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Final Submittal to the US Environmental Protection Agency**High Production Volume Challenge Program**

Carbamodithioic acid, dibutyl-,methylene ester

CAS Registry Number 10254-57-6

April 2009

Summary

The R. T. Vanderbilt Company, Inc. is pleased to provide this final submittal for Carbamodithioic acid, dibutyl-,methylene ester (Vanlube® 7723) under the Environmental Protection Agency's High Production Volume (HPV) Challenge Program. This document was revised following receipt of comments from the US EPA following the initial test plan submission.

Vanlube® 7723 is a general purpose, ashless antioxidant which should find application in petroleum lubricants of all types. All of the requirements of the US EPA High Production Volume Chemical Testing Program have been met.

BACKGROUND

Background Information: Manufacturing and Commercial Applications

Manufacturing

Vanlube 7723 has been manufactured since 1977. It is manufactured by batch rather than continuous process. Vanlube 7723 process is confidential.

Commercial Applications

Carbamodithioic acid, dibutyl-,methylene ester (VANLUBE 7723) is a general purpose, ashless antioxidant which should find application in petroleum lubricants of all types. It is effective at economical concentrations, readily soluble, and easy to blend. VANLUBE 7723 has been tested in a variety of base stocks commonly used in compounding turbine, hydraulic and circulating oils. In addition to being an effective antioxidant, VANLUBE 7723 also exhibits good extreme pressure performance alone and in combination with other additives. This material is useful as a component of additive packages.

Shipping/Distribution

Vanlube 7723 is shipped extensively throughout the world from manufacturing plants located in North America.

Worker/Consumer Exposure

To the best of our knowledge, all Vanlube 7723 is used by the lubrication additive industry, mostly by large industrial users as a component of their petroleum oil lubricating compounds. This additives industry has a long safety record and only sophisticated industrial users handle this material. It is only available as a liquid and most large industrial users have mechanized materials handling systems, so employee exposure is minimal. The greatest potential for skin and inhalation exposure is at the packing station at the manufacturing site and, to a lesser extent, during weighing activities at the customer site.

Consumer exposure is very minimal. The usage level is less than 5 weight percent in the lubricating fluid formulations.

Background Information: HPV Endpoints

Table 1 presents the HPV endpoint data for this material. Robust study summaries are provided in the attached IUCLID dossier.

Physical chemical properties

The physical chemical properties of carbamodithioic acid, dibutyl-, methylene ester have not been determined. EPIWIN modeling was used to predict boiling point,

vapor pressure, and partition coefficient of this material. Carbamodithioic acid, dibutyl-, methylene ester is not water soluble, such that determination of the partition coefficient is not applicable.

All physical/chemical properties endpoints have been filled.

Environmental Fate

This water-insoluble material does not appear to be readily hydrolysable, as it does not contain common hydrolysable organic functional groups such as carboxyl esters, nitriles and imines (see Figure 1). An OECD TG 111 was conducted to determine hydrolysis; however the solubility of Vanlube® 7723 in the buffer solutions pH 4.0, pH 7.0 and pH 9.0 was very low. It was not possible to increase the solubility of the test item with the use of different solubilizers (acetone, acetonitrile and ethanol). The photodegradation half-life was estimated using EPIWIN; the half-life is predicted to be .52 hours. This material is not readily biodegradable. Fugacity modeling indicates this material would be found primarily in sediment and soil, which is consistent with its low water solubility.

All environmental fate endpoints have been filled.

Environmental Effects

The acute aquatic toxicity of this material is well characterized. This material has low water solubility, and this property is characterized in the results of the testing. There was no acute (fish, daphnia or algae) or chronic (daphnia) toxicity when tested at the limit of water solubility.

All aquatic toxicity testing endpoints have been filled.

Mammalian Toxicity

Acute Toxicity: The acute oral LD₅₀ for carbamodithioic acid, dibutyl-, methylene ester is 16000 mg/kg. The acute dermal LD₅₀ is greater than 2,000 mg/kg.

Repeated Dose/Reproductive/Developmental Effects: A repeat dose toxicity study with screening reproductive and developmental endpoints (OECD 422) has been conducted with the test substance. The parental NOAEL was 1000 ppm; the NOAEL for F1 offspring was greater than 20000 ppm.

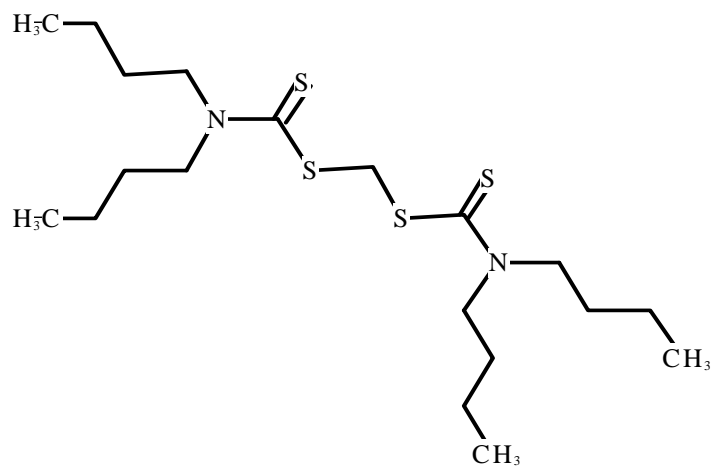
Genotoxicity: A *Salmonella*/mammalian-microsome plate incorporation mutagenicity assay has been conducted with carbamodithioic acid, dibutyl-, methylene ester. The results of the bacterial mutagenicity test were negative.

All mammalian toxicity endpoints have been filled.

Table 1. Matrix of Available and Adequate Data

Test	CAS No. 10254-57-6
Chemical/physical Properties	
Melting Point	-38.3 C (measured)
Vapor Pressure	.0000000638 hPa at 25 °C (estimated)
Boiling Point	490 C at 1013 hPa (estimated)
Partition Coefficient	6.73 (estimated)
Water Solubility	0.243 mg/L
Environmental Fate	
Hydrolysis	No hydrolysable functional groups; low water solubility prohibited study completion
Photodegradation	t1/2 = .5 hours
Biodegradation	21% in 28 days
Environmental Transport	Air 0.08% Water 7.14% Soil 33.6% Sediment 59.2%
Aquatic Toxicity	
Acute Fish 96 hr LC50	>0.06 mg/L
Acute Daphnid 48 hr EC50	>0.052 mg/L
Algae 72 hr EC50	>0.0325 mg/L
21-d NOEC Daphnid	>0.247 mg/L (water solubility limit)
21 d EC50 for inhibition of the reproduction rate Daphnid	>0.247 mg/L (water solubility limit)
Mammalian Toxicity	
Acute Oral	16000 mg/kg (rat)
Acute Dermal	>2000 mg/kg (rabbit)
Repeated Dose	NOAEL = 1000 ppm
Genotoxicity (<i>in vitro</i> -bacteria)	negative
Genotoxicity (<i>in vitro</i> mammalian)	negative
Reproductive/Developmental	NOAEL F ₁ offspring >20000 ppm

Figure 1 Carbamodithioic acid, dibutyl-,methylene ester structure



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I U C L I D

Data Set

Existing Chemical : ID: 10254-57-6
CAS No. : 10254-57-6
EINECS Name : 4,4'-methylene bis(dibutyldithiocarbamate)
EC No. : 233-593-1
Molecular Formula : C19H38N2S4

Producer related part
Company : Epona Associates, LLC
Creation date : 30.01.2004

Substance related part
Company : Epona Associates, LLC
Creation date : 30.01.2004

Status :
Memo : RT Vanderbilt

Printing date : 03.04.2009
Revision date :
Date of last update : 03.04.2009

Number of pages : 31

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 : typical for marketed substance
Substance type : organic
Physical status : liquid
Purity : = 100 % w/w
Colour : amber
Odour : not available

15.11.2005 (5)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Vanlube (R) 7723

19.03.2007 (5)

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

1.13 REVIEWS

2.1 MELTING POINT

Value	: = -38.3 °C
Sublimation	:
Method	: OECD Guide-line 102 "Melting Point/Melting Range"
Year	: 2007
GLP	: yes
Test substance	: as prescribed by 1.1 - 1.4
Method	: A preliminary test was performed to check the approximate freezing temperature of Vanlube® 7723. The test item was stored about 21 hours at -22°C in a freezer. As the sample was not frozen after this time the freezing temperature of Vanlube® 7723 is below 22°C.
	During the main tests, about 2 ml of the test item placed in a small test tube were cooled down from room temperature to about -47°C using a dry ice and acetone mixture.
Result	: At -38.0°C (1st test) and -38.5°C (2nd test), respectively, the test item was frozen by visual judgement.
	The freezing point was determined to be -38.3°C ± 0.4°C which is equal to 235.0 K ± 0.4 K.
Test substance	: Purity 100%
Reliability	: (1) valid without restriction Guideline study, GLP
Flag	: Critical study for SIDS endpoint
12.03.2007	(7)

2.2 BOILING POINT

Value	: = 490.4 °C at 1013 hPa
Decomposition	:
Method	: other: estimated with EPIWIN
Year	: 2009
GLP	: no
Test substance	: as prescribed by 1.1 - 1.4
Result	: Boiling Pt (deg C): 490.44 (Adapted Stein & Brown method)
Test condition	: MPBVP v1.43
Test substance	: SMILES : N(C(=S)SCSC(N(CCCC)CCCC)=S)(CCCC)CCCC CHEM : Carbamodithioic acid, dibutyl-, methylene ester CAS NUM: 010254-57-6 MOL FOR: C19 H38 N2 S4 MOL WT : 422.77
Reliability	: (2) valid with restrictions Acceptable calculation method
Flag	: Critical study for SIDS endpoint
03.04.2009	(1)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : .0000000638 hPa at 25 °C
Decomposition :
Method : other (calculated)
Year : 2009
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : VP(mm Hg,25 deg C): 4.79E-08 (6.38-06 Pa) (Modified Grain method)
Test condition : MPBVP v1.43
Test substance : SMILES : N(C(=S)SCSC(N(CCCC)CCCC)=S)(CCCC)CCCC
 CHEM : Carbamodithioic acid, dibutyl-, methylene ester
 CAS NUM: 010254-57-6
 MOL FOR: C19 H38 N2 S4
 MOL WT : 422.77

Reliability : (2) valid with restrictions
 Acceptable calculation method
Flag : Critical study for SIDS endpoint
 03.04.2009 (1)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = 6.73 at °C
pH value :
Method : other (calculated)
Year : 2009
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : Log Kow(version 1.67 estimate) = 6.73
Test condition : KOWWIN v1.67 estimate
Test substance : SMILES : N(C(=S)SCSC(N(CCCC)CCCC)=S)(CCCC)CCCC
 CHEM : Carbamodithioic acid, dibutyl-, methylene ester
 CAS NUM: 010254-57-6
 MOL FOR: C19 H38 N2 S4
 MOL WT : 422.77

Reliability : (2) valid with restrictions
 Acceptable calculation method
Flag : Critical study for SIDS endpoint
 03.04.2009 (1)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : = .243 mg/l at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other
Year : 2004

2. Physico-Chemical Data

Id 10254-57-6

Date 03.04.2009

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

Test substance : Vanlube® 7723
Reliability : (1) valid without restriction
Published data

Flag : Critical study for SIDS endpoint
25.02.2004 (12)

Solubility in Value : Water
: = .2344 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: estimated using EPIWIN
Year : 2009
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Result : WSKOW v1.41 Results -----
Log Kow (estimated) : 6.73
Log Kow (experimental): not available from database
Log Kow used by Water solubility estimates: 6.73

Equation Used to Make Water Sol estimate:
Log S (mol/L) = 0.693-0.96 log Kow-0.0092(Tm-25)-0.00314 MW +
Correction

Melting Pt (Tm) = -38.30 deg C (Use Tm = 25 for all liquids)

Correction(s):	Value
-----	-----
Amine, aliphatic	0.838

Log Water Solubility (in moles/L) : -6.256
Water Solubility at 25 deg C (mg/L): 0.2344

Test condition : Water Solubility Estimate from WSKOW v1.41
Test substance : SMILES : N(C(=S)SCSC(N(CCCC)CCCC)=S)(CCCC)CCCC
CHEM : Carbamodithioic acid, dibutyl-, methylene ester
CAS NUM: 010254-57-6
MOL FOR: C19 H38 N2 S4
MOL WT : 422.77

Reliability : (2) valid with restrictions
Acceptable calculation method

Flag : Critical study for SIDS endpoint
03.04.2009 (2)

Solubility in Value : Water
: at °C
pH value concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :

2. Physico-Chemical Data

Id 10254-57-6

Date 03.04.2009

Method :
Year : 2003
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : Insoluble in cold water
Reliability : (2) valid with restrictions
Safety data sheet

25.02.2004

(5)

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

DIRECT PHOTOLYSIS

Half-life t_{1/2} : = .5 hour(s)
 Degradation : % after
 Quantum yield :

INDIRECT PHOTOLYSIS

Sensitizer : OH
 Conc. of sensitizer :
 Rate constant : ca. .000000000245 cm³/(molecule*sec)
 Degradation : % after
 Deg. product :
 Method : other (calculated)
 Year : 2009
 GLP : no
 Test substance : as prescribed by 1.1 - 1.4

Result : SUMMARY (AOP v1.92): HYDROXYL RADICALS (25 deg C) -----
 Hydrogen Abstraction = 110.4773 E-12 cm³/molecule-sec
 Reaction with N, S and -OH = 135.4000 E-12 cm³/molecule-sec
 Addition to Triple Bonds = 0.0000 E-12 cm³/molecule-sec
 Addition to Olefinic Bonds = 0.0000 E-12 cm³/molecule-sec
 Addition to Aromatic Rings = 0.0000 E-12 cm³/molecule-sec
 Addition to Fused Rings = 0.0000 E-12 cm³/molecule-sec

 OVERALL OH Rate Constant = 245.8773 E-12 cm³/molecule-sec
 HALF-LIFE = 0.044 Days (12-hr day; 1.5E6 OH/cm³)
 HALF-LIFE = 0.522 Hrs
 ----- SUMMARY (AOP v1.91): OZONE REACTION (25 deg C) ---

***** NO OZONE REACTION ESTIMATION *****
 (ONLY Olefins and Acetylenes are Estimated)

Experimental Database: NO Structure Matches
 Fraction sorbed to airborne particulates (phi):
 0.959 (Junge-Pankow, Mackay avg)
 0.317 (Koa method)

Note: the sorbed fraction may be resistant to atmospheric oxidation

Test condition : Atmospheric Oxidation (25 deg C) [AopWin v1.92]
Test substance : SMILES : N(C(=S)SCSC(N(CCCC)CCCC)=S)(CCCC)CCCC
 CHEM : Carbamodithioic acid, dibutyl-, methylene ester
 CAS NUM: 010254-57-6
 MOL FOR: C19 H38 N2 S4
 MOL WT : 422.77

Reliability : (2) valid with restrictions
 Acceptable calculation method

03.04.2009

(1)

3.1.2 STABILITY IN WATER

Type : abiotic
 t_{1/2} pH4 : at °C
 t_{1/2} pH7 : at °C
 t_{1/2} pH9 : at °C
 Deg. product :
 Method : OECD Guide-line 111 "Hydrolysis as a Function of pH"

3. Environmental Fate and Pathways

Id 10254-57-6
Date 03.04.2009

Year : 2007
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : According to the EEC Directive 92/69, Section C.7, the method is applicable only to water soluble substances. The test item shows no significant solubility in the different solvent systems. Therefore, no further testing could be performed with Vanlube® 7723 at pH 4.0, pH 7.0 and pH 9.0.

Result : The solubility of Vanlube® 7723 in the buffer solutions pH 4.0, pH 7.0 and pH 9.0 was very low. It was not possible to increase the solubility of the test item with the use of different solubilizers (acetone, acetonitrile and ethanol).

Peaks obtained, if any, were too small to allow quantification or even to follow a degradation curve.

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : Critical study for SIDS endpoint
02.04.2009 (6)

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: estimated using EPIWIN
Year : 2009

Result :
Level III Fugacity Model (Full-Output):

=====
Chem Name : Carbamodithioic acid, dibutyl-, methylene ester
Molecular Wt: 422.77
Henry's LC : 5.55e-006 atm-m3/mole (Henrywin program)
Vapor Press : 4.79e-008 mm Hg (Mpbpwin program)
Log Kow : 6.73 (Kowwin program)
Soil Koc : 1.8e+006 (KOCWIN MCI method)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.0769	1.04	1000
Water	7.14	208	1000
Soil	33.6	416	1000
Sediment	59.2	1.87e+003	0

3. Environmental Fate and Pathways

Id 10254-57-6

Date 03.04.2009

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	4.17e-014	947	14.3	31.6	0.475
Water	2.2e-012	441	133	14.7	4.42
Soil	1.05e-014	1.04e+003	0	34.6	0
Sediment	8.37e-013	407	22	13.6	0.732

Persistence Time: 618 hr
Reaction Time: 655 hr
Advection Time: 1.1e+004 hr
Percent Reacted: 94.4
Percent Adverted: 5.62

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):

Air: 1.044
Water: 208.1
Soil: 416.2
Sediment: 1873
Biowin estimate: 3.365 (days-weeks)

Advection Times (hr):

Air: 100
Water: 1000
Sediment: 5e+004

Test substance : SMILES : N(C(=S)SCSC(N(CCCC)CCCC)=S)(CCCC)CCCC
CHEM : Carbamodithioic acid, dibutyl-, methylene ester
CAS NUM: 010254-57-6
MOL FOR: C19 H38 N2 S4
MOL WT : 422.77

Reliability : (2) valid with restrictions
Acceptable calculation method

Flag : Critical study for SIDS endpoint
03.04.2009 (1)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : domestic sewage
Concentration : 10 mg/l related to Test substance
related to
Contact time : 29 day(s)
Degradation : = 21 (±) % after 28 day(s)
Result : other: not readily biodegradable
Kinetic of testsubst. : 0 day(s) = 0 %
6 day(s) = 5 %
14 day(s) = 7 %
20 day(s) = 19 %
28 day(s) = 21 %
Control substance : Benzoic acid, sodium salt
Kinetic : 28 day(s) = 50 %
%
Deg. product :

3. Environmental Fate and Pathways

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Method : OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO₂ evolution)"
Year : 2003
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Test condition : The test material, at a concentration of 10 mg C/l, was exposed to activated sewage sludge micro-organisms with a culture medium in sealed culture vessels in the dark at 21 deg C for 28 days. The degradation of the test material was assessed by the determination of carbon dioxide produced. Control solutions with inoculum and the standard material, sodium benzoate, together with a toxicity control were used for validation purposes.

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : Critical study for SIDS endpoint
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(8)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : semistatic
Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : = .06 measured/nominal
LC50 : > .06 measured/nominal
Limit test : no
Analytical monitoring : yes
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 2004
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : The results of the media preparation trials indicated that at a test concentration of 0.243 mg/l prepared using a preliminary solution in auxiliary solvent to spike test medium a significant proportion of undissolved/dispersed test material would be present. Samples taken from the test preparations throughout the test were therefore analysed untreated and after centrifugation (40000 g, 30 minutes) in order to give an indication of the dissolved and hence bioavailable test material concentration.

Chemical analysis of the untreated test samples showed measured test concentrations to range from 104% to 129% of the nominal test concentration with a mean measured value of 118%, indicating that the test system was correctly dosed during the test.

In the centrifuged test samples the measured test concentration were shown to range from 11% to 42% of the nominal test concentration, indicating the amount of dissolved and hence bioavailable test material in the test system. No significant decline was shown in the measured test concentrations over each 24-hour dosing period during the test, indicating that the dissolved test material was stable during testing.

Given there was no significant decline in the measured test concentrations over each 24-hour dosing period, it was considered justifiable to base the results on the mean measured test concentrations of the centrifuged test media to give a "worst case" analysis of the data.

Test condition : The maximum concentration employed in the study was 0.243 mg/l, which is the water solubility value of the test material. In order to enable the accurate and consistent preparation of this test concentration, it was determined that using a preliminary solution in auxiliary solvent (dimethylformamide) to spike the test medium was the most suitable method of test media preparation.

A semistatic test regime was employed in the test involving a daily renewal of the test preparations to ensure that the concentrations of the test material remained near nominal and to prevent the build up of nitrogenous waste products.

Following a preliminary range-findings test, fish were

exposed in two groups of 10 to an aqueous dispersion of the test material at a single concentration of 0.243 mg/l for a period of 96 hours at a temperature of approximately 14 deg C under semi-static conditions. The number of mortalities and any sub-lethal effects of exposure in each test and control vessel were determined 3 and 6 hours after the start of exposure and then daily throughout the test until termination after 96 hours.

Test substance : Vanlube® 7723
Conclusion : The 96-hour LC50 based on the mean measured test concentrations of the centrifuged test media was greater than 0.060 mg/l and correspondingly the No Observed Effect Concentration was 0.060 mg/l.
Reliability : (1) valid without restriction
 Guideline study, GLP
Flag : Critical study for SIDS endpoint
 02.04.2009 (13)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : semistatic
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : = .052 measured/nominal
EC50 : > .052 measured/nominal
Limit Test : no
Analytical monitoring : yes
Method : OECD Guide-line 202
Year : 2004
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : The results of the media preparation trials indicated that at a test concentration of 0.243 mg/l prepared using a preliminary solution in auxiliary solvent to spike test medium a significant proportion of undissolved/dispersed test material would be present. Samples taken from the test preparations at 0 (fresh test media), 24 (old or expired and fresh test media) and 48 hours (old or expired test media) were therefore analysed untreated and after centrifugation (40000 g, 30 minutes) in order to give an indication of the dissolved and hence bioavailable test material concentration.

Chemical analysis of the untreated test samples taken at 0 (fresh media), 24 (old and fresh media) and 48 hours (old media) showed the measured test concentrations to be 80% to 106% of the nominal value with the exception of replicates R3-R4 at 24 hours (fresh media) and replicates R1-R2 and R3-R4 at 48 hours, which showed measured values of 150%, 135% and 134% of the nominal value, respectively. However, analysis of frozen duplicate samples taken during the test showed measured test concentrations of 124%, 113%, and 110% of nominal, respectively, for these test samples, indicating that the initial results from analysis did not reflect the true dosed test concentrations and that the test system was correctly dosed.

In the centrifuged samples the measured concentrations were

shown to range from 15% to 32% of the nominal test concentration. No significant decline in the measured test concentrations was observed over each dosing period indicating that the dissolved test material was stable in the test medium during testing.

Given that no significant losses of test material were shown over each dosing period, it was considered justifiable to base the results on the mean measured test concentrations of the centrifuged test media in order to give a "worst case" analysis of the data.

Test condition : The maximum concentration employed in the study was 0.243 mg/l, which is the water solubility value of the test material. In order to enable the accurate and consistent preparation of this test concentration, it was determined that using a preliminary solution in auxiliary solvent (dimethylformamide) to spike the test medium was the most suitable method of test media preparation.

A semi-static test regime was employed in the test in an effort to maintain near nominal test concentrations. For the test media renewal at 24 hours, the test concentrations were freshly prepared and the daphnids transferred by wide bore pipette from the 24-hour old test media into the fresh test media.

Following a preliminary range-finding test, forty daphnids (4 replicated of 10 animals) were exposed to an aqueous dispersion of the test material at a concentration of 0.243 mg/l for 48 hours at a temperature of approximately 21 deg C under semi-static conditions in the dark. Immobilization and any adverse reactions to exposure were recorded after 24 and 48 hours.

Test substance : Vanlube® 7723
Conclusion : The 48-hour EC50 based on the mean measured test concentrations of the centrifuged test media was greater than 0.052 mg/l and correspondingly the No Observed Effect Concentration was 0.052 ml/L.

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : Critical study for SIDS endpoint
02.04.2009

(12)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Scenedesmus subspicatus (Algae)
Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/l
NOEC : = .0325 measured/nominal
EC50 : > .0325 measured/nominal
Limit test : no
Analytical monitoring : yes
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 2004
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : The results of the media preparation trials indicated that at a test concentration of 0.243 mg/l prepared using a

preliminary solution in auxiliary solvent to spike test medium a significant proportion of undissolved/dispersed test material would be present. Samples taken from the test preparations at 0 and 72 hours were therefore analysed untreated and after centrifugation (40000 g, 30 minutes) in order to give an indication of the dissolved and hence bioavailable test material concentration.

Chemical analysis of the untreated test samples at 0 hours showed the measured test concentrations to be 90% and 96% of the nominal value (Replicates R1-R3 and R4-R6 pooled, respectively). After 72 hours there was a marked decline in the measured concentrations in the untreated test samples to 52% and 39% of nominal.

In the centrifuged samples the measured concentrations at 0 hours were 24% and 23% of the nominal value and a decline in measured test concentration was also observed after 72 hours to 9% and 7% of the nominal value.

The test material was shown to be stable in the culture medium over a 72-hour period and hence the decline in test concentrations observed in the definitive test was considered to be due to adsorption to algal cells.

Given this decline in measured test concentrations it was considered justifiable to base the results on the mean measured test concentration of the centrifuged test media in order to give a "worst case" analysis of the data.

Test condition : The maximum concentration employed in the study was 0.243 mg/l, which is the water solubility value of the test material. To enable the accurate and consistent preparation of this test concentration, it was determined that using a preliminary solution in auxiliary solvent (dimethylformamide) to spike the test medium was the most suitable method of test media preparation.

Following a preliminary range-finding test, *Scenedesmus subspicatus* was exposed to an aqueous dispersion of the test material at a concentration of 0.243 mg/l (six replicate flasks) for 72 hours under constant illumination and shaking at a temperature of 24 +/- 1 deg C.

Test substance : Samples of the algal population were removed daily and cell concentrations determined for each control and treatment group, using a Coulter® Multisizer Particle Counter.
Conclusion : Vanlube® 7723
: The EC50 values based on the geometric mean measured test concentrations of the centrifuged test media were greater than 0.0325 mg/l and correspondingly the No Observed Effect Concentration was 0.0325 mg/l.

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : Critical study for SIDS endpoint

02.04.2009

(4)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Daphnia magna (Crustacea)
Endpoint : other: survival, growth (body length), and reproduction
Exposure period : 21 day(s)
Unit : mg/l
NOEC : $\geq .247$
LOEC : $\geq .247$
EC50 : $> .247$
Analytical monitoring : yes
Method : OECD Guide-line 211
Year : 2009
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The test method is based on the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (2000).

Remark : The biological results were based on mean measured concentrations calculated as time-weighted means of the test item concentrations measured at the start of the test medium renewals and the concentrations measured in the stability control samples without food at the end of the renewal periods.

Result : The nominal concentrations tested were 15.6, 31.3, 62.5, 125 and 250 µg/L. Additionally, a control and a solvent control were tested in parallel. The test item Vanlube® 7723 had no toxic effects on survival, growth and reproduction of Daphnia magna after the exposure period of 21 days up to the water solubility limit of the test item. Thus, the 21-day NOEC of the test item was determined to be at least 247 µg/L. This value might be even higher but concentrations far above the water solubility limit of the test item were not tested in accordance with the test guidelines. The 21 day LOEC was above the water solubility limit of the test item. The MATC (Maximum Acceptable Toxicant Concentration) was determined to be higher than 247 µg/L and thus, above the water solubility limit of the test item.

Reliability : The 21 day EC50 for the inhibition of the reproduction rate of the daphnids was above the water solubility limit of the test item.

Flag : (1) valid without restriction
Guideline study, GLP

02.04.2009

(3)

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 : = 16000 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year : 2003
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (4) not assignable
Safety data sheet

19.03.2007

(5)

5.1.2 ACUTE INHALATION TOXICITY**5.1.3 ACUTE DERMAL TOXICITY**

Type : LD50
Value : > 2000 mg/kg bw
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year : 2003
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (4) not assignable
Safety data sheet

19.03.2007

(5)

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-acute
Species	: rat
Sex	: male/female
Strain	: Sprague-Dawley
Route of admin.	: oral feed
Exposure period	: For two weeks prior to mating, during mating, gestation, and up to Day 5 of lactation
Frequency of treatm.	: daily
Post exposure period	: none
Doses	: 1000, 5000 and 20000 ppm; reduced to 900, 4500 and 18000 ppm on Day 29 to account for the anticipated increase in female food consumption during late gestation
Control group	: yes, concurrent no treatment
NOAEL	: = 1000 ppm
Method	: other: OECD 422
Year	: 2006
GLP	: yes
Test substance	: as prescribed by 1.1 - 1.4

Result : At 20000 ppm there were no mortalities and no clinical signs of toxicity. The behavioural evaluations showed no evidence of toxicity. There were inconsistent differences in bodyweight gain for males throughout, and females prior to pairing compared to controls. Female bodyweight gain during gestation was lower than controls resulting in significant bodyweight differences during the final week of gestation and early lactation. There were no significant effects upon food consumption except for a significant difference in female food consumption during the final week of gestation. Laboratory investigations showed a significant increase in both Activated Partial Thromboplastin Time and Clotting time for males only when compared to control values. There were no significant blood chemistry changes. Post mortem macroscopic examination showed an increase in absolute and relative liver weight for females only when compared to control values. There were no significant macroscopic abnormalities. Histopathology showed a reduction in the severity grades for splenic extramedullary haemopoiesis for both males and females compared to controls but this is of questionable toxicological relevance.

At 5000 ppm there were no mortalities or clinical signs of toxicity. A similar pattern of reduction in bodyweight gain during gestation for females was observed but no significant effect upon female food consumption. There were no significant effects seen for blood chemistry and haematological analysis. Significant post mortem changes were limited to an increase in liver weight for females only and lower severity grades of splenic extramedullary haemopoiesis for males only. There were no treatment-related effects upon fertility, reproductive performance or offspring viability, growth and development up to early lactation.

At 1000 ppm there were no mortalities or effects on adults

Test condition

seen during the in-life phase of the study. There were no significant effects on blood chemistry or haematology. Post mortem findings were limited to lower severity grades of splenic extramedullary haemopoiesis for males only. There were no effects on fertility or reproductive performance. Offspring viability, growth and development up to Day 5 of lactation was comparable to controls.

- : The test material was administered orally, by dietary inclusion, to groups of ten male and ten female rats throughout maturation, mating, gestation and up to Day 5 of lactation. The dose levels were 1000, 5000 and 20000 ppm of Vanlube 7723 in the diet. These dose levels were reduced to 900, 4500 and 18000 ppm respectively on study Day 29 to account for the anticipated increase in female food consumption during late gestation.

Following two weeks of dosing, male and female rats were paired within their dose groups to produce litters. At Day 5 post partum, all surviving females and offspring together with all adult males were killed and examined macroscopically.

Parental animals were observed daily for clinical signs of toxicity. Bodyweights and food consumption were recorded weekly during the maturation phase which was continued for males after the mating phase. Neurotoxicological assessments were performed at specific time points during the study. Mated females were weighed and food consumption recorded on specific days post coitum and post partum up to Day 5 of lactation.

Blood sampling for haematology and clinical chemistry was performed on five selected males and five selected females per dose group one day prior to pairing.

The offspring were observed daily for clinical signs. The offspring clinical signs and individual pup bodyweights were recorded on specific days post partum up to Day 5 of lactation.

Post mortem macroscopic examinations were performed on all adults and offspring, including decedents. Selected reproductive organs were weighed and/or preserved together with any significant abnormalities from all parental animals. In addition an extended list of organs/tissues were weighed and/or preserved in fixative for selected males and females. Histopathology was carried out on specific organs from selected parental animals. Histopathology was also performed on the extended list of tissues preserved from selected males and females.

**Test substance
Conclusion**

- : Vanlube® 7723
- : At dose levels of 5000 ppm Vanlube 7723 and above there was evidence of treatment-related effects upon the adult. At a dose level of 1000 ppm and above the only significant finding was lower grades of severity splenic extramedullary haemopoiesis which is considered not to be an adverse finding. No evidence of effects upon reproductive performance or subsequent offspring viability in utero and early lactation was seen. Offspring development was comparable to control values. The "No Observed Adverse Effect Level" for effects upon adults was 1000 ppm and for reproductive

5. Toxicity

Id 10254-57-6

Date 03.04.2009

performance and offspring viability was in excess of 20000 ppm.

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : Critical study for SIDS endpoint
02.04.2009 (9)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Bacterial reverse mutation assay
System of testing : Salmonella typhimurium strains TA1535, TA1537, TA102, TA98 and TA100
Test concentration : 50, 150, 500, 1500 and 5000 ug/plate
Cytotoxic concentr. : > 5000 ug/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year : 2003
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : The test material caused no visible reduction in the growth of the bacterial background lawn at any dose level. The test material was, therefore, tested up to the maximum recommended dose level of 5000 ug/plate. An oily precipitate was observed at and above 1500 ug/plate; this did not prevent the scoring of revertant colonies.

No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test material, either with or without metabolic activation.

The vehicle control plates gave counts of revertant colonies within the normal range. All of the positive control chemicals used in the test induced marked increases in the frequency of revertant colonies, both with and without metabolic activation. Thus, the sensitivity of the assay and the efficacy of the S9-mix were validated.

Test condition : Salmonella typhimurium strains TA1535, TA1537, TA102, TA98 and TA100 were treated with the test material using the Ames plate incorporation method at five dose levels, in triplicate, both with and without the addition of a rat liver homogenate metabolising system (10% liver S9 in standard co-factors). The dose range was determined in a preliminary toxicity assay and was 50 to 5000 ug/plate in the first experiment. The experiment was repeated on a separate day using the same dose range as Experiment 1. The vehicle was dimethyl sulphoxide.

Test substance : Vanlube® 7723
Conclusion : The test material was considered to be non-mutagenic under the conditions of this test.

Reliability : (1) valid without restriction
Guideline study, GLP
Flag : Critical study for SIDS endpoint

02.04.2009 (11)

Type : Chromosomal aberration test
System of testing : Human lymphocytes
Test concentration : 0, 7.5, 15, 30, 60, 120 ug/ml
Cytotoxic concentr. : >4220 ug/ml

Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 473
Year : 2005
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : A preliminary toxicity test was conducted at a dose range of 16.48 to 4220 ug/ml using a 4-hour exposure time with and without metabolic activation followed by a 20-hour recovery period, and a continuous exposure of 24 hours without metabolic activation. In the main study, duplicate cultures of human lymphocytes, treated with the test material, were evaluated for chromosome aberrations at up to three dose levels, together with vehicle and positive controls. Four treatment conditions were used for the study, ie, in Experiment 1, 4 hours in the presence of metabolic activation, at a 2% final concentration with cell harvest after a 20-hour expression period and a four-hour exposure in the absence of metabolic activation with a 20-hour expression period. In Experiment 2, the 4-hour exposure with addition of metabolic activation was repeated (using a 1% final metabolic activation system concentration), while in the absence of metabolic activation the exposure time was increased to 24 hours.

Result : The test material exhibited no evidence of toxicity in any of the exposure groups in the preliminary toxicity assay. A precipitate of the test material was observed in the parallel blood-free cultures at the end of the exposure periods, at and above 65.94 ug/ml. The dose selection for the chromosome aberration study used the lowest precipitating dose level as the maximum dose level and was 120 ug/ml for all exposure groups with and without activation.

All vehicles (solvent) controls had frequencies of cells with aberrations within the range expected for normal human lymphocytes. All of the positive control materials induced statistically significant increases in the frequency of cells with aberrations indicating the satisfactory performance of the test and of the activity of the activation system. The test material was not toxic and did not induce any statistically significant increases in the frequency of cells with aberrations, in either of two separate experiments, using a dose range that included a dose level that was the lowest precipitating dose level.

Conclusion : The test material was considered to be non-clastogenic to human lymphocytes in vitro.

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : Critical study for SIDS endpoint

02.04.2009

(10)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type	:	One generation study
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	For two weeks prior to mating, during mating, gestation, and up to Day 5 of lactation
Frequency of treatm.	:	daily
Premating exposure period	:	
Male	:	14 days
Female	:	14 days
Duration of test	:	up to Day 5 of lactation
No. of generation studies	:	2
Doses	:	1000, 5000 and 20000 ppm; reduced to 900, 4500 and 18000 ppm on Day 29 to account for the anticipated increase in female food consumption during late gestation
Control group	:	yes, concurrent no treatment
NOAEL parental	:	= 1000 ppm
NOAEL F1 offspring	:	> 20000 ppm
Result	:	The "No Observed Adverse Effect Level" for effects upon adults was 1000 ppm and for reproductive performance and offspring viability was in excess of 20000 ppm.
Method	:	OECD combined repeated dose and reproductive/developmental toxicity screening test
Year	:	2006
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	At 20000 ppm there were no mortalities and no clinical signs of toxicity. The behavioural evaluations showed no evidence of toxicity. There were inconsistent differences in bodyweight gain for males throughout, and females prior to pairing compared to controls. Female bodyweight gain during gestation was lower than controls resulting in significant bodyweight differences during the final week of gestation and early lactation. There were no significant effects upon food consumption except for a significant difference in female food consumption during the final week of gestation. Laboratory investigations showed a significant increase in both Activated Partial Thromboplastin Time and Clotting time for males only when compared to control values. There were no significant blood chemistry changes. Post mortem macroscopic examination showed an increase in absolute and relative liver weight for females only when compared to controls. There were no significant macroscopic abnormalities. Histopathology showed a reduction in the severity grades for splenic extramedullary haemopoiesis for both males and females compared to controls but this is of questionable toxicological relevance. There were no significant effects upon fertility or reproductive performance and no effect upon offspring development in utero and up to Day 5 of lactation. At 5000 ppm there were no mortalities or clinical signs of toxicity. A similar pattern of reduction in bodyweight gain during gestation for females was observed but no significant effect upon female food consumption. There were no significant effect seen for blood chemistry and

haematological analysis. Significant post mortem changes were limited to an increase in liver weight for females only and lower severity grades of splenic extramedullary haemopoiesis for males only. There were no treatment-related effects upon fertility, reproductive performance or offspring viability, growth and development up to early lactation.

At 1000 ppm there were no mortalities or effects on adults seen during the in-life phase of the study. There were no significant effects on blood chemistry or haematology. Post mortem findings were limited to lower severity grades of splenic extramedullary haemopoiesis for males only. There were no effects on fertility or reproductive performance. Offspring viability, growth and development up to Day 5 of lactation were comparable to controls.

Test condition

: The test material was administered orally, by dietary inclusion, to groups of ten male and ten female rats throughout maturation, mating, gestation and up to Day 5 of lactation. The dose levels were 1000, 5000 and 20000 ppm of Vanlube 7723 in the diet. These dose levels were reduced to 900, 4500 and 18000 ppm respectively on study Day 29 to account for the anticipated increase in female food consumption during late gestation.

Following two weeks of dosing, male and female rats were paired within their dose groups to produce litters. At Day 5 post partum, all surviving females and offspring together with all adult males were killed and examined macroscopically.

Parental animals were observed daily for clinical signs of toxicity. Bodyweights and food consumption were recorded weekly during the maturation phase which was continued for males after the mating phase. Neurotoxicological assessments were performed at specific time points during the study. Mated females were weighed and food consumption recorded on specific days post coitum and post partum up to Day 5 of lactation.

Blood sampling for haematology and clinical chemistry was performed on five selected males and five selected females per dose group one day prior to pairing.

The offspring were observed daily for clinical signs. The offspring clinical signs and individual pup bodyweights were recorded on specific days post partum up to Day 5 of lactation.

Post mortem macroscopic examinations were performed on all adults and offspring, including decedents. Selected reproductive organs were weighed and/or preserved together with any significant abnormalities from all parental animals. In addition an extended list of organs/tissues were weighed and/or preserved in fixative for selected males and females. Histopathology was carried out on specific organs from selected parental animals. Histopathology was also performed on the extended list of tissues preserved from selected males and females.

**Test substance
Conclusion**

: Vanlube® 7723
: There was
no evidence of effects upon reproductive

performance or subsequent offspring viability in utero and early lactation. The "No Observed Adverse Effect Level" for reproductive performance and offspring viability was in excess of 20000 ppm.

Reliability : (1) valid without restriction
Guideline study, GLP

Flag : Critical study for SIDS endpoint
02.04.2009 (9)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : For two weeks prior to mating, during mating, gestation, and up to Day 5 of lactation
Frequency of treatm. : daily
Duration of test :
Doses : 1000, 5000 and 20000 ppm; reduced to 900, 4500 and 18000 ppm on Day 29 to account for the anticipated increase in female food consumption during late gestation
Control group : yes, concurrent no treatment
NOAEL maternal tox. : = 1000 ppm
NOAEL teratogen. : > 20000 - ppm
Method : other: OECD 422
Year : 2006
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : At 20000 ppm there were no significant effects upon fertility or reproductive performance and no effect upon offspring development in utero and up to Day 5 of lactation.

At 5000 ppm there were no treatment-related effects upon fertility, reproductive performance or offspring viability, growth and development up to early lactation.

At 1000 ppm there were no effects on fertility or reproductive performance. Offspring viability, growth and development up to Day 5 of lactation were comparable to controls

Test condition : The test material was administered orally, by dietary inclusion, to groups of ten male and ten female rats throughout maturation, mating, gestation and up to Day 5 of lactation. The dose levels were 1000, 5000 and 20000 ppm of Vanlube 7723 in the diet. These dose levels were reduced to 900, 4500 and 18000 ppm respectively on study Day 29 to account for the anticipated increase in female food consumption during late gestation.

Following two weeks of dosing, male and female rats were paired within their dose groups to produce litters. At Day 5 post partum, all surviving females and offspring together with all adult males were killed and examined macroscopically.

Parental animals were observed daily for clinical signs of toxicity. Bodyweights and food consumption were recorded weekly during the maturation phase which was continued for males after the mating phase. Neurotoxicological assessments were performed at specific time points during the study. Mated females were weighed and food consumption recorded on specific days post coitum and post partum up to Day 5 of lactation.

Blood sampling for haematology and clinical chemistry was performed on five selected males and five selected females per dose group one day prior to pairing.

The offspring were observed daily for clinical signs. The offspring clinical signs and individual pup bodyweights were recorded on specific days post partum up to Day 5 of lactation.

Post mortem macroscopic examinations were performed on all adults and offspring, including decedents. Selected reproductive organs were weighed and/or preserved together with any significant abnormalities from all parental animals. In addition an extended list of organs/tissues were weighed and/or preserved in fixative for selected males and females. Histopathology was carried out on specific organs from selected parental animals. Histopathology was also performed on the extended list of tissues preserved from selected males and females.

**Test substance
 Conclusion**

: Vanlube® 7723
 : There was no evidence of effects upon reproductive performance or subsequent offspring viability in utero and early lactation. Offspring development was comparable to control values. The "No Observed Adverse Effect Level" for for reproductive performance and offspring viability was in excess of 20000 ppm.

Reliability

: (1) valid without restriction
 Guideline study, GLP

Flag
 02.04.2009

: Critical study for SIDS endpoint

(9)

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

- (1) EPI SUMMARY (v4.00)
- (2) EPIWIN SUMMARY (v3.11)
- (3) Harlan Laboratories Ltd. (2009) Effect of Vanlube® 7723 on Survival, Growth and Reproduction of *Daphnia magna* in a Semi-Static Test over Three Weeks. Harlan Laboratories Study B10855
- (4) Mead, C. and McKenzie, J. (2004) Vanlube® 7723: Algal Inhibition Test. SafePharm Laboratories Limited, SPL Project Number: 860/087.
- (5) R.T. Vanderbilt Company, Inc (2003) Material Safety Data Sheet Vanlube (R) 7723. 4/14/2003
- (6) RCC Ltd (2007) HYDROLYSIS DETERMINATION OF Vanlube® 7723 AT DIFFERENT pH VALUES RCC Study Number: B10844
- (7) RCC Ltd. (2007) Determination of the Freezing Point/Freezing Range of Vanlube® 7723. Study Number B10833
- (8) SafePharm Laboratories (2004) Vanlube (R) 7723: Assessment of Ready Biodegradability; CO₂ Evolution Test. SPL Project Number: 860/088.
- (9) SafePharm Laboratories (2006) Vanlube® 7723: Dietary Combined Repeat Dose Toxicity Study with Reproductive/Developmental Screening Test in the Rat. SafePharm Laboratories Limited, SPL Project Number: 860/083.
- (10) SafePharm Laboratories Ltd (2005) Vanlube (R) 7723: Chromosome Aberration Test in Human Lymphocytes in vitro. SPL Project number 860/109.
- (11) Thompson, P.W. (2003) Vanlube® 7723: Reverse Mutation Assay "Ames Test" Using *Salmonella Typhimurium*. SafePharm Laboratories Limited, SPL Project Number: 860/084, February 13, 2003.
- (12) Wetton, P.M. and McKenzie, J. (2004) Vanlube® 7723: Acute Toxicity to *Daphnia magna*. SafePharm Laboratories Limited, SPL Project Number: 860/086.
- (13) Wetton, P.M. and McKenzie, J. (2004) Vanlube® 7723: Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*). SafePharm Laboratories Limited, SPL Project Number: 860/085.

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT