculation by MPBPWIN ver. 1.40 using calculation method of Grain.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Reliability	:	(2) valid with restrictions The result is a calculated value based on the chemical structure and represents a potential vapor pressure for the substance with the CAS number listed under test substance.

15.11.2006 EPI Suite (2004)

Value	:	= 1.9 x 10^{-4} Pa
Decomposition	:	
Method	:	other (calculated)
Year	:	2006
GLP	:	no data
Test substance	:	other TS: CAS No. 112-80-1, oleic acid
Reliability	:	(2) valid with restrictions Although the original data were not retrieved and reviewed for quality, they were developed following acceptable test methods and therefore considered reliable. Value was provided by the experimental database of the EPIWIN program. Reference given in EPI Suite: Perry and Green (1984).
Flag	:	Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log Kow	:	14.71
pH value	:	
Method	:	Other (calculated)
Year	:	2003
GLP	:	No
Test substance	:	CAS No. 14666-94-5; cobalt oleate
Method	:	Calculated values using KOWWIN version 1.67, a subroutine of the computer program EPIWIN version 3.12
Test condition	:	Octanol / Water Partition Coefficient estimations performed by KOWWIN are based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. J. Pharm. Sci. 84:83-92.
Reliability	:	(2) valid with restrictions The result is a calculated value based on the chemical structure and represents a potential partition coefficient for the substance with the CAS number listed under test substance.

15.11.2006 EPI Suite (2004)

Partition coefficient	:	octanol-water
Log Kow	:	= 7.64 at 25 °C
pH value	:	
Method	:	other (measured)
Year	:	1993
GLP	:	no data
Test substance	:	CAS No. 6863-58-7; sec-butyl ether
Test condition	:	
Reliability	:	(2) valid with restrictions Value was provided by the experimental database of the EPIWIN program. Reference given in EPI Suite: Sangster (1993).
Flag	:	Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	
concentration	:	3.2 x10^{-11} mg/L
Description	:	
Stable	:	
Method	:	other: calculated
Year	:	2006
GLP	:	No
Test substance	:	CAS No. 14666-94-5; cobalt oleate
Method	:	Calculated values using WSKOWWIN version 1.41, a subroutine of the computer program EPIWIN version 3.12
Test condition	:	Water Solubility estimations performed by WSKOWWIN are based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". Environ. Toxicol. Chem. 15:100-106. 1995.
Reliability	:	(2) valid with restrictions The result is a calculated value based on the chemical structure and represents a potential water solubility for the substance with the CAS number listed under test substance.

15.11.2006 EPI Suite (2004)

Solubility in	:	Water
Value	:	
concentration	:	0.01 mg/L
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: calculated
Year	:	2006
GLP	:	No
Test substance	:	Other TS: CAS No. 112-80-1, oleic acid
Method	:	Calculated values using WSKOWWIN version 1.41, a subroutine of the computer program EPIWIN version 3.12
Test condition	:	Water Solubility estimations performed by WSKOWWIN are based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". Environ. Toxicol. Chem. 15:100-106. 1995.
Reliability	:	(2) valid with restrictions The result is a calculated value based on the chemical structure and represents a potential water solubility for the substance with the CAS number listed under test substance.

15.11.2006 EPI Suite (2004)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	Air
Light source	:	Sun light
Light spectrum	:	Nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	cm³/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (calculated): Calculated values using AOPWIN version 1.91, a subroutine of the computer program EPIWIN version 3.12
Year	:	2006
GLP	:	No
Test substance	:	Other TS:CAS No. 112.80-1
Result	:	Atmospheric Oxidation Potential

In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH-) radicals (Atkinson, 1988, 1989). The rate at which an organic compound reacts with OH- radicals is a direct measure of its atmospheric persistence (Meylan and Howard, 1993).

AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon average atmospheric concentrations of hydroxyl radicals.

Since the reactions only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day.

Calculated* half-life (hours)	OH- Rate Constant (cm3/molecule-sec)
1.7	75.5×10^{-12}

References:

Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. Environ. Toxicol. Chem. 7:435-442.

Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J. Phys. Chem. Ref. Data Monograph No. 1, Amer. Inst. Physics & Amer. Chem. Soc., NY.

Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. Chemosphere 12:2293-2299.

Test condition :

Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson.

Temperature: 25°C

Sensitizer: OH radical
Concentration of Sensitizer: 1.5 E6 OH radicals/cm3

Reliability : (2) valid with restrictions
The results include calculated data based on chemical structure as modeled by AOPWIN. The data represent a potential atmospheric half-life range for the test substance.

Flag : Critical study for SIDS endpoint
15.11.2006 EPI Suite (2004)

3.1.2 STABILITY IN WATER

Type : Abiotic
t1/2 pH4 : At °C
t1/2 pH7 : At °C
t1/2 pH9 : At °C
Deg. product :
Method : Other: technical discussion
Year : 2006
GLP :
Test substance : CAS No. 14666-94-5; cobalt oleate

Result : Hydrolysis as a Function of Molecular Structure

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (Gould, 1959; Harris, 1982). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule.

Chemicals that are susecptible to hydrolysis contain functional groups that can be displaced by a nucleophilic substitution reaction. Substances 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). The lack of a suitable leaving group renders a compound resistant to hydrolysis.

Cobalt oleate is expected to be resistant to hydrolysis because it lacks a functional group that is hydrolytically reactive (Harris, 1982). Therefore, hydrolysis will not contribute to its removal from the environment.

References:

Gould, E.S. (1959), Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA.

Harris, J.C. (1982), "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA.

Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.

Flag : Critical study for SIDS endpoint
15.11.2006

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	other: air – sediment - soil - water
Air	:	% (Fugacity Model Level III)
Water	:	% (Fugacity Model Level III)
Soil	:	% (Fugacity Model Level III)
Sediment	:	% (Fugacity Model Level III)
Method	:	other: Calculation according Mackay, Level III
Year	:	2006
Test substance	:	CAS No. 14666-94-5; cobalt oleate
Method	:	The Level III fugacity model is a steady state model that is useful for determining how the medium of release affects environmental fate. Level III fugacity allows non-equilibrium conditions to exist between connected media as steady state, and illustrate important transport and transformation processes. Physicochemical input values for the model were calculated using the EPIWIN Estimation v 3.12 program. Measured input values were also used where available and obtained from the EPIWIN database or other reliable sources. Distribution data from the equilibrium model provide basic information on the potential partitioning behavior of chemicals between selected environmental compartments (i.e., air, water, soil, and sediment). Input values used: Molecular mass = 621.86 g/mol Vapour pressure = 1.3 x10^{-15} mm Hg log Kow = 14.7 Melting point = 291 ° C This model was run assuming the default emissions.
Result	:	Air – 0.01% Water – 1.89% Soil – 28.4% Sediment – 69.7%
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data are calculated and not measured.
Flag	:	Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

Type	:	fugacity model level III
Media	:	other: air – sediment - soil – water
Air	:	% (Fugacity Model Level III)
Water	:	% (Fugacity Model Level III)
Soil	:	% (Fugacity Model Level III)
Sediment	:	% (Fugacity Model Level III)
Method	:	other: Calculation according Mackay, Level III
Year	:	2006
Test substance	:	other TS CAS No. 112-80-1; oleic acid
Method	:	The Level III fugacity model is a steady state model that is useful for determining how the medium of release affects environmental fate. Level III fugacity allows non-equilibrium conditions to exist between connected media

as steady state, and illustrate important transport and transformation processes.

Physicochemical input values for the model were calculated using the EPIWIN Estimation v 3.12 program. Measured input values were also used where available and obtained from the EPIWIN database or other reliable sources. Distribution data from the equilibrium model provide basic information on the potential partitioning behavior of chemicals between selected environmental compartments (i.e., air, water, soil, and sediment).

Input values used:
Molecular mass = 282.47 g/mol
Vapour pressure = 5.13 x10^{-5} mm Hg
log Kow = 7.64
Melting point = 133 ° C

This model was run assuming the default emissions.

Result : Air – .05%
Water – 3.86%
Soil – 18.2%
Sediment – 67.9%

Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : Aerobic
Inoculum :
Contact time :
Degradation : (±) % after
Result : other: not readily biodegradable
Deg. product :
Method : other: calculated using BIOWIN version 4.02
Year : 2006
GLP : No
Test substance : CAS No. 14666-94-5; cobalt oleate
Remark : Calculation of biodegradation and the timeframe for Primary and Ultimate biodegradation using BIOWIN version 4.02, a subroutine of the computer program EPI Suite version 3.12 as described by Howard, et al, 1994.

BIOWIN contains six models (linear regression (BIOWIN 1), non-linear regression (BIOWIN 2), ultimate degradation to CO2 and H2O (BIOWIN 3), primary degradation (BIOWIN 4), linear regression estimate of the probability of passing the OECD 301C / MITI-1 ready biodegradation test (BIOWIN 5), and non-linear regression estimate of the probability of passing the OECD 301C / MITI-1 ready biodegradation test (BIOWIN 6).

BIOWIN 1 - "Biodegrades Fast"
BIOWIN 2 - "Does Not Biodegrade Fast"
BIOWIN 3 - "Weeks-Months"
BIOWIN 4 - "Days-Weeks"

BIOWIN 5 - "Does Not Biodegrade Fast"
BIOWIN 6 - "Does Not Biodegrade Fast"

According to the USEPA, BIOWIN 6 is better predictor of whether a chemical will pass or fail the OECD 301C / MITI-1 ready biodegradation test than BIOWIN 5.

The test compound will dissociate to oleic acid and cobalt. The metal will not degrade, but based on predictions, and data supporting analog compounds, cobalt oleate is likely moderately biodegradible.

Reliability : (2) valid with restrictions
The value was calculated based on the chemical structure as modeled by EPI Suite. This robust summary has a reliability rating of 2 because the data are modeled.

Flag : Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

Type : Aerobic
Inoculum :
Contact time :
Degradation : (±) % after
Result : other: readily biodegradable
Deg. product :
Method : other: calculated using BIOWIN version 4.02
Year : 2006
GLP : No
Test substance : Other TS: CAS No. 112-80-1; oleic acid
Remark : Calculation of biodegradation and the timeframe for Primary and Ultimate biodegradation using BIOWIN version 4.02, a subroutine of the computer program EPI Suite version 3.12 as described by Howard, et al, 1994.

BIOWIN contains six models (linear regression (BIOWIN 1), non-linear regression (BIOWIN 2), ultimate degradation to CO2 and H2O (BIOWIN 3), primary degradation (BIOWIN 4), linear regression estimate of the probability of passing the OECD 301C / MITI-1 ready biodegradation test (BIOWIN 5), and non-linear regression estimate of the probability of passing the OECD 301C / MITI-1 ready biodegradation test (BIOWIN 6).

BIOWIN 1 - "Biodegrades Fast"
BIOWIN 2 - "Biodegrades Fast"
BIOWIN 3 - "Weeks"
BIOWIN 4 - "Days"
BIOWIN 5 - "Biodegrades Fast"
BIOWIN 6 - "Biodegrades Fast"

According to the USEPA, BIOWIN 6 is better predictor of whether a chemical will pass or fail the OECD 301C / MITI-1 ready biodegradation test than BIOWIN 5.

Reliability : (2) valid with restrictions
The value was calculated based on the chemical structure as modeled by EPI Suite. This robust summary has a reliability rating of 2 because the data are modeled.

Flag : Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other: calculated
Species	:	other: freshwater fish
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	Unlikely to see effects at saturation.
Method	:	other: ECOSAR Computer Model
Year	:	2006
GLP	:	
Test substance	:	CAS No. 14666-94-5; cobalt oleate
Test condition	:	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPISuite computer model (2). 1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92. 2. EPI Suite (2004) Estimation Program Interface Suite, version 3.12. Syracuse Research Corporation, Syracuse, NY, USA.
Conclusion	:	ECOSAR results indicated that based on the low predicted solubility of this comopund, effects were unlikely to be seen at saturation.
Reliability	:	(2) valid with restrictions The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured.
Flag	:	Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

Type	:	other: calculated
Species	:	other: freshwater fish
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	Unlikely to see effects at saturation.
Method	:	other: ECOSAR Computer Model
Year	:	2006
GLP	:	
Test substance	:	Other TS: CAS No. 112-8-1; oleic acid
Test condition	:	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPISuite computer model (2). 1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92. 2. EPI Suite (2004) Estimation Program Interface Suite, version 3.12. Syracuse Research Corporation, Syracuse, NY, USA.
Conclusion	:	ECOSAR results indicated that based on the low predicted solubility of this comopund, effects were unlikely to be seen at saturation. This conclusion is supported by data for tall oil fatty acid indicating an LL50 of >1000mg/L

(Metal Carboxylates Coalition, 2005).

Reliability : (2) valid with restrictions
The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint

14.11.2006 EPI Suite (2004)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : other: calculated
Species : Daphnia sp. (Crustacea)
Exposure period : 48 h
Unit : mg/l
LC50 : Unlikely to see effects at saturation.
Method : other: ECOSAR Computer Model
Year : 2006
GLP :
Test substance : CAS No. 14666-94-5; cobalt oleate
Test condition : Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPISuite computer model (2).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.

2. EPI Suite (2004) Estimation Program Interface Suite, version 3.12. Syracuse Research Corporation, Syracuse, NY, USA.

Conclusion : ECOSAR results indicated that based on the low predicted solubility of this comopund, effects were unlikely to be seen at saturation.

Reliability : (2) valid with restrictions
The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

Type : other: calculated
Species : Daphnia sp. (Crustacea)
Exposure period : 48 h
Unit : mg/l
LC50 : Unlikely to see effects at saturation.
Method : other: ECOSAR Computer Model
Year : 2006
GLP :
Test substance : Other TS: CAS No. 112-8-1; oleic acid
Test condition : Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPISuite computer model (2).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for

estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.

2. EPI Suite (2004) Estimation Program Interface Suite, version 3.12. Syracuse Research Corporation, Syracuse, NY, USA.

Conclusion : ECOSAR results indicated that based on the low predicted solubility of this comopund, effects were unlikely to be seen at saturation. This conclusion is supported by data for tall oil fatty acid indicating an LL50 of >1000mg/L (Metal Carboxylates Coalition, 2005).

Reliability : (2) valid with restrictions
The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint

15.11.2006 (1)

4.3.1 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Type : other: calculated
Species : other algae: green algae
Exposure period : 96 h
Unit : mg/l
LC50 : Unlikely to see effects at saturation.
Method : other: ECOSAR Computer Model
Year : 2006
GLP :
Test substance : CAS No. 14666-94-5; cobalt oleate
Test condition : Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPISuite computer model (2).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.

2. EPI Suite (2004) Estimation Program Interface Suite, version 3.12. Syracuse Research Corporation, Syracuse, NY, USA.

Conclusion : ECOSAR results indicated that based on the low predicted solubility of this comopund, effects were unlikely to be seen at saturation.

Reliability : (2) valid with restrictions
The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint

15.11.2006 EPI Suite (2004)

Type : other: calculated
Species : other algae: green algae
Exposure period : 96 h
Unit : mg/l
LC50 : Unlikely to see effects at saturation.
Method : other: ECOSAR Computer Model
Year : 2006
GLP :
Test substance : Other TS: CAS No. 112-8-1; oleic acid

Test condition	:	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPISuite computer model (2).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.

2. EPI Suite (2004) Estimation Program Interface Suite, version 3.12. Syracuse Research Corporation, Syracuse, NY, USA.

Conclusion	:	ECOSAR results indicated that based on the low predicted solubility of this comopund, effects were unlikely to be seen at saturation. This conclusion is supported by data for tall oil fatty acid indicating an LL50 of 854 mg/L (Metal Carboxylates Coalition, 2005).
Reliability	:	(2) valid with restrictions The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured.
Flag	:	Critical study for SIDS endpoint

14.11.2006 EPI Suite (2004)

Type	:	Static
Species	:	*Selenastrum capricornutum*
Endpoint	:	Growth inhibition
Exposure period	:	96 h
Unit	:	mg/L
EC50	:	0.58
Limit test	:	No
Analytical monitoring	:	No
Method	:	EPA method 1003.0, Algal, *Selenastrum capricornutum* growth test. In: Short-term methods for estimating chronic toxicity of effluent and receiving waters to freshwater organisms. EPA 600/4-89/001.
Year	:	2003
GLP	:	No
Test substance	:	other TS: oleic acid (CAS # 112-80-1)
Test condition	:	*Selenastrum capricornutum* NIES-35 was obtained from the culture collection of Global Environment Forum (GEF),Tsukuba, Japan, and was maintained at 21 +/- 1°C with a 12 h light:12 h dark photoperiod (500 lux) on slopes of C(S) medium. Cultures were prepared in 100-mL Erlenmeyer flasks containing 20 mL of the filtersterilized (0.22 μm) test medium (initial pH: 7.45) in triplicate. Test chemicals were dissolved in DMSO and added to each culture (final concentration of DMSO: less than 0.3%); DMSO can be used at up to a 1% concentration level in the bioassay with *S. capricornutum*. Each chemical was tested in a dilution series of at least 5 concentrations. Both controls and test flasks were inoculated with exponentially growing algae at an initial concentration of *S. capricornutum* of 1 x 10^4 cells/mL. The cultures were incubated at a temperature of 24 +/- 1°C, and shaken at 100 rpm under a constant illumination of 4000 +/- 400 lux. After 72 and 96 h cell counts were determined using a microscope and a hemocytometer. The median inhibition concentration (IC50) values were calculated by the linear interpolation method (U.S. EPA, 1989). The concentrations of test chemicals were not analyzed; therefore, their nominal concentration was used as the exposure concentration in the calculation of IC50 values.
Remark	:	The use of a carrier solvent was employed in this study to achieve

concentrations of test substance greater than the solubility limits. The IC50 value of 0.58 mg/L is greater than the solubility of oleic acid. Nominal, not measured concentrations were employed.

Conclusion : Oleic acid exhibited toxicity to algae at levels likely greater than maximum aqueous solubility through the use of a carrier solvent. Both modellng, and data on tall oil fatty acid indicate that the value presented may not be appropriate for read accross to cobalt oleate.

Reliability : (2) valid with restrictions

15.11.2006 Kamaya Y, Kurogi Y and Suzuki K. (2003). Acute toxicity of fatty acids to the freshwater green alga *Selenastrum capricornutum*. Environ. Toxicol. 18(5): 289-294.

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	**:**	LD50
Value	**:**	>21.5 mL/kg bw
Species	**:**	rat
Strain	**:**	
Sex	**:**	male
Number of animals	**:**	5
Vehicle	**:**	
Doses	**:**	0.464, 1.00, 2.15, 4.64, 10.0, 21.5 mL/kg bw
Method	**:**	other: not specified
Year	**:**	1987
GLP	**:**	
Test substance	**:**	other TS: oleic acid (CAS # 112-80-1)
Remark	**:**	Administration of doses up to 21.5 mL/kg of oleic acid by oral gavage to albino rats resulted in no deaths and no significant gross lesions at necropsy.
Result	**:**	LD50 >21.5 mL/kg
Conclusion	**:**	Oleic acid has a low order of toxicity by the oral route of exposure.
Reliability	**:**	(2) valid with restrictions

06.11.2006 Cosmetic Ingredient Review (1987). Final report on the safety assessment of oleic acid, lauric acid, palmitic acid, myristic acid, and stearic acid. J. Am. Coll. Toxicol. 6(3):321-401.

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type	**:**	LD50
Value	**:**	>3000 mg/kg bw
Species	**:**	Guinea pig
Strain	**:**	
Sex	**:**	male/female
Number of animals	**:**	6
Vehicle	**:**	
Doses	**:**	3000 mg/kg
Method	**:**	other: not specified
Year	**:**	1987
GLP	**:**	
Test substance	**:**	other TS: oleic acid (CAS # 112-80-1)
Remark	**:**	Application of commercial grade oleic acid to the skin of quinea pigs produced no deaths and no signs of toxicity.
Result	**:**	LD50 >3000 mg/kg
Conclusion	**:**	Oleic acid has a low order of toxicity by the dermal route of exposure.
Reliability	**:**	(2) valid with restrictions

06.11.2006 Cosmetic Ingredient Review (1987). Final report on the safety assessment of oleic acid, lauric acid, palmitic acid, myristic acid, and stearic acid. J. Am. Coll. Toxicol. 6(3):321-401.

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic, fertility study
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	other: Oral feeding
Exposure period	:	10-16 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	15% in diet (~12 g/kg/day)
Control group	:	
NOAEL	:	<15% in diet (~12 g/kg/day) for females; 15% in diet (~12 g/kg/day) for males
Method	:	
Year	:	1957
GLP	:	No
Test substance	:	other TS: 88.1% oleic acid (CAS # 112-80-1), 3.0% linoleic acid, 0.6% linolenic acid, 7.4% saturated acids, preformed diene

Remark :

Number of animals: 4-7/sex/dose group
Sprague-Dawley rats were fed to the stock powdered diet mixed with 15% oleic acid for 10-16 weeks. Animals were observed for mortality or obvious signs of toxicity. Body weights were measured during the study.

Vaginal smears were taken daily from all females. A complete and detailed chart of the estrous cycles of each animal was obtained. The presence of a vaginal plug or sperm in the vaginal smear provided evidence that mating had occurred. Implantation was assumed to have occurred if the following signs appeared: cessation of the estrous cycle, appearance of blood in the vaginal smear after the 10th day, a rapid increase in body weight. If parturition did not occur and the body weight decreased, resorption of the fetus was assumed to have taken place. Careful observation was made of the number and state of health of the newborn.

At autopsy, the testes, seminal vesicles, and prostate were removed, and fixed in formalin or Bouin's solution before weighing. Other organs were weighed in the natural state.

Result : Feeding 15% oleic acid diets to rats for 10-16 weeks had no adverse effects on growth or general health. All of the animals appeared normal except for the reproductive capacity of females. Postmorterm examination showed no lesions in other organs than those of reproduction. All animals showed a normal rate of gain in body weight.

Of 4 female weanling rats fed the diet, all 4 were able to become pregnant; however, 2 died at parturition, a litter was eaten at birth, and the remaining litter died within 3 days of birth. Mating of 7 adult female rats fed the diet for 10 weeks resulted in rpoduction of 52 young, 44 of which survived 1 week and 11 of which survived 3 weeks. In all cases mammary development which normally occurs during pregnancy was markedly reduced, and lactation failed to occur. A few rats had ovarian cysts.

The feeding of the diet supplemented with 15% oleic acid had no impairment of the fertility of the male rats.

Conclusion : The NOAEL for subchronic toxicity for males and females were equal to or greater than 15% in diet (~12 g/kg/day), respectively.

Reliability : (4) not assignable

06.11.2006 Carroll, K.K. and Noble, R.L. (1957). Influence of a dietary supplement of erucic acid and other fatty acids on fertility in the rat. Can. J. Biochem. Physiol. 35: 1093-1106.

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Bacterial reverse mutation assay
System of testing : Salmonella typhimurium
Test concentration : Doses ranging from 0.1 to 333 ug per plate
Cycotoxic concentr. : >10,000 ug/plate
Metabolic activation : with and without
Result : negative
Method : other
Year : 1986
GLP :
Test substance : other TS: oleic acid (CAS # 112-80-1)

Remark : Strains tested: Salmonella typhimurium tester strains TA98, TA100, TA1535, TA1537

Test substance doses/concentration levels: The concentration of oleic acid ranged from 0.1 to 333 ug per plate

Metabolic activation: With and without (S9 fraction mix of livers of Aroclor 1254 pretreated rats and hamsters)

Vehicle: Dimethyl sulfoxide (DMSO)

Positive Controls: 2-aminoanthracene, sodium azide, 9-aminoacridine and 4-nitro-o-phenylenediamine.

The criteria used for data evaluation: 1) mutagenic response: a dose-related, reproducible increase in the number of revertants over background, even if the increase was less than twofold; 2) nonmutagenic response: when no increase in the number of revertants was elicited by the chemical; 3) questionable response: when there was an absence of a clear-cut-dose-related increase in revertants, when the dose-related increases in the number of revertants were not reproducible, or when the response was of insufficient magnitude to support a determination of mutagenicity.

Cytotoxicity study: A toxicity screening test conducted with strain TA 100 prior to the full assay indicated a lack of toxicity at concentrations as high as 10,000 ug per plate.

Result : Oleic acid did not induce reverse gene mutation in any Salmonella strain with or without metabolic activation. A satisfactory response was obtained

with the positive control substances (2-aminoanthracene, sodium azide, 9-aminoacridine and 4-nitro-o-phenylenediamine).

Conclusion : Under the conditions of this study, the test material was not mutagenic.
Reliability : (2) valid with restrictions
06.11.2006 Mortelmans K, Haworth S, Lawlor T, Speck W., Tainer B and Zeiger E. (1986). Salmonella Mutagenicity tests: II. Results from the testing of 270 chemicals. Enviro. Mutagen. 8(Suppl 7): 1-119

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type : other
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : other: Oral feeding
Exposure period : 10-16 weeks
Frequency of treatm. :
Premating exposure period
Male :
Female :
Duration of test :
No. of generation studies : 1
Doses : 15% in diet (~7500 mg/kg/day)
Control group :
Method :
Year : 1957
GLP : no
Test substance : other TS: 88.1% oleic acid (CAS # 112-80-1), 3.0% linoleic acid, 0.6% linolenic acid, 7.4% saturated acids, preformed diene

Remark : Number of animals: 4-7/sex/dose group
Sprague-Dawley rats were fed to the stock powdered diet mixed with 15% oleic acid for 10-16 weeks. Animals were observed for mortality or obvious signs of toxicity. Body weights were measured during the study.

Vaginal smears were taken daily from all females. A complete and detailed chart of the estrous cycles of each animal was obtained. The presence of a vaginal plug or sperm in the vaginal smear provided evidence that mating had occurred. Implantation was assumed to have occurred if the following signs appeared: cessation of the estrous cycle, appearance of blood in the vaginal smear after the 10th day, a rapid increase in body weight. If parturition did not occur and the body weight decreased, resorption of the fetus was assumed to have taken place. Careful observation was made of the number and state of health of the newborn.

At autopsy, the testes, seminal vesicles, and prostate were removed, and fixed in formalin or Bouin's solution before weighing. Other organs were weighed in the natural state.

Result : Feeding 15% oleic acid diets to rats for 10-16 weeks had no adverse effects on growth or general health. All of the animals appeared normal except for the reproductive capacity of females. Postmorterm examination showed no

lesions in other organs than those of reproduction. All animals showed a normal rate of gain in body weight.

Of 4 female weanling rats fed the diet, all 4 were able to become pregnant; however, 2 died at parturition, a litter was eaten at birth, and the remaining litter died within 3 days of birth. Mating of 7 adult female rats fed the diet for 10 weeks resulted in reproduction of 52 young, 44 of which survived 1 week and 11 of which survived 3 weeks. In all cases mammary development which normally occurs during pregnancy was markedly reduced, and lactation failed to occur. A few rats had ovarian cysts.

The feeding of the diet supplemented with 15% oleic acid had no impairment of the fertility of the male rats.

Conclusion : The NOAEL for subchronic toxicity for males and females were equal to or greater than 15% in diet (~7500 mg/kg/day, assuming 20 g/day of average feed consumption and 400g average body weight), respectively.

Reliability : (4) not assignable
06.11.2006

Carroll, K.K. and Noble, R.L. (1957). Influence of a dietary supplement of erucic acid and other fatty acids on fertility in the rat. Can. J. Biochem. Physiol. 35: 1093-1106.

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

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8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

EPI Suite (2004) Estimation Program Interface Suite, version 3.12. Syracuse Research Corporation, Syracuse, NY, USA.

Mortelmans K, Haworth S, Lawlor T, Speck W., Tainer B and Zeiger E. (1986). Salmonella Mutagenicity tests: II. Results from the testing of 270 chemicals. Enviro. Mutagen. 8(Suppl 7): 1-119.

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT

201-16041A

U.S. High Production Volume (HPV) Chemical Challenge Program

CATEGORY DEVELOPMENT AND JUSTIFICATION, AND PROPOSED TEST PLAN FOR COBALT STEARATE AND FATTY ACIDS, TALL OIL, COBALT SALTS

Prepared by

MorningStar Consulting, Inc.

on behalf of

The Metal Carboxylates Coalition

A SOCMA Affiliated Consortium

Specifically Sponsored By

OM Group, Inc.
Shepard Chemical Co.

September 2005

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SUMMARY

Cobalt Stearate and Fatty acids, Tall Oil, Cobalt Salts are two sponsored chemicals organized under the Metal Carboxylates Coalition (The Coalition), an HPV testing consortium managed by the Synthetic Organic Chemical Manufacturers Association's (SOCMA) VISIONS Department. The Coalition member companies sponsoring these compounds are OM Group (OMG) and The Shepherd Chemical Company.

The Metal Carboxylates Coalition has sponsored 19 compounds that are metal salts of carboxylic acids (metal carboxylates). These compounds readily dissociate to the corresponding metal and carboxylic acid. The HPV endpoints are fulfilled using a combination of data from the parent molecule, as well as for the dissociation products; that is, a metal salt and/or a carboxylic acid. Selected testing of the parent molecules has been proposed to further fulfill HPV endpoints. Robust summaries are provided for the parent molecules as well as the dissociation products.

This submittal provides the information for:

Cobalt Stearate	CASRN 13586-84-0
Fatty acids, Tall Oil, Cobalt Salts	CASRN 61789-52-4

The proposed testing is presented in the attached Test Plan matrix (Table 6)

1.0 BACKGROUND

This submittal provides the information for:

Cobalt Stearate	CASRN 13586-84-0
Fatty Acids, Tall Oil, Cobalt Salts	CASRN 61789-52-4

Cobalt stearate is the cobalt salt of stearic acid. Because cobalt is divalent, two stearic acid molecules are involved. The structural formula is $Co(C_{18}H_{35}O_2)_2$. The cobalt salts of fatty acids, tall oil are more difficult to characterize chemically because the tall oil fatty acids are derived from the fractional distillation of crude tall oil, which is a by-product from the pulping of pine trees. The mixture of fatty acids in pine trees varies by species and even within species (Pine Chemicals Association, 2004). The composition of a typical tall oil fatty acid includes oleic acid (48%), linoleic acid (35%), conjugated linoleic acid (7%), stearic acid (2%), palmitic acid (1%), and other acids and unsaponifiable matter (Pine Chemicals Association, 2004). Oleic acid and linoleic acid, like stearic acid, are C18 fatty acids with slightly differing degrees of saturation.

Cobalt stearate and fatty acids, tall oil, cobalt salts are high molecular weight compounds. The molecular weight for cobalt stearate is 625.9. The molecular weight of fatty acids, tall oil, cobalt salt is undefined due to the undefined nature of the acid component; however, the typical composition would be largely oleic and linoleic acid, both of which are C18 unbranched aliphatic acids, as is stearic acid. Thus the molecular weight of fatty acids, tall oil, cobalt salts would be similar to that of cobalt stearate.

Figure 1 provides the structure of cobalt stearate. Figure 2 provides the structures of oleic acid and linoleic acid, major components of fatty acids, tall oil. The cobalt salts of fatty acids, tall oil consist of cobalt associated with the various acid moieties, similar to cobalt stearate.

1.1 Use Patterns for Metal Carboxylates

The metal carboxylates function to deliver a metal ion into chemical reactions. The carboxylic acids (acids) are tailored for use in different products or chemical reactions.

In general the cobalt carboxylates are used as oxidative polymerization catalysts in many product areas. These areas include, but are not limited to: ink and paint driers; unsaturated polyester resins, and hydrodesulfurization in their manufacturing; and the making of the insecticide DEET (diethyltoluamide). Some of these carboxylate compounds are used in oxygen scavenger plastics as well (for example, plastic bottles). The tire industry also uses cobalt carboxylate compounds as adhesion promoters in tire manufacturing. These compounds facilitate adhesion between the rubber in the steel cords. The metal (not salt) loadings range from 0.01 – 0.5% depending upon the application.

1.2 Common Characteristics of Metal Carboxylates

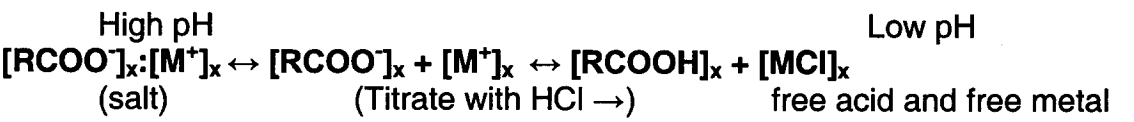
These two metal carboxylates (cobalt stearate and fatty acids, tall oil, cobalt salts) are functionally similar and have the same ionizable substituents, the same metal cation, and a structurally similar carboxylic acid group (RCOOH). These compounds are divalent compounds and have two carboxylic acid moieties per molecule. The metal carboxylate salts are designed to add metals to chemical reactions; therefore, they are designed to readily dissociate into the free metal and free acid.

2.0 Dissociation Studies

One key characteristic of metal carboxylates is that they readily dissociate from an ion pair into free metal and free acid. They are found as partially dissociated products in the ambient environment (i.e., neutral pH). Dissociation is a reversible process and the proportion of dissociated salt present is dependent on the pH and pKa (the dissociation constant), which is the pH at which 50% dissociation occurs. In the low pH environment of the digestive tract (e.g., pH 1.2) complete dissociation will occur for these metal carboxylates. The transport and bioavailability of the metals and acids are determined by their solubility in environmental media and biological fluids which is determined by environmental parameters such as pH.

The Metal Carboxylates Coalition conducted studies to determine the dissociation constants of each of these compounds. The mean pKa value for cobalt stearate was 7.5 at 20ºC while the mean pKa value for fatty acids, tall oil, cobalt salts was 5.82. These results indicate that significant dissociation will occur at approximately neutral pH (i.e., representative of aquatic and marine ecosystems), while complete dissociation will occur at physiologically relevant pH of the mammalian stomach (pH 1.2). These findings are particularly important in relating available data for the respective acids and metals to support the existing data for cobalt stearate and fatty acids, tall oil, cobalt salts in the fulfillment of critical endpoints.

Dissociation is a reversible reaction, splitting the parent compound into two or more chemical species which may be ionic, but are not necessarily so. The process can be generally represented as:



The pKa and pH are equal when the metal carboxylate salt is 50% dissociated. The parent compounds, the metal carboxylate salts, are associated ionized molecules.

The dissociation constant is important for two reasons. First, it determines the proportion of any specific acid or metal that is dissociated at a given pH. The free acid and corresponding free metal are often much different than the salt (ion pair) moiety in characteristics such as solubility, adsorption, and toxicity. The proportion of dissociation influences the behavior of the substance in the environment and bioavailability of the acid and metal constituents of metal carboxylate salts.

The dissociation constants for 18 related metal carboxylate compounds tested have pKa (pKb) values (pKa1) in the neutral range (5.088 to 8.448). This indicates that in the neutral pH range, significant portions of the metal carboxylates will be dissociated. In addition, at the low pH of the mammalian stomach (pH 1.2) all of the metal carboxylates would be expected to be completely or nearly completely dissociated. This indicates that the absorption and any observed toxicity would be independent for the respective acid and metal when administered orally.

The dissociation constants show that at the pH of the stomach and at the pH of environmental media, the important moieties are the ionized free acid and metal. Because of this, environmental fate, ecotoxicity, and mammalian toxicity of the free acid, or that for a simple salt which would readily dissociate (e.g., the sodium salt), can serve as surrogate data for the acid component of respective metal carboxylates. Similarly, under these conditions, data for the metal ion can be represented by fate and toxicity data on free metal ion or simple metal salts (e.g., metal chlorides). Therefore, the role in any observed toxicity for acids and metals can be evaluated independently (i.e., as the free metal and/or free acid).

3.0 Bioequivalency

The work described below by Stopford et al. (unpublished)[1] shows that cobalt chloride is similar to, or more bioavailable than, the corresponding cobalt carboxylate salts, which makes the chloride a conservative surrogate in estimating bioavailability and toxicity of dissociated metal. Cobalt chloride has thus been emphasized during preparation of the attached robust summaries and provides the preferred surrogate data for cobalt carboxylate salts.

The recent studies by Stopford et al. to evaluate the "bioequivalency" (an estimate of bioavailability) of cobalt compounds included three cobalt carboxylates and cobalt chloride. The solubility of these compounds in synthetic

[1] Stopford, W., J. Turner, D. Cappellini, and T. Brock. (unpublished) Bioequivalency Testing of Cobalt Compounds (Oct 15, 2002 Draft). Conducted by Duke University Medical Center, Division of Occupational and Environmental Medicine for the Cobalt Development Institute, Research Triangle Park, N.C.

biological fluids (gastric juices, intestinal juices, several interstitial fluids, and cytosol) showed that these salts were completely dissociated and dissolved at gastric pH and cytosolic pH. The dissolution of these compounds ranged from 26.1% to 80.4 % of available cobalt at neutral pH (Table 1). The results for cobalt chloride and cobalt 2-ethyl-hexanoate were very similar at acidic and neutral pH. Cobalt neodecanoate and cobalt naphthenate showed similar levels of dissolution at acidic (gastric and cytosolic) pH, but smaller proportions of the metal component of these compounds were dissolved at neutral pH. The differences in dissolution for these metal carboxylates at neutral pH in synthetic body fluids could be related to differences in their dissociation constants.

These data are valuable in understanding cobalt stearate and fatty acid, tall oil, cobalt salts for three reasons:

1. They confirm the prediction that these compounds would be expected to be completely dissociated in the gastrointestinal tract (low pH) and a substantial proportion would be expected to be dissociated and bioavailable at neutral pH (7.4).

2. The fraction of the three cobalt carboxylates evaluated by Stopford et al. that was dissolved at acidic and neutral pH was very similar for different acid constituents with a range of molecular weights and chain lengths. This finding greatly strengthens the extrapolation of the results to cobalt stearate and fatty acids, tall oil, cobalt salts.

3. The work by Stopford et al. shows that cobalt chloride is similar to, or more bioavailable than, the corresponding cobalt carboxylate salts, which makes the chloride a conservative surrogate in estimating bioavailability and toxicity of dissociated metals. Cobalt chloride has been emphasized during preparation of the attached robust summaries and provides the preferred surrogate data for the cobalt carboxylate salts.

Work by Firriolo[2] demonstrated that absorption, distribution, and excretion of cobalt from cobalt carboxylic acids is independent of the acid. This work was based on cobalt chloride and cobalt naphthenate and confirms observations by Stopford et al. that dissociation of the carboxylate is complete at the pH of the stomach.

[2] Firriolo, J.M. 1992. Disposition and toxicity after oral and intravenous administration of cobalt naphthenate and cobalt chloride in rats. Ph.D. Dissertation, University of Arizona.

4.0 Supporting Data for HPV Chemicals and their Dissociation Products

Data for cobalt stearate (Appendix A) and fatty acids, tall oil, cobalt salts (Appendix B) and their dissociation products (cobalt chloride, stearic acid, and fatty acids, tall oil [Appendixes C, D, and E, respectively]) are provided in robust summary format.

Consistent with discussions between the Metal Carboxylates Coalition and the EPA, data for the dissociation products (metals and acids) are recognized as being essential to understanding the environmental fate and toxicological characteristics of the respective metal carboxylate salts. Data for stearic acid, fatty acids, tall oil, and cobalt are useful in characterizing the hazard of the cobalt stearate and fatty acids, tall oil, cobalt salts.

In summary, the key points relative to these two HPV chemicals are:

- Dissociation to the carboxylic acids and cobalt (described as cobalt chloride);
- Dissociation constants (pKa) in the circum neutral range (5.82 to 7.5);
- Complete or nearly complete dissociation at gastric and cytosolic pH levels;
- A moderate to high proportion of dissociation in the neutral pH range;
- General bioequivalency for salts with the same metal cation (e.g., cobalt) and different acids or the chloride salt;
- Cobalt carboxylates have the same use pattern, to provide free metal ion to chemical reactions.
- Existing data for the parent molecule or both of its dissociation products will be sufficient to address specific endpoints.

5.0 Proposed Test Plan

The Metal Carboxylates Coalition has relied on the fact that these compounds will dissociate and that the respective acid (stearic acid or fatty acids, tall oil), and metal (cobalt) are the chemicals of interest. Studies conducted by the Metals Carboxylates Coalition have demonstrated that dissociation of these materials will occur readily in water at neutral pH's and completely at the pH of the stomach (pH 1.2). This is consistent with data for other metal carboxylates.

The Metal Carboxylates Coalition is relying on the data for cobalt and for stearic acid to support cobalt stearate and to minimize unnecessary testing. A robust summary document has been prepared for cobalt chloride, which describes the necessary endpoint data under the HPV Program (Appendix C). A robust summary document has also been prepared for stearic acid (Appendix D).

Stearic acid has a long history of safe use in foods and cosmetics. This compound is sponsored within the Aliphatic Acids Category under the HPV Challenge Program. More complete or more robust data may become available following the Aliphatic Acids Category submission to the EPA by The Soap and Detergent Association. If needed, the Metal Carboxylates Coalition will then revise the current robust summary document to include more complete stearic acid data and will make a supplemental submission.

To support fatty acids, tall oil, cobalt salts, the Metal Carboxylates Coalition is relying on the data for cobalt and for fatty acids, tall oil. As mentioned previously, the robust summary document prepared for cobalt chloride is attached as Appendix C. Fatty acids, tall oil is sponsored by the Pine Chemicals Association, Inc. as part of the category Tall Oil Fatty Acids and Related Substances. The robust summaries for fatty acids, tall oil submitted to EPA as part of the final submission from the Pine Chemicals Association, dated August 2004, are included as Appendix E. Also included in Appendix E is the IUCLID dataset for fatty acids, tall oil, dated February 2000.

Tables 2 - 5 provide a summary of the data for cobalt stearate and fatty acids, tall oil, cobalt salts, as well as their dissociation products

Physicochemical Properties

The physicochemical properties are summarized in Table 2. The Metal Carboxylates Coalition conducted GLP studies to determine several properties of cobalt stearate and fatty acids, tall oil, cobalt salts, including melting point, boiling point, water solubility and dissociation constant. Melting point studies were performed to generate data for both HPV compounds (see Table 2). In studies conducted to determine the boiling points, cobalt stearate decomposed before boiling could occur and a boiling point was not observed for fatty acids, tall oil, cobalt salts. Based upon the properties of the respective acids, the vapor pressure of the two HPV compounds is expected to be low. Studies indicated the water solubility of the two compounds was fairly low, but greater than their respective acids. This result may be related to the procedure used, which quantified the amount of test compound in solution by measuring the amount of cobalt. Since cobalt stearate and fatty acids, tall oil, cobalt salts dissociate, the water solubility test results may reflect dissociation rather than solubility per se. The octanol-water partition coefficient (Kow) is a property that is determined on unionized, undissociated chemicals and therefore is not an appropriate property to measure for metal carboxylates. The Kow of the respective acids provides surrogate data to estimate this property for the dissociated cobalt stearate and fatty acids, tall oil, cobalt salts.

No additional physical chemical properties testing is necessary or proposed.

Environmental Fate

Table 3 provides a summary of the available environmental fate data for the two HPV chemicals, as well as their dissociation products. The Metal Carboxylates Coalition conducted studies to determine the dissociation constants of cobalt stearate and fatty acids, tall oil, cobalt salts; the resulting pKa values were 7.50 and 5.82, respectively. These results indicate that the environmental fate characteristics of these chemicals will be dependent upon the characteristics of their dissociation products, data for which are presented in Table 3. The dissociated cobalt metal, of course, will not photodegrade or biodegrade. The respective acids, however, are amenable to these degradation processes. Predictions based upon structure-activity models (e.g., EPIWIN) indicate that stearic acid is photodegradable and would tend to be found in the sediment or soil compartments of the environment. Several laboratory studies indicate that both stearic acid and fatty acids, tall oil are readily biodegradable. Predictions for photodegradation and transport (fugacity) have been calculated using EPIWIN for oleic acid and linoleic acid, the two major components of a typical fatty acid, tall oil. These results are similar to those for stearic acid.

A biodegradation study with cobalt stearate is proposed. Biodegradation data will show that the rate of degradation for the cobalt stearate salt is the same as stearate alone and that the cobalt does not inhibit biodegradation of the stearate. Both cobalt stearate and fatty acids, tall oil, cobalt salts would have the same combined effect on biodegradation; therefore only one study with cobalt stearate is proposed.

Environmental Effects

Table 4 provides a summary of the available environmental effects data for cobalt stearate, and fatty acids, tall oil, cobalt salts, as well as their dissociation products. No information is available for the two HPV chemicals. For the dissociation products, adequate data exist to characterize the aquatic toxicity of cobalt. Studies have been conducted to determine the acute toxicity of fatty acids, tall oil to fish, invertebrates and algae, providing sufficient information for these endpoints. However, for stearic acid, only data on toxicity to fish are available, and this is for a study of time to lethality (LT50 endpoint), so it is marginally useful. It is anticipated that additional aquatic toxicity data for stearic acid will be generated by the Aliphatic Acids Consortium. When available, the Metal Carboxylates Coalition will amend this test plan with these data. To demonstrate that dissociation product data is representative of the aquatic toxicity for the two HPV chemicals, it is proposed that acute toxicity studies for fish, daphnia and algae be conducted with cobalt stearate.

Acute toxicity studies with fish, daphnia and algae are proposed to characterize the aquatic toxicity of cobalt stearate. In addition, an acute daphnia study with

fatty acids, tall oil, cobalt salts is proposed as a bridging study to demonstrate that the dissociation product data are representative for this metal carboxylate salt..

Human Health Effects

Data elements for human health effects endpoints were examined for cobalt stearate and fatty acids, tall oil, cobalt salts, and their dissociation products (Table 5). Mammalian toxicity will be represented by data available for the salt where available (e.g., Acute Oral LD50) and dissociation products. For cobalt chloride, several studies are available to document acute oral toxicity and repeated dose toxicity. Male reproductive effects have been demonstrated in rats and mice and developmental toxicity studies exist for both rats and mice. Cobalt (II) is generally not mutagenic in bacterial assays but has genotoxic effects in mammalian systems. For fatty acids, tall oil, data are available for acute oral toxicity, repeated dose toxicity, and reproductive/developmental toxicity. In addition, tests have demonstrated that fatty acids, tall oil was not mutagenic in bacterial assays but was clastogenic to mammalian cells (though at cytotoxic concentrations).

All endpoints are filled for cobalt chloride and fatty acids, tall oil. Data gaps exist for stearic acid. However, the Coalition will supplement this Test Plan with data being generated by the Aliphatic Acids Consortium on stearic acid, when these studies become available.

An oral LD50 study is proposed for fatty acids, tall oil, cobalt salts as part of establishing the category approach, i.e., that the dissociation products can be used to predict the toxicity of the salts. An OECD 422 study with cobalt stearate is proposed as a bridging study to show that dissociation product data is representative of the mammalian toxicity for these two metal carboxylate salts. Because there is no data available on the genetic toxicity of stearic acid to mammalian systems, a chromosomal aberration study is proposed for cobalt stearate. A chromosomal aberration study is also proposed for fatty acids, tall oil, cobalt salts based on reported clastogenicity of both dissociation products (cobalt and fatty acids, tall oil).

5.1 TEST PLAN SUMMARY

Table 6 provides the test plan for cobalt stearate and fatty acids, tall oil, cobalt salts. A biodegradation study is proposed for cobalt stearate. For ecotoxicity, acute testing with fish, daphnia, and algae are also proposed with cobalt stearate. An oral acute LD50 test, a combined Repeated Dose w/Repro/Developmental Screen (OECD 422) and a chromosomal aberration test are also proposed with cobalt stearate. For fatty acids, tall oil, cobalt salts, an acute daphnia test, an acute oral LD50 test, and a chromosomal aberration test are proposed.

FIGURES

Figure 1: Cobalt Stearate

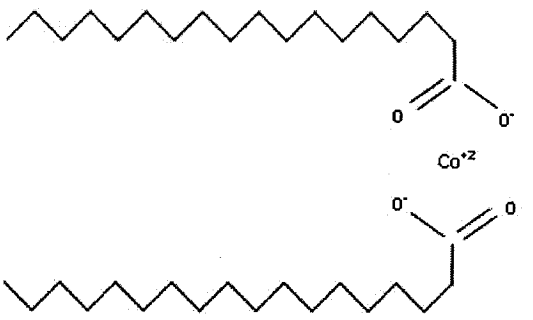
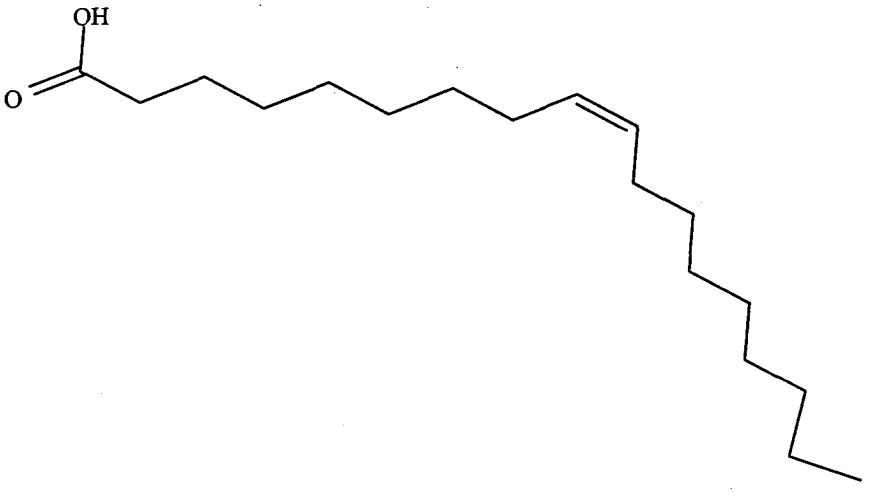
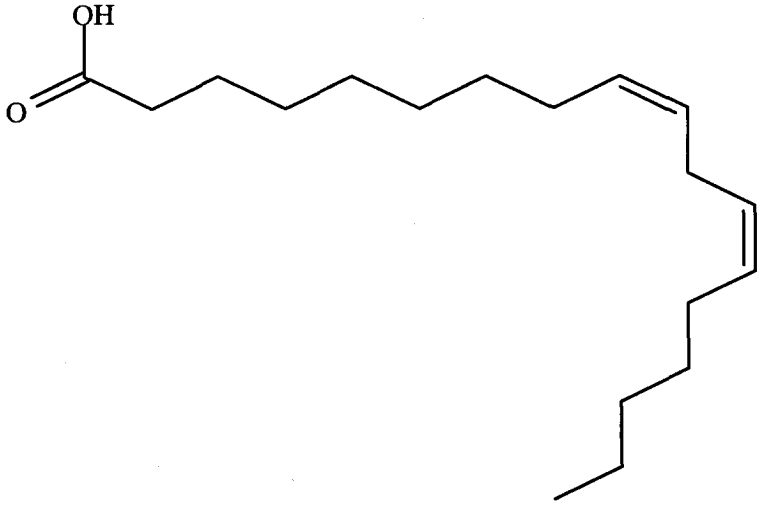


Figure 2: Fatty acids, tall oil: typical major components

Oleic acid
$C_{18}H_{34}O_2$



Linoleic acid
$C_{18}H_{32}O_2$



TABLES

Table 1. Results of Extraction of Cobalt from Surrogate Biological Fluids

Matrix (pH)	Maximum Solubility (% of available metal)			
	$CoCl_2$	Co 2-ethyl-hexanoate	Co naphthenate	Co neodecanoate
Gastric pH (1.5)	>91.6	100	>85.7	100
Intestinal pH (7.4)	>79.4	50.8*	45.4*	30.8*
Alveolar pH (7.4)	>68	>59.6	35.4*	26.1*
Interstitial pH (7.4)	78.4	>80.4	40*	43.1*
Serum	>85	>66.9	42.9*	46.6*
Intracellular pH (4.5)	>89.6	100	>79.1	>78.1

* maximum extraction level at 72 hours

All data is taken from Stopford et al. (unpublished) Bioequivalency Testing of Cobalt Compounds. Conducted by Duke University Medical Center, Division of Occupational and Environmental Medicine for the Cobalt Development Institute.

Table 2. Summary of Available and Relevant Physical/Chemical Properties Data for Cobalt Stearate, Fatty Acids, Tall Oil, Cobalt Salts, and their Dissociation Products

Compound	Physical/Chemical Properties				
	Melting Point (deg C)	Boiling Point (deg C)	Vapor Pressure (hPa)	Partition coefficient (log Kow)	Water Solubility (mg/L)
Dissociation Product: Cobalt chloride	735	1,049	NA	NA	450,000
Cobalt stearate	45.1 – 79.3	ND	-	NA	6.4 @ 20ºC
Dissociation Product: Stearic acid	69 - 70	383	1.33 @173.7	8.42	0.568 @ 25ºC
Fatty acids, tall oil, cobalt salts	-38 to -39	ND	-	NA	149 @ 20ºC
Dissociation Product: Fatty acids, tall oil	NA	160 - 210 @ 6.6 hPa	negligible	4.4 – 8.3 @ pH 2; 3.6 – 7.4 @ pH 7.5	12.6

ND = no data; testing did not yield results for boiling point
NA = not applicable due to substance properties

Table 3: Summary of Available and Relevant Environmental Fate Data for Cobalt Stearate, Fatty Acids, Tall Oil, Cobalt Salts, and their Dissociation Products

Compound	Environmental Fate			
	Stability in Water	Photo-degradation	Level III Fugacity Model	Biodegradation
Dissociation Product: Cobalt chloride	(high water solubility)	NA	NA	NA
Cobalt stearate	Dissociates: pKa = 7.50 @ 20ºC	-	-	-
Dissociation Product: Stearic acid	(low water solubility)	T ½ = 0.5 days	Air: 0.676 Water: 7.19 Soil: 28.9 Sediment: 63.3	Readily biodegradable
Fatty acids, tall oil, cobalt salts	Dissociates: pKa = 5.82 @ 20ºC	-	-	-
Dissociation Product: Fatty acids, tall oil [(1)]	(low water solubility)	T ½ = 2 hours or less	Air: <0.1 Water: 7-8 Soil: 28-29 Sediment: 63-64	Readily biodegradable

NA = not applicable due to substance properties

[(1)] Photodegradation and fugacity results are averages of modeled results for oleic acid and linoleic acid, two components of fatty acids, tall oil

Table 4. Summary of Available and Relevant Environmental Effects Data for Cobalt Stearate, Fatty Acids, Tall Oil, Cobalt Salts, and their Dissociation Products

Compound	Environmental Effects		
	Acute Toxicity to Fish (mg/L)	Acute Toxicity to Daphnia (mg/L)	Acute Toxicity to Algae (mg/L)
Dissociation Product: Cobalt chloride	1.41 – 333 (96-h LC50)	1.52 – 5.5 (48-h EC50)	0.52 (96-h EC50)
Cobalt stearate	-	-	-
Dissociation Product: Stearic acid	LT50 data (marginally useful)	-	-
Fatty acids, tall oil, cobalt salts	-	-	-
Dissociation Product: Fatty acids, tall oil	10 (96-h LC50) to > 1000 (96-h LL50)	55.7 (48-h EC50) to > 1000 (48-h LL50)	0.79 – 9 (EC50) to 854 (72-h EL50)

Table 5. Summary of Available and Relevant Human Health Effects Data for Cobalt Stearate, Fatty Acids, Tall Oil, Cobalt Salts, and their Dissociation Products

Compound	Human Health Effects				
	Acute Toxicity (mg/kg)	Repeat Dose Toxicity	Reproductive Effects	Developmental Effects	Genetic Toxicity
Dissociation product: Cobalt chloride	LD50 = 42.4 – 190 (rat) LD50 = 89.3 (mouse)	NOAEL = 0.6 mg Co/kg; LOAELs 0.5 – 30.2 mg Co/kg/day	Effects in rats at 13.2 – 30.2 mg Co/kg/d; mice at 23-58.9 mg Co/kg/d	NOAEL = 24.8 mg/kg/d (mice); 81.7 mg Co/kg in screening study (mice)	Co (2+) generally non-mutagenic in bacterial assays; genotoxic/mutagenic/ clastogenic in mammalian systems
Cobalt stearate	LD50 = 9.82 gm/kg-	-	-	-	-
Dissociation Product: Stearic acid	LD50 = 4600 (rat) LD50 > 10,000 (rat)	50 g/kg/d for 24 weeks produced reversible lipogranulomas in rats; Severe effects in rats, including mortality, at 3000 ppm	-	-	Not mutagenic in bacterial assays
Fatty acids, tall oil, cobalt salts	-	-	-	-	-
Dissociation Product: Fatty acids, tall oil	LD50 > 10,000 (rat)	NOEL = 2500 mg/kg/d (rat 90-d, diet)	NOAEL = 5000 mg/kg/d (rat, 2 gen study)	NOAEL = 5000 mg/kg/d (rat, 2 gen study)	Not mutagenic in bacterial assays; clastogenic to mammalian cells but at cytotoxic concentrations

Table 6: Test Plan for Cobalt Stearate and Fatty Acids, Tall Oil, Cobalt Salts

Endpoint	Cobalt Stearate					Fatty Acids, Tall Oil, Cobalt Salts				
	Co stearate	Stearic acid	Co chloride	Data Used or Test required	OECD Guideline	FA,Tall Oil, Cobalt Salts	FA,Tall Oil	Co chloride	Data Used or Test required	OECD Guideline
Physicochemical Properties										
Melting point	Y	Y	Y	A		Y	NA	Y	A	
Boiling point	Y	Y	Y	A		Y	Y	Y	A	
Vapor pressure	N	Y	NA	DP		N	Y	NA	DP	
Partition coefficient	NA	Y	NA	NA		NA	Y	NA	NA	
Water Solubility	Y	Y	Y	A		Y	Y	Y	A	
Environmental Fate										
Photodegradation	N	Y	NA	DP		N	Y	NA	DP	
Stability in water	Y	Y	Y	A		Y	Y	Y	A	
Fugacity	N	Y	NA	DP		N	Y	NA	DP	
Biodegradation	N	Y	NA	Test	301	N	Y	NA	DP	
Ecotoxicity										
Acute Fish	N	N	Y	Test	203	N	Y	Y	R/DP	
Acute Daphnia	N	N	Y	Test	202	N	Y	Y	Test	202
Acute Algae	N	N	Y	Test	208	N	Y	Y	R/DP	
Mammalian Toxicity										
Acute	N	Y	Y	Test	425	N	Y	Y	Test	425
Repeated Dose	N	Y	Y	Test	422	N	Y	Y	R/DP	
Reproductive	N	N	Y	Test	422	N	Y	Y	R/DP	
Developmental	N	N	Y	Test	422	N	Y	Y	R/DP	
Genetic Toxicity (Bacteria)	N	Y	Y	DP		N	Y	Y	DP	
Genetic Toxicity (Mammalian)	N	N	Y	Test	473	N	Y	Y	Test	473

Y = Acceptable data available
N = No acceptable data available
NA = Not applicable due to physical/chemical properties of the substance
A = Endpoint requirement fulfilled with adequate existing data
Test = Endpoint requirements to be fulfilled with testing
DP = Endpoint requirements to be fulfilled using data for dissociation products
R = Use of category approach, e.g. that these two compounds are essentially the same and toxicity for one salt can be predicted from data for the other salt, when dissociation product data is available.

APPENDIX A

COBALT STEARATE ROBUST SUMMARIES

1. General Information

ID 6865-35-6
Date January 31, 2005

1.0 SUBSTANCE INFORMATION

Generic Name	:	Cobalt Stearate
Chemical Name	:	
CAS Registry No.	:	13586-84-0
Component CAS Nos.	:	
EINECS No.	:	
Structural Formula	:	$Co(C_{18}H_{35}O_2)_2$
Molecular Weight	:	625.9
Synonyms and Tradenames	:	Octadecanoic acid, cobalt salt; stearic acid, cobalt salt

2.1 MELTING POINT

Type	:	Melting Point/Melting Range Determination
Guideline/method	:	OECD 102; EPA OPPTS 830.7200
Value	:	45.1º to 79.3°C
Decomposition	:	Starts at 177°C
Sublimation	:	
Year	:	2003
GLP	:	Yes
Test substance	:	Cobalt stearate, batch H08 M23, 9.41% cobalt, purple solid, provided by Alfa Aesar
Method	:	OECD 102, Melting Point/Melting Range, July 1995; EPA Product Properties Test Guidelines, OPPTS 830.7200, Melting Point/Melting Range, March 1998
Method detail	:	A differential scanning colorimeter (DSC 821, Fa, Mettler Toledo) was used to determine the melting point/range (the temperature or temperature range at which phase transition from solid to liquid state occurs). A preliminary test was conducted at a heating rate of 20 K/min from 25ºC to 400ºC and the quantities of heat absorbed or released were measured and recorded. The weight and appearance of the sample were recorded before and after the test. Based upon the preliminary test results, two definitive runs were made at a heating rate of 5 K/min from 25ºC to 120ºC to determine the onset and end of the endothermic reaction.
Result	:	The melting range was determined from the mean of two definitive runs to be between 45.1ºC and 79.3ºC (318.3 K and 340.7 K)
Remark	:	**Supporting data for dissociation products:** **Acid:** The melting point reported for stearic acid is 69 - 70°C (Appendix D). **Metal:** The melting point reported for cobalt chloride is 735ºC (Appendix C).
Reliability	:	[1] Reliable without restriction
Reference	:	Tognucci, A., 2003. Determination of the Melting Point/Melting Range of Cobalt Stearate, RCC Study No. 849123, 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	:	Decomposition observed before boiling could occur
Decomposition	:	Starts at 177°
Year	:	2003
GLP	:	Yes
Test substance	:	Cobalt stearate, batch H08 M23, 9.41% cobalt, purple solid, provided by Alfa Aesar
Method	:	OECD 103, Boiling Point, 1995; EPA Product Properties Test Guidelines, OPPTS 830.7220, Boiling Point/Boiling Range, August 1996
Method detail	:	A differential scanning colorimeter (DSC 821, Fa, Mettler Toledo) was used to determine the boiling point/range (the temperature or temperature range at which the vapor pressure of a liquid is the same as the standard pressure). A preliminary test was conducted at a heating rate of 20 K/min from 25ºC to 400ºC and the quantities of heat absorbed or released were measured and recorded. The weight and appearance of the sample were recorded before and after the test. A definitive run was made at a heating rate of 5 K/min from 130ºC to 300ºC; however no peak was observed from which boiling could be deduced.
Result	:	The boiling point was not observed because the test material decomposed prior to boiling.

Remark	:	**Supporting data for dissociation products:** **Acid:** The reported boiling point for stearic acid is 383 °C (Appendix D). **Metal:** The reported boiling point for cobalt chloride is 1,049ºC (Appendix C).
Reliability	:	[1] Reliable without restriction
Reference	:	Tognucci, A., 2003. Determination of the Boiling Point/Boiling Range of Cobalt Stearate, RCC Study No. 849124, conducted for the Metal Carboxylates Coalition by RCC Ltd., Switzerland.

2.3 DENSITY

Type	:	
Guideline/method	:	
Value	:	1.035
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting data for dissociation products:** **Acid:** Reported value for stearic acid is 0.9408 at 20°C (HSDB 8/16/02). **Metal:** Reported value for cobalt chloride is 3.367 at 25ºC (Appendix C).
Reliability	:	
Reference		Certificate of Analysis for Cobalt Stearate, Lot Number H08M23, 9.41% cobalt, prepared by Alfa Aesar, Ward Hill, MA.

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 stearic acid is 1.33 hPa at 173.7°C (Appendix D).
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	:	Determination of octanol/water partition coefficient (Kow) is inappropriate for metal carboxylate compounds such as cobalt stearate. Kow is determined on unionized, undissociated chemicals. Due to the complex water chemistry of cobalt stearate, and the presence of dissociated ionized constituents, measuring Kow would be extremely difficult if not impossible, and would not provide meaningful data. A worst-case estimate of log Kow, calculated for the salt ion pairs using EPIWIN, is 15.1; however, this value most probably over-predicts the potential for bioaccumulation of cobalt stearate under environmentally-relevant conditions. **Supporting data for dissociation products:** **Acid:** Log Kow for stearic acid is reported as 8.42 (Appendix D). **Metal:** not applicable (ionizes in water)
Reliability	:	
Reference	:	

2.6.1 SOLUBILITY IN WATER

Type	:	Water Solubility Determination
Guideline/method	:	OECD 105; EPA OPPTS 830.7840
Value	:	6.4 mg/L at 20ºC
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
PKa	:	at °C
Description	:	
Stable	:	
Deg. product	:	
Year	:	2003
GLP	:	Yes
Test substance	:	Cobalt stearate, Batch H08 M23, 9.41% cobalt, purple solid, provided by Alfa Aesar
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 solubility was below 10 mg/L; therefore, the column elution method was used in the definitive test. The column was prepared by adding 6.05 g of glass beads into a flask, adding 0.120 g ground test material and mixing for 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 stearate from the carrier material. Temperature was 20ºC. The flow rate was 0.52 mL/min for 71 hours, followed by a period of 24 hours at 0.26 mL/min. 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 sampled at 1 hour intervals to determine the concentration of cobalt, using atomic absorption spectroscopy.
Result	:	Based on the results of 12 samples, the cobalt solubility was 0.6 mg/L (SD ± 0 mg/L) which corresponds to a water solubility of cobalt stearate of 6.4 mg/L (calculated based on cobalt content of 9.41%). The pH during the test ranged from 7.04 to 7.98.
Remark	:	**Supporting data for dissociation products:** **Acid:** The reported water solubility for stearic acid is 0.568 mg/L at 25 °C (Appendix D).

		Metal: The reported water solubility for cobalt chloride is 450 g/L at 7ºC (Appendix C).
Reliability	:	[1] Reliable without restriction
Reference	:	Tognucci, A., 2003. Determination of the Water Solubility of Cobalt Stearate, RCC Study No. 849126, conducted for the Metal Carboxylates Coalition by RCC Ltd., Switzerland.

2.7 FLASH POINT

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

3.1.1 PHOTODEGRADATION

Type		
Guideline/method	:	
Light source	:	
Light spectrum	:	
Relative intensity	:	based on
Spectrum of substance	:	lambda (max, >295nm) : epsilon (max) : epsilon (295) :
Conc. of substance	:	at °C
DIRECT PHOTOLYSIS		
Halflife (t1/2)	:	
Degradation	:	% after
Quantum yield	:	
INDIRECT PHOTOLYSIS		
Sensitizer	:	
Conc. of sensitizer	:	
Rate constant	:	
Degradation	:	
Deg. product	:	
Year	:	
GLP	:	
Test substance	:	
Deg. products CAS#	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting data for dissociation products:** **Acid**: Half life of 0.5 days for stearic acid, calculated using AopWin v1.91 (Appendix D). **Metal:** not applicable, metal does not degrade
Reliability	:	
Reference	:	

3.1.2 DISSOCIATION

Type	:	Dissociation constant determination
Guideline/method	:	OECD 112
pKa	:	7.50 at 20°C
Year	:	2002
GLP	:	Yes
Test substance	:	Cobalt stearate, lot number F26L13, received from Alfa Aesar. Dark pellets, purity of 9.6% cobalt.
Approximate water solubility	:	0.17 mg/L, determined by Inductively Coupled Plasma Atomic Emission Spectrometry during preliminary study
Method	:	OECD Guideline 112, Dissociation Constants in Water
Method detail	:	Three replicate samples of cobalt stearate were prepared at a nominal concentration of 0.10 mg/L by fortification of 100 mL of degassed water (ASTM Type II) with a 0.10 mg/mL stock solution of the test substance in tetrahydrofuran. Each sample was titrated against 0.00025 N sodium hydroxide while maintained at a test temperature of 20±1°C. At least 10 incremental additions were made before the equivalence point and the titration was carried past the equivalence point. Values of pK were calculated for a minimum of 10 points on the titration curve. Phosphoric acid and 4-nitrophenol were used as reference substances.
Result	:	Mean (N = 3) pKa value was 7.50 (SD = 0.0356) at 20°C

Remark	:	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	:	[1] Reliable without restriction.
Reference	:	Lezotte, F.J. and W.B. Nixon, 2002. Determination of the dissociation constant of cobalt stearate, Wildlife International, Ltd. Study No. 534C-113, 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**: Using EPIWIN v. 3.11, the Level III fugacity model predicts distribution of stearic acid primarily to sediment (63.3%), followed by soil (28.9%), water (7.19%) and air (<1%). See Appendix D.
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	:	**Supporting data for dissociation products:** **Acid**: Stearic acid is readily biodegradable in activated sludge under aerobic conditions: 77% degraded in 28 days in BOD test; 95% in 21 days in Sturm CO_2 evolution test; reported half-life of 3 -10 days in additional studies (Appendix D). **Metal:** not applicable, metal does 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	:	

4.1 ACUTE TOXICITY TO FISH

Type	:	
Guideline/method	:	
Species	:	
Exposure period	:	
NOEC	:	
LC0	:	
LC50	:	
LC100	:	
Other	:	
Other	:	
Limit test	:	
Analytical monitoring	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting information for dissociation products:** **Acid:** For stearic acid, the LT50 was > 96 hours at 12 mg/L for *Oncorhynchus kisutch* (Appendix D). **Metal:** For cobalt chloride, the 96-h LC50 was 1.41 mg Co/L for the highly sensitive rainbow trout, *Onchorynchus mykiss*. Toxicity to other fish species ranges from LC50 values of 22 – 333 mg Co/L. Toxicity is dependent upon water hardness (Appendix C).
Reliability	:	
Reference	:	

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	
Guideline/method	:	
Species	:	
Exposure period	:	
NOEC	:	
EC0	:	
EC50	:	
EC100	:	
Other	:	
Other	:	
Other	:	
Limit test	:	
Analytical monitoring	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting information for dissociation products:** **Metal:** For cobalt chloride, the 48-h EC50 for *Daphnia magna* was 1.52 mg Co/L. In other studies, and with other species, 48-h LC50 values ranged from 1.52 – 5.5 mg Co/L. (Appendix C).
Reliability	:	
Reference	:	

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

Type	:	
Guideline/method	:	
Species	:	
Endpoint	:	
Exposure period	:	
NOEC	:	
LOEC	:	
EC0	:	
EC10	:	
EC50	:	
Other	:	
Other	:	
Limit test	:	
Analytical monitoring	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting information for dissociation products:** **Metal:** For cobalt chloride, the 96-h EC50 for *Chorella vulgaris* was 0.52 mg Co/L. Other aquatic plants were less sensitive with EC50 values from 16.9 – 23.8 mg Co/L. (Appendix C).
Reliability	:	
Reference	:	

4.4 CHRONIC TOXICITY TO FISH

Type	:	
Guideline/method	:	
Species	:	
Exposure period	:	
NOEC	:	
LOEC	:	
LC0	:	
LC50	:	
LC100	:	
Other	:	
Other	:	
Limit test	:	
Analytical monitoring	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	
Reliability	:	
Reference	:	

4.5 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type	:	

Guideline/method	:
Species	:
Exposure period	:
NOEC	:
LOEC	:
EC0	:
EC50	:
EC100	:
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	:	1st.: 2nd.: 3rd.:
Toxic behavior	:	
Deg. product	:	
Deg. products CAS#	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting information for dissociation products:** **Metal:** Absorption of cobalt in the digestive tract is influenced by the chemical form of the metal, with increasing solubility resulting in increased absorption. 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(2):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 (Appendix C).
Reliability	:	
Reference	:	

5.1.1 ACUTE ORAL TOXICITY

Type	:	Single dose
Guideline/Method	:	
Species	:	Rat
Strain	:	
Sex	:	Both male and females
Number of animals	:	Five per dose level (30 overall)
Vehicle	:	Propylene Glycol
Doses	:	1.0, 2.0, 4.0, 8.0, 16.0, and 32.0 gm /kg

LD50	:	9.82 gm /kg (± 95% CI 7.45-12.95 gm /kg)
Year	:	1977
GLP	:	No
Test substance	:	Co Stearate
Method	:	Oral gavage
Method detail	:	Young rats 200-300 gms wererandomized and dosed via oral gavage and observed for 14 days
Result	:	Observations included: lethargy, unkempt coat, diarrhea, nasal hemorrhage, and at 16.0 gm /kg loss of mototr control . In the high dose the mortalities occurred within 24 hours. At 16.0 and 8.0 gm /kg moptalities occurred between 4 and 6 days post treatment.
Remark	:	**Supporting information for dissociation products:** **Acid:** Rat LD50 = 4600 mg/kg bw for stearic acid (Appendix D). Additional data: Male rats (5 males per treatment) were dosed with 0.464 to 10.0 g/kg of eutectic (triple pressed) stearic acid. The LD50 was reported as >10.0 g/kg (>10,000 mg/kg). Reference: Cosmetic, Toiletries, and Fragrance Association (1987) Cosmetic Ingredient Review, Final Report on the Safety Assessment of Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid and Stearic Acid. J. Am. Coll. Toxicol. Vol. 6, No. 3, pp321-401. (Subsequently referred to as CTFA#3.) **Metal:** Reported LD50s of cobalt chloride to rats range from 42.4 to 190 mg $CoCl_2$/kg bw (equivalent to 19.8 to 85.5 mg Co/mg bw). Toxicity of cobalt sulfate is reported to be similar to the chloride with oral LD50s for rats ranging from 123 to 161 mg/kg bw (equivalent to 46.7 to 61.2 mg Co/kg bw). For the mouse, LD50 values are 89.3 and 123 mg/kg for cobalt chloride and cobalt sulfate, respectively, which are equivalent to 40.2 and 56.7 mg/kg bw when expressed as the metal only (ATSDR Sept 2001 Draft; see Appendix C).
Reliability	:	(2) Reliable with resptriction. Consucted prior to the the implementation of GLP.
Reference	:	Study conducted by Bio-Toxicology Laboratories, Inc. Moorestown, NJ, for The Shepherd Chemical Company Reported May 31, 1977.

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:** **Metal:** No acute inhalation studies have been located for cobalt chloride.
Reliability	:	
Reference	:	

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	:	**Supporting information for dissociation products:** **Acid:** Stearic acid, 10-100 mM in olive oil was dosed intradermally in guinea pigs and rabbits which resulted in mild erythema and slight induration of skin. CTFA#3 ref 157. Stearic acid as a 20% formulations was applied at 2.0 ml/kg of product to abraded/intact sites on the backs of rabbits. After four weeks no mortaltities and slight edema and sesqumation were observed. CTFA#3 ref 163. **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 C).
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:** **Metal:** Dermatitis is a common result of dermal exposure to cobalt in humans and has been verified in a large number of studies. The dermatitis is probably caused by an allergic reaction to cobalt. (Appendix C).
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	:	
Method	:	
Method detail	:	
Result	:	**Supporting information for dissociation products:** **Acid:** Stearic acid (eutectic, commercial grade) was applied to the eyes of albino rabbits following the Draise method. Results ranged from no irritation to mild conjunctival erythema in 2 rabbits subsiding by 72 hours. Stearic acid in various formulations at lower strengths showed similar results (CTFA#3).
Remark	:	
Reliability	:	
Reference	:	

5.4 REPEATED DOSE TOXICITY

Type	:	
Guideline/method	:	
Species	:	
Strain	:	
Sex	:	
Number of animals	:	
Route of admin.	:	
Exposure period	:	
Frequency of treatment	:	
Post exposure period	:	
Doses	:	
Control group	:	
NOAEL	:	
LOAEL	:	
Other	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting information for dissociation products:** **Acid:** Rats fed for 24 weeks with stearic acid (50 g/kg/day) developed foreign body type reaction in perigenital fat. Lipogranulomas were oberved to be reversible. Rats fed stearic acid (3000 ppm) for 30 weeks developed anorexia, severe pulmonary infection, and high mortality. No significant pathological lesions were observed. (CTFA#3 ref 151,152). (Appendix D). **Metal:** Repeated oral dosing of rats for 150-210 days with cobalt chloride

at 4 and 10 mg Co/kg indicated a LOAEL of 4 mg Co/kg, based upon increased organ weights. Eight weeks' oral exposure of rats to cobalt chloride hexahydrate indicated a LOAEL of 2.5 mg Co/kg (changes in hemoglobin and red blood cell count) and a NOAEL of 0.6 mg Co/kg. Other studies using repeated oral dosing for periods ranging from 12-16 days up to 7 months indicated LOAELs ranging from 0.5 to 30.2 mg Co/kg/day (as cobalt chloride) based upon observations such as reduced weight gain, increases in some organ weights (heart, liver and lungs); increased hematocrit, hemoglobin, and RBCs; renal tubular necrosis; and various changes on cardiac physiology (left ventricular hypertrophy, impaired ventricular function, and degeneration of myofibrils). Cardiac effects were observed in rats at LOAELs 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 (Appendix C).

Reliability :
Reference :

5.5 GENETIC TOXICITY 'IN VITRO'

Type :
Guideline/method :
System of testing :
Species :
Strain :
Test concentrations :
Cytotoxic concentr. :
Metabolic activation :
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark :

Supporting information for dissociation products:
Acid: Stearic acid was not mutagenic in *S. typhimurium* with and without metabolic activation. Stearic acid was tested for mutagenicity using the Ames test with *Salmonella typhumurium* strains TA98, TA100, TA1535, TA1537, TA1538. Spot tests were performed suing 50 mg/ml stearic acid suspensions in the distilled waster (50 µg/plate) with and without microsomal activation from hepatic S9 fractions from rats induced with Aroclor 1254 (50 µg/plate). Positive controls were 2-aminoanthracene and 4-nitro—o-phenylenediamine in dimethyl sulfoxide, 9-aminoacridinein ethanol, and sodium azide in distilled water with and without metabolic acitivation. (CTFA#3.)
MetalCobalt compounds with a valence state of II, the form of cobalt released by dissociation of cobalt chloride, are reported to be generally non-mutagenic in *in vitro* bacterial assays, although weak positive responses have been observed under some conditions (Appendix C).

Reliability :
Reference :

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	:	
Result	:	
Remark	:	**Supporting information for dissociation products:** **Metal:** Cobalt compounds, including soluble salts, are observed to be clastogenic (cause chromosomal aberrations) in a range of mammalian assay systems. 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). In the mouse micronucleus test, a dose-dependent increase in the frequency of micronucleated polychromatic erythrocytes was observed with i.p. exposure to cobalt chloride hexahydrate (Appendix C).
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	:	**Supporting information for dissociation products:** **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, stunted pup growth was seen at all dose levels. 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. In a screening study, 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 C).

Reliability	:
Reference	:

5.8.3 TOXICITY TO REPRODUCTION

Type	:
Guideline/method	:
In vitro/in vivo	:
Species	:
Strain	:
Sex	:
Route of admin.	:
Exposure period	:
Frequency of treatment	:
Duration of test	:
Doses	:
Control group	:
Year	:
GLP	:
Test substance	:
Method	:
Method detail	:
Result	:
Remark	: **Supporting information for dissociation products:** **Metal:**Male mice exposed to cobalt chloride hexahydrate in drinking water for 12-13 weeks demonstrated effects on testicular weight and sperm concentration at all dose levels (23 - 58.9 mg Co/kg bw). Rats exposed to 20 mg Co/kg bw (as cobalt chloride hexahydrate) through the diet showed degenerative and necrotic lesions in seminiferous tubules and testicular atrophy (Appendix C).
Reliability	:
Reference	:

6.0 OTHER INFORMATION

6.1 CARCINOGENICITY

Supporting information for dissociation products:
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 (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).

APPENDIX B

FATTY ACID, TALL OIL, COBALT SALTS ROBUST SUMMARIES

1. General Information

ID 61789-52-4

Date January 31, 2005

1.0 SUBSTANCE INFORMATION

Generic Name	:	
Chemical Name	:	Fatty acids, tall oil, cobalt salts
CAS Registry No.	:	61789-52-4
Component CAS Nos.	:	
EINECS No.	:	
Structural Formula	:	
Molecular Weight	:	
Synonyms and Tradenames	:	Cobalt tallate; Tall oil fatty acids, cobalt salts
References	:	

2.1 MELTING POINT

Type	:	Melting Point/Melting Range Determination
Guideline/method	:	OECD 102; EPA OPPTS 830.7200
Value	:	-38 to -39°C
Decomposition	:	at °C
Sublimation	:	
Year	:	2003
GLP	:	Yes
Test substance	:	Fatty acids, tall oil, cobalt salts, Lab batch 1022-49, 8.85% cobalt, very tacky red-purple solid, provided by OMG Americas
Method	:	OECD 102, Melting Point/Melting Range, July 1995; EPA Product Properties Test Guidelines, OPPTS 830.7200, Melting Point/Melting Range, March 1998
Method detail	:	The freezing point, defined as the temperature at which phase transition from liquid to solid state at normal atmospheric temperature occurs, corresponds to the melting point. To determine the freezing point, 5 mL of test material was preheated in a waterbath at about 80ºC and then cooled using acetone and dry ice until solidification. A thermocouple probe in the center of the sample was used to measure temperature over time; the physical state was observed as well. The test was run in duplicate.
Result	:	The freezing point (melting point) was determined to be between -38ºC and -39ºC (equal to 234 – 235 K)
Remark	:	**Supporting data for dissociation products:** **Metal**: The melting point reported for cobalt chloride is 735ºC (Appendix C).
Reliability	:	[1] Reliable without restriction
Reference	:	Tognucci, A., 2003. Determination of the Melting Point/Melting Range of Fatty Acids, Tall Oil, Cobalt Salts, RCC Study No. 849114, 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	:	Boiling point was not observed
Decomposition	:	
Year	:	2003
GLP	:	Yes
Test substance	:	Fatty acids, tall oil, cobalt salts, Lab batch 1022-49, 8.85% cobalt, very tacky red-purple solid, provided by OMG Americas
Method	:	OECD 103, Boiling Point, 1995; EPA Product Properties Test Guidelines, OPPTS 830.7220, Boiling Point/Boiling Range, August 1996
Method detail	:	A differential scanning colorimeter (DSC 821, Fa, Mettler Toledo) was used to determine the boiling point/range (the temperature or temperature range at which the vapor pressure of a liquid is the same as the standard pressure). A preliminary test was conducted at a heating rate of 20 K/min from 25ºC to 400ºC and the quantities of heat absorbed or released were measured and recorded. The weight and appearance of the sample were recorded before and after the test. A definitive run was made at a heating rate of 10 K/min; however no peak was observed from which boiling could be deduced.
Result	:	The boiling point was not observed.
Remark	:	**Supporting data for dissociation products:** **Acid**: For tall oil fatty acids, the boiling point is reported as approx. 160 - 210 °C at 6.6 hPa. Union Camp Chemicals (Durham. UK); cited in year 2000 IUCLID dataset.

Metal: The reported boiling point for cobalt chloride is 1,049ºC (Appendix C).

Reliability : [1] Reliable without restriction

Reference : Tognucci, A., 2003. Determination of the Boiling Point/Boiling Range of Fatty Acids, Tall Oil, Cobalt Salts, RCC Study No. 849115, conducted for the Metal Carboxylates Coalition by RCC Ltd., Switzerland.

2.3 DENSITY

Type : Specific gravity
Guideline/method :
Value : 1.02 at 25°C
Year :
GLP :
Test substance :
Method :
Method detail :
Result :
Remark : **Supporting data for dissociation products:**
Metal: Reported value for cobalt chloride is 3.367 at 25ºC (Appendix C).
Reliability :
Reference Material Safety Data Sheet for cobalt tallate, OMG Americas, Inc.

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: For tall oil fatty acids, the vapor pressure is negligible at 25°C. Union Camp Chemicals (Durham. UK); cited in year 2000 IUCLID dataset.
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 : Determination of octanol/water partition coefficient (Kow) is inappropriate for metal carboxylate compounds such as fatty acids, tall oil, cobalt salts. Kow is determined on unionized, undissociated chemicals. Due to the complex

water chemistry of fatty acids, tall oil, cobalt salts, and the presence of dissociated ionized constituents, measuring Kow would be extremely difficult if not impossible, and would not provide meaningful data.
Supporting data for dissociation products:
Acid: When tested according to OECD Test Method 117, at pH 2, the log P_{ow} values for seven compounds in tall oil fatty acid were 4.4, 7.0, 7.3, 7.5, 7.7, 8.0, and 8.3. At pH 7.5, the log P_{ow} values for six compounds in tall oil fatty acid were 3.6, 3.8, 4.2, 4.5, 4.7, and 7.4. (Dybdahl, H.P. 1993). See robust summary prepared by the Pine Chemicals Association (Appendix E).
Metal: not applicable (ionizes in water).

Reliability :
Reference :

2.6.1 SOLUBILITY IN WATER

Type	:	Water Solubility Determination
Guideline/method	:	OECD 105; EPA OPPTS 830.7840
Value	:	149 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	:	Fatty acids, tall oil, cobalt salts, Lab Batch 1022-49, 8.85% cobalt, very tacky red-purple solid, provided by OMG Americas
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 solubility was below 10 mg/L; therefore, the column elution method was used in the definitive test. The column was prepared by adding 6.09 g of glass beads into a flask, adding 0.12 g of test material dissolved in 5 mL dichloromethane, and evaporating the solvent under a stream of nitrogen. 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 test material from the carrier material. Temperature was 20ºC. The flow rate was 0.52 mL/min for 120 hours, followed by a period of 23 hours at 0.26 mL/min. 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 sampled at 1 hour intervals to determine the concentration of cobalt, using atomic absorption spectroscopy.
Result	:	Based on the results of 12 samples, the cobalt solubility was 13.2 mg Co/L (SD ± 2.8 mg/L) which corresponds to a water solubility of fatty acids, tall oil, cobalt salts of 149 mg FA Tall Oil Co Salt/L (calculated based upon cobalt content of 8.85% w/w). The pH during the test ranged from 5.59 to 5.62.
Remark	:	**Supporting data for dissociation products:** **Acid**: The water solubility of tall oil fatty acid, in its entirety as a complex mixture, was reported as 12.6 mg/L (Dinwoodie, N.B., 2003; see robust summary prepared by the Pine Chemicals Association in Appendix E).

Metal: The reported water solubility for cobalt chloride is 450 g/L at 7°C (Appendix C).

Reliability : [1] Reliable without restriction

Reference : Tognucci, A., 2003. Determination of the Water Solubility of Fatty Acids, Tall Oil, Cobalt Salts, RCC Study No. 849117, conducted for the Metal Carboxylates Coalition by RCC Ltd., Switzerland.

2.7 FLASH POINT

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

3.1.1 PHOTODEGRADATION

Type		
Guideline/method	:	
Light source	:	
Light spectrum	:	
Relative intensity	:	based on
Spectrum of substance	:	lambda (max, >295nm) :
		epsilon (max) :
		epsilon (295) :
Conc. of substance	:	at °C
DIRECT PHOTOLYSIS		
Halflife (t1/2)	:	
Degradation	:	% after
Quantum yield	:	
INDIRECT PHOTOLYSIS		
Sensitizer	:	
Conc. of sensitizer	:	
Rate constant	:	
Degradation	:	
Deg. product	:	
Year	:	
GLP	:	
Test substance	:	
Deg. products CAS#	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting data for dissociation products:** **Acid:** AOPWIN v.191 was used to calculate photodegradation for two major components of fatty acids, tall oil. The half-life for oleic acid was 1-2 hours and the half-life for linoleic acid was 0.7 -1 hours. **Metal:** not applicable, metal does not degrade.
Reliability	:	(1) Reliable without restriction
Reference	:	

3.1.2 DISSOCIATION

Type	:	Dissociation constant determination
Guideline/method	:	OECD 112
pKa	:	5.82 at 20°C
Year	:	2002
GLP	:	Yes
Test substance	:	Cobalt tallate, CAS number 61789-52-4, received from OMG. Dark solid, purity of 20.6% cobalt
Approximate water solubility	:	3.5 mg/L, determined by Inductively Coupled Plasma Atomic Emission Spectrometry during preliminary study
Method	:	OECD Guideline 112, Dissociation Constants in Water
Method detail	:	Three replicate samples of cobalt tallate were prepared at a nominal concentration of 1.5 mg/L by fortification of 100 mL of degassed water (ASTM Type II) with a 1.0 mg/mL stock solution of the test substance in methanol. Each sample was titrated against 0.00025 N sodium hydroxide while maintained at a test temperature of 20±1°C. At least 10 incremental additions were made before the equivalence point and the titration was carried past the equivalence point. Values of pK were calculated for a minimum of 10 points on the titration curve. Phosphoric acid and 4-nitrophenol were used as reference substances.

Result	:	Mean (N = 3) pKa value was 5.82 (SD = 0.108) at 20°C
Remark	:	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	:	[1] Reliable without restriction.
Reference		Lezotte, F.J. and W.B. Nixon, 2002. Determination of the dissociation constant of tall oil, cobalt salts, Wildlife International, Ltd. Study No. 534C-117, 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**: EPIWIN v3.11 was used to determine fugacity (Level III) for two major components of fatty acids, tall oil. Results are:

	Mass amount (%)	Half-life (hr)	Emissions (kg/hr)
Oleic acid			
Air	0.0999	1.3	1000
Water	7.49	360	1000
Soil	28.1	360	1000
Sediment	64.3	1440	0
Persistence time: 616 hr			
Linoleic acid			
Air	0.0546	0.691	1000
Water	8.07	360	1000
Soil	28.7	360	1000
Sediment	63.1	1440	0
Persistence time: 603 hr			

Reliability	:	(1) Reliable without restriction
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	:	**Supporting data for dissociation products:** **Acid:** The biodegradability of tall oil fatty acids has been studied in several different tests. In a ready biodegradability closed bottle test (OECD 301D), the test material degraded 50% in 7 days and 56% in 28 days (Madsen, 1993). In a manometric respiratory test (OECD 301 F), the substance degraded 84% in 28 days (Aniol, 1999). In a ready biodegradability modified Sturm test (OPPTS 853.110), 74% of the test article degraded in 28 days (Sewell, 1994). See robust summaries prepared by the Pine Chemicals Association (Appendix E). **Metal:** not applicable, metal does 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	:	

4.1 ACUTE TOXICITY TO FISH

Type	:
Guideline/method	:
Species	:
Exposure period	:
NOEC	:
LC0	:
LC50	:
LC100	:
Other	:
Other	:
Other	:
Limit test	:
Analytical monitoring	:
Year	:
GLP	:
Test substance	:
Method	:
Method detail	:
Result	:
Remark	: **Supporting data for dissociation products:** **Acid:** In a study conducted according to OECD 203, fathead minnows (*Pimephales promelas*) were exposed to water accommodated fractions of tall oil fatty acid. The 96-h LL50 was > 1000 mg/L, which was the highest loading rate tested. The NOEL was 1000 mg/L. (Kelly, 2002. See robust summary prepared by the Pine Chemicals Association (Appendix E). The 96-h LC50 for zebrafish is reported to be 10 to 20 mg/L for tall oil fatty acids. Arizona Chemical Company letter to U.S EPA dated November 2, 1999. [Available from the National Technical Information Service in microfiche OTS0559827, Initial submission letter from attorneys of Arizona Chemical Co. to USEPA regarding 17 health and ecotoxicity studies of various chemicals with attachments and dated 110299 (sanitized)]. **Metal:** For cobalt chloride, the 96-h LC50 was 1.41 mg Co/L for the highly sensitive rainbow trout, *Onchorynchus mykiss*. Toxicity to other fish species ranges from LC50 values of 22 – 333 mg Co/L. Toxicity is dependent upon water hardness (Appendix C).
Reliability	:
Reference	:

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:
Guideline/method	:
Species	:
Exposure period	:
NOEC	:
EC0	:
EC50	:
EC100	:
Other	:
Other	:
Other	:
Limit test	:
Analytical monitoring	:
Year	:
GLP	:

Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting data for dissociation products:** **Acid:** In a study conducted according to OECD 202, Part 1, *Daphnia magna* were exposed to water accommodated fractions of tall oil fatty acid. The 48-h EL50 was > 1000 mg/L, which was the highest loading rate tested. The NOEL was 1000 mg/L. (Kelly, 2002. See robust summary in attached document prepared by the Pine Chemicals Association (Appendix E). The 48-h EC50 for *Daphnia magna* is reported as 55.7 mg/L for tall oil fatty acids. Arizona Chemical Company letter to U.S EPA dated November 2, 1999. [Available from the National Technical Information Service in microfiche OTS0559827, Initial submission letter from attorneys of Arizona Chemical Co. to USEPA regarding 17 health and ecotoxicity studies of various chemicals with attachments and dated 110299 (sanitized)]. **Metal:** For cobalt chloride, the 48-h EC50 value for *Daphnia magna* was 1.52 mg Co/L. In other studies, and with other species, 48-h LC50 values ranged from 1.52 – 5.5 mg Co/L (Appendix C).
Reliability	:	
Reference	:	

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	:	**Supporting data for dissociation products:** **Acid:** In a study conducted according to OECD 201, the green alga *Selenastrum capricornutum* was exposed to water accommodated fractions of tall oil fatty acid. The 72-h EL50 based on area under the growth curve was 854 mg/L with a corresponding NOEL of 500 mg/L. The 72-h EL50 based on average specific growth rate was > 1000 mg/L with a corresponding NOEL of 750 mg/L. (Kelly, 2002. See robust summary in attached document prepared by the Pine Chemicals Association (Appendix E). The growth inhibition EC50 values for three algal species were reported to range from 0.79 to 9 mg/L for tall oil fatty acids. Arizona Chemical Company letter to U.S EPA dated November 2, 1999. [Available from the

National Technical Information Service in microfiche OTS0559827, Initial submission letter from attorneys of Arizona Chemical Co. to USEPA regarding 17 health and ecotoxicity studies of various chemicals with attachments and dated 110299 (sanitized)].
Metal: For cobalt chloride, the 96-h EC50 for *Chorella vulgaris* was 0.52 mg Co/L. Other aquatic plant species were less sensitive, with EC50 values from 16.9 – 23.8 mg Co/L (Appendix C).

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	:	1st: 2nd: 3rd:
Toxic behavior	:	
Deg. product	:	
Deg. products CAS#	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting data for dissociation products:** **Metal:** Absorption of cobalt in the digestive tract is influenced by the chemical form of the metal, with increasing solubility resulting in increased adsorption. 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(2):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 (Appendix C).
Reliability	:	
Reference	:	

5.1.1 ACUTE ORAL TOXICITY

Type	:	
Guideline/Method	:	
Species	:	
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	

Doses	:	
LD50	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	
Reliability	:	**Supporting data for dissociation products:** **Acid:** The acute oral LD50 of tall oil fatty acids has been reported as >10,000 mg/kg in rats using a test procedure consistent with OECD Test Method 401. (Mallory, 1983). See robust summary in attached document prepared by the Pine Chemicals Association (Appendix E). **Metal:** Reported LD50s of cobalt chloride to rats range from 42.4 to 190 mg $CoCl_2$/kg bw (equivalent to 19.1 to 85.5 mg Co/mg bw). Toxicity of cobalt sulfate is reported to be similar to the chloride with oral LD50s for rats ranging from 123 to 161 mg/kg bw (equivalent to 46.7 to 61.2 mg Co/kg bw). For the mouse, LD50 values were reported as 89.3 and 123 mg/kg for cobalt chloride and the cobalt sulfate, respectively, which are equivalent to 40.2 and 56.7 mg/kg bw when expressed as cobalt (ATSDR Sept 2001 Draft; see Appendix C).
Reference	:	

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:** **Metal:** No acute inhalation studies have been located for cobalt chloride.
Reliability	:	
Reference	:	

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	:	**Supporting data for dissociation products:** **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 C).
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:** **Metal:** Dermatitis is a common result of dermal exposure to cobalt in humans and has been verified in a large number of studies. The dermatitis is probably caused by an allergic reaction to cobalt (Appendix C).
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	:	
Method	:	

Method detail	:
Result	:
Remark	:
Reliability	:
Reference	:

5.4 REPEATED DOSE TOXICITY

Type	:
Guideline/method	:
Species	:
Strain	:
Sex	:
Number of animals	:
Route of admin.	:
Exposure period	:
Frequency of treatment	:
Post exposure period	:
Doses	:
Control group	:
NOAEL	:
LOAEL	:
Other	:
Year	:
GLP	:
Test substance	:
Method	:
Method detail	:
Result	:
Remark	: **Supporting data for dissociation products:** **Acid:** Two repeated dose oral toxicity studies in rats have been conducted using tall oil fatty acids. In a 28-d dietary feeding study, the NOAEL was 15% when expressed in terms of total calories fed (Seppanen, 1969). Growth was significantly decreased at a feeding level of 30% of total calories. In a 90-d dietary feeding study, the NOEL was 5% in the diet or approximately 2,500 mg/kg/day (Fancher, 1969). The most sensitive effect was a reduction food consumption (but not body weight) at 10% in the diet. No effects on clinical signs or histopathology were reported at feeding levels up to 25% in the diet. See robust summaries in attached document prepared by the Pine Chemicals Association (Appendix E). **Metal:** Repeated oral dosing of rats for 150-210 days with cobalt chloride at 4 and 10 mg Co/kg indicated a LOAEL of 4 mg Co/kg, based upon increased organ weights. Eight weeks' oral exposure of rats to cobalt chloride hexahydrate indicated a LOAEL of 2.5 mg Co/kg (changes in hemoglobin and red blood cell count) and a NOAEL of 0.6 mg Co/kg. Other studies using repeated oral dosing for periods ranging from 12-16 days up to 7 months indicated LOAELs ranging from 0.5 to 30.2 mg Co/kg/day (as cobalt chloride) based upon observations such as reduced weight gain, increases in some organ weights (heart, liver and lungs); increased hematocrit, hemoglobin, and RBCs; renal tubular necrosis; and various changes on cardiac physiology (left ventricular hypertrophy, impaired ventricular function, and degeneration of myofibrils). Cardiac effects were observed in rats at LOAELs 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 (Appendix C).
Reliability	:
Reference	:

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	
Guideline/method	:	
System of testing	:	
Species	:	
Strain	:	
Test concentrations	:	
Cytotoxic concentr.	:	
Metabolic activation	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting data for dissociation products:** **Acid:** Tall oil fatty acids tested negative in the Ames *Salmonella*/microsome plate test both with and without metabolic activation (Godek, 1983). Testing was conducted following OECD 471 with five different strains of *S. typhimurium* at doses up to 10,000 µg/plate. In the chromosomal aberration assay with Chinese hamster ovary cells (OECD 473), tall oil fatty acid was clastogenic with S9 mix at 20 ug/mL and without S9 mix at 156 ug/L; both concentrations were overtly toxic to the cells (Murie, 2001). See robust summaries in attached document prepared by the Pine Chemicals Association. (Appendix E). **Metal:** Cobalt compounds with a valence state of II, the form of cobalt released by dissociation of cobalt chloride, are reported to be generally non-mutagenic in *in vitro* bacterial assays, although weak positive responses have been observed under some conditions (Appendix C).
Reliability	:	
Reference	:	

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	:	
Result	:	
Remark	:	**Supporting data for dissociation products:** **Metal:** Cobalt compounds, including soluble salts, are observed to be clastogenic (cause chromosomal aberrations) in a range of mammalian assay systems. 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). In the mouse micronucleus test, a dose-

dependent increase in the frequency of micronucleated polychromatic erythrocytes was observed with i.p. exposure to cobalt chloride hexahydrate (Appendix C).

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 :

Supporting data for dissociation products:
Acid: The effects of tall oil fatty acids on rat developmental parameters have been studied in a two-generation feeding study (Tegeris, 1975). The study was generally consistent with OECD 416 except the initial treatment period for the parental generation was approximately three weeks prior to mating. Feeding levels were 0, 5, or 10% in the diet. Following weaning, the F_1 generation was fed the test article and mated at 100 days. The F_2 generation survived to weaning. Treatment did not affect the number of liveborn or stillborn F_1 litters and pups, or F_1 weaning weight. No treatment-related changes in fertility, viability, lactation, or gestation indices were measured. Clinical chemistry and pathological examinations also did not reveal treatment-related effects. It was concluded that tall oil fatty acid had no reproductive or developmental effects on rats at doses as high as 10% (approx. 5,000 mg/kg/day). See robust summary in attached document prepared by the Pine Chemicals Association (Appendix E).
Metal: In a developmental toxicity study with cobalt chloride exposure (5.4 or 21.8 mg Co/kg/day) in rats from gestation day 14 to lactation day 21, stunted pup growth was seen at all dose levels. 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. In a screening study, 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 C).

Reliability :
Reference :

5.8.3 TOXICITY TO REPRODUCTION

Type	:	
Guideline/method	:	
In vitro/in vivo	:	
Species	:	
Strain	:	
Sex	:	
Route of admin.	:	
Exposure period	:	
Frequency of treatment	:	
Duration of test	:	
Doses	:	
Control group	:	
Year	:	
GLP	:	
Test substance	:	
Method	:	
Method detail	:	
Result	:	
Remark	:	**Supporting data for dissociation products:** **Acid:** The effects of tall oil fatty acids on rat reproductive parameters have been studied in a two-generation feeding study (Tegeris, 1975). The study was generally consistent with OECD 416 except the initial treatment period for the parental generation was approximately three weeks prior to mating. Feeding levels were 0, 5, or 10% in the diet. Following weaning, the F_1 generation was fed the test article and mated at 100 days. The F_2 generation survived to weaning. Treatment did not affect the number of liveborn or stillborn F_1 litters and pups, or F_1 weaning weight. No treatment-related changes in fertility, viability, lactation, or gestation indices were measured. Clinical chemistry and pathological examinations also did not reveal treatment-related effects. It was concluded that tall oil fatty acid had no reproductive or developmental effects on rats at doses as high as 10% (approx. 5,000 mg/kg/day). See robust summary in attached document prepared by the Pine Chemicals Association (Appendix E). **Metal:** Male mice exposed to cobalt chloride hexahydrate in drinking water for 12-13 weeks demonstrated effects on testicular weight and sperm concentration at all dose levels (23 – 58.9 mg Co/kg bw). Rats exposed to 20 mg Co/kg bw (as cobalt chloride hexahydrate) through the diet showed degenerative and necrotic lesions in seminiferous tubles and testicular atrophy (Appendix C).
Reliability	:	
Reference	:	

6.0 OTHER INFORMATION

Supporting data for dissociation products:
Acid: A safety assessment of tall oil acid (a purified form of tall oil fatty acids) has been performed for use in cosmetic products by an Expert Panel (Expert Panel, 1989). Based on its review of available data for tall oil acid and its primary constituent (oleic acid), the Expert Panel concluded that tall oil acid is safe for use in cosmetics. The Expert Report includes a clinical assessment of safety for dermal exposure based on testing in human subjects. Several studies were conducted with liquid soaps containing 12% tall oil acid. These studies included a 4-week hand washing study with a diluted soap (final concentration of 3% tall oil acid) and two repeated dose patch studies with undiluted soap. None

of the subjects in these studies had positive reactions and the soap was found to be non-irritating and non-sensitizing.

Expert Panel. 1989. Final report on the safety assessment of tall oil acid. J. Amer. Coll. Toxicol. 8:769-776.

6.1 CARCINOGENICITY

Supporting data for dissociation products:
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 (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).

APPENDIX C

COBALT CHLORIDE ROBUST SUMMARIES

1. General Information

ID 7646-79-9

Date January 31, 2005

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).

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

2.4 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.

2.7 FLASH POINT

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

3.1.1 PHOTODEGRADATION

Type				
Guideline/method	:			
Light source	:			
Light spectrum	:			
Relative intensity	:	based on		
Spectrum of substance	:	lambda (max, >295nm)	:	
		epsilon (max)	:	
		epsilon (295)	:	
Conc. of substance	:		at	°C
DIRECT PHOTOLYSIS				
Halflife (t1/2)	:			
Degradation	:	% after		
Quantum yield	:			
INDIRECT PHOTOLYSIS				
Sensitizer	:			
Conc. of sensitizer	:			
Rate constant	:			
Degradation	:			
Deg. product	:			
Year	:			
GLP	:			
Test substance	:			
Deg. products CAS#	:			
Method	:			
Method detail	:			
Result	:			
Remark	:	Not applicable – metal does not degrade		
Reliability	:			
Reference	:			

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	:	
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	:	

4.1 ACUTE TOXICITY TO FISH

Type	:	Acute
Guideline/method	:	Flow-through, freshwater
Species	:	Rainbow trout (*Onchorhynchus mykiss*)
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 ($CoCl_2 \cdot 2H_20$)
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 mninnow (*Pimephales promelas*), 333 mg Co/L for the carp (*Cyprinus carpio*), and 275 mg Co/L for the mummichog (*Fundulus heteroclitus*) (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	:	*Daphnia magna* (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 ($CoCl_2 \cdot 6H_20$)
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 *Daphnia magna* 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, *Daphnia hyaline*, 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 *Ceriodaphnia dubia* 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. *Daphnia magna* 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	:	*Chlorella vulgaris* (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 *Spirulina platensis* (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 *Lemna minor* (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 *Chlorella vulgaris* 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	:	1st: 2nd: 3rd:
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

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 ($CoCl_2 \cdot 6H_20$)
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/kg 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 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 (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	:	
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% $CoCl_2$ (equivalent to 10.8, 27, or 54.1 mg Co/kg/day), rats exposed to 2.5 or 5% $CoCl_2$ (equivalent to 9.6 or 19.2 mg Co/kg/day), and guinea pigs exposed to 5% $CoCl_2$ (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	:	
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 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.
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 ($CoCl_2 \cdot 6H_20$)
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 *in vitro*
Species	:	*Salmonella typhimurium* 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 ($CoCl_2 \cdot 6H_20$)
Method	:	Ames, B.N., J. McCann, and E. Yamasaki. 1975. Mutat. Res., 31:347-364.
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 *in vitro* bacterial assays (ATSDR Sept 2001 Draft). For example, cobalt chloride was not mutagenic in plate incorporation and fluctuation assays with *Salmonella* TA strains or a *Escherichia coli* 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 *Bacillus subtilis* 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 *in vitro*
Species	:	*Salmonella typhimurium* 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 *Salmonella typhimurium*. Mutat. Res., 172: 97-104.

5.6 GENETIC TOXICITY - CLASTOGENICITY

Type	:	Chromosomal aberrations in bone marrow cells
Guideline/method	:	*In vivo*
Species	:	Mouse (*Mus musculus*)
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 ($CoCl_2 \cdot 6H_20$)
Method	:	Preston, R.J. et al., 1987. Mutat. Res., 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 form 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. Occup. Environ. Med., 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. Biol. Trace Elem. Res., 29:139-145.

Type	:	Micronucleus Test
Guideline/method	:	In vivo
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 ($CoCl_2 \cdot 6H_20$)
Method	:	Von Ledbur, M. and W. Schmid. 1973. Mutat. Res., 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.

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 ($CoCl_2 \cdot 6H_20$)
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 ($P388D_1$ 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.

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 21st 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. Rev. Esp. Fisiol., 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

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 ($CoCl_2 \cdot 6H_20$)
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	:	

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 ($CoCl_2 \cdot 6H_20$)
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

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 ($CoCl_2 \cdot 6H_20$)
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).

APPENDIX D

STEARIC ACID ROBUST SUMMARIES

APPENDIX E

FATTY ACIDS, TALL OIL ROBUST SUMMARIES

IUCLID

Data Set

Existing Chemical	:	ID: 57-11-4
EINECS Name	:	stearic acid
EC No.	:	200-313-4
Molecular Formula	:	C18H36O2

Producer related part

Company	:	Epona Associates, LLC
Creation date	:	04.12.2003

Substance related part

Company	:	Epona Associates, LLC
Creation date	:	04.12.2003
Status	:	
Memo	:	SOCMA MCC
Printing date	:	05.12.2003
Revision date	:	
Date of last update	:	05.12.2003
Number of pages	:	22
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	organic
Physical status	:	solid
Purity	:	-
Colour	:	Colorless, waxy solid
Odour	:	SLIGHT TALLOW-LIKE ODOR
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

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1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

Type of measure :
Legal basis : other: Generally Recognized as Safe

Remark : [Code of Federal Regulations]
[Title 21, Volume 3]
[Revised as of April 1, 2003]
From the U.S. Government Printing Office via GPO Access
[CITE: 21CFR184.1090]

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
PART 184--DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

Subpart B--Listing of Specific Substances Affirmed as GRAS

Sec. 184.1090 Stearic acid.

(a) Stearic acid (C16H36O2, CAS Reg. No. 57-11-4) is a white to yellowish white solid. It occurs naturally as a glyceride in tallow and other animal or vegetable fats and oils and is a principal constituent of most commercially hydrogenated fats. It is produced commercially from hydrolyzed tallow derived from edible sources or from hydrolyzed, completely hydrogenated vegetable oil derived from edible sources.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 313, which is incorporated by reference, and the requirements of Sec. 172.860(b)(2) of this chapter. Copies of the Food Chemicals Codex are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) In accordance with Sec. 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as a flavoring agent and adjuvant as

defined in Sec. 170.3(o)(12) of this chapter.
(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice.
(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

[48 FR 52445, Nov. 18, 1983, as amended at 50 FR 49536, Dec. 3, 1985]

Reliability : (1) valid without restriction
05.12.2003

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= 69 - 70 °C
Sublimation	:	
Method	:	
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.
Flag	:	Critical study for SIDS endpoint

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2.2 BOILING POINT

Value	:	= 383 - °C at 1013 hPa
Decomposition	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.
Flag	:	Critical study for SIDS endpoint

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2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= 1.33 - hPa at 173.7 °C
Decomposition	:	
Method	:	
Year	:	1969
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.
Flag	:	Critical study for SIDS endpoint

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2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 8.42 - at °C
pH value	:	-
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

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2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= .568 - mg/l at 25 °C
pH value	:	-
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: measured
Year	:	1966
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Water solubility = .0001 mg/L at 30 deg C
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

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2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= .5 - day(s)
Degradation	:	- % after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Estimated using AopWin v1.91
Result	:	Atmospheric Oxidation (25 deg C) [AopWin v1.91]: Hydroxyl Radicals Reaction: OVERALL OH Rate Constant = 22.4804 E-12 cm3/molecule-sec Half-Life = 0.476 Days (12-hr day; 1.5E6 OH/cm3) Half-Life = 5.710 Hrs Ozone Reaction: No Ozone Reaction Estimation
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

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Type	:	air
Light source	:	
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 17 - hour(s)
Degradation	:	- % after
Quantum yield	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor phase stearic acid is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with a half-life of about 17 hours.
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

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3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	
Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	other: modeling
Year	:	2003
Method	:	EPI v3.11
Result	:	Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.676	11.4	1000
Water	7.19	360	1000
Soil	28.9	360	1000
Sediment	63.3	1.44e+003	0

Persistence Time: 640 hr

Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

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3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge
Contact time	:	
Degradation	:	= 77 - (±) % after 28 day(s)
Result	:	readily biodegradable
Kinetic of testsubst.	:	10 day(s) = 65 - % 14 day(s) = 69 - % 28 day(s) = 77 - % - % - %
Deg. product	:	
Method	:	other: BOD test
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Results are an average of 11 participating laboratories.

Result	:	65, 69 and 77 % degradation after 10, 14 and 28 days, respectively.
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.
05.12.2003		(7)

Type	:	aerobic
Inoculum	:	activated sludge
Concentration	:	100 g/l related to Test substance related to
Contact time	:	5 day(s)
Degradation	:	- (±) % after
Result	:	readily biodegradable
Deg. product	:	
Method	:	other: BOD5
Year	:	1985
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Rate: .0088 1/HR Half-Life [Days]: 3.3
Source	:	Epona Associates, LLC
Test condition	:	BOD test conducted at 20 deg C.
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.
05.12.2003		(14)

Type	:	aerobic
Inoculum	:	other: sewage sludge
Contact time	:	21 day(s)
Degradation	:	= 95 - (±) % after 21 day(s)
Result	:	readily biodegradable
Deg. product	:	
Method	:	other: Sturm CO2 evolution
Year	:	1984
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.
Flag	:	Critical study for SIDS endpoint
05.12.2003		(13)

Type	:	aerobic
Inoculum	:	activated sludge
Contact time	:	
Degradation	:	- (±) % after
Result	:	readily biodegradable
Deg. product	:	
Method	:	other: Warburg
Year	:	1973
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Rate: .0077; .0052; .00217 Rate Units: 1/HR Half-Life [Days]: 3.75; 5.55; 10.7
Source	:	Epona Associates, LLC

Test condition	:	Test Method: WARBURG Oxygen Condition: AEROBIC Analysis Method: 02 UPTAKE Inoculum: ACTIVATED SLUDGE Temperature [øC]: 20; 25; 30
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

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3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus kisutch (Fish, fresh water, marine)
Exposure period	:	> 96 hour(s)
Unit	:	µg/l
LC50	:	= 12000 - measured/nominal
Method	:	The test result is actually LT50 not LC50
Year	:	1977
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Epona Associates, LLC
Test substance	:	"pure"
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

05.12.2003 (8)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 4600 - mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

05.12.2003 (2)

Type	:	LD100
Value	:	= 14286 - mg/kg bw
Species	:	human
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Minimum/Potential Fatal Human Dose: 1. 1= PRACTICALLY NONTOXIC: PROBABLE ORAL LETHAL DOSE (HUMAN) MORE THAN 1 QT (2.2 LB) FOR 70 KG PERSON (150 LB).
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

05.12.2003 (4)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	24 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	50g/kg/day
Control group	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Rats fed 50 g/kg/day stearic acid for 24 weeks developed reversible lipogranulomas in adipose tissue. No significant pathological lesions were observed in rats fed 3000 ppm stearic acid orally for about 30 weeks, but anorexia, increased mortality, and a greater incidence of pulmonary infection were observed. Stearic acid is one of the least effective fatty acids in producing hyperlipemia, but the most potent in diminishing blood clotting time.
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

05.12.2003 (2)

Type	:	Sub-acute
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	6 or 9 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	5 or 6%
Control group	:	
Result	:	Rats fed 5% stearic acid as part of a high-fat diet for 6 weeks, or 6% stearic acid for 9 weeks, showed a decreased blood clotting time and hyperlipemia.
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

05.12.2003

Type	:	Sub-acute
Species	:	mouse

Sex	:	
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	3 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	5 to 50%
Control group	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	When diets containing 5 to 50% stearic acid (as the monoglyceride) were fed to weanling mice for 3 weeks, depression of weight gain was seen above the 10% dietary level. Mortality occurred only with the 50% diet. The effects were less noticeable in adult mice.
Source	:	Epona Associates, LLC
Reliability	:	(2) valid with restrictions Information taken from a peer-reviewed publication.

05.12.2003 (2)

5.5 GENETIC TOXICITY 'IN VITRO'

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT

Final Submission for Tall Oil Fatty Acids and Related Substances

Pine Chemicals Association
August 2004

VII. Robust Summaries of Data for Tall Oil Fatty Acids and Related Substances

PHYSICO-CHEMICAL PROPERTY – WATER SOLUBILITY	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 105, Water Solubility
Test Type	Water solubility
GLP (Y/N)	Y
Year (Study Performed)	2003
Test conditions	Tall oil fatty acid (TOFA) was tested for water solubility by weighing 0.5 g of the test material into an Erlenmeyer flask and adding 120 to 150 ml of Milli-Q water. Samples were prepared in triplicate. The flasks were then shaken orbitally at 150 r.p.m. at 30 ^{0}C ± 1 ^{0}C for 72 h. A Milli-Q water blank was prepared in the same manner, without test material. At the end of the shaking period, the flasks were transferred to a water bath at 20 ^{0}C ± 1 ^{0}C for 24 h. 100 ml of the clear supernatant/filtrate was then adjusted to pH2 with phosphoric acid and extracted using solid phase extraction cartridges, evaporated to residue, reconstituted in an internal standard solution and derivatized with trimethylphenylammonium hydroxide (TMPAH). The test samples were then assayed by gas chromatography (GC) using flame ionization detection (FID). Myristic acid methyl ester was used as the internal standard.
Results	The water solubility of tall oil fatty acid, in its entirety as a complex mixture, is 12.6 mg/l at 20 ^{0}C.
Data Quality	Reliable without restrictions – Klimisch Code 1a
References	Dinwoodie, N.B. 2003. Determination of the Water Solubility of Tall Oil Fatty Acids and Related Products. Report No. 23304, Inveresk Research, Tranent, Scotland.

PHYSICO-CHEMICAL PROPERTY – WATER SOLUBILITY	
Test Substance	
Chemical Name	Fatty acids, tall oil, low boiling
CAS #	65997-03-7
Remarks	This substance is also referred to as tall oil heads in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 105, Water Solubility
Test Type	Water solubility
GLP (Y/N)	Y

Year (Study Performed)	2003
Test conditions	Fatty acids, tall oil, low boiling was tested for water solubility by weighing 0.5 g of the test material into an Erlenmeyer flask and adding 120 to 150 ml of Milli-Q water. Samples were prepared in triplicate. The flasks were then shaken orbitally at 150 r.p.m. at 30 ^{0}C ± 1 ^{0}C for 72 h. A Milli-Q water blank was prepared in the same manner, without test material. At the end of the shaking period, the flasks were transferred to a water bath at 20 ^{0}C ± 1 ^{0}C for 24 h. 100 ml of the clear supernatant/filtrate was then adjusted to pH2 with phosphoric acid and extracted using solid phase extraction cartridges, evaporated to residue, reconstituted in an internal standard solution and derivatized with trimethylphenylammonium hydroxide (TMPAH). The test samples were then assayed by gas chromatography (GC) using flame ionization detection (FID). Myristic acid methyl ester was used as the internal standard.
Results	The water solubility of fatty acids, tall oil, low boiling, in its entirety as a complex mixture, is 22.8 mg/l at 20 ^{0}C.
Data Quality	Reliable without restrictions – Klimisch Code 1a
References	Dinwoodie, N.B. 2003. Determination of the Water Solubility of Tall Oil Fatty Acids and Related Products. Report No. 23304, Inveresk Research, Tranent, Scotland.

PHYSICO-CHEMICAL PROPERTY – WATER SOLUBILITY	
Test Substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear
CAS #	68955-98-6
Remarks	This substance is also referred to as monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 105, Water Solubility
Test Type	Water solubility
GLP (Y/N)	Y
Year (Study Performed)	2003
Test conditions	Monomer acid was tested for water solubility by weighing 0.5 g of the test material into an Erlenmeyer flask and adding 120 to 150 ml of Milli-Q water. Samples were prepared in triplicate. The flasks were then shaken orbitally at 150 r.p.m. at 30 ^{0}C ± 1 ^{0}C for 72 h. A Milli-Q water blank was prepared in the same manner, without test material. At the end of the shaking period, the flasks were transferred to a water bath at 20 ^{0}C ± 1 ^{0}C for 24 h. 100 ml of the clear supernatant/filtrate was then adjusted to pH2 with phosphoric acid and extracted using solid phase extraction cartridges, evaporated to residue, reconstituted in an internal standard solution and derivatized with trimethylphenylammonium hydroxide (TMPAH). The test samples were then assayed by gas chromatography (GC) using flame ionization detection (FID). Myristic acid methyl ester was used as the internal standard.

Results	The water solubility of monomer acid, in its entirety as a complex mixture, is 15.0 mg/l at 20 ^{0}C.
Data Quality	Reliable without restrictions – Klimisch Code 1a
References	Dinwoodie, N.B. 2003. Determination of the Water Solubility of Tall Oil Fatty Acids and Related Products. Report No. 23304, Inveresk Research, Tranent, Scotland.

PHYSICO-CHEMICAL PROPERTY – WATER SOLUBILITY	
Test Substance	
Chemical Name	Octadecanoic acid, branched and linear
CAS #	68201-37-6
Remarks	This substance is also referred to as hydrogenated monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 105, Water Solubility
Test Type	Water solubility
GLP (Y/N)	Y
Year (Study Performed)	2003
Test conditions	Octadecanoic acid, branched and linear was tested for water solubility by weighing 0.5 g of the test material into an Erlenmeyer flask and adding 120 to 150 ml of Milli-Q water. Samples were prepared in triplicate. The flasks were then shaken orbitally at 150 r.p.m. at 30 ^{0}C ± 1 ^{0}C for 72 h. A Milli-Q water blank was prepared in the same manner, without test material. At the end of the shaking period, the flasks were transferred to a water bath at 20 ^{0}C ± 1 ^{0}C for 24 h. 100 ml of the clear supernatant/filtrate was then adjusted to pH2 with phosphoric acid and extracted using solid phase extraction cartridges, evaporated to residue, reconstituted in an internal standard solution and derivatized with trimethylphenylammonium hydroxide (TMPAH). The test samples were then assayed by gas chromatography (GC) using flame ionization detection (FID). Myristic acid methyl ester was used as the internal standard.
Results	The water solubility of octadecanoic acid, branched and linear, in its entirety as a complex mixture, is 2.5 mg/l at 20 ^{0}C.
Data Quality	Reliable without restrictions – Klimisch Code 1a
References	Dinwoodie, N.B. 2003. Determination of the Water Solubility of Tall Oil Fatty Acids and Related Products. Report No. 23304, Inveresk Research, Tranent, Scotland.

PHYSICO-CHEMICAL PROPERTY – OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 117, *"Partition Coefficient (n-Octanol/Water) High Performance Liquid Chromatograph (HPLC) Method"*

Test Type	Partition coefficient
GLP (Y/N)	Y
Year (Study Performed)	2002
Test conditions	Tall oil fatty acid and reference materials were dissolved in methanol and the solutions were analyzed in duplicate by HPLC with Refractive Index (RI) and Photodiode Array (PDA) detection using a mobile phase of 25:75 (v/v) Milli-Q water/methanol at pH 2. A mixture of seven materials with known log P_{ow} values was used for reference.
Results	At pH 2, tall oil fatty acid had a partition coefficient range of 4.9 to 7.6.
Data Quality	Reliable without restrictions – Klimisch Code 1a
Reference	Lightbody, S.M., Fisher, K. and Dinwoodie, N.B. 2002. Determination of the Partition Coefficient of Fatty Acids and Fatty Acid Salts. Report No. 20976. Inveresk Research, Tranent, Scotland.

PHYSICO-CHEMICAL PROPERTY – OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 117, *"Partition Coefficient (n-Octanol/Water) High Performance Liquid Chromatograph (HPLC) Method"*
Test Type	Partition coefficient
GLP (Y/N)	Y
Year (Study Performed)	1993
Test conditions	Tall oil fatty acid was dissolved in methanol and the solution was analyzed by HPLC with UV detection using a mobile phase of methanol:buffer (3:1) at pH 2 and pH 7.5. A mixture of seven materials with known log P_{ow} values was used for reference.
Results	At pH 2, the log P_{ow} values of seven components in tall oil fatty acid were 4.4, 7.0, 7.3, 7.5, 7.7, 8.0, and 8.3. At pH 7.5, the log K_{ow} values of six components in tall oil fatty acid were 3.6, 3.8, 4.2, 4.5, 4.7, and 7.4.
Data Quality	Reliable without restrictions – Klimisch Code 1a
Reference	Dybdahl, H.P. 1993. Determination of log P_{ow} for single components in tall oil fatty acid. GLP Study No. 408335/472. Water Quality Institute, Horsh□lm, Denmark.

PHYSICO-CHEMICAL PROPERTY – OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Tall oil fatty acids, low boiling
CAS #	65977-03-7
Remarks	This substance is also referred to as tall oil heads in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 117, *"Partition Coefficient (n-Octanol/Water) High Performance Liquid*

	Chromatograph (HPLC) Method"
Test Type	Partition coefficient
GLP (Y/N)	Y
Year (Study Performed)	1993
Test conditions	Tall oil heads was dissolved in methanol and the solution was analyzed by HPLC with UV detection using a mobile phase of methanol:buffer (3:1) at pH 2 and pH 7.5. A mixture of seven materials with known log P_{ow} values was used for reference.
Results	At pH 2, the log P_{ow} values of nine components in tall oil heads were 4.4, 6.7, 6.9, 7.0, 7.2, 7.2, 7.4, 7.7, and 7.8. At pH 7.5, the log P_{ow} values of seven components in tall oil heads were 4.6, 6.5, 6.9, 6.9, 7.3, 7.4, and 8.0.
Data Quality	Reliable without restrictions – Klimisch Code 1a
Reference	Dybdahl, H.P. 1993. Determination of log Pow for single components in tall oil heads. GLP Study No. 408335/474. Water Quality Institute, Horsh□lm, Denmark.

PHYSICO-CHEMICAL PROPERTY – OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear
CAS #	68955-98-6
Remarks	This substance is also referred to as monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to Method A8 of Commission Directive 92/69/EEC
Test Type	Partition coefficient
GLP (Y/N)	N
Year (Study Performed)	1994
Test conditions	Not specified
Results	Fatty acids, C16 - C18 and C18 unsaturated, branched and linear had a partition coefficient of 7.93×10^4 at 25°C, or a Log_{10} P_{ow} of 4.90.
Data Quality	Reliable with restrictions – Klimisch Code 2a
Reference	Mullee, D.M. 1994. Determination of partition coefficient. Project ID No. 508/027. SafePharm Laboratories Ltd., Derby, England.

PHYSICO-CHEMICAL PROPERTY – OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Octadecanoic acid, branched and linear
CAS #	68201-37-6
Remarks	This substance is also referred to as hydrogenated monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 117, *"Partition Coefficient (n-Octanol/Water) High Performance Liquid Chromatograph (HPLC) Method"*
Test Type	Partition coefficient
GLP (Y/N)	Y
Year (Study Performed)	2002
Test conditions	Octadecanoic acid, branched and linear and reference materials

	were dissolved in methanol and the solutions were analyzed in duplicate by HPLC with Refractive Index (RI) and Photodiode Array (PDA) detection using a mobile phase of 25:75 (v/v) Milli-Q water/methanol at pH 2. A mixture of seven materials with known log P_{ow} values was used for reference.
Results	At pH 2, octadecanoic acid, branched and linear had a partition coefficient range of 5.6 to 6.1.
Data Quality	Reliable without restrictions – Klimisch Code 1a
Reference	Lightbody, S.M., Fisher, K. and Dinwoodie, N.B. 2002. Determination of the Partition Coefficient of Fatty Acids and Fatty Acid Salts. Report No. 20976. Inveresk Research, Tranent, Scotland.

PHYSICO-CHEMICAL PROPERTY – OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Fatty acids, tall oil, potassium salts
CAS #	61790-44-1
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 117, *"Partition Coefficient (n-Octanol/Water) High Performance Liquid Chromatograph (HPLC) Method"*
Test Type	Partition coefficient
GLP (Y/N)	Y
Year (Study Performed)	2002
Test conditions	Fatty acids, tall oil, potassium salts and reference materials were dissolved in methanol and the solutions were analyzed in duplicate by HPLC with Refractive Index (RI) and Photodiode Array (PDA) detection using a mobile phase of 25:75 (v/v) Milli-Q water/methanol at pH 2. A mixture of seven materials with known log P_{ow} values was used for reference.
Results	At pH 2, fatty acids, tall oil, potassium salts had a partition coefficient range of 4.9 to 7.6.
Data Quality	Reliable without restrictions – Klimisch Code 1a
Reference	Lightbody, S.M., Fisher, K. and Dinwoodie, N.B. 2002. Determination of the Partition Coefficient of Fatty Acids and Fatty Acid Salts. Report No. 20976. Inveresk Research, Tranent, Scotland.

PHYSICO-CHEMICAL PROPERTY – OCTANOL/WATER PARTITION COEFFICIENT	
Test Substance	
Chemical Name	Fatty acids, tall oil, sodium salts
CAS #	61790-45-2
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 117, *"Partition Coefficient (n-Octanol/Water) High Performance Liquid Chromatograph (HPLC) Method"*
Test Type	Partition coefficient
GLP (Y/N)	Y
Year (Study Performed)	2002
Test conditions	Fatty acids, tall oil, sodium salts and reference materials were dissolved in methanol and the solutions were analyzed in duplicate by HPLC with Refractive Index (RI) and Photodiode Array (PDA) detection using a mobile phase of 25:75 (v/v) Milli-Q water/methanol at pH 2. A mixture of seven materials with known log P_{ow} values was used for reference.

Results	At pH 2, fatty acids, tall oil, sodium salts had a partition coefficient range of 4.9 to 7.6.
Data Quality	Reliable without restrictions – Klimisch Code 1a
Reference	Lightbody, S.M., Fisher, K. and Dinwoodie, N.B. 2002. Determination of the Partition Coefficient of Fatty Acids and Fatty Acid Salts. Report No. 20976. Inveresk Research, Tranent, Scotland.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 301 D, *"Ready Biodegradability: Closed Bottle Test"*
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1993
Contact time	28 days
Inoculum	Secondary effluent from Rungsted Treatment plant
Test conditions	Inoculum: Secondary effluent was collected from Rungsted Treatment plant. Concentration of test chemical: A stock solution of the test material (2 g/L) was prepared in demineralized water by ultra sonication for 5 minutes. Test Setup: Test medium was prepared by adding 1 mL each of four solutions (potassium phosphate, magnesium sulfate, calcium chloride, ferric chloride) to 1 liter of demineralized water, which was aerated to an initial oxygen concentration of 9 mg O_2/L and inoculated with 1 drop of secondary effluent per liter. The test article was added at 2 mg/L to a part of the inoculated test medium, equivalent to a chemical oxygen demand of 5.03 mg O_2/L. Sodium benzoate, the reference compound, was added at 2 mg/L to another part of the inoculated medium (to assess the activity of the inoculum), equivalent to a theoretical oxygen demand of 3.34 mg O_2/L. Both the test and reference articles (2 mg/L) were added to a third part of the inoculated medium (to assess possible inhibitory effects of the test article), at a theoretical oxygen demand of 8.37 mg O_2/L. Blank controls were prepared using the inoculated medium without test or reference materials. After the samples were prepared, the medium was transferred to calibrated respirometric bottles (BOD bottles), and placed in the dark at 20°C. The study was performed in triplicate. Sampling frequency: Samples were collected for BOD analysis on days 0, 7, 14, 21, and 28. Controls: Yes.

	Method of calculating oxygen demand: Oxygen demand was calculated as the difference between the measured oxygen concentrations at time t and the start of the test. Biological oxygen demand was calculated by subtracting the oxygen demand for the blank controls from the oxygen demand in the bottles containing test and reference compounds.
Results Degradation % after time	50% after 7 days and 56% after 28 days (test article); 63% after 7 days and 77% after 28 days (sodium benzoate)
Conclusions	The biological oxygen demand for tall oil fatty acid was 50 and 56% of the theoretical oxygen demand after 7 and 28 days, respectively. The rapid oxygen consumption in the first week and the total oxygen demand at the termination of the experiment indicate that the test material was dominated by readily biodegradable compounds. Tall oil fatty acid did not inhibit the respiratory activity of the inoculum.
Data Quality	Reliable without restrictions– Klimisch Code 1a
Reference	Madsen, T. 1993. Biodegradation of tall oil fatty acid. GLP Study No. 308067/472. Water Quality Institute, Horsh□lm, Denmark.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 301 F, *"Manometric respiratory test for biological degradation"*
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1999
Contact time	28 days
Inoculum	Activated sludge from a municipal sewage treatment plant
Test conditions	Inoculum: Activated sludge from the municipal sewage treatment plant in Reutlingen was washed twice with tap water and centrifuged. Concentration of test chemical: A stock solution of the test material (101.5 mg/L) was prepared. Test Setup: Mineral medium was prepared by adding 10 mL of a potassium phosphate solution and 1 mL each of three other solutions (magnesium sulfate, calcium chloride, ferric chloride) to make a total volume of 1 liter in demineralized water. Six flasks were prepared: two of the test article in mineral medium with inoculum (24 mg/L); two of the mineral medium plus the inoculum (24 mg/L); one of the reference substance [sodium benzoate (98.5 mg/L)] with inoculum (24 mg/L); and one of the test article

	in water with sterilized medium. Sampling frequency: Samples were collected for analysis on days 14 and 28. Controls: Yes. Method of calculating oxygen demand: Biological oxygen demand was calculated by subtracting the oxygen demand for the blank controls from the oxygen demand in the flasks containing test and reference compounds.
Results	
Degradation % after time	84% after 28 days (test article); 97% after 28 days (sodium benzoate)
Conclusions	Eighty-four percent of tall oil fatty acid was biodegraded after 28 days indicating that the organic portion of the test material was readily biodegradable.
Data Quality	Reliable without restrictions– Klimisch Code 1a
Reference	Aniol, S. 1999. Biological degradation (Manometric respirometry test). STZ Project No. 03/99. Steinbeis-Transferzentrum Angewandte und Umwelt-Chemie, Reutungen.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to the CO_2 Evolution Test (Modified Sturm Test), EPA guideline number OPPTS 853.110, *"Ready Biodegradability"*
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	N
Year (Study Performed)	1994
Contact time	29 days
Inoculum	Activated sludge from the Servern Trent water sewage treatment plant
Test conditions	Inoculum: Activated sludge microorganisms were obtained from the Servern Trent water sewage treatment plant at Belper, Derbyshire. A 1% inoculum was prepared. Concentration of test chemical: The test material was used at a concentration of 20 mg/L. Test Setup: Culture medium was prepared by adding 10 mL of a potassium phosphate solution and 1 mL each of three other solutions (magnesium sulfate, calcium chloride, ferric chloride) to a final volume of 1 liter in purified water. Twenty-four hours prior to study initiation, vessels were filled with 2400 mL of culture medium and 30 mL of inoculum and aerated over night. On day

	0 of the study, the test and reference material (sodium benzoate, 10 mg/L) were added and the total volume was increased to 3 liters. The following series of vessels was prepared: culture medium with inoculum; culture medium with inoculum and sodium benzoate; and culture medium with inoculum and test material. The CO_2 absorption bottles were connected to the outlet and were sealed. CO_2-free air was bubbled through the solution and they were stirred continuously. All experiments were performed in the dark at 20 to 22°C. Sampling frequency: Samples (2 mL) were collected from the first CO_2 absorber vessel on days 0, 1, 2, 3, 6, 8, 10, 14, 16, 18, 20, 22, 24, 27, 28, and 29, and from the second absorber on days 0 and 29. Controls: Yes. Analysis: Samples from the CO_2 absorbers were injected into the inorganic carbon channel of the total carbon analyzer for direct analysis of evolved CO_2. The analyses were conducted in triplicate.
Degradation % after time	74% after 28 days (test article); 80% after 28 days (sodium benzoate)
Conclusions	The test article was degraded 74% after 28 days and sodium benzoate was degraded 80% after 28 days. Under the conditions of the OECD guidelines, the test article cannot be considered to be readily biodegradable.
Data Quality	Reliable without restrictions– Klimisch Code 1b
Reference	Sewell, I.G. 1994. Assessment of ready biodegradability using the CO_2 evolution test (modified Sturm test). Project No. 508/28. SafePharm Laboratories Ltd., Derby, England.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acids, low boiling
CAS #	65997-03-2
Remarks	This substance is also referred to as tall oil heads in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD Test Method 301 D, *"Ready Biodegradability: Closed Bottle Test"*
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1993
Contact time	28 days
Inoculum	Secondary effluent from Rungsted Treatment plant
Test conditions	Inoculum: Secondary effluent was collected from Rungsted Treatment plant. Concentration of test chemical: A stock solution of the test material (2 g/L) was prepared in demineralized water by ultra sonication for 5 minutes.

	Test Setup: Test medium was prepared by adding 1 mL each of four solutions (potassium phosphate, magnesium sulfate, calcium chloride, ferric chloride) to 1 liter of demineralized water, which was aerated to an initial oxygen concentration of 9 mg O_2/L and inoculated with 1 drop of secondary effluent per liter. The test article was added at 2.4 mg/L to a part of the inoculated test medium, equivalent to a chemical oxygen demand of 4.94 mg O_2/L. Sodium benzoate, the reference compound, was added at 2 mg/L to another part of the inoculated medium (to assess the activity of the inoculum), equivalent to a theoretical oxygen demand of 3.34 mg O_2/L. Both the test and reference articles were added to a third part of the inoculated medium (to assess possible inhibitory effects of the test article), at a theoretical oxygen demand of 8.28 mg O_2/L. Blank controls were prepared using the inoculated medium without test or reference materials. After the samples were prepared, the medium was transferred to calibrated respirometric bottles (BOD bottles), and placed in the dark at 20°C. The study was performed in triplicate. Sampling frequency: Samples were collected for BOD analysis on days 0, 7, 14, 21, and 28. Controls: Yes. Method of calculating oxygen demand: Oxygen demand was calculated as the difference between the measured oxygen concentrations at time t and the start of the test. Biological oxygen demand was calculated by subtracting the oxygen demand for the blank controls from the oxygen demand in the bottles containing test and reference compounds.
Results Degradation % over time	33% after 7 days and 41% after 28 days (test article); 63% after 7 days and 77% after 28 days (sodium benzoate)
Conclusions	The biological oxygen demand for tall oil heads was 33 and 41% of the theoretical oxygen demand after 7 and 28 days, respectively. These results indicate that the test material contains readily biodegradable and recalcitrant compounds. Tall oil heads did not inhibit the respiratory activity of the inoculum.
Data Quality	Reliable without restrictions– Klimisch Code 1a
Reference	Madsen, T. 1993. Biodegradation of tall oil heads. GLP Study No. 308067/474. Water Quality Institute, Horsh□lm, Denmark.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Fatty acids, C16 - C18 and C18 unsaturated, branched and linear
CAS #	68955-98-6
Remarks	This substance is also referred to as monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	

Method/Guideline followed	Testing was conducted according to the CO_2 Evolution Test (Modified Sturm Test), EPA guideline number OPPTS 853.110, *"Ready Biodegradability"*
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	N
Year (Study Performed)	1994
Contact time	29 days
Inoculum	Activated sludge from the Severn Trent water sewage treatment plant
Test conditions	Inoculum: Activated sludge microorganisms were obtained from the Severn Trent water sewage treatment plant at Belper, Derbyshire. A 1% inoculum was prepared. Concentration of test chemical: The test material was used at a concentration of 20 mg/L. Test Setup: Culture medium was prepared by adding 10 mL of a potassium phosphate solution and 1 mL each of three other solutions (magnesium sulfate, calcium chloride, ferric chloride) to a final volume of 1 liter in purified water. Twenty-four hours prior to study initiation, vessels were filled with 2400 mL of culture medium and 30 mL of inoculum and aerated over night. On day 0 of the study, the test and reference material (sodium benzoate, 10 mg/L) were added and the total volume was increased to 3 liters. The following series of vessels was prepared: culture medium with inoculum; culture medium with inoculum and sodium benzoate; and culture medium with inoculum and test material. The CO_2 absorption bottles were connected to the outlet and were sealed. CO_2-free air was bubbled through the solution and they were stirred continuously. All experiments were performed in the dark at 21 to 22°C. Sampling frequency: Samples (2 mL) were collected from the first CO_2 absorber vessel on days 0, 1, 2, 3, 6, 8, 10, 12, 14, 16, 20, 22, 24, 27, 28, and 29, and from the second absorber on days 0 and 29. Controls: Yes. Analysis: Samples from the CO_2 absorbers were injected into the inorganic carbon channel of the total carbon analyzer for direct analysis of evolved CO_2. The analyses were conducted in triplicate.
Results Degradation % after time	67% after 28 days (test article); 87% after 28 days (sodium benzoate)
Conclusions	The test article was degraded 67% after 28 days. Under the conditions of the OECD guidelines, it cannot be considered to be readily biodegradable.
Data Quality	Reliable without restrictions– Klimisch Code 1b
Reference	Sewell, I.G. 1994. Assessment of ready biodegradability using the CO2 evolution test (modified Sturm test). Project No. 508/23. SafePharm Laboratories Ltd., Derby, England.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Octadecanoic acid, branched and linear
CAS #	68201-37-6
Remarks	This substance is also referred to as hydrogenated monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Testing was conducted according to OECD (1992) 301B Modified Sturm Test
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	2002
Contact time	28 days
Inoculum	Activated sludge from the Haddington Municipal Sewage Treatment Works
Test conditions	Inoculum: Activated sludge microorganisms were obtained from the Haddington Municipal Sewage Treatment Works. The solids content of the sludge was 3.2 g/l. Concentration of test chemical: The test material was used at a concentration of 20 mg DOC/L. Based on the percentage carbon content, a target weight of 53.6 mg of test material was weighed for direct addition to each appropriate bioreactor. Test Setup: Each test item bioreactor contained 1980 ml of mineral media, 20 ml of microbial inoculum and 54 mg of test item. The reference bioreactor contained 1911 ml of mineral media, 20 ml of microbial inoculum and 69 ml of reference material (sodium benzoate) stock. The control bioreactors each contained 1980 ml of mineral media and 20 ml of microbial inoculum. The toxicity control bioreactor contained 1911 ml of mineral media, 20 ml of microbial inoculum, 53.9 mg of test item and 69 ml reference material stock. Each bioreactor was connected to three traps, each trap containing 100 ml of 0.0125 M $Ba(OH)_2$. At trap collection, the trap closes to the bioreactor was taken for titration, the two remaining traps were moved closer to the bioreactor and a fresh trap was placed third in line from the bioreactor. Trap changes were conducted on days 1, 4, 6, 8, 11, 15, 18, 21, 26, and 29. Each sampled trap was titrated with a few drops of phenolphthalein indicator against 0.05M HCl. The pH was determined in each bioreactor on days 0, 28 and 29; if necessary, the pH on day 0 was adjusted to 7.2-7.8. Calculation of Results: The weight of CO_2 evolved was calculated from the titre. The actual titre for each batch of $Ba(OH)_2$ was used as the background titre. The mean titre for the test, reference and control vessels was calculated according to the following equation: Weight CO_2 produced (mg) = 1.1 x (background titre – ml HCl

	titrated) The net CO_2 production was then calculated by subtracting the control mean CO_2 production from the test and reference material mean CO_2 production values. The percentage biodegradation was calculated by comparing actual CO_2 evolved in test and reference vessels with the theoretical CO_2 evolution. For the test item this was calculated using the DOC addition rate: $\% \text{ degradation} = \frac{\text{Mg } CO_2 \text{ produced}}{\text{mg DOC added} \times 3.67^{*}} \times 100$ * = where 3.67 is the conversion factor (44/12) for carbon to CO_2
Results Degradation % after time	46.72% after 28 days (test article); 68.39% after 28 days (sodium benzoate)
Conclusions	The test article was degraded 47% after 28 days. Under the conditions of the OECD guidelines, it cannot be considered to be readily biodegradable.
Data Quality	Reliable without restrictions– Klimisch Code 1a
Reference	Kelly, C.R. 2002. Octadecanoic acid, branched and linear, CAS No. 68201-37-6 Determination of Ready Biodegradability by the Modified Sturm Test. Report No. 21136. Inveresk Research, Tranet, Scotland.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Fatty acids, tall oil, sodium salt
CAS #	61790-45-2
Method	
Method/Guideline followed	Testing was conducted according to OECD (1992) 302B Modified Zahn-Wellens Test
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	2002
Contact time	28 days
Inoculum	Activated sludge from the Haddington Municipal Sewage Treatment Works
Test conditions	Inoculum: Activated sludge microorganisms were obtained from the Haddington Municipal Sewage Treatment Works. The solids content of the sludge was 4.0 g/l. Concentration of test chemical: The test material was used at a concentration of 200 mg DOC/L equivalent to 4480 mg of fatty acid, tall oil, sodium salt per 2.5 liter bioreactor based on percentabe carbon content. To prepare the reference material (aniline) 8.09 ml was added to 1000 ml DI water and sonicated for *ca* 30 min. to aid dissolution; from this stock 125 ml aliquots were added to each appropriate bioreactor.

	Test Setup: The activated sludge was introduced to the test system at a ratio of 2.5:1 sludge solids/l to test item DOC/l which required the addition of 250 ml of 4 g/l sludge to each bioreactor. A total of six bioreactors were used. Each bioreactor had a final volume of 2000 ml; the control bioreactors each contained 250 ml sludge and 1750 ml of mineral medium; the reference bioreactor contained 250 ml sludge, 125 ml of aniline stock solution and 1625 of mineral medium; the test item bioreactors each contained 250 ml sludge, the appropriate weight of test item and 1750 ml of mineral medium; the toxicity control bioreactor contained 250 ml sludge, the appropriate weight of test item, 125 ml aniline stock and 1625 ml mineral medium. The test was conducted over 28 days. DOC measurements were conducted on duplicate samples 3 h after test initiation, and on Days 14 and 28. Sampling Procedure: Prior to each sampling point the liquid in each vessel was replenished to its starting level. The pH and dissolved oxygen concentration were recorded. If necessary the pH was adjusted to 6.5-8.0 using H_2SO_4 as appropriate. A *ca* 25 ml sample was extracted from each vessel using a syringe and allowed to settle after which it was passed through a 0.45um filter for DOC analysis. Determination of DOC, total organic carbon (TOC), total carbon (TC) and inorganic carbon (IC) were determined. Calculation of Results: All measurements were conducted on duplicate samples. Dissolved organic carbon (DOC) values were calculated as follows: $DOC = TC - IC$ The percentage degradation (Dt) at each timepoint was calculated using mean DOC measurements from the duplicate samples, using the following equation: $Dt = \left(1 - \frac{Ct - Cb}{Ca - Cba}\right) \times 100$ Where: Ct = mean DOC concentration in test/reference at time t Cb = mean DOC concentration in controls at time t Ca = mean DOC concentration in test/reference at 3 h ± 0.5 h Cba = mean DOC concentration in controls at 3 h ± 0.5 h
Results Degradation % after time	The test item reached 73.8 % degradation by Day 14 and 98.4 % by Day 28; the material reached 97% degradation by Day 14.
Conclusions	The test article was degraded 98% after 28 days under the conditions of the test.
Data Quality	Reliable without restrictions– Klimisch Code 1a
Reference	Kelly, C.R. 2002. Fatty acid, tall oil, sodium salt, CAS No. 61790-45-2 Determination of Inherent Biodegradability by the

	Modified Zahn-Wellens Test. Report No. 21485. Inveresk Research, Tranet, Scotland.

ENVIRONMENTAL FATE – BIODEGRADATION	
Test Substance	
Chemical Name	Tall oil fatty acids, potassium salt
CAS #	61790-44-1
Method	
Method/Guideline followed	Testing was conducted according to a modified OECD test for ready biodegradability, EPA guideline number OPPTS 853.110, *"Ready Biodegradability"*
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (Study Performed)	1991
Contact time	28 days
Inoculum	Activated sludge from Bergen County sewage treatment plant
Test conditions	Inoculum: Activated sludge from Bergen County sewage treatment plant was mixed with soil extract and surface water to prepare the inoculum. Concentration of test chemical: The test article was tested at a concentration of 20 to 25 ppm. Test Setup: OECD test medium was used. Aniline was the reference material and was tested at a concentration of 20 to 25 ppm. The experiments were performed in the dark at 20 to 25°C. Sampling frequency: Samples were collected for analysis on days 0, 7, 14, 21, and 28. Controls: Yes. Method of calculating degradation: The mean initial concentration of soluble organic carbon (SOC) in the controls is subtracted from the initial concentration in the test sample. From this is subtracted, the mean initial concentration of SOC in the test and control samples at time t. This value is divided by the mean initial concentration of SOC in the controls subtracted from the initial concentration in the test sample.
Results	
Degradation % after time	79% after 28 days (test article); 97% after 28 days (aniline)
Conclusions	The test material degraded 79% and is considered to be readily biodegradable as defined by OECD.
Data Quality	Reliable without restrictions– Klimisch Code 1b
Reference	Drozdowki, D. 1991. Modified OECD test for ready biodegradability of [product name deleted] tall oil fatty acid potassium salt. Report No. 063383-1. United States Testing Company, Inc., Hoboken, New Jersey.

ECOTOXICITY – ACUTE TOXICITY TO FISH	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 203, *"Testing of Chemicals, Fish Acute Toxicity Test"* and following procedures in OECD (2000) Guidance Document No. 23 on Testing Difficult Substances.
Year	2002
GLP (Y/N)	Y
System of testing	Fathead minnows (*Pimephales promelas)* under static conditions.
Concentration	0, 1, 10, 100 and 1000 mg/l
Results	The 96 hr LL_{50} was > 1000 mg/l the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 1000 mg/l.
Detailed Summary	Tall oil fatty acid (TOFA) was tested in fathead minnows under static conditions to determine the acute toxicity. Water accommodated fractions (WAF) were prepared using the same conditions as those used to determine the water solubility of this substance. Appropriate weights of TOFA were added to a stirring medium in glass vessels which were sealed to avoid loss of volatile fractions. Using magnetic stirrers, the stirring speed was adjusted to give a stirring vortex 5-10% of the water column. After a stirring period of approximately 48 hr. the test solutions were allowed to settle for ca hour. The WAF was then removed via a glass siphon taking care not to remove undissolved material at the top of bottom of the water column. The test organisms were exposed to this WAF. This procedure was adopted to maximize the solubility of the test item under specific test exposure conditions, but to reduce exposure to the test organisms to insoluble fractions. A control medium without the addition of the test item was stirred and extracted in an identical ways as the treated media. The effects of both filtering and adjusting pH were investigated in a range finding test using the highest loading rate (i.e., 1000 mg/l). Because no mortality or other effects were observed in the range finding tests, a definitive-limit test was conducted at the maximum loading rate of 1000 mg/l. The 96 hr LL_{50} was > 1000 mg/l, the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 1000 mg/l.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Kelly, C. 2002. Fatty acids, tall oil, CAS No. 61790-12-3 Determination of Acute Toxicity (LL_{50}) to Fathead Minnows (96 h, Static). Report No. 20621. Inveresk Research, Tranent, Scotland.

ECOTOXICITY – ACUTE TOXICITY TO FISH	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear
CAS #	68955-98-6
Remarks	This substance is also referred to as monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.

Method	
Method/Guideline followed	OECD Test Method 203, *"Testing of Chemicals, Fish Acute Toxicity Test."*
Year	1994
GLP (Y/N)	Y
System of testing	Golden orfe (*Leuciscus idus.*) under static conditions.
Concentration	1000 mg/l
Results	The 96 hr LL_{50} was > 1000 mg/l the highest loading rate tested. The No Observed Effect Concentration Loading Rate ($NOEC_r$) was 1000 mg/l.
Detailed Summary	Fatty acid, C16 and C18 and C18 unsaturated, branched and linear was tested in golden orfe under static conditions to determine the acute toxicity. A range finding test was conducted during which no mortality was observed at a concentration of 1000 mg/l. For the definitive test, water accommodated fractions (WAF) were prepared by placing 1000 mg/l of test material on the surface of dechlorinated tap water. This was stirred using a magnetic stirrer for 24 hr prior to the test with care taken to avoid the formation of a vortex during mixing. After 24 hr. the mixture was allowed to stand for 1 hr. prior to removing the aqueous phase (i.e., WAF) by a siphon to glass exposure vessels for testing. The test organisms were exposed to this WAF. Because no mortality or other effects were observed in the range finding tests, a definitive-limit test was conducted at the maximum loading rate of 1000 mg/l. There were no mortalities or other adverse reactions in 20 fish exposed to a 1000 mg/l WAF loading rate for a period of 96 hr. The 96 hr LL_{50} was > 1000 mg/l, the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 1000 mg/l.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Sewell, I.G. 1994. [Fatty acid, C16 and C18 and C18 unsaturated, branched and linear] Acute Toxicity to Golden Orfe. SafePharm Laboratories Ltd. Durham, England.

ECOTOXICITY – ACUTE TOXICITY TO FISH	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear, calcium salt
CAS #	Not assigned
Remarks	This substance is also referred to as monomer acid calcium salt in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 203, *"Testing of Chemicals, Fish Acute Toxicity Test."*
Year	2002
GLP (Y/N)	Y
System of testing	Rainbow trout (*Oncorhynchus mykiss.*) under static conditions.
Concentration	100 mg/l
Results	The 96 hr LL_{50} was > 100 mg/l the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 100 mg/l.
Detailed Summary	Monomer acid, calcium salt was tested in rainbow trout under

	static conditions to determine the acute toxicity. A range finding test was conducted during which no mortality was observed at a concentration of 100 mg/l. It was considered unnecessary and unrealistic to test at loading rates in excess of 100 mg/l. For the definitive test, water accommodated fractions (WAF) were prepared by placing 2100 mg of test material on the surface of 21L of dechlorinated tap water to yield the 100 mg/l loading rate. This was stirred using a magnetic stirrer for 23 hr prior to the test with care taken to ensure that the vortex formed was only a dimple on the water surface. After 23 hr. the mixture was allowed to stand for 1 hr. prior to removing the aqueous phase (i.e., WAF) by a siphon to glass exposure vessels for testing. Microscopic inspection of the WAF showed no micro-dispersions or undissolved test material. The test organisms were exposed to this WAF. Because no mortality or other effects were observed in the range finding tests, a definitive-limit test was conducted at the maximum loading rate of 100 mg/l. There were no mortalities or other adverse reactions in 20 fish exposed to a 100 mg/l WAF loading rate for a period of 96 hr. The 96 hr LL_{50} was > 100 mg/l, the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 100 mg/l.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Shacklady, L.G. and Mullee, D.M. 2002. [Monomer acid, calcium salt] Acute Toxicity to Rainbow Trout (*Oncorhynchus* mykiss). SPL Proj. No. 1078/087. SafePharm Laboratories Ltd. Durham, U.K.

ECOTOXICITY – ACUTE TOXICITY TO DAPHNIA	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 202, Part 1 *"Testing of Chemicals, Daphnia sp. Acute Immobilization Test"* and following procedures in OECD (2000) Guidance Document No. 23 on Testing Difficult Substances.
Year	2002
GLP (Y/N)	Y
System of testing	*Daphnia magna* (water fleas) under static conditions.
Concentration	0, 1, 10, 100 and 1000 mg/l
Results	The 48 hr EL_{50} was > 1000 mg/l the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 1000 mg/l.
Detailed Summary	Tall oil fatty acid (TOFA) was tested in daphnia under static conditions to determine the acute toxicity. Water accommodated fractions (WAF) were prepared using the same conditions as those used to determine the water solubility of this substance. Appropriate weights of TOFA were added to a stirring medium in glass vessels which were sealed to avoid loss of volatile fractions. Using magnetic stirrers, the stirring speed was adjusted to give a stirring vortex 5-10% of the water column. After a stirring period of approximately 48 hr. the test solutions

	were allowed to settle for ca hour. The WAF was then removed via a glass siphon taking care not to remove undissolved material at the top of bottom of the water column. The test organisms were exposed to this WAF. This procedure was adopted to maximize the solubility of the test item under specific test exposure conditions, but to reduce exposure to the test organisms to insoluble fractions. A control medium without the addition of the test item was stirred and extracted in an identical ways as the treated media. The effects of both filtering and adjusting pH were investigated in a range finding test. Because no mortality or other effects were observed in the range finding tests, a definitive-limit test was conducted at the maximum loading rate of 1000 mg/l. The 48 hr EL_{50} was > 1000 mg/l, the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 1000 mg/l.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Kelly, C. 2002. Fatty acids, tall oil, CAS No. 61790-12-3 Determination of Acute Toxicity (EL_{50}) to Daphnia (48 h, Static). Report No. 20468. Inveresk Research, Tranent, Scotland.

ECOTOXICITY – ACUTE TOXICITY TO DAPHNIA	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear
CAS #	68955-98-6
Remarks	This substance is also referred to as monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 202, Part 1 *"Testing of Chemicals, Daphnia sp. Acute Immobilization Test"*
Year	1994
GLP (Y/N)	Y
System of testing	Daphnia (*Daphnia magna.)* under static conditions.
Concentration	1000 mg/l
Results	The 48 hr Effective Loading Rate (ELR_{50}) was > 1000 mg/l the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) at both 24 and 48 hr. was 1000 mg/l.
Detailed Summary	Fatty acid, C16 and C18 was tested in daphnia under static conditions to determine the acute toxicity. A range finding test was conducted during which no mortality was observed at a concentration (i.e., loading rate) of 1000 mg/l. For the definitive test, water accommodated fractions (WAF) were prepared by placing 1000 mg/l of test material on the surface of appropriate daphnia media. This was stirred using a magnetic stirrer for 24 hr prior to the test with care taken to avoid the formation of a vortex during mixing. After 24 hr. the mixture was allowed to stand for 1 hr. prior to removing the aqueous phase (i.e., WAF) by a siphon to glass exposure vessels for testing. The test organisms were exposed to this WAF. Because no mortality or other effects were observed in the range finding tests, a definitive-limit test was conducted at the maximum loading rate of 1000 mg/l. There were no immobilized daphnia or other adverse reactions in 40 daphnids exposed to a 1000 mg/l WAF loading rate for a period of 48 hr. The 48 hr Effective Loading Rate (ELR_{50}) was > 1000

	mg/l the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) at both 24 and 48 hr. was 1000 mg/l.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Sewell, I.G. 1994. [Fatty acid, C16 and C18] Acute Toxicity to Daphnia Magna. SafePharm Laboratories Ltd. Durham, England.

ECOTOXICITY – ACUTE TOXICITY TO DAPHNIA	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear, calcium salt
CAS #	Not assigned
Remarks	This substance is also referred to as monomer acid calcium salt in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 202, Part 1 *"Testing of Chemicals, Daphnia sp. Acute Immobilization Test"*
Year	2002
GLP (Y/N)	Y
System of testing	Daphnia (*Daphnia* magna) under static conditions.
Concentration	100 mg/l
Results	The 48 hr EL_{50} was > 100 mg/l the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 100 mg/l.
Detailed Summary	Monomer acid, calcium salt was tested in daphnia under static conditions to determine the acute toxicity. A range finding test was conducted during which no mortality was observed at a concentration of 100 mg/l. It was considered unnecessary and unrealistic to test at loading rates in excess of 100 mg/l. For the definitive test, water accommodated fractions (WAF) were prepared by placing 1000 mg of test material on the surface of 10L of daphnia media to yield the 100 mg/l loading rate. This was stirred using a magnetic stirrer for 23 hr prior to the test with care taken to ensure that the vortex formed was only a dimple on the water surface. After 23 hr. the mixture was allowed to stand for 1 hr. prior to removing the aqueous phase (i.e., WAF) by a siphon to glass exposure vessels for testing. Microscopic inspection of the WAF showed no micro-dispersions or undissolved test material. The test organisms were exposed to this WAF. Because no mortality or other effects were observed in the range finding tests, a definitive-limit test was conducted at the maximum loading rate of 100 mg/l. There were no mortalities or other adverse reactions in 40 daphnia exposed to a 100 mg/l WAF loading rate for a period of 48 hr. The 48 hr EL_{50} was > 100 mg/l, the highest loading rate tested. The No Observed Effect Loading Rate ($NOEL_r$) was 100 mg/l.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Shacklady, L.G. and Mullee, D.M. 2002. [Monomer acid, calcium salt] Acute Toxicity to *Daphnia Magna* SPL Proj. No. 1078/088. SafePharm Laboratories Ltd. Durham, U.K.

ECOTOXICITY – ALGA, GROWTH INHIBITION	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 201, *"Testing of Chemicals, Alga, Growrh Inhibition Test"* and following procedures in OECD (2000) Guidance Document No. 23 on Testing Difficult Substances.
Year	2002
GLP (Y/N)	Y
System of testing	Green alga (*Selenastrum capriconutum)* growth inhibition.
Concentration	0, 125, 250, 500 and 1000 mg/l
Results	The 72 hr EL_{50} for area under growth curve (AUC) was 854.90 mg/l with a corresponding No Observed Effect Loading Rate ($NOEL_r$) of 500 mg/l. The 72 hr. EL_{50} based on Average Specific Growth Rate was > 1000 mg/l with a corresponding $NOEL_r$ of 500 mg/l. at 0-48 hr and 750 mg/l at 0-72 hr. indicating some inhibition (<50%) compared to the control.
Detailed Summary	Tall oil fatty acid (TOFA) was tested in alga to determine the median effective loading (EL_{50}) for growth inhibition. Water accommodated fractions (WAF) were prepared using the same conditions as those used to determine the water solubility of this substance. Appropriate weights of TOFA were added to a stirring medium in glass vessels which were sealed to avoid loss of volatile fractions. Using magnetic stirrers, the stirring speed was adjusted to give a stirring vortex 5-10% of the water column. After a stirring period of approximately 48 hr. the test solutions were allowed to settle for ca hour. The WAF was then removed via a glass siphon taking care not to remove undissolved material at the top of bottom of the water column. The test organisms were exposed to this WAF. This procedure was adopted to maximize the solubility of the test item under specific test exposure conditions, but to reduce exposure to the test organisms to insoluble fractions. A control medium without the addition of the test item was stirred and extracted in an identical ways as the treated media. The effects of both filtering and adjusting pH were investigated in a range finding test at the highest loading rate. In the range finding test there was a 29% inhibitioin of growth at 1000 mg/l; after 72 hr. exposure cell numbers in all test solutions < 100 mg/l were higher than the standard controls. Based on the results of the range-finding test a definitive test was conducted at loading rates of 0, 125, 250, 500, 750 and 1000 mg/l. This test was conducted using an unfiltered WAF with no pH adjustment. The 72 hr EL_{50} for area under growth curve (AUC) was 854.90 mg/l with a corresponding No Observed Effect Loading Rate ($NOEL_r$) of 500 mg/l. The 72 hr. EL_{50} based on Average Specific Growth Rate was > 1000 mg/l with a corresponding $NOEL_r$ of 500 mg/l. at 0-48 hr and 750 mg/l at 0-72 hr. indicating some inhibition (<50%) compared to the control.

Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Kelly, C. 2002. Fatty acids, tall oil, CAS No. 61790-12-3 Alga, Growth Inhibition Test (72 h, EL_{50}). Report No. 20706. Inveresk Research, Tranent, Scotland.

ECOTOXICITY – ALGA, GROWTH INHIBITION	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear
CAS #	68955-98-6
Remarks	This substance is also referred to as monomer acid in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 201, *"Testing of Chemicals, Alga, Growrh Inhibition Test"*
Year	1994
GLP (Y/N)	Y
System of testing	Alga (*Scenedesmus subspicatus)* under static conditions.
Concentration	1000 mg/l
Results	The 72 hr Effective Loading Rate that reduced biomass by 50% (E_bLR_{50}) was > 1000 mg/l WAF loading rate and the 24 hr Effective Loading Rate that reduced specific growth rate by 50% (E_rLR_{50}) was > 1000 mg/l WAF loading rate.
Detailed Summary	Fatty acid, C16 and C18 was tested in alga under static conditions to determine the extent of growth inhibition. A water accommodated fraction (WAF) was prepared by placing 2000 mg/l of test material on the surface of alga culture medium. This was stirred using a magnetic stirrer for 24 hr prior to the test with care taken to avoid the formation of a vortex during mixing. After 24 hr. the mixture was allowed to stand for 1 hr. prior to removing the aqueous phase (i.e., WAF) for testing. This 2000 mg/l WAF loading rate was diluted 50:50 with algal suspension to give a 1000 mg/l WAF loading rate. The test organisms were exposed to this WAF; six replicates were used. Samples were taken at 0, 24, 48 and 72 hrs. Cell densities of control and test cultures at 0 and 72 hrs. were determined by direct counting with a haemocytometer. Neither the growth nor the biomass of alga were affected by the presence of the test compound over the 72 hr. exposure period. The 72 hr Effective Loading Rate that reduced biomass by 50% (E_bLR_{50}) was > 1000 mg/l WAF loading rate and the 24 hr Effective Loading Rate that reduced specific growth rate by 50% (E_rLR_{50}) was > 1000 mg/l WAF loading rate.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Sewell, I.G. 1994. Assessment of the Algistatic Effect of [Fatty acid, C16 and C18]. SafePharm Laboratories Ltd. Durham, England.

ACUTE TOXICITY – ORAL	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data

	Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was consistent with OECD Test Method 401, *"Acute Oral Toxicity"*
GLP (Y/N)	Y
Year (Study Performed)	1983
Species	Rat
Strain	Sprague-Dawley
Route of administration	Oral
Dose levels	10,000 mg/kg
Sex and number/group	5 male and 5 female rats
Frequency of treatment	Single oral gavage
Duration of test	14 day observation post-treatment
Control group (Y/N)	N
Result	
Acute Oral LD_{50}	>10,000 mg/kg
Detailed Summary	Sprague-Dawley rats (n = 5/sex) received a single oral (gavage) dose of 10,000 mg/kg of fatty acid, tall oil (CAS #61790-12-3) and were observed for 14 days. Parameters evaluated included clinical signs, mortality, body weight, and gross pathology. None of the animals died. One hour post-dosing, piloerection was observed in one male and abnormal stance was observed in one male and one female. By four hours, these effects had resolved. No body weight effects were observed. Gross necropsy revealed no treatment-related effects. The acute oral LD_{50} was greater than 10,000 mg/kg.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Mallory, V.T. 1983. Acute oral toxicity study in rats: fatty acid [product name deleted]. Study No. PH 402-AC-009-83. Pharmakon Research International, Inc., Waverly, Pennsylvania.

ACUTE TOXICITY – ORAL	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear, sodium salt
CAS #	Not assigned
Remarks	This non-HPV substance is also referred to as monomer acid sodium salt in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was OECD Test Method 423, *"Acute Oral Toxicity- Acute Toxic Class Method"*
GLP (Y/N)	Y
Year (Study Performed)	2002
Species	Rat
Strain	Sprague-Dawley
Route of administration	Oral
Dose levels	2000 mg/kg
Sex and number/group	3 male and 3 female rats
Frequency of treatment	Single oral gavage
Duration of test	14 day observation post-treatment
Control group (Y/N)	N

Result	
Acute Oral LD_{50}	>2500 mg/kg
Detailed Summary	Sprague-Dawley rats (n = 3/sex) received a single oral (gavage) dose of 2000 mg/kg of monomer acid, sodium salt and were observed for 14 days. Parameters evaluated included clinical signs, mortality, body weight, and gross pathology. None of the animals died. No body weight effects were observed. Gross necropsy revealed no treatment-related effects. The acute oral LD_{50} was estimated as being greater than 2500 mg/kg.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Sanders, A. 2002. Acute oral toxicity study in the rat – Acute Toxic Class Method. Project No. 1078/031. SafePharm Laboratories, Derby, UK.

ACUTE TOXICITY – ORAL	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear, calcium salt
CAS #	Not assigned
Remarks	This non-HPV substance is also referred to as monomer acid calcium salt in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was OECD Test Method 423, *"Acute Oral Toxicity- Acute Toxic Class Method"*
GLP (Y/N)	Y
Year (Study Performed)	2002
Species	Rat
Strain	Sprague-Dawley
Route of administration	Oral
Dose levels	2000 mg/kg
Sex and number/group	3 male and 3 female rats
Frequency of treatment	Single oral gavage
Duration of test	14 day observation post-treatment
Control group (Y/N)	N
Result	
Acute Oral LD_{50}	>2500 mg/kg
Detailed Summary	Sprague-Dawley rats (n = 3/sex) received a single oral (gavage) dose of 2000 mg/kg of monomer acid, calcium salt and were observed for 14 days. Parameters evaluated included clinical signs, mortality, body weight, and gross pathology. None of the animals died. No body weight effects were observed. Gross necropsy revealed no treatment-related effects. The acute oral LD_{50} was estimated as being greater than 2500 mg/kg.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Sanders, A. 2002. Acute oral toxicity study in the rat – Acute Toxic Class Method. Project No. 1078/031. SafePharm Laboratories, Derby, UK.

REPEAT DOSE TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was similar to OECD Test Method 407, *"Repeat Dose 28-Day Oral Toxicity Study in Rodents,"* but failed to collect data on several parameters (hematology, clinical chemistry, histopathology) and was only conducted in male animals.
Year	1969
GLP (Y/N)	N (pre-GLP)
Species	Rat
Strain	Sprague-Dawley
Sex	Male
Route of Administration	Oral, diet
Exposure Period	28 days
Frequency of Treatment	Daily
Post-exposure observation period	None
Dose Levels	0, 15, 30, and 60% of total calories
Control group (Y/N)	Y
Results	
NOAEL:	15%
Detailed Summary	Male Sprague-Dawley rats (n = 10/group) were fed diets containing tall oil acid distillate (CAS #61790-12-3) as 0, 15, 30 or 60% of the total calories for four weeks. Parameters evaluated included mortality, body weight, and food consumption. One animal treated with 15% died (day of death not specified) and all animals treated with 60% died within four days of dose initiation. It is unlikely that this single death was a treatment related effect since similar mortality did not occur at 30%. No effect on growth rate was reported at 15%, but a significant decrease in growth was reported at 30%.
Data Quality	Not assignable – Klimisch Code 4b
Reference	Seppanen 1969 as cited in: Anon. 1989. Final report on the safety assessment of tall oil acid. J. Amer. Coll. Toxicol. 8:769-776.

REPEAT DOSE TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure is consistent with OECD Test Method 407, *"Repeat Dose 28-Day Oral Toxicity Study in Rodents"*
Year	1969
GLP (Y/N)	N (pre-GLP)
Species	Rat

Strain	Charles River
Sex	Male, female
Route of Administration	Oral, diet
Exposure Period	90 days
Frequency of Treatment	Daily
Post-exposure observation period	None
Dose Levels	5, 10, and 25% (approximately equivalent to 2500, 5000, and 12,500 mg/kg/day)
Control group (Y/N)	Y
Results	
NOEL:	5%, approximately 2500 mg/kg/day
Detailed Summary	Tall oil fatty acid was administered to Charles River rats (n = 10/sex/group) in the diet at concentrations 0, 5, 10, or 25% for 90 days. The approximate doses were 0, 2,500, 5,000, or 12,500 mg/kg/day, based on standard conversion factors provided by WHO (1990). Parameters evaluated included clinical signs, mortality, body weight, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, gross pathology, organ weights (liver, kidneys, spleen, gonads, heart, adrenal glands, thyroid gland, brain), and microscopic pathology (esophagus, stomach, small intestine, cecum, colon, liver, kidneys, spleen, pancreas, urinary bladder, pituitary gland, adrenal gland, testes, seminal vesicle, ovary, bone marrow, thyroid gland, parathyroid gland, salivary gland, prostate gland, heart, aorta, lung, lymph node, skeletal muscle, peripheral nerve, bone, spinal cord, uterus, trachea, eye, optic nerve, brain). Two control rats died during blood sampling. No other deaths occurred and no clinical signs were observed. Body weight and body weight gain were not affected by treatment, but food consumption was slightly decreased at 10 and 25%. No changes in hematology, clinical chemistry or urinalysis parameters occurred at any dose. At gross pathology, no treatment-related effects were noted at any dose. No consistent organ weight changes and no histopathological effects were reported at any dose. Based on these data, the NOEL was 5% (approximately 2,500 mg/kg/day).
Data Quality	Valid without restriction – Klimisch Code 1b
References	Fancher, O.E. 1969. Ninety-day subacute oral toxicity of [trade name deleted; tall oil fatty acid] in albino rats. IBT No. B7067. Industrial Bio-Test Laboratories, Inc., Northbrook, Illinois. World Health Organization (WHO). 1990. Principles for the Toxicological Assessment of Pesticide Residues in Food.

IN VITRO GENETIC TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test was consistent with OECD Test Method 471, *"Bacterial*

	Reverse Mutation Test"
Year	1984
GLP (Y/N)	Y
System of testing	*S. typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538
Concentration	0, 100, 333, 1000, 3333, 10000 µg/plate
Metabolic activation	With and without addition of S-9 fraction from Aroclor 1254-treated Sprague-Dawley rats.
Results	Non-mutagenic
Detailed Summary	Tall oil fatty acid was tested against *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 for mutagenic activity. The test article was tested at concentrations of 100, 333, 1000, 3333 and 10,000 µg/plate with and without metabolic activation with S-9 fraction. Positive controls not requiring metabolic activation included sodium azide, 9-aminoacridine and 2-nitrofluorene; the positive control requiring metabolic activation was 2-aminoanthracene. No increases in mutation frequency were reported at any concentration of tall oil fatty acid with or without metabolic activation. Tall oil fatty acid was not mutagenic in this assay.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Godek, E.G. 1983. Ames Salmonella/microsome plate test: fatty acid [trade name deleted]. Study No. PH 301D-AC-018-83. Pharmakon Research International, Inc., Waverly, Pennsylvania.

IN VITRO GENETIC TOXICITY	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear, sodium salt
CAS #	Not assigned
Remarks	This substance is also referred to as monomer acid sodium salt in the Final Summary document for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 471, *"Bacterial Reverse Mutation Test"*
Year	2002
GLP (Y/N)	Y
System of testing	*S. typhimurium* strains TA98, TA100, TA102, TA1535 and TA15378
Concentration	50, 150, 500, 1500, and 5000 µg/plate
Metabolic activation	With and without addition of S-9 fraction from phenobarbitone/â-naphthoflavone-treated Sprague-Dawley rats.
Results	Non-mutagenic with or without metabolic activation
Detailed Summary	Monomer acid sodium salt was tested against *S. typhimurium* strains TA98, TA100, TA102, TA1535 and TA1537 for mutagenic activity at concentrations of 50, 150, 500, 1500 and 5000 µg/plate with and without metabolic activation. Positive controls not requiring metabolic activation included N-ethyl-N-nitro-N-nitrosoguanidine, mytomycin C, , 4-nitroquinoline-1-oxide and 9-aminoacridine; the positive controls requiring metabolic activation were 2-aminoanthracene, benzo(a)pyrene, and 1,8-dihydroxyanthraquinone. No increases in mutation frequency were reported at any concentration of monomer acid sodium salt with or without metabolic activation. Monomer acid sodium salt

	was not mutagenic in this assay either with or without metabolic activation.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Thompson, P.W. 2002. [Monomer Acid Sodium Salt] Reverse Mutation Assay "Ames Test" Using *Salmonella Typhimurium*. Proj. No. 1078/038. SafePharm Laboratories, Derby, UK.

IN VITRO GENETIC TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 473, *"Chromosomal Aberration Assay with Chinese Hamster Ovary Cells in vitro."*
Year	2001
GLP (Y/N)	Y
System of testing	Chinese Hamster Ovary (CHO) cells *in vitro*
Concentration	With S9 mix: 5, 10 and 20 ug/ml Without S9 mix: 39, 78 and 156 ug/ml
Metabolic activation	With and without addition of S-9 fraction from Aroclor 1254-treated adult male Fisher rats.
Results	Clastogenic with S9 mix at 20 ug/ml and without S9 mix at 156 ug/ml; both concentrations were overtly toxic to the cells.
Detailed Summary	Tall oil fatty acid was tested in Chinese hamster ovary (CHO) cells for clastogenic activity both with and with metabolic activation with rat liver S9 mix. The test article was tested with metabolic activation with S9 mix at concentrations of 5, 10 and 20 ug/ml and without metabolic activation with S9 mix at concentrations of 39, 78 and 156 ug/ml. The positive controls requiring and not requiring metabolic activation were cyclophosphamide (CPH) and methanesulphonate (MMS), respectively. Treatments with test item or controls were performed on duplicate cell cultures. Two slides per culture up to 50 metaphase cells per slide were examined. A dose level was considered to be toxic if the cell count was reduced to less than 50% of the mean vehicle control values or if consistent evidence of changes to cell morphology was observed. In both the presence and absence of S9 mix, positive levels of structural aberrations were observed. In the presence of S9 mix, this response was observed in the cultures treated with 20 ug/ml and in the absence of S9 mix, in the cultures treated with 156 ug/ml. Both of these concentrations were judged overtly toxic to the cultures. Therefore, tall oil fatty acid was a clastogen at toxic concentrations.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Murie, E. 2001. Fatty Acids, CAS No. 61790-12-3 Chromosomal Aberration Assay with Chinese Hamster Ovary Cells in vitro (Complying with EC (Annex V) and OECD 473 Guidelines). Report No. 20712. Inveresk Research, Tranent, Scotland.

IN VITRO GENETIC TOXICITY	
Test substance	
Chemical Name	Fatty acids, C16-C18 and C18 unsaturated, branched and linear, calcium salt
CAS #	Not assigned
Remarks	This substance is also referred to as monomer acid calcium salt in the Final Summary document for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	OECD Test Method 473, *"Genetic Toxicology: Chromosomal Aberration Test."*
Year	2002
GLP (Y/N)	Y
System of testing	Human lymphocytes *in vitro*
Concentration	With S9 mix: 0, 31.25, 62.5, 125, 250, 375 and 500 ug/ml Without S9 mix: 0, 31.25, 62.5, 125, 250, 375 and 500 ug/ml
Metabolic activation	With and without addition of S-9 fraction from phenobarbitone/â-naphthoflavone-treated male Sprague-Dawley rats.
Results	Monomer acid calcium salt was non-clastogenic to human lymphocytes *in vitro* both with and without metabolic activation.
Detailed Summary	Monomer acid calcium salt was tested *in vitro* in human lymphocyrtes for clastogenic activity both with and with metabolic activation with rat liver S9 mix. Lymphocytes were obtained from a volunteer who had been previously sereened for suitability (not exposed to radiation, hazardous chemicals or recently suffereing from a viral infection). Cells were grown in Eagle's minimal essential medium with HEPES buffer, supplemented with L-glutamine, penicillin/streptomycin, amphotericin B and 15% fetal calf serum. Following a preliminary toxicity rangefinding test, the test article was tested both with and without metabolic activation with S9 mix at concentrations of 0, 31.25, 62.5, 125, 250, 375 and 500 ug/ml. The positive controls requiring and not requiring metabolic activation were cyclophosphamide and mitomycin C, respectively. A total of 2000 lymphocyte cell nuclei were counted and the number of cells in metaphase recorded and expressed as the mitotic indec and as a percentage of the vehicle control value. Due to cellular toxicity the maximum dose level selected for metaphase analysis was 150 ug/ml in both exposure groups. The test material did not induce a toxicologically significant increase in the frequency of cells with chromosomal aberrations in either the absence or presence of a liver enzyme metabolizing system in either of two separate experiments. Monomer acid calcium salt was therefore considered to be non-clastogenic to human lymphocytes *in vitro*.
Data Quality	Valid without restriction – Klimisch Code 1a
Reference	Jenkinson, P.C. and Durward, R. 2002. [Monomer acid calcium salt] Chromosomal Aberration Test in Human Lymphocytes *In* Vitro. SPL Proj. No. 1078/086. SafePharm Laboratories, Derby, UK.

REPRODUCTION AND DEVELOPMENTAL TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was consistent with OECD Test Method 416, *"Two-Generation Reproduction Toxicity Study"* with one exception: the initial treatment period was decreased (three weeks versus ten weeks).
Year	1975
GLP (Y/N)	N
Species	Rat
Strain	Sprague-Dawley
Sex	Male and female
Route of Administration	Oral, diet
Frequency of Treatment	Daily
Dose	5 and 10% (approximately equivalent to 2500 and 5000 mg/kg/day)
Control group (Y/N)	Y
Pre-mating exposure period for males	20 days (parental generation)
Pre-mating exposure period for females	20 days (parental generation)
Results	
NOEL	10%, approximately 5000 mg/kg/day, for reproductive and systemic toxicity
Detailed Summary	Sprague-Dawley rats (n = 30 females/group and 15 males/group) were administered tall oil fatty acid (CAS #61790-12-3) in the diet at concentrations of 0, 5 or 10%. The approximate doses were 0, 2,500, or 5,000 mg/kg/day, based on standard conversion factors provided by WHO (1990). The parental (F_0) generation began treatment at 80 days of age and were mated at 100 days of age. Treatment continued through the weaning of the first generation (F_1). After weaning, 20 F_1 males and 20 F_1 females per group were maintained on the parental diet. At 100 days of age, these rats were mated and allowed to deliver pups (F_2). Parameters evaluated included F_1 reproductive parameters, F_1 fertility, viability, lactation, and gestation indices, hematology, serum chemistry, urinalysis, and microscopic pathology of the F_2 pups (brain, pituitary gland, spinal cord, eye, sub-maxillary gland, thyroid, lungs, heart, liver, kidneys, spleen, adrenals, pancreas, stomach, intestines, lymph nodes, bladder, gonads, skin, bone, bone marrow, nerve, muscle). Treatment did not affect the number of liveborn or stillborn F_1 litters and pups, or F_1 weaning weight. No treatment-related changes in fertility, viability, lactation, or gestation indices were measured. Hematology, clinical chemistry and urinalysis parameters were similarly unchanged, and gross and microscopic pathology revealed no treatment-related effects. Tall oil fatty acid had no effect on the reproductive or developmental capabilities of rats at doses as high as 10% (approximately 5,000 mg/kg/day).

Data Quality	Valid without restriction – Klimisch Code 1b
References	Tegeris, A.S. 1975. Sub-acute reproduction in the rat on tall oil fatty acid [trade name deleted]. Report No. 75-106. Pharmacopathics Research Laboratories, Inc., Laurel, Maryland. World Health Organization (WHO). 1990. Principles for the Toxicological Assessment of Pesticide Residues in Food.

REPRODUCTION AND DEVELOPMENTAL TOXICITY	
Test substance	
Chemical Name	Tall oil fatty acid
CAS #	61790-12-3
Remarks	This substance is also referred to as TOFA in the Final Data Summary for Tall Oil Fatty Acids and Related Substances.
Method	
Method/Guideline followed	Test procedure was consistent with OECD Test Method 416, *"Two-Generation Reproduction Toxicity Study"* with one exception: the initial treatment period was decreased (three weeks versus ten weeks).
Year	1977
GLP (Y/N)	N
Species	Rat
Strain	Sprague-Dawley
Sex	Male and female
Route of Administration	Oral, diet
Frequency of Treatment	Daily
Dose	5 and 10% (approximately equivalent to 2500 and 5000 mg/kg/day)
Control group (Y/N)	Y
Pre-mating exposure period for males	20 days (parental generation)
Pre-mating exposure period for females	20 days (parental generation)
Results	
NOEL	10%, approximately 5000 mg/kg/day, for reproductive and systemic toxicity
Detailed Summary	Sprague-Dawley rats (n = 30 females/group and 15 males/group) were administered tall oil fatty acid (CAS #61790-12-3) in the diet at concentrations of 0, 5 or 10%. The approximate doses were 0, 2,500, or 5,000 mg/kg/day, based on standard conversion factors provided by WHO (1990). The parental (F_0) generation began treatment at 80 days of age and were mated at 100 days of age. Treatment continued through the weaning of the first generation (F_1). After weaning, 20 F_1 males and 20 F_1 females per group were maintained on the parental diet. At 100 days of age, these rats were mated and were allowed to deliver pups (F_2). The F_2 generation survived to weaning. Parameters evaluated included F_1 reproductive parameters, F_1 fertility, viability, lactation, and gestation indices, hematology, serum chemistry, urinalysis, organ weights for F_1 animals (thyroids, heart, liver, adrenals, kidneys, gonads), gross pathology of F_1 and F_2 animals, and microscopic pathology of the F_2 pups (brain, pituitary gland, spinal cord, eye, sub-maxillary gland, thyroid, lungs, heart, liver, kidneys, spleen,

	adrenals, pancreas, stomach, intestines, lymph nodes, bladder, gonads, skin, bone, bone marrow, nerve, muscle). There were no treatment effects on reproductive performance, the number of liveborn or stillborn F_1 litters and pups, or weaning weight of the F_1 pups. No treatment-related changes in fertility, viability, lactation, or gestation indices were measured. Hematology, clinical chemistry and urinalysis parameters were similarly unchanged, organ weights were unchanged, and gross and microscopic pathology revealed no treatment-related effects. Tall oil fatty acid had no effect on the reproductive or developmental capabilities of rats at doses as high as 10% (approximately 5,000 mg/kg/day).
Data Quality	Valid without restriction – Klimisch Code 1b
References	Tegeris, A.S. 1977. Tall oil fatty acid: two-generation reproduction study in the rat. Report No. 77-124. Pharmacopathics Research Laboratories, Inc., Laurel, Maryland. World Health Organization (WHO). 1990. Principles for the Toxicological Assessment of Pesticide Residues in Food.