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APPENDIX

Robust Summaries for Substances in The HPV Test Plan for the Glycol Esters Category of the Aliphatic Esters Chemicals

- Part I. HPV Substances in the Glycol Esters Category**
- Part II. Surrogate Glycol Esters**

December 24, 2003

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

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Part II - Robust Summaries for Surrogate Glycol Esters

Five Surrogate Glycol Esters Substances

The five structurally analogous surrogate glycol esters are:

- Heptanoic acid, ester with 2,2,4-trimethyl-1,3-pentanediol (CAS No. 71839-38-8)
- Triethylene glycol, diheptanoate (CAS No. 7434-40-4)
- Propylene glycol, monostearate (CAS No. 1323-39-3)
- Propylene glycol, dilaurate (CAS No. 22788-19-8)
- Propylene glycol, diisostearate (CAS No. 68958-54-3)

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Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

PART I. HPV Substances in the Glycol Esters Category**Melting Point, Boiling Point (CAS No. 111-60-4)**

Test Substance	Stearic acid, 2-hydroxyethyl ester
CAS Number	111-60-4
Remarks	Purity not indicated
Method/guideline	Not specified
Test type	Melting point and boiling point
GLP	Not specified
Year	1997
Remarks	Method of melting point and boiling point determination was not given. Physical chemical properties were cited in Handbook of Chemistry and Physics, 78th ed. (1997)
Conclusions	Melting Point 60.5 °C Boiling Point 189-191°C (3 mm Hg)
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature.
References	CRC Handbook of Chemistry and Physics. D.R. Lide (ed.), 78th Ed., CRC Press Inc., Boca Raton FL, 1997, pg. 3-227, No. 8260.
Other	Date: November 21, 2003.

Acute Oral Toxicity (CAS No. 111-60-4)

Test Substance	Stearic acid, 2-hydroxyethyl ester
CAS Number	111-60-4
Remarks	Purity not specified
Method/guideline	Not indicated
Test type	Acute oral toxicity
GLP	Not indicated
Year	1984
Test system	Species (Strain) Rats (Wistar) Sex: Male and female No. of animals: 5 males and 5 females/treatment Route: Oral gavage Dosage: 5.0 g/kg Statist. Methods: Not specified
Test conditions	Five male and 5 female Wistar rats weighing 200-300 grams were fasted for 18 hrs and dosed by gavage with 5.0 g/kg body weight of the test material. The test material was mixed with corn oil and administered as a 25% w/w solution. The rats were observed for mortality or other signs of gross toxicity for 14 days. Observations were unremarkable and necropsy was unremarkable.
Results/Remarks	The oral LD50 was > 5.0 gm/kg as reported in IUCLID data set.
Conclusions	The acute oral LD ₅₀ for the test substance was > 5.0 g/kg in rats.

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Data Quality	Reliable with restrictions [Klimisch reliability 2] as assigned by Environ Corp. in an IUCLID document provided to Soap and Detergent Association (SDA).
References	IUCLID data set for CAS No. 111-60-4 (dated 30-Jan-2001) as provided by the Soap and Detergent Association (SDA) to ACC Aliphatic Esters Panel in December 2001.
Other	Date: November 21, 2003.

Acute Oral Toxicity (CAS No. 111-60-4)

Test Substance CAS Number Remarks	Stearic acid, 2-hydroxyethyl ester 111-60-4 Purity not specified
Method/guideline Test type GLP Year	Not indicated Acute oral toxicity No 1982
Test system	Species (Strain) Rat (not specified) Sex: Not specified No. of animals: See below for each of the four studies Route: Oral gavage (undiluted or diluted in corn oil), single dose Dosage: Range from 0.464 g/kg to 21.3 g/kg
Test conditions Results/Remarks	Elder (1982) has reported following LD ₅₀ values determined from four acute oral toxicity studies in rats (single oral dose). 1) LD ₅₀ >10 g/kg. Groups of 5 rats/treatment with dosage 0.464 –10 g/kg; diluted 50% corn oil. 2) LD ₅₀ >21.3 g/kg Group of 5 rats/treatment with dosage 0.7 to 21.3 g/kg, 1:2 dilution in corn oil. 3) LD ₅₀ >10 g/kg. Group of 10 rats, oral gavage undiluted at 10 g/kg. 4) LD ₅₀ > 5 g/kg. Group of 10 rats, oral gavage undiluted at 5 g/kg Doses at above 13 g/kg b.w. were noted to produce effects which included diarrhea, wet oil coats, nasal hemorrhage; symptoms appeared within 4 days after dosing but disappeared after day 10. No other adverse effects reported by Elder (1982).
Conclusions	The acute oral LD ₅₀ was reported to be > 10 g/kg, >21.3 g/kg, >10 g/kg and >5 g/kg in four oral gavage studies in rats, respectively (see above).
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature.
References	Elder RL (1982). Final report on the safety assessment of glycol stearate, glycol stearate SE and glycol distearate. J. Amer. Coll. Toxicol. 1(2) : 1-11.
Other	Date: November 21, 2003.

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Melting Point (CAS No. 94-28-0)

Test Substance	Hexanoic acid, 2-ethyl-, diester with triethylene glycol
CAS Number	94-28-0
Remarks	Purity not specified
Method/guideline	Not indicated
Test type	Melting point
GLP	Not specified
Year	Not specified
Remarks	Methods of determination were not given. Physical chemical properties were supplied by a member company to the ACC Aliphatic Esters Panel.
Conclusions	Melting Point < -40 °C
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature.
References	Unpublished confidential business information supplied to ACC Aliphatic Esters Panel
Other	Date: November 21, 2003.

Boiling Point (CAS No. 94-28-0)

Test Substance	Hexanoic acid, 2-ethyl-, diester with triethylene glycol
CAS Number	94-28-0
Remarks	Purity was not indicated
Method/guideline	Not indicated
Test type	Boiling point
GLP	Not specified
Year	1996
Remarks	Method of boiling point determination was not given. This physical chemical property was cited in 1996 BIBRA Toxicity Profile for this test material.
Conclusions	Boiling Point 344 °C
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature: BIBRA (1996)
References	BIBRA (1996). Toxicity Profile for Triethylene Glycol Bis(2-Ethylhexanoate), CAS No. 94-28-0. British Industrial Biological Research Association (BIBRA). 4 pp. and references therein.
Other	Date: November 21, 2003.

Acute Oral Toxicity (CAS No. 94-28-0)

Test Substance	Hexanoic acid, 2-ethyl-, diester with triethylene glycol
CAS Number	94-28-0
Remarks	Purity not specified
Method/guideline	Not indicated
Test type	Acute oral toxicity

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GLP Year	No 1941, 1981
Test system	Species (Strain) Rat (not specified) Sex: Not specified No. of animals: Not specified Route: Oral gavage Dosage: Not specified
Test conditions/ Results/Remarks	BIBRA (1996) cited the two oral toxicity studies in rats [Smyth et al. (1941); Timofievskaya (1981)]. No experimental information given in BIBRA toxicity profile review for these two oral toxicity studies. In addition, BIBRA reported oral LD50 values for mice (16.0 g/kg) and for guinea pig (20.58 g/kg) as well. Rats and mice given lethal doses were reported to have died in state of narcosis.
Conclusions	The acute oral LD ₅₀ was 12.5 g/kg (Timofievskaya , 1981). The acute oral LD ₅₀ was 31.37 g/kg (Smyth et al., 1941).
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature.
References	1) BIBRA (1996). Toxicity Profile for Triethylene Glycol Bis(2-Ethylhexanoate). British Industrial Biological Research Association (BIBRA). 4 pp. and references therein. 2) Smyth HF, Seaton J, Fischer L (1941). The single dose toxicity of some glycols and their derivatives. J. Ind. Hyg. Toxicol. 23 : 259-268. 3) Timofievskaya LA (1981). Gig Sanit. 46 (5) : 87.
Other	Date: November 24, 2003.

Repeated-Dose Toxicity (CAS No. 94-28-0)

Test Substance CAS Number Remarks	Hexanoic acid, 2-ethyl-, diester with triethylene glycol 94-28-0 Purity not indicated
Method/guideline Test type GLP Year	Not specified 12 Day Oral Dietary Feeding Study Not indicated 1991
Species/strain Route of Administ. Duration of test No. of animals Dose/Conc. Levels Sex Frequency of treatment Control Group	Rats (strain not specified) Diet containing test material at 0.1% and 1% 12 Days Not indicated 0.1 and 1.0% in diet Not indicated Daily administration in diet for 12 days Not specified
Post-exposure observat.	Mortality, survival, growth, food consumption, clinical signs/symptoms, clinical chemistry, hematology, necropsy, gross morphology and histopathology appear to have been carried out.
Statist. Methods	Not specified.
Test Conditions/Results	Limited experimental information available in secondary literature.
Conclusions	BIBRA (1996) cited that rats fed dietary levels of 0.1% or 1% of the test material for 12 days showed <u>no</u> adverse effects with respect to food consumption, weight gain, behavior, hematology, clinical serum chemistry, liver or kidney weight, or gross or

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Data Quality	microscopic appearance of organs. The dietary 0.1 and 1% concentrations corresponded approximately to daily doses of ~80 and 800 mg/kg/day, respectively.
References	Not assignable [Klimisch reliability 4]. BIBRA reviewed toxicity data. 1) BIBRA (1996). Toxicity Profile for Triethylene Glycol Bis(2-Ethylhexanoate) (CAS No. 94-28-0). British Industrial Biological Research Association (BIBRA). 4 pp. and references therein. 2) Confidential business information (1991). Findings from the 12-day oral dietary study as well as other toxicity data were reported to US EPA as a TSCA Section 8(d) report, EPA-OTS 86-920000021; NTIS/OTS 0533587.
Other	Date: November 24, 2003.

Acute fish toxicity (CAS No. 94-28-0)

Test Substance	Hexanoic acid, 2-ethyl-, diester with triethylene glycol						
CAS Number	94-28-0						
Remarks	Purity not specified						
Method/guideline	Not indicated (static limit test)						
Type (test type)	96-hr Acute Fish Toxicity						
Test System	Fish, freshwater						
GLP	No						
Year	1977						
Species/Strain	Fish: Fathead minnow (<i>Pimephales promelas</i>)						
Analyt. Monitoring	No analysis performed						
Exposure period	96 hours						
Statist. Methods	Not specified						
Remarks on Test Conditions	96-hr static test at limited concentration. Test performed in 20-L glass vessels containing dilution water (Lake Ontario water, charcoal-filtered and dechlorinated), 19-20 °C, aerated . No. of fish: 10/treatment, 10 for control Concentration: 100 µl /L nominal loading rate and control (0 mg/L, untreated). If density of ~0.97 g/ml is assumed, the 100 µl /L concentration was equivalent to ~97 mg/L. Observations for mortality, abnormal behavior and treatment-related effects were performed at 0, 24, 48, 72 and 96 hrs. Daily physical measurement of pH, dissolved oxygen and temperature was carried out. The pH was 7.5 to 8.0, dissolved oxygen was 5.9 to 9.4 mg/L, temperature was 19-20 °C. Light 16 hr/dark 8 hr cycle was maintained. The average wet weight per fish in this study was not reported.						
Remarks	Detailed procedure for preparation of exposure solutions was not available but there was note in report that acetone (0.5 ml/L final test volume) was mixed with test substance to enhance dispersion. No mention of whether acetone was similarly added to control group exposure solution. Test substance was reported to be partially dissolved at 96 hr and the exposure solution surface had an oily appearance. There was no oily surface observed in the control solution.						
Results	<table> <thead> <tr> <th><u>Nominal test conc.</u></th> <th><u>Mortality (96h)</u></th> </tr> </thead> <tbody> <tr> <td>0 (Untreated controls)</td> <td>0 %</td> </tr> <tr> <td>100 µl /L (equivalent to 97 mg/L)</td> <td>0 %</td> </tr> </tbody> </table>	<u>Nominal test conc.</u>	<u>Mortality (96h)</u>	0 (Untreated controls)	0 %	100 µl /L (equivalent to 97 mg/L)	0 %
<u>Nominal test conc.</u>	<u>Mortality (96h)</u>						
0 (Untreated controls)	0 %						
100 µl /L (equivalent to 97 mg/L)	0 %						

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Conclusions	96-hr LC ₅₀ > 100 µl /L (or ~97 mg/L) (nominal loading rate). No mortality was observed in the exposed (100 µl /L, nominal) or control groups of fish. In addition, fish in the control and in the exposed group exhibited normal behavior and appearance throughout the 96-hr test. Hence, the data would suggest that test substance did not cause mortality at or above its water solubility limits or water saturated level (WSL).
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP and no chemical analyses or measurements were performed.
References	Unpublished confidential business information.
Other	Date: November 24, 2003.

Acute toxicity to aquatic invertebrate (CAS No. 94-28-0)

Test Substance	Hexanoic acid, 2-ethyl-, diester with triethylene glycol																						
CAS Number	94-28-0																						
Remarks	Purity not specified																						
Method/guideline	Not indicated																						
Type (test type)	<i>Daphnia sp.</i> , Acute immobilization test																						
Test System	Freshwater invertebrate																						
GLP	No																						
Year	1977																						
Species/Strain	Freshwater invertebrate, <i>Daphnia magna</i> , < 24 hrs old																						
Analyt. Monitoring	No analysis performed																						
Exposure period	96 hr																						
Statist. Methods	Not specified																						
Test Conditions	96-hr static test at limited concentration. Test performed in glass culture vessels containing dilution water (charcoal-filtered and dechlorinated), 19-20 °C, aerated. No. of daphnids: 10/treatment, 10 for control Concentration: 100 µl /L nominal loading rate and control (0 mg/L, untreated). If density of ~0.97 g/ml is assumed, the 100 µl /L concentration was equivalent to ~97 mg/L. Observations for immobility and signs of stress were performed at 0, 6, 24, 48, 72 and 96 hrs. Daily physical measurement of pH, dissolved oxygen and temperature was carried out. The pH was 7.5 to 8.0, dissolved oxygen was 5.9 to 9.4 mg/L, temperature was 19-20 °C. Light 16 hr/dark 8 hr cycle was maintained.																						
Remarks	Detailed procedure for preparation of exposure solutions was not available but there was note in report that acetone (0.5 ml/L final test volume) was mixed with test substance to enhance dispersion. No mention of whether acetone was similarly added to control group exposure solution. Test substance was reported to be partially dissolved at 96 hr and that the exposure solution surface had an oily appearance. There was no oily surface observed in the control solution.																						
Results	<table border="1"> <thead> <tr> <th rowspan="2">Nominal test conc.</th> <th colspan="4">% Immobilization at</th> </tr> <tr> <th>24-hr</th> <th>48 hr</th> <th>72 hr</th> <th>96 hr</th> </tr> </thead> <tbody> <tr> <td>0 (Untreated controls)</td> <td>0 %</td> <td>0%</td> <td>0%</td> <td>20%</td> </tr> <tr> <td>100 µl /L (equivalent to 97 mg/L)</td> <td>0 %</td> <td>0%</td> <td>0%</td> <td>10%</td> </tr> </tbody> </table>				Nominal test conc.	% Immobilization at				24-hr	48 hr	72 hr	96 hr	0 (Untreated controls)	0 %	0%	0%	20%	100 µl /L (equivalent to 97 mg/L)	0 %	0%	0%	10%
Nominal test conc.	% Immobilization at																						
	24-hr	48 hr	72 hr	96 hr																			
0 (Untreated controls)	0 %	0%	0%	20%																			
100 µl /L (equivalent to 97 mg/L)	0 %	0%	0%	10%																			
Conclusions	48-hr EC ₅₀ > 100 µl /L (or ~97 mg/L) (nominal loading rate) for daphnid immobilization. No immobilization or signs of abnormal behavior mortality was observed at 24 hr or 48 hr																						

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Data Quality	(typical time period used for current OECD 202 acute daphnia toxicity studies). Hence, the data at 48 hrs would suggest that test substance did not cause immobilization of daphnids at or above its water solubility limits or water saturated level (WSL). Reliable with restrictions [Klimisch reliability 2]. Not GLP and no chemical analyses or measurements were performed.
References	Unpublished confidential business information.
Other	Date: November 24, 2003.

Partition Coefficient (CAS No. 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanedioyl) ester					
CAS Number	70729-68-9					
Remarks	Test material purity was 88% with remainder comprised of 6% triethylene glycol di-n-heptanoate, 4% mixed ester of tetraethylene glycol with n-heptanoic and 2 methylhexanoic acids, 2% other mixed esters					
Method/guideline	OECD 107 (1981)					
Test type	Partition coefficient					
GLP	No					
Year	1981					
Test conditions	Octanol and water were mutually saturated with each other. Test substance (20.0 mg in 5 mL octanol) was mixed with octanol (total volume 5, 7 and 10 mL in flask A, B and C, resp.) and water (40, 38 and 35 mL in flask A, B and C, resp.) in duplicate vessels at 25°C. The mixtures were shaken for 15 min., centrifuged and re-equilibrated to 25°C for 24h. Concentrations were determined using gas chromatographic analysis.					
Results/Remarks						
Treatment	A1	A2	B1	B2	C1	C2
TS (mg)	20	20	20	20	20	20
Volume octanol [ml]	5	5	7	7	10	10
Volume water [ml]	40	40	38	38	35	35
Conc. in octanol phase [mg/L]	3880	3940	2885	2875	1990	2020
Conc. in aqueous phase [mg/L]	5.57	4.97	3.69	3.44	3.77	2.77
Recovery [%]	98	100	102	101	100	101
Partition coeff.= Pow	7.0×10^2	7.9×10^2	7.8×10^2	8.4×10^2	5.3×10^2	7.3×10^2
Average Pow \pm RSD	$7.4 \times 10^2 \pm 9.5\%$		$8.1 \times 10^2 \pm 4.9\%$		$6.3 \times 10^2 \pm 22\%$	
Average Pow \pm SD	$7.3 \times 10^2 \pm 1.1 \times 10^2$					
log(Pow)	2.86					
Conclusions	log P _{ow} 2.86 at 25°C					
Data Quality	Reliable without restrictions [Klimisch reliability 1]					
References	Unpublished confidential business information.					
Other	Date: November 25, 2003.					

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Acute Oral Toxicity (CAS No. 70729-68-9)

Test Substance CAS Number Remarks	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanediyl) ester 70729-68-9 Purity was 94.5% and contained ~2% monoesters
Method/guideline Test type GLP Year	OECD 401, 84/449/EEC Acute oral toxicity Yes 1991
Test system	Species (Strain) Rats (Wistar) Sex: Male and female No. of animals: 5/sex/treatment Route: Oral gavage Dosage: Single oral administration (gavage) of 2000 mg/kg bw Animals were fasted 16 h prior to dosing and did not have access to food until 3-4 h after dosing Control: No control group Statist. Methods: Not specified
Test conditions	Mortality/clinical signs 10 min, 1, 2, 6 and 24 h post-dosing and daily thereafter for 14 days. Body weight on day 0, 7 and 14. Necropsy and gross pathological examinations were performed on all animals on day 14.
Results/Remarks	No mortality was reported in any of dosed animals. Weight gains were normal in all animals. Gross pathological examination at terminal necropsy revealed no treatment-related findings. No abnormal clinical signs were observed apart from slight piloerection and sporadic findings (e.g., ventral or limb position, reduced activity, reduced turgor) up to 6 hrs after oral administration.
Conclusions	The acute oral LD ₅₀ > 2.0 g/kg
Data Quality	Reliable without restrictions [Klimisch reliability 1]
References	Unpublished confidential business information.
Other	Date: November 25, 2003.

Acute Oral Toxicity (CAS No. 70729-68-9)

Test Substance CAS Number Remarks	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanediyl) ester 70729-68-9 Test material purity was 88% with remainder comprised of 6% triethylene glycol di-n-heptanoate, 4% mixed ester of tetraethylene glycol with n-heptanoic and 2 methylhexanoic acids, 2% other mixed esters
Method/guideline Test type GLP Year	Not indicated Acute oral toxicity No 1980
Test system	Species (Strain) Rats (ChR:CD) Sex: Male, weight 261 g No. of animals: 10 Males/treatment Route: Oral gavage

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Remarks	Abbreviation: + = Clinical signs observed x= dose-related effect (A) All deaths occurred within 2 days (B) Clinical observations included flat body posture, moribundness, labored breathing, stained/wet perineal area, lacrimation, stained face, weakness, ataxia, lethargy, prostration, salivation and chromodacryorrhea Other remarks: Only females are used in this test. The frequency of the observations was not indicated. Necropsy was not performed.
Conclusions	Acute oral LD50 was estimated to be 24-25 g/kg
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP. Only female animals tested.
References	Unpublished confidential business information.
Other	Date last updated: November 25, 2003

Repeated-Dose Toxicity (CAS No. 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanediyl) ester						
CAS Number	70729-68-9						
Remarks	Test material purity was 88% with remainder comprised of 6% triethylene glycol di-n-heptanoate, 4% mixed ester of tetraethylene glycol with n-heptanoic and 2 methylhexanoic acids, 2% other mixed esters.						
Method/guideline	Not indicated						
Test type	28-Day Oral Toxicity Study						
GLP	No						
Year	1981						
Species/strain	Rats /Wistar						
Route of Administ.	Oral gavage						
Duration of test	28 days						
No. of animals	5/sex/treatment						
Dose/Conc. Levels	Oral administration (gavage) for 28 days at 0 and 1000 mg/kg bw; vehicle corn oil (11-15% solution); 14 day recovery period for 5 additional animals/sex receiving 1000 mg/kg bw.						
Sex	Male and female						
Frequency of treatment	Oral gavage, daily for 28 consecutive days						
Control Group	Yes						
Post-exposure observat.	Mortality, clinical signs and body weight daily. Macroscopic gross observation, organ weights and limited histopathology on day 28 (main group and control) and on day 42 (recovery group). Hematology and clinical chemistry performed.						
Statist. Methods	ANOVA						
Results							
Dose Group	0 mg/kg/day		1000 mg/kg/day		1000 mg/kg/d (recovery group)		Dose-Related Effect
Sex	M	F	M	F	M	F	M F
Mortality	0/5	0/5	0/5	0/5	0/5	0/5	
Clinical signs ^(A)			+				
Body weight gain			d	d	d	d	
Hematology	No treatment related effects						
Leukocytes (day 0, 28, 42)			i		i		
Clinical chemistry			i				
ASAT (day 28)							
ALP (day 40)				d	d	d	

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Bilirubin (day 28)	i	i	
Organ weight		Not reported	
Necropsy		No treatment related effects	
Histopathology ^(B)		No treatment related effects	
Conclusions	<p>Abbreviations + = Effect reported d = decrease i = increase</p> <p>Footnotes: (A) Congestion was seen. (B) In all treatment groups and control lung lesions were seen (pneumonitis, peribronchiolitis and/or perivasculitis). Other findings were incidental and included cysts in K�rsteiners duct of the thyroid, thyroid C-cell hyperplasia, periportal vacuolization, hepatitis, trachitis, nephritis, atrophy and degeneration of the seminiferous tubules of the testes and epididymitis</p>		
Remarks	<p>NOAEL 1000 mg/kg/day (no adverse systemic effects)</p> <p>1) No analytical determination of the test concentrations. No analyses for stability and homogeneity of the test substance. 2) Organ weights were not reported. All histopathological changes were associated to macroscopic effects. 3) Leukocyte counts were decreased compared to pretest values in both treated and control animals. In treated males pretest, 28-day and 42-day values were increased compared to the values in control males. Therefore, these effects were not considered toxicologically relevance. 4) The decreased levels of alkaline phosphatase were considered to be of no toxicological relevance. 5) The increased bilirubin level was found both in treated and control animals. 6) Since body weight loss was reported to be sporadic and effects on liver enzymes were not very clearly treatment related, 1000 mg/kg bw is considered to be a NOAEL. 7) Food intake was not measured. No information was available on age and weight of the animals, on housing conditions. Histopathology was limited (female sex organs, spinal cord, heart, urinary bladder and peripheral nerve tissue were not investigated) 8) Only the results for clinical chemistry, hematology and histopathology were reported. Other findings were summarized (no actual values and no individual data). Some of the blood parameters were stated to differ significantly from control values, however, this was not indicated in the tables in the report</p>		
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP. Limited report.		
References	Unpublished confidential business information.		
Other	Date last updated: November 26, 2003.		

Genetic Toxicity in Vitro (CAS No. 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanedioyl) ester
CAS Number	70729-68-9
Remarks	Test material purity was 88% with remainder comprised of 6% triethylene glycol di-n-heptanoate, 4% mixed ester of tetraethylene glycol with n-heptanoic and 2 methylhexanoic acids, 2% other mixed esters.
Method/guideline	Not indicated
Type of Study	Bacterial Reverse Mutation Assay
Test System	Bacterial (<i>Salmonella typhimurium</i>)
GLP	No
Year	1979

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Species/Strain	<i>Salmonella typhimurium</i> / TA98, TA100, TA1535, TA1537
Metab. Activation	Aroclor 1254-induced rat liver preparations (S9 mixture)
Concentrations	500-10,000 µg/plate, 100-2500 µg/plate (based on toxicity with TA1535)
Statist. Methods	Z-test based on Poisson distribution
Test Conditions/Remarks	Negative control: DMSO (vehicle) Positive control: N-methyl-N'-nitro-N-nitroguanidine (TA100 and TA1535 without S9), 9-aminoacridine (TA1537 without S9), 2-nitrofluorene (TA98 without S9) and 2-aminoanthracene (all strains with S9) Procedure: Plate incorporation test similar to OECD 471 procedure with independent repeat.
Results/Remarks	The test substance was negative for mutagenic activity in the four <i>Salmonella</i> tester strains, with or without metabolic activation. No mutagenic activity was observed at concentrations tested. The positive controls gave the appropriate responses as expected. Only 2 replicates were plated per test. Current OECD 471 guidelines require evaluation using 5 different strains.
Conclusions	The test substance was <u>not</u> mutagenic, with or without metabolic activation in the <i>Salmonella</i> /Mammalian Microsome Reverse Mutation assay.
Data Quality	Reliable without restrictions [Klimisch reliability 1].
References	Unpublished confidential business information.
Other	Date last updated: November 26, 2003.

Genetic Toxicity In Vitro (CAS No. 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanedioyl) ester
CAS Number	70729-68-9
Remarks	Test material purity was 88% with remainder comprised of 6% triethylene glycol di-n-heptanoate, 4% mixed ester of tetraethylene glycol with n-heptanoic and 2 methylhexanoic acids, 2% other mixed esters.
Method/guideline	Not indicated
Type of Study	Chinese hamster ovary cell assay for mutagenicity
Test System	Chinese hamster ovary cell - HGPRT locus
GLP	No
Year	1981
Species/Strain	Cell Line: CHO-cells (BH4 clone)
Metab. Activation	Rat S9 mix (Aroclor 1254 induced)
Concentrations	-S9: 0.27 to 23.9 mM, based on solubility; vehicle DMSO +S9: 0.25 to 23.9 mM, based on solubility; vehicle DMSO
Statist. Methods	Student's <i>t</i> -test, ANOVA
Test Conditions/Remarks	Negative control: vehicle controls (DMSO). Positive controls: ethylmethane-sulfonate (-S9), 7,12-dimethylbenzanthracene (+S9). Procedure: Three independent tests; duplicate cultures/treatment; no. of cells 10 ⁶ ; exposure period 18-19 hours (-S9) and 5 hours (+S9); expression period 7 days; endpoint: forward mutation on HGPRT locus.

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Results				
Test Number	Metabolic act.	Doses tested [mM]	Cytotoxicity [% of control survival] at highest dose	Test result
1	Without S9	0.27, 1.2, 2.7, 5.5, 13.6, 23.9	100	Negative
	With S9	0.25, 1.2, 2.5, 7.5, 16.0, 23.9	96	Negative
2	Without S9	0.27, 1.2, 2.7, 5.5, 13.6, 23.9	83	Negative
	With S9	0.25, 1.2, 2.5, 7.5, 16.0, 23.9	75	Negative
3	Without S9	0.27, 2.7, 13.6, 23.9	88	Negative
	With S9	0.25, 1.2, 2.5, 7.5, 16.0, 23.9	99	Negative
Remarks	It is not clear from the report at which concentrations a precipitate was observed. Individual data were not presented. Positive and negative controls gave the appropriate responses as expected.			
Conclusions	The test substance was <u>not</u> mutagenic using the Chinese hamster ovary cell forward mutation assay on the HGPRT locus, with or without metabolic activation.			
Data Quality	Reliable without restrictions [Klimisch reliability 1].			
References	Unpublished confidential business information.			
Other	Date last updated: November 26, 2003.			

Acute fish toxicity (CAS No. 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanediyl) ester
CAS Number	70729-68-9
Remarks	Purity was 94.5% and contained ~2% monoesters
Method/guideline	DIN 38412, part 15
Type (test type)	Acute fish toxicity study
Test System	Fish, freshwater
GLP	Yes
Year	1991
Species/Strain	Fish: Golden orfe (<i>Leuciscus idus</i>), mean length 53 mm
Analyt. Monitoring	No analyses were performed.
Exposure period	48 hours
Statist. Methods	Not specified
Test Conditions	48-hr static test at eight nominal concentrations from 18 mg/L to 1000 mg/L Golden orfe (<i>Leuciscus idus</i>), mean length 53 mm Test performed in 12 L vessel containing 10 L of dechlorinated tap water (hardness 250 mg CaCO ₃ /L) at 17.5-20°C, aerated, 16 h light, unfed, loading 0.74 g fish/L. No. of fish: 5/vessel; 2 vessels/treatment Concentrations: Nominal dispersions of 0 (untreated control), 18, 32, 56, 100, 180, 320, 560 and 1000 mg/L Analysis: No analyses were performed Physical Measurements: Daily, overall range for pH was 7.9-8.2; dissolved O ₂ was 60-100% of saturation; temperature was 17.5-20.0°C over course of study. Observations: Mortality/symptoms at 2-4, 24 and 48 hr

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Results	Nominal test conc.	
	<u>Loading Level (mg/L)</u>	<u>Mortality (48-h)</u>
	0 Control (untreated)	0
	18	0
	32	0
	56	0
	100	0
	180	0
	320	0
	560	20
1000	90	
	Oil drops on the water surface were observed in test solutions for nominal concentrations 100 mg/L to 1000 mg/L.	
Conclusion	48-h LC ₅₀ was estimated to be 720 mg/L (graphical determination using observed data). No mortality was observed at 320 mg/L (nominal). Test concentrations were all above the water solubility of the test material (calculated to be 0.34 mg/L, EpiWin). Hence, data indicate that the test material would not be expected to cause acute toxicity in fish at its water saturation limit or water solubility limit (WSL).	
Remarks	1) There is limited information on the homogeneity of the test “solutions” and no analyses were performed to confirm the nominal test concentrations. The mortality found in this study may be related to possible physical effects (sorption of oily substance to the fish). 2) The test duration was only 48 hours. 3) <i>Leuciscus idus</i> was not recommended by current OECD 203 guidelines. However in the EG guidelines <i>Leuciscus idus</i> was included as a recommended fish species. The test temperature was rather low (17.5-20°C, EG 20-24°C).	
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Test duration was 48 hr only. Other reasons discussed above.	
References	Unpublished confidential business information.	
Other	Date last updated: December 1, 2003.	

Acute fish toxicity (CAS No. 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanedioyl) ester
CAS Number	70729-68-9
Remarks	Test material purity was 88% with remainder comprised of 6% triethylene glycol di-n-heptanoate, 4% mixed ester of tetraethylene glycol with n-heptanoic and 2 methylhexanoic acids, 2% other mixed esters.
Method/guideline	Not indicated
Type (test type)	Acute fish toxicity study
Test System	Fish, freshwater
GLP	No
Year	1981
Species/Strain	Fish: Zebra fish (<i>Brachydanio rerio</i>)
Analyt. Monitoring	No analyses were performed
Exposure period	24 hours
Statist. Methods	Not specified

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Test Conditions	<p>24-hr static acute fish toxicity test at nine nominal concentrations from 0.56 g/L to 10 g/L Species: Zebra fish (<i>Brachydanio rerio</i>), mean length 25 mm Test performed in glass vessels containing 15 L of laboratory supply water (hardness 90 mg CaCO₃/L) at 20°C, not aerated, 16 hr light/8hr dark, unfed, loading 0.2 g fish/L No. of fish: 10/treatment Concentrations (nominal): 0.56, 0.75, 1.0, 2.4, 3.2, 4.2, 5.6, 7.5 and 10 g/L, untreated controls (0 g/L) Physical Measurement: The pH, temperature and dissolved were performed at 0 and 24 hr. At 0 and 24 h in control, 0.56, 4.2 and 10 g/L, the ranges for pH was 7.0-7.3; range for dissolved O₂ was 7.0 to 8.9 mg/L; temperature was maintained at 20°C. Observations: Mortality/symptoms at 24 h</p>																						
Result	<p>Nominal test conc.</p> <table border="1" data-bbox="440 590 974 926"> <thead> <tr> <th><u>Loading Level (g/L)</u></th> <th><u>Mortality (24-hr)</u></th> </tr> </thead> <tbody> <tr> <td>0 Control (untreated)</td> <td>0</td> </tr> <tr> <td>0.56</td> <td>0</td> </tr> <tr> <td>0.75</td> <td>0</td> </tr> <tr> <td>1.0</td> <td>0</td> </tr> <tr> <td>2.4</td> <td>10</td> </tr> <tr> <td>3.2</td> <td>20</td> </tr> <tr> <td>4.2</td> <td>0</td> </tr> <tr> <td>5.6</td> <td>90</td> </tr> <tr> <td>7.5</td> <td>100</td> </tr> <tr> <td>10</td> <td>100</td> </tr> </tbody> </table> <p>Observations of symptoms such as darkening of the fish, loss of equilibrium and/or erratic swimming were reported at nominal concentrations 2.4 g/L or higher.</p>	<u>Loading Level (g/L)</u>	<u>Mortality (24-hr)</u>	0 Control (untreated)	0	0.56	0	0.75	0	1.0	0	2.4	10	3.2	20	4.2	0	5.6	90	7.5	100	10	100
<u>Loading Level (g/L)</u>	<u>Mortality (24-hr)</u>																						
0 Control (untreated)	0																						
0.56	0																						
0.75	0																						
1.0	0																						
2.4	10																						
3.2	20																						
4.2	0																						
5.6	90																						
7.5	100																						
10	100																						
Conclusion	<p>24-h LC₅₀ was calculated to be 4.8 g/L or 4800 mg/L using 20% trimmed Spearman-Kärber analysis.</p> <p>No mortality was observed at 1.0 g/L or 1000 mg/L (nominal). Test concentrations were all above the water solubility of the test material (calculated to be 0.34 mg/L, EpiWin). Hence, data indicate that the test material would not be expected to cause acute toxicity in fish at its water saturation limit or water solubility limit (WSL).</p>																						
Remarks	<ol style="list-style-type: none"> 1) There is no information on the homogeneity of the test “solutions” and no analyses were performed to confirm the nominal test concentrations. The mortality found in this study may be related to possible physical effects (sorption of oily substance to the fish). 2) The test duration was only 24 hours. It cannot be excluded that the LC₅₀ after 96 hours may be significantly different from that after 24 hours. The test data reliability was lowered because of this. 3) Reason for lack of mortality in fish at 4.2 g/L nominal concentration was not explained or discussed in report. 4) The test temperature was rather low based on current guidelines (20°C, OECD 203 21-25°C) 																						
Data Quality	<p>Not reliable [Klimisch reliability 3]. Test duration was 24 hr only. Other reasons discussed above.</p>																						
References	<p>Unpublished confidential business information.</p>																						
Other	<p>Date last updated: December 1, 2003.</p>																						

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Acute toxicity to aquatic invertebrate (CAS No. 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanedioyl) ester																						
CAS Number	70729-68-9																						
Remarks	Test material purity was 88% with remainder comprised of 6% triethylene glycol di-n-heptanoate, 4% mixed ester of tetraethylene glycol with n-heptanoic and 2 methylhexanoic acids, 2% other mixed esters.																						
Method/guideline	Not indicated																						
Type (test type)	<i>Daphnia sp.</i> , Acute immobilization test																						
Test System	Freshwater invertebrate																						
GLP	No																						
Year	1981																						
Species/Strain	Freshwater invertebrate, <i>Daphnia magna</i>																						
Analyt. Monitoring	No analyses were performed																						
Exposure period	24 hours																						
Statist. Methods	Probit analysis (Finney, 1971)																						
Remarks on Test Conditions	24-hr static immobilization study Species <i>Daphnia magna</i> , <24 h old Test was performed at 20°C in 250 mL glass beakers containing 200 mL laboratory test water of hardness 104 mg/L (CaCO ₃), 16 h light, unfed No. of daphnids: 10 /replicate, 2 replicates/treatment Physical measurements: At 0 and 24 h in control, 0.56, 4.2 and 10 g/L: range for pH was 6.6-7.5; dissolved O ₂ was less than 60% saturation at 24 hr for the dose levels monitored; temperature was maintained at 20°C. Observations: Immobility and symptoms at 24 hr																						
Results	<p>Nominal test conc.</p> <table border="1"> <thead> <tr> <th><u>Loading Level (g/L)</u></th> <th><u>Immobility % (24-hr)</u></th> </tr> </thead> <tbody> <tr> <td>0 Control (untreated)</td> <td>0 %</td> </tr> <tr> <td>0.56</td> <td>5</td> </tr> <tr> <td>0.75</td> <td>0</td> </tr> <tr> <td>1.0</td> <td>15</td> </tr> <tr> <td>2.4</td> <td>15</td> </tr> <tr> <td>3.2</td> <td>55</td> </tr> <tr> <td>4.2</td> <td>70</td> </tr> <tr> <td>5.6</td> <td>35</td> </tr> <tr> <td>7.5</td> <td>90</td> </tr> <tr> <td>10</td> <td>100</td> </tr> </tbody> </table>	<u>Loading Level (g/L)</u>	<u>Immobility % (24-hr)</u>	0 Control (untreated)	0 %	0.56	5	0.75	0	1.0	15	2.4	15	3.2	55	4.2	70	5.6	35	7.5	90	10	100
<u>Loading Level (g/L)</u>	<u>Immobility % (24-hr)</u>																						
0 Control (untreated)	0 %																						
0.56	5																						
0.75	0																						
1.0	15																						
2.4	15																						
3.2	55																						
4.2	70																						
5.6	35																						
7.5	90																						
10	100																						
Remarks	<p>1) Test concentrations were all above the water solubility of the test material (calculated to be 0.34 mg/L, EpiWin). Hence, data indicate that the test material would not be expected to cause immobilization or adverse effects in daphnids at its water saturation limit or water solubility limit (WSL).</p> <p>2) There is no information on the homogeneity of the test “solutions” and no analyses were performed to confirm the nominal test concentrations.</p> <p>3) The oxygen concentration fell below 60% of saturation during the study. This will most probably affect the study outcome, but is acceptable in a worst case approach</p>																						
Conclusions	24-hr EC ₅₀ was estimated to be 3.8 g/L (or 3800 mg/L) The data would suggest that test substance did not cause immobilization at or close to its water saturation levels or water solubility limits (WSL).																						
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP and there are some issue with dissolved oxygen levels.																						

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

References	Unpublished confidential business information.
Other	Date last updated: December 1, 2003.

Acute toxicity to aquatic plants (e.g., algae) (CAS No, 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanedioyl) ester		
CAS Number	70729-68-9		
Remarks	Test material purity was 88% with remainder comprised of 6% triethylene glycol di-n-heptanoate, 4% mixed ester of tetraethylene glycol with n-heptanoic and 2 methylhexanoic acids, 2% other mixed esters.		
Method/guideline	Not indicated		
Type (test type)	Algae, growth inhibition test 5 day study		
Test System	Aquatic plant (e.g., algae)		
GLP	No		
Year	1981		
Species/Strain	Green algae / <i>Selenastrum capricornutum</i>		
Analyt. Monitoring	No analyses were performed		
Exposure period	120 hours		
Statist. Methods	Not specified		
Remarks on Test Conditions	<p>120 hr static algae growth inhibition study carried out at three concentrations</p> <p>Species: Green algae (<i>Selenastrum capricornutum</i>)</p> <p>Tests were performed in 250 mL flasks containing 50 mL of algal medium (pH 7.1, hardness 18 mg CaCO₃/L); temperature: 24 ± 2°C; continuous illumination (~4300 lux); continuously shaken at 100 rpm</p> <p>Initial Cell Conc.: 1 x 10⁴ cells/mL</p> <p>No. of replicates: 4/treatment</p> <p>Concentrations (nominal): 25, 50, 100 ppm, untreated and vehicle (acetone) controls. The test solutions were prepared using a 20% stock solution (in acetone vehicle) to give the final test concentrations of 25, 50 and 100 ppm. Density of test material reported as 0.996 g/ml</p> <p>Physical Measurements: Not indicated</p> <p>Observations: Cell density at least at 0 and 120 h by electronic particle counting, verified by spot hemacytometer counts (at 0 and 120 h)</p>		
Results	Nominal test conc.	Mean Cell Density	0-120 hr
	<u>Loading Level (ppm)</u>	<u>at 120 hr (10⁴ cells/mL)</u>	<u>Inhibition %</u>
	Control (untreated)	20.7	0
	Control vehicle (acetone)	20.3	1.9
	25	9.3	55.1
	50	5.3	74.4
	100	4.7	77.3
Conclusions	120-hr EC ₅₀ was estimated to be 25 ppm or 25 mg/L.		
Remarks	Test concentrations were all above the water solubility of the test material (calculated to be 0.34 mg/L, EpiWin). The data suggest that test substance would not be expected to cause acute aquatic toxicity at or close to its water saturation levels or water solubility limits (WSL).		
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP. Limited experimental information given in summary report.		
References	Unpublished confidential business information.		
Other	Date last updated: December 1, 2003.		

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Biodegradation (CAS No. 70729-68-9)

Test Substance	Heptanoic acid, oxybis(2,1-ethanedioxy-2,1-ethanediyl) ester																							
CAS Number	70729-68-9																							
Remarks	Purity was 95%																							
Method/guideline	OECD 301E; EEC 79/831																							
Test type	Aerobic Ready Biodegradability, Modified OECD Screening Test (OECD 301E)																							
GLP	Yes																							
Year	1991																							
Test system	Exposure Period: 28 Days Inoculum: Activated sludge Kinetics: Not Reported Monitoring: Dissolved Organic Carbon (DOC)																							
Test Conditions	Test Sample: mineral nutrient soln + inoculum + test material (at DOC of 47.3 mg/L) Positive control: mineral nutrient soln + inoculum + sodium benzoate (at DOC of 20 mg /L) Blank control: mineral nutrient solution + inoculum. The number of replicate flasks was not indicated. Procedure: Aliquots of a stock solution of the test substance (tested concentration 74.9 mg/l providing 47.3 mg DOC/L), inoculum from an treatment plant (secondary effluent) and mineral nutrient solution (1.5 mL) were mixed. Water was added to give a final volume of 1.5 L. The test mixture (it was not indicated that the test was performed in duplicate) was incubated at 22 ± 1 °C for 32 days being shielded from light (initial pH 7.2-7.8 at start of studies). Aeration was accomplished by diffusion facilitated by shaking (120 rpm). Samples were taken on days 0, 7, 14, 21 and 28. For DOC-determination, samples were centrifuged and analyzed in duplicate for TC (total carbon) and IC (inorganic carbon), and the DOC was calculated.																							
Results	<p>Biodegradation Results:</p> <table border="1"> <thead> <tr> <th rowspan="2">Day</th> <th colspan="5">% Biodegradation [% of DOC]</th> </tr> <tr> <th>0</th> <th>7</th> <th>14</th> <th>21</th> <th>28</th> </tr> </thead> <tbody> <tr> <td>Test Substance</td> <td>0</td> <td>49</td> <td>72</td> <td>92</td> <td>98</td> </tr> <tr> <td>Positive Control (sodium benzoate)</td> <td>0</td> <td>91</td> <td>91</td> <td>90</td> <td>100</td> </tr> </tbody> </table>	Day	% Biodegradation [% of DOC]					0	7	14	21	28	Test Substance	0	49	72	92	98	Positive Control (sodium benzoate)	0	91	91	90	100
Day	% Biodegradation [% of DOC]																							
	0	7	14	21	28																			
Test Substance	0	49	72	92	98																			
Positive Control (sodium benzoate)	0	91	91	90	100																			
Conclusions	Biodegradation was 98% in 28 days for the test material.																							
Remarks	<ol style="list-style-type: none"> 1) In the mineral nutrient solution two components were replaced by other components (MnCl₂ instead of MnSO₄; yeast extract instead of vitamin solution). However it is anticipated that this replacement will not influence the results. 2) The DOC of test substance (47 mg DOC/L) slightly exceeded the prescribed amount of 10-40 mg DOC/L. 3) Not enough samples were taken to determine whether the test material met the 10-day window criteria for readily biodegradable classification. 4) The number of replicates used for the test material and positive controls was not indicated. 5) No information on the concentration of secondary effluent was given. 																							
Data Quality	Reliable with restrictions [Klimisch reliability 2]. No information was indicated for number of replicates used in study. See above for other reasons.																							
References	Unpublished confidential business information.																							
Other	Date last updated: December 1, 2003																							

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Acute Oral Toxicity (CAS No. 67989-24-6)

Test Substance CAS Number Remarks	9-Octadecenoic acid (Z)-, ester with 2,2-dimethyl-1,3-propanediol 67989-24-6 Purity not specified. Mixture containing CAS No. 67989-24-6 and CAS No. 70024-57-4 was tested; composition not specified.						
Method/guideline Test type GLP Year	Not indicated Acute oral toxicity No 1976						
Test system	Species (Strain) Rats (strain not specified) Sex: Male rats, weight 205-237 g No. of animals: 5 males/dose group Route: Oral gavage Dosage: Single oral administration (gavage) of 0.464, 1.00, 2.15, 4.64 and 10.0 ml/kg bw; no controls; feeding <i>ad libitum</i> but food was withheld ~18 h prior to dosing. Statist. Methods: Not specified.						
Test conditions	Test material was administered to groups of 5 male rats, fasted for 18 hrs at the six dose concentrations cited above. Observations included: (1) Mortality/clinical signs several times on day 1 and at least once daily for 14 days. (2) body weights on day 1 and 14; (3) necropsy on day 14.						
Results	Dosage Levels						
Endpoint or Effect , Observ.	Day	0.464 ml/kg	1.00 ml/kg	2.15 ml/kg	4.64 ml/kg	10.0 ml/kg	Dose related Effect
Mortality	1-14	None					
Clinical signs ^(A)	1-14	+ + +					x
Body weight gain	1-14	No treatment related effects					
Necropsy	14	No treatment related effects					
Remarks	Abbreviations/footnotes: + = Clinical observations reported were diarrhea, oily rough fur, depression, depressed righting and placement reflexes x = does-related effect observed Other remarks: males/dose group were used instead of 5/sex/dose group. No measurements of body weight were performed on day 7.						
Conclusions	The oral LD50 was > 10 ml/kg.						
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP. Limited report.						
References	Unpublished confidential business information.						
Other	Date last updated: December 1, 2003.						

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Acute fish toxicity (CAS No. 67989-24-6)

Test Substance	9-Octadecenoic acid (Z)-, ester with 2,2-dimethyl-1,3-propanediol															
CAS Number	67989-24-6															
Remarks	Purity not specified. Mixture containing CAS No. 67989-24-6 and CAS No. 70024-57-4 was tested; composition not specified															
Method/guideline	OECD 203 (1981 guidelines)															
Type (test type)	Acute fish toxicity study															
Test System	Fish, freshwater															
GLP	No															
Year	1993															
Species/Strain	Fish: Rainbow trout (<i>Oncorhynchus mykiss</i>)															
Analyt. Monitoring	No analyses were performed.															
Exposure period	96 hours															
Statist. Methods	Trimmed Spearman Karber analysis															
Test Conditions	<p>96 hr static test acute fish toxicity study at five nominal test concentrations</p> <p>Species: Rainbow trout (<i>Oncorhynchus mykiss</i>), length ~50 mm</p> <p>Test was performed in 20 L glass vessels containing 6 L of water (hardness 66-68 mg/L CaCO₃); 15±1°C; 16 h light/8hr dark cycle; unfed; aerated.</p> <p>No. of fish: 10/vessel, 2 vessels/treatment</p> <p>Concentrations (nominal): 40.5, 135, 450, 1500 and 5000 ppm (v/v), untreated controls</p> <p>The test substance (oil) was emulsified using a blender</p> <p>Physical measurements: Daily in all vessels: overall ranges for pH 7.1-7.5; O₂ 60-83%; temperature 14-16°C</p> <p>Observations: Mortality/symptoms at 24, 48, 72 and 96 h</p>															
Results	<p>Nominal test conc.</p> <table border="1"> <thead> <tr> <th><u>Loading Level (ppm, v/v)</u></th> <th><u>Mortality (96-hr)</u></th> </tr> </thead> <tbody> <tr> <td>0 Control (untreated)</td> <td>0</td> </tr> <tr> <td>40.5</td> <td>0</td> </tr> <tr> <td>135</td> <td>0</td> </tr> <tr> <td>450</td> <td>5</td> </tr> <tr> <td>1500</td> <td>20</td> </tr> <tr> <td>5000</td> <td>100</td> </tr> </tbody> </table>		<u>Loading Level (ppm, v/v)</u>	<u>Mortality (96-hr)</u>	0 Control (untreated)	0	40.5	0	135	0	450	5	1500	20	5000	100
<u>Loading Level (ppm, v/v)</u>	<u>Mortality (96-hr)</u>															
0 Control (untreated)	0															
40.5	0															
135	0															
450	5															
1500	20															
5000	100															
Conclusion	<p>The 96-h LC₅₀ was estimated to be 2027 ppm (v/v) (equivalent to ~2000 mg/L if density of ~1.0 was assumed).</p> <p>The 96-h LC₀ was 135 ppm (nominal) in which no mortality was observed. Test concentrations were all above the water solubility of the test material (calculated to be 0.0010 mg/L, EpiWin). Hence, data indicate that the test material would not be expected to cause acute toxicity in fish at its water saturation limit or water solubility limit (WSL).</p>															
Remarks	<p>1) The biological loading was not specified in the report. It is not clear if the biological loading exceeded 1 g fish/L, since a mean weight of 0.6 gram for fish with a length of ~50 mm appears to be rather low.</p> <p>2) Because the test substance is not soluble in water, a suspension of the test substance in water is used. The emulsions were reported to be reasonable stable, but surface pooling was observed.</p>															
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP and for reasons discussed above.															
References	Unpublished confidential business information.															
Other	Date last updated: December 1, 2003.															

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Biodegradation (CAS No. 67989-24-6)

Test Substance	9-Octadecenoic acid (Z)-, ester with 2,2-dimethyl-1,3-propanediol																																																																		
CAS Number	67989-24-6																																																																		
Remarks	Purity not specified. Mixture containing CAS No. 67989-24-6 and CAS No. 70024-57-4 was tested; composition not specified																																																																		
Method/guideline	Modified Sturm Test, 40 CFR 796.3260																																																																		
Test type	Aerobic Ready Biodegradability test (CO ₂ evolution method)																																																																		
GLP	No																																																																		
Year	1992																																																																		
Test system	Exposure Period: 28 Days and extended to 34 Days Inoculum: Activated sludge from municipal sewage wastewater treatment plant Kinetics: Reported																																																																		
Test Conditions	Inoculum: activated sludge from municipal wastewater treatment plant Microbial density was 6.1x 10 ³ CFU/ml; 1 flask Treated [medium + inoculum + test material (7.8 mg C/l)]; 1 flask Treated [medium + inoculum + tewst material (15.6 mg C/l)]; 1 flask Positive Control [medium + inoculum + sodium acetate (20 mg/l acetate)]; 1 flask Blank Control[medium + inoculum] Procedure: Biodegradation experiments were performed in 3L test vessels containing medium solution, test substance and/or inoculum. Inoculum and medium solution were purged with CO ₂ -free air for 24 hours prior to addition of test material. The test system, containing 4 vessels, was carried out for 34 days at 21±2 ⁰ C, under a constant gas flow. The outgoing air from the biodegradation vessels was passed through CO ₂ -traps containing Ba(OH) ₂ solutions. The amount of CO ₂ produced during the course of the test was monitored, days 2, 5, 7, 9, 12, 15, 18, 25, 28 as well as day 30, 32, 34, 37. Biodegradation findings up to day 28 are reported in table below. Concentrations for Test Substance were 7.8 and 15.6 mg C /L Concentration for sodium acetate (positive control) was 20 mg C/L.																																																																		
Results	<p>Biodegradation Results:</p> <table border="1"> <thead> <tr> <th rowspan="2">Day</th> <th colspan="11">% Biodegradation [% of ThCO₂]</th> </tr> <tr> <th>2</th> <th>5</th> <th>7</th> <th>9</th> <th>12</th> <th>15</th> <th>18</th> <th>22</th> <th>25</th> <th>28</th> </tr> </thead> <tbody> <tr> <td>Conc (7.8 mg C/L)</td> <td>5.1</td> <td>23</td> <td>39</td> <td>42</td> <td>49</td> <td>58</td> <td>64</td> <td>68</td> <td>68</td> <td>68</td> </tr> <tr> <td>Conc (15.6 mg C/L)</td> <td>7.2</td> <td>27</td> <td>48</td> <td>53</td> <td>60</td> <td>67</td> <td>72</td> <td>76</td> <td>77</td> <td>78</td> </tr> <tr> <td>Mean Value ==></td> <td>6.2</td> <td>25</td> <td>44</td> <td>48</td> <td>55</td> <td>63</td> <td>68</td> <td>72</td> <td>73</td> <td>73</td> </tr> <tr> <td>Positive Control (sodium acetate)</td> <td>18</td> <td>33</td> <td>46</td> <td>50</td> <td>55</td> <td>67</td> <td>77</td> <td>83</td> <td>85</td> <td>85</td> </tr> </tbody> </table>	Day	% Biodegradation [% of ThCO ₂]											2	5	7	9	12	15	18	22	25	28	Conc (7.8 mg C/L)	5.1	23	39	42	49	58	64	68	68	68	Conc (15.6 mg C/L)	7.2	27	48	53	60	67	72	76	77	78	Mean Value ==>	6.2	25	44	48	55	63	68	72	73	73	Positive Control (sodium acetate)	18	33	46	50	55	67	77	83	85	85
Day	% Biodegradation [% of ThCO ₂]																																																																		
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Mean Value ==>	6.2	25	44	48	55	63	68	72	73	73																																																									
Positive Control (sodium acetate)	18	33	46	50	55	67	77	83	85	85																																																									
Conclusions	Biodegradation occurred to the extent of 73% in 28 days for the test substance (mean of biodegradation at the two tested concentrations). The test substance met the "10-day window" criterion for "readily biodegradable".																																																																		
Remarks	1) Limited report; no information on whether experiments were performed in dark, no information on stirring regime, amount of inoculum; pH, test medium solution, number of absorption bottles and the volume of Ba(OH) ₂ used; the way of determination of CO ₂ -amount in the absorption traps; amount of total CO ₂ evolution in the blank control 2) No replicates for test flasks, positive and for blank control flasks.																																																																		
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP and limited information in report. Number of replicates used.																																																																		
References	Unpublished confidential business information																																																																		

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Other	Date last updated: December 1, 2003
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Melting Point, Boiling Point (CAS No. 627-83-8)

Test Substance	Stearic acid, ethylene ester
CAS Number	627-83-8
Remarks	Purity not specified
Method/guideline	Not specified
Test type	Melting point and boiling point
GLP	Not specified
Year	1997
Remarks	Method of melting point and boiling point determination was not given. Physical chemical properties were cited in Handbook of Chemistry and Physics, 78th ed. (1997)
Conclusions	Melting Point 79 °C Boiling Point 241 °C (20 mm Hg)
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature.
References	CRC Handbook of Chemistry and Physics. D.R. Lide (ed.), 78th Ed., CRC Press Inc., Boca Raton FL, 1997, pg. 3-227, No. 8256.
Other	Date: December 1, 2003.

Acute Oral Toxicity (CAS No. 627-83-8)

Test Substance	Stearic acid, ethylene ester
CAS Number	627-83-8
Remarks	Purity not indicated
Method/guideline	Not indicated
Test type	Acute oral toxicity
GLP	No
Year	1982
Test system	Species (Strain) Rat (strain not specified), weight 220-241 gm Sex: Male No. of animals: 5 Male/treatment Route: Oral gavage (diluted in corn oil 50% w/v) Dosage: 0.464, 1.00, 2.15, 4.64 and 10.0 g/kg
Test conditions/ Results/Remarks	<p>Test substance was administered by oral gavage to male rats at the five dosages described above. Rats were fasted for approx. 18 hrs prior to dosing. Following administration, food and water were available <i>ad libitum</i>. All animals were observed for mortality, and clinical signs of systemic toxicity at frequent intervals during the first day and at least once daily thereafter for 14 days. At the end of the 14 days, animals were sacrificed and gross necropsy performed. Body weight gains were monitored. Statistical method of mortality data was carried out using Weil's moving average method.</p> <p>No mortality was reported at any of the test doses for the test material. No clinical signs or systemic toxicity or gross necropsy or histopathological abnormalities were reported.</p>

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Conclusions	The acute oral LD ₅₀ >10 g/kg
Data Quality	Reliable with restrictions [Klimisch reliability 2]. Not GLP.
References	Confidential business information. These findings have been cited by Elder RL in J. Amer. Coll. Toxicol. 1(2) : 1-11 (1982). Final report on the safety assessment of glycol stearate, glycol stearate SE and glycol distearate.
Other	Date: December 1, 2003.

Acute Oral Toxicity (CAS No. 627-83-8)

Test Substance	Stearic acid, ethylene ester
CAS Number	627-83-8
Remarks	Purity not specified
Method/guideline	Not indicated
Test type	Acute oral toxicity
GLP	No
Year	1982
Test system	Species (Strain) Rat (not specified) Sex: Not specified No. of animals: See below for number of rats used in each of the four studies Route: Oral gavage (undiluted or diluted in corn oil), single dose. Dosage: Dosage ranged from 0.464 g/kg to 16 g/kg.
Test conditions/ Results/Remarks	Elder (1982) has reported following LD50 values from four separate acute oral toxicity studies in rats (single oral dose). 1) LD50 >10 g/kg. Groups of 5 rats/treatment with dosage 0.464 –10 g/kg; diluted 50% corn oil. 2) LD50 >16 g/kg Group of 5 rats/treatment with dosage 0.5 to 16 g/kg , 1:4 dilution in corn oil. 3) LD50 >10 g/kg. Group of 10 rats, oral gavage undiluted at 10 g/kg. 4) LD50 > 5 g/kg. Group of 10 rats, oral gavage undiluted at 5 g/kg Doses at above 13 g/kg b.w. were noted to produce effects which included diarrhea, wet oil coats, nasal hemorrhage; symptoms appeared within 4 days after dosing but disappeared by day 10. No other adverse effects reported.
Conclusions	The acute oral LD ₅₀ was reported to be > 5 g/kg, >16 g/kg, >10 g/kg and >5 g/kg in four oral gavage studies, respectively (see above).
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature.
References	Elder RL (1982). Final report on the safety assessment of glycol stearate, glycol stearate SE and glycol distearate. J. Amer. Coll. Toxicol. 1(2) : 1-11.
Other	Date: December 1, 2003.

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Part II. Surrogate Glycol Esters**Melting Point, Boiling Point, Vapor Pressure,
Partition Coefficient, Water Solubility (CAS No. 71839-38-8)
Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol - Surrogate Glycol Ester**

Test Substance CAS Number Remarks	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol 71839-38-8 Purity was 100%		
	GLP (Yes/No)	METHOD/ GUIDELINE	RESULTS / CONCLUSIONS
Physicochemical Properties			
Melting Point	Yes	OECD 102	< -50 °C
Boiling Point	Yes	OECD 103	> 300 °C
Vapor Pressure	Yes	OECD 104	2.8 x 10 ⁻⁵ Pa at 25 °C
Partition Coeffic.	Yes	OECD 107/117	log P > 6.3 (HPLC method)
Water Solubility	Yes	OECD 105	2.7 mg/L (GC analysis)
Year	1997		
Remarks	Determination of a complete battery of physicochemical properties for the test substance CAS No. 71839-38-8, including those designated above has been carried out under GLP and by methods, which are in compliance with the OECD and EEC Commission Directive 92/69/EEC guidelines. These physicochemical properties determination studies were performed at Huntingdon Life Sciences Ltd., Suffolk, United Kingdom.		
Data Quality	Reliable without restrictions [Klimisch reliability 1].		
References	Unpublished confidential business information.		
Other	Date: December 2, 2003		

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Acute Oral Toxicity CAS No. 71839-38-8)

Test Substance CAS Number Remarks	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol 71839-38-8 Purity was 100%
Method/guideline Test type GLP Year	OECD 401, Commission Directive 92/69/EC, Method B1 Acute oral toxicity test – fixed dose method Yes 1997
Test system	Species (Strain) Rat (CrI:CD-BR) Sex: Male and female: weight: 195-219 g (males), 189-199 g (females) No. of animals: 5 /sex Vehicle: Corn oil Route: Oral gavage Dosage: 2000 mg/kg body weight
Test conditions	Group of five female and five male rats (fasted) were dosed by oral gavage at dose of 2000 mg/kg of body weight as a single dose in corn oil as a vehicle. The animals were observed daily for a period of 14 days for mortality and signs of systemic toxicity. Body weights were measured on Day -1, 1, 8 and 15. The animals were necropsied at the end of the observation period on Day 15.
Results	Oral LD ₅₀ > 2000 mg/kg
Remarks	No mortality was observed in any of the animals. All animals were free of clinical signs of pharmacologic and toxicologic signs throughout the study. No significant macroscopic postmortem abnormalities were noted at necropsy.
Conclusions	The acute oral LD ₅₀ was > 2000 mg/kg in rats.
Data Quality	Reliable without restrictions [Klimisch reliability 1].
References	Unpublished confidential business information.
Other	Date: December 2, 2003

Repeated-Dose Toxicity/Reproductive Toxicity (CAS No. 71839-38-8)

Test Substance CAS Number Remarks	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol 71839-38-8 Purity was 100%
Method/guideline Test type GLP Year	OECD 407 Repeated 28 day Oral Toxicity 28-Day Oral Toxicity Study Yes 1997
Species/strain Route of Administ. Duration of test No. of animals Dose/Conc. Levels	Rats / CrI:CD-BR Oral gavage, administered in corn oil vehicle 28 days 30 /sex (see below for sex/dose group) 0, 30, 180, and 1000 mg/kg/day

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Sex Frequency of treatment Control Group	Male and female, ~ 8 weeks-old, weight: 262-335 g (males); 200-237 g (females) Daily oral gavage for 28 days 10/sex
Test System/Dose Group	Set of five female and five male rats from control group (Group 1) and from high dose group (Group 4)(1000 mg/kg) will be retained after the 28 day treatment phase for 14 day recovery period (see below).
Statist. Methods	ANOVA, ANCOVA, two-way ANOVA test for variance, Kruski-Wallis non-parametric, Wilcoxon rank-sum test, Terpstra-Jonckheere test, Dunnett's test, Levene's test.
Test Conditions	The test substance was administered orally (gavage) to Crl:CD-BR rats for 28 consecutive days at dose levels of 0, 30, 180 and 1000 mg/kg body weight. Group 1 consisted of 10 males and 10 females that were treated with vehicle alone (corn oil) and served as the control group. A set of 5 males and 5 females from Group 1 were retained after the 28-day treatment phase for a 14-day recovery period (i.e., treatment-free period). Group 2 (low dose) and Group 3 (intermediate dose) consisted of 5 males and 5 females per group, were administered 30 and 180 mg/kg/dose, respectively. Group 4 (high dose) consisted of 10 males and 10 females that were administered 1000 mg/kg/dose of the test substance. A set of 5 males and 5 females from Group 4 were also retained after the 28-day treatment phase for a 14-day recovery period. After 28-days of treatment, 40 animals (5/sex/group) were euthanized and subjected to necropsy. After a recovery period of 2 weeks, the remaining 20 animals (5/sex from the control and high-dose groups) were euthanized. Histopathological evaluation of selected tissues from the 4-week high dose (1000 mg/kg/day) and control animals was performed.
Post-exposure observat./ Remarks	Mortality, clinical observations, signs of ill health, behavioral changes or overt toxicity, body weights and food consumption were carried out. Hematology, coagulation, clinical chemistry and bone marrow smears were performed. A complete necropsy was performed after 28 days for designated groups or at the end of the 14 day recovery period as described above. Organ weights were recorded and tissues collected, fixed, prepared, sectioned and stained for histopathology examination. Tissues examined microscopically also included testes, epididymides, ovaries and uterus.
Results/Remarks	<p>Oral (gavage) administration of the test substance to Crl:CD-BR rats at dose levels up to 1000 mg/kg/day for 28 days, produced no mortality and no clinical signs of systemic toxicity during the test. All groups of treated females gained less body weight than controls. There was no indication of an effect on male body weight. There were no differences in the group mean food consumption.</p> <p>Hematological parameters after 4 weeks of treatment revealed platelet counts for females at the nominal dose levels of 30, 180 or 1000 mg/kg/day to be slightly lower than those of the controls but this is considered to be of doubtful biological significance.</p> <p>Clinical chemistry parameters revealed glucose levels for high dose animals and females receiving 180 mg/kg/day to be lower than that of the controls. After the 14-day recovery, glucose levels were increased for the high dose animals.</p> <p>Liver weights were higher for the high dose animals than controls at the end of the treatment and recovery periods. This is believed to be a metabolic change associated with the metabolism of the test material and not toxicity as such. The NOEL for this change is 180 mg/kg/day.</p> <p>There was no macroscopic evidence of toxicity for the test material. Microscopically, there was a treatment-related increase in hyaline droplets and tubular basophilia in the kidneys of high dose males. The NOEL was established at 180 mg/kg/day. Partial reversal of these findings was observed in the 14-day recovery animals. Hyaline droplet nephropathy is a male rat-specific condition, which is of little relevance to risk assessment in humans.</p>

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Conclusions	<p>1) The no-observed effect level (NOEL) was 180 mg/kg/day based on liver weight changes and hyaline droplet formation in male rats.</p> <p>2) Doses up to 1000 mg/kg/day were well-tolerated in animals with no mortality or clinical signs of toxicity.</p> <p>3) After 28 days of repeated dose exposure to up to 1000 mg/kg/day, there was no indication that the test material adversely affected the reproductive organs in male and female rats. No histopathological or gross abnormalities were reported for testes, epididymides and ovaries.</p>
Data Quality	Reliable without restrictions [Klimisch reliability 1]
References	Unpublished confidential business information. Study was GLP and met requirements of the OECD 407 guidelines.
Other	Date: December 2, 2003.

Genetic Toxicity In Vitro (CAS No. 71839-38-8)

Test Substance CAS Number Remarks	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol 71839-38-8 Purity was 100%
Method/guideline Type of Study Test System GLP Year	OECD 471 (1997 Guideline) Bacterial Reverse Mutation Assay Bacterial (<i>Salmonella</i> - <i>Escherichia coli</i>) Yes 1997
Species/Strain	<i>Salmonella typhimurium</i> / TA1535, TA1537, TA1538, TA98, TA100 and <i>Escherichia coli</i> / WP2uvrA
Metab. Activation Concentrations Statist. Methods	Aroclor 1254-induced rat liver preparations (S9 mixture) 10, 33, 100, 333, and 1000 µg/plate of the test material (solubilized in DMSO) Not specified but positive controls were run concurrently with test substance.
Test Conditions/ Remarks	Concurrent positive control materials were 2-nitrofluorene, sodium azide, 2-aminoanthracene, 9-aminoacridine for the <i>Salmonella</i> tester strains; and methane methanesulfonate and 2-aminonanthracene for the <i>E. coli</i> strain. DMSO was used a vehicle (negative) control.
Results	The test substance was negative for mutagenic activity in the five <i>Salmonella</i> tester strains and in the <i>E. coli</i> strain, with or without metabolic activation. No mutagenic activity was observed at concentrations ranging from 10µg/plate to the highest concentration of 1000 µg/plate. The bacterial strains tested included <i>Salmonella typhimurium</i> strains TA1535, TA1537, TA 1538, TA98; TA100 and <i>Escherichia coli</i> strain WP2uvrA. The positive controls gave the appropriate responses as expected.
Conclusions	The test substance was <u>not</u> mutagenic, with or without metabolic activation in the <i>Salmonella-Escherichia coli</i> / Mammalian Microsome Reverse Mutation assay.
Data Quality	Reliable without restrictions [Klimisch reliability 1].
References	Unpublished confidential business information.
Other	Date: December 2, 2003.

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Genetic Toxicity In Vitro (CAS No. 71839-38-8)

Test Substance CAS Number Remarks	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol 71839-38-8 Purity was 100%
Method/guideline Type of Study Test System GLP Year	OECD 473 In Vitro Mammalian Chromosomal Aberration Test In vitro human lymphocyte cytogenetic system Yes 1997
Species/ cell type Metab. activation Concentrations Statist. Methods	Human lymphocyte in whole blood culture Arochlor 1254-induced rat liver S9 mixture (Sprague Dawley rat) 157, 313, 625, 1250, 2500, and 5000 µg/ml (vehicle used was ethanol) Fisher's test
Test Conditions /Remarks	<p>Study was carried out to assess the ability of test substance to induce chromosomal aberrations in human lymphocytes cultured in vitro. Human lymphocytes in whole blood culture were stimulated to divide by addition of phytohemagglutinin and exposed to the test substance both in the presence and absence of S-9 mix derived from rat liver (Arochlor 1254-induced S-D rat). Solvent and positive control cultures were also prepared. Two hours before the end of the incubation period, cell division was arrested with Colomid, the cells harvested and slides prepared so that the metaphase cells could be examined for chromosomal damage. The mitotic index was calculated for all cultures treated with the test substance and the solvent control. On the basis of these data, the following concentrations were selected for metaphase analysis:</p> <ol style="list-style-type: none"> 1) 625, 1250, 2500 and 5000 µg/ml dose levels were selected for microscopic analysis in the 20 and 44 hr harvest without S9 2) 625, 1250, 2500 and 5000 µg/ml dose levels were selected for microscopic analysis in the 4 hr exposure with S9 <p>Positive controls used were mitomycin C (in absence of S9 mix) and cyclophosphamide (in presence of S9 mix).</p>
Results/Remarks	<ol style="list-style-type: none"> 1) In both the absence and presence of S9 mix, the test substance caused no statistically significant increase in the proportion of metaphase figures containing chromosomal aberrations, at any dose level, when compared with the solvent control. 2) No toxicity (as measured by mitotic inhibition) was observed in doses as high as 5000 µg/ml in both non-activated and S9-activated studies. No statistically significant increases in structural chromosome aberrations were observed with or without S9 metabolic activation, regardless of dose level or harvest time. No statistically significant increases in numerical chromosome observed were observed at the 44-hr harvest time in either the non-activated or S9-activated studies, regardless of dose level. 3) The positive, untreated and solvent controls gave the expected responses to fulfill the requirements of a valid test. Positive controls gave statistically significant increases in the proportion of aberrant cells, demonstrating the sensitivity of the test system and the efficacy of the S9 mix.
Conclusions	The test material is <u>not</u> clastogenic in the <i>in vitro</i> human lymphocyte cytogenetics test system, with or without metabolic activation. Regardless of dose level (as high as 5000 µg/ml) and dosing regimen, the test substance was concluded to be negative for structural and numerical chromosome aberrations, with or without S-9.
Data Quality	Reliable without restrictions [Klimisch reliability 1].
References	Unpublished confidential business information.

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Other	Date: December 2, 2003.
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Acute fish toxicity (CAS No. 71839-38-8)

Test Substance	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol	
CAS Number	71839-38-8	
Remarks	Purity was 100%	
Method/guideline	OECD 203	
Type (test type)	96-hr Acute Fish Toxicity	
Test System	Fish, freshwater	
GLP	Yes	
Year	1998	
Species/Strain	Fish: Rainbow trout (<i>Oncorhynchus mykiss</i>), length 47 mm (mean), weight 1.06 g (mean)	
Analyt. Monitoring	GC-FID analysis of test substance in control group medium solution and in five dose level test medium solutions	
Exposure period	96 hours	
Statist. Methods	Not spec	
Remarks on Test Conditions	<p>96-hr static test (mechanically stirred dispersion of test material) at five concentrations</p> <p>Test was performed in glass aquarium capable of holding 24 L of dechlorinated laboratory tap water, charcoal filtered, hardness ~58 mg/L CaCO₃; 14.0-15.1°C, aerated.</p> <p>No. of fish: 20/treatment, 20 for control</p> <p>Concentrations: control (0 mg/L , untreated) and 63, 125, 250, 500 and 1000 mg/L (nominal loading rate)</p> <p>Observations for mortality, abnormal behavior, and treatment-related effects were performed at 1, 24, 48, 72 and 96 hrs. Daily physical measurement of pH, dissolved oxygen and temperature was carried out. The pH was 6.9 to 7.5, dissolved oxygen was 86-100% of saturation, temperature was 14.0 - 15.1 °C, total hardness was ~58 mg/L as CaCO₃. Light 16 hr/dark 8 hr cycle was maintained.</p>	
Results/Remarks	<u>Nominal test conc. (mg/L)</u>	<u>Mortality (96h)</u>
	0 (Untreated controls)	0 %
	63 mg/L	0 %
	125 mg/L	0 %
	250 mg/L	0 %
	500 mg/L	0 %
	1000 mg/L	0 %
Remarks	Fish were exposed to test material concentrations of 63, 125, 250, 500 and 1000 mg/L which were maintained as distributions of small droplets using shielded propeller stirrers to give a mechanical dispersion of the test material. Test solutions were not renewed during course of the study. No mortality, abnormal behavioral or treatment-related effects were reported at any of the tested concentrations. GC analysis of test solutions indicated that the test material was present in the water.	
Conclusions	96-hr LC ₅₀ >1000 mg/L (nominal loading rate). Analytical data indicated the presence of test material at the water solubility limit (~2.7 mg/L) or higher. No mortality was observed at any of the exposure doses including the highest tested nominal concentration of 1000 mg/L. Hence, the test substance did not cause mortality at or above its water solubility or water saturated level (~2.7 mg/L).	
Data Quality	Reliable without restrictions [Klimisch reliability 1].	

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References	Unpublished confidential business information.
Other	Date: December 2, 2003.

Acute toxicity to aquatic invertebrate (CAS No. 71839-38-8)

Test Substance	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol															
CAS Number	71839-38-8															
Remarks	Purity was 100%															
Method/guideline	OECD 202															
Type (test type)	<i>Daphnia sp.</i> , Acute immobilization test															
Test System	Freshwater invertebrate															
GLP	Yes															
Year	1998															
Species/Strain	Freshwater invertebrate, <i>Daphnia magna</i> , <24 hr-old															
Analyt. Monitoring	GC-FID analysis of test substance in control and WAF solutions generated from nominal loading rate of 125, 250, 500, 1000 and 2000 mg/L.															
Exposure period	48 hours															
Statist. Methods	Not specified															
Remarks on Test Conditions	<p>48-hr static test without renewal of test solution media. Test was performed in glass containers with 125 ml of the WAF solutions or dilution water (untreated controls) at 19.3-19.5 °C.</p> <p>No. of daphnids: 20/treatment, 20/control.</p> <p>Concentrations: Water accommodated fraction (WAF) generated at 125, 250, 500, 1000 and 2000 mg/L (nominal loading rate) and control (0 mg/L, untreated).</p> <p>Observations for immobilized daphnids were performed after 24 and 48 hr. Daily physical measurements of pH, dissolved oxygen and temperature were carried out. The pH was 7.8 to 8.0, dissolved oxygen was 100% of saturation and temperature was 19.3- 19.5 °C during the study. A light 16 hr/dark 8 hr cycle was maintained.</p> <p>The WAF solution was prepared by stirring test material (five nominal loading rate as cited above) in dilution water for approximately 20 hours and allowing mixture to settle for 4 hours before the aqueous WAF solution was taken for study.</p>															
Results	<table border="1"> <thead> <tr> <th><u>Nominal test conc. (mg/L)</u></th> <th><u>% Immobilized (48h)</u></th> </tr> </thead> <tbody> <tr> <td>0 (Untreated controls)</td> <td>0 %</td> </tr> <tr> <td>125 mg/L WAF</td> <td>0 %</td> </tr> <tr> <td>250 mg/L WAF</td> <td>0 %</td> </tr> <tr> <td>500 mg/L WAF</td> <td>0 %</td> </tr> <tr> <td>1000 mg/L WAF</td> <td>0 %</td> </tr> <tr> <td>2000 mg/L WAF</td> <td>0 %</td> </tr> </tbody> </table>	<u>Nominal test conc. (mg/L)</u>	<u>% Immobilized (48h)</u>	0 (Untreated controls)	0 %	125 mg/L WAF	0 %	250 mg/L WAF	0 %	500 mg/L WAF	0 %	1000 mg/L WAF	0 %	2000 mg/L WAF	0 %	
<u>Nominal test conc. (mg/L)</u>	<u>% Immobilized (48h)</u>															
0 (Untreated controls)	0 %															
125 mg/L WAF	0 %															
250 mg/L WAF	0 %															
500 mg/L WAF	0 %															
1000 mg/L WAF	0 %															
2000 mg/L WAF	0 %															
Remarks	<p>No immobilization and no adverse effects on the daphnids were observed during this study, even at the highest WAF solution (nominal load rate 2000 mg/L).</p> <p>The analytical results (GC-FID) indicated that concentrations of the test substance in the test WAF solutions were in the range of 0.3 to 6.9 mg/L.</p>															
Conclusions	<p>48-hr EC₅₀ >2000 mg/L (WAF, nominal loading rate). Analytical data (GC-FID) indicated presence of test material in WAF solutions, albeit relatively low measured concentrations, which were close or slightly above its water solubility limit (WSL) or water saturated levels. Data would suggest that test substance did not cause immobilization at or close to its water saturation limit.</p>															

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Data Quality	Reliable without restrictions [Klimisch reliability 1].
References	Unpublished confidential business information.
Other	Date: December 2, 2003.

Acute toxicity to aquatic plants (e.g., algae) (CAS No. 71839-38-8)

Test Substance CAS Number Remarks	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol 71839-38-8 Purity was 100%
Method/guideline Type (test type) Test System GLP Year	OECD 201 Algae, growth inhibition test Aquatic plant (e.g., algae) Yes 1998
Species/Strain Analyt. Monitoring Exposure period Statist. Methods	Algae / <i>Raphidocelis subcapitata</i> GC-FID analysis of test substance in WAF solutions 72 hours Dunnett's test
Remarks on Test Conditions	72-hr static algae study exposed to water accommodated fractions (WAFs) in 250 mL loosely cotton-plugged flasks containing 100 mL of algal medium (pH 7.6-7.9) test WAF solutions or control solutions; temperature: 22.3-25.3°C; continuous illumination (8220-8310 lux); continuously shaken at 100 rpm. Initial cell conc: 1×10^4 cells/ml in controls No. of replicates: 4 replicates/treatment, 7 replicates/control. 1 replicate flask for water quality measurements Concentrations: Water accommodated fraction (WAF) generated at 125, 250, 500, 1000 and 2000 mg/L nominal loading rate and untreated controls (0 mg/L). Observations: Cell density determined at 0, 24, 48 and 72 hr by counting with an improved Neubauer hemacytometer and light microscope. Measurement of pH: pH 7.6-7.7 at 0 hr and pH 7.8-7.9 at 72 hr
Results	In this study, a series of five WAF solutions were prepared by the direct addition of test material to algal nutrient medium to provide the nominal loading rate as summarized above. The WAFs were stirred for approximately 20 hours and allowed to for approx. 4 hours before the final WAF solution was taken for use in the study. Sufficient algal inocula were added to give an initial cell density of 1×10^4 cells/ml in each test flask or control flask. GC-FID analysis of WAF and control samples indicated that the presence of the test material in samples of the test algal culture at 0 hrs and at 72 hours. Analytical results indicate that measured concentrations at 72 hr ranged from 1.4 to 4.3 mg/L, which are below or close to the water-solubility limit of the test material.
Conclusion	72-hr EC ₅₀ >2000 mg/L (WAF, nominal loading rate) based on both area under the growth curves and specific growth rates. Compared to controlled cultures, neither the areas under the growth curves nor the growth rates were significantly reduced by the test substance, even at the highest nominal loading rate (2000 mg/L). The NOEL (no-observed effect loading rate) was >2000 mg/L based on both area under the curves and specific growth rates. No inhibition of algal growth was observed with any of the WAF solutions of the test material. Data suggest that test substance would not be expected to inhibit algal growth at its

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

	water saturation limit.
Data Quality	Reliable without restrictions [Klimisch reliability 1].
References	Unpublished confidential business information.
Other	Date: December 2, 2003.

Biodegradation (CAS No. 71839-38-8)

Test Substance CAS Number Remarks	Heptanoic acid, ester with 2,2,4-trimethyl-1,3-propanediol 71839-38-8 Purity was 100%																																
Method/guideline Test type GLP Year	OECD 301B Modified Sturm Aerobic Ready Biodegradability test (CO ₂ evolution method) Yes 1997																																
Test system	Exposure Period: 28 Days Inoculum: Activated sludge from municipal sewage treatment plant Kinetics: Not Reported																																
Test Conditions	Inoculum: activated sludge from domestic wastewater treatment plant. Sufficient inoculum (34.6 ml) to provide final 30 mg suspended solids/L medium. Blank control [medium + inoculum] (n=2) Positive control [medium + inoculum + sodium benzoate (20.02 mg C/L)] (n=2) Treated [medium + inoculum + test material (21.93 mg C/L)]. (n=2) Medium was buffered mineral medium solution (initial pH 7.5) as outline in OECD 301B guidelines. Biodegradation experiments were performed in the dark under continuous stirring in 4 L glass vessels. The inoculum and medium (3 L) were pre-acclimated during 24 hours, and subsequently treated and aerated for 28 days at 23-24°C with CO ₂ -free air. The outflowing air from the biodegradation vessel was passed through 3 consecutive CO ₂ -traps containing 100 ml 0.0125 M Ba(OH) ₂ . The amount of CO ₂ was determined in the traps by back-titrating with standardized 0.05M HCl at various time intervals (duplicate determinations). Traps were taken on day 1, 3, 6, 10, 14, 21 and 28. The pH was measured on day 28 in the individual vessels and was found to range from 7.4 to 7.5. Concentrations for Test Substance was 21.93 mg C /L for test substance. Concentration for sodium benzoate (positive control) was 20.02 mg C/L.																																
Results	Biodegradation occurred to the extent of 87.3% in 28 days for the test substance. The test substance <u>did not</u> meet the “10-day window” criterion for “readily biodegradable”. Positive controls (sodium benzoate) achieved 85.6% biodegradation in 28 days and met the readily biodegradable classification. Biodegradation values were corrected for background CO ₂ with blank controls. Biodegradation Results: <table border="1"> <thead> <tr> <th></th> <th colspan="7">% Biodegradation [% of ThCO₂]</th> </tr> <tr> <th>Day</th> <th>1</th> <th>3</th> <th>6</th> <th>10</th> <th>14</th> <th>21</th> <th>28</th> </tr> </thead> <tbody> <tr> <td>Test Substance</td> <td>0.0</td> <td>4.7</td> <td>22.9</td> <td>41.6</td> <td>59.6</td> <td>74.1</td> <td>87.3</td> </tr> <tr> <td>Positive Control (sodium benzoate)</td> <td>7.8</td> <td>27.6</td> <td>47.7</td> <td>67.5</td> <td>77.6</td> <td>82.3</td> <td>85.6</td> </tr> </tbody> </table> From the biodegradation time plot, the test material was estimated to reach the 10% biodegradation mark on Day 3.87 and 10 days later, on Day 13.87, the biodegradation was 59.0%.		% Biodegradation [% of ThCO ₂]							Day	1	3	6	10	14	21	28	Test Substance	0.0	4.7	22.9	41.6	59.6	74.1	87.3	Positive Control (sodium benzoate)	7.8	27.6	47.7	67.5	77.6	82.3	85.6
	% Biodegradation [% of ThCO ₂]																																
Day	1	3	6	10	14	21	28																										
Test Substance	0.0	4.7	22.9	41.6	59.6	74.1	87.3																										
Positive Control (sodium benzoate)	7.8	27.6	47.7	67.5	77.6	82.3	85.6																										

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Conclusions	The test substance was biodegraded to the extent of 87.3% in 28 days but did not meet the 10-day window criterion required for "readily biodegradable" classification. Sodium benzoate (positive control) was found to be readily biodegradable and was biodegraded to the extent of 85.6% in 28 days.
Data Quality	Reliable without restrictions [Klimisch reliability 1].
References	Unpublished confidential business information
Other	Date: December 2, 2003

Melting Point, Boiling Point, Water Solubility (CAS No. 7434-40-4)

Test Substance	Triethylene glycol, diheptanoate
CAS Number	7434-40-4
Remarks	Purity not specified
Method/guideline	Not specified
Test type	Melting point, boiling point and water solubility
GLP	Not specified
Year	1996
Remarks	Method of melting point, boiling point and water solubility determination was not given. Physical chemical properties were cited in IUCLID datasheet for CAS No. 7434-40-4.
Conclusions	Melting Point -24 °C Boiling Point Not determined, decomposes at > 250°C Water solubility ca. 30 mg/L
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature. Limited experimental information given. Cited in IUCLID dataset for CAS No. 7434-40-4. Data were unpublished proprietary information reported by business company to ECB for inclusion into IUCLID database.
References	IUCLID (1996). ECB Existing Chemicals Datasheet for Ethane-1,2-diylbis(oxyethane-2,1-diyl) bisheptanoate, CAS No. 7434-40-4. 14 pages. October 23, 1995. Information from IUCLID CD-ROM (version 1996).
Other	Date: December 2, 2003

Genetic Toxicity In vitro (CAS No. 7434-40-4)

Test Substance	Triethylene glycol, diheptanoate
CAS Number	7434-40-4
Remarks	Purity not specified
Method/guideline	Directive 84/449/EEC, B.14
Type of Study	Ames <i>Salmonella typhimurium</i> Reverse Mutation Assay
Test System	Bacterial
GLP	Yes
Year	1979

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Species/Strain	<i>Salmonella typhimurium</i> /TA98, TA100, TA1535, TA1537, TA1538
Metab. Activation	Yes. Metabolic activation system used in Ames assay but specific information not given
Concentrations	Range from 0 to 5000 µg/plate.
Statist. Methods	Not specified
Remarks on Test Conditions	Limited experimental information given but Ames assay was performed with and without metabolic activation.
Conclusions	The test substance was <u>negative</u> in the strains tested. No mutagenic activity was reported over a dose range from 0 to 5000 µg/plate, with or without metabolic activation.
Data Quality	Not assignable [Klimisch reliability 4]. Limited experimental information given. Cited in IUCLID dataset for CAS No. 7434-40-4. Data were unpublished proprietary information reported by business company to ECB for inclusion into IUCLID database.
References	IUCLID (1996). ECB Existing Chemicals Datasheet for Ethane-1,2-diylbis(oxyethane-2,1-diyl) bisheptanoate, CAS No. 7434-40-4. 14 pages. October 23, 1995. Information from IUCLID CD-ROM (version 1996).
Other	Date: December 2, 2003

Acute fish toxicity (CAS No. 7434-40-4)

Test Substance	Triethylene glycol, diheptanoate
CAS Number	7434-40-4
Remarks	Purity not specified
Method/guideline	DIN 38412, Part 15
Type (test type)	48-hr Acute Fish Toxicity
Test System	Fish, freshwater
GLP	No
Year	1989
Species/Strain	Fish: Golden orfe (<i>Leuciscus idus</i>)
Analyt. Monitoring	Not indicated.
Exposure period	48 hours
Statist. Methods	Not specified
Remarks on Test Conditions	Limited experimental information given. Test material was tested with and without emulsifier, Marlowet EF.
Result/Conclusion	No mortality was observed at concentrations up to the water solubility limit or up to 1000 mg/L (with emulsifier).
Conclusions	48-hr LC50 was reported to be greater than water solubility limit (WSL). Water solubility of test material was reported to be ~30 mg/L in the IUCLID database. With emulsifier, 48-hr LC50 was greater than 1000 mg/L. Hence, the data indicate that the test substance did not cause mortality in fish at or close to its water saturation levels or water solubility limits (WSL).
Data Quality	Not assignable [Klimisch reliability 4]. Limited experimental information given. Cited in IUCLID dataset for CAS No. 7434-40-4. Data were unpublished proprietary information reported by business company to ECB for inclusion into IUCLID database.
References	IUCLID (1996). ECB Existing Chemicals Datasheet for Ethane-1,2-diylbis(oxyethane-2,1-diyl) bisheptanoate, CAS No. 7434-40-4. 14 pages. October 23, 1995. Information from IUCLID CD-ROM (version 1996).

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

Other	Date: December 3, 2003
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Acute toxicity to aquatic invertebrate (CAS No. 7434-40-4)

Test Substance	Triethylene glycol, diheptanoate
CAS Number	7434-40-4
Remarks	Purity not indicated
Method/guideline	Directive 84/449/EEC, C.2 (Acute toxicity for Daphnia test)
Type (test type)	Daphnia sp. Acute immobilization test .
Test System	Freshwater invertebrate
GLP	Yes
Year	1984
Species/Strain	Freshwater invertebrate, <i>Daphnia magna</i>
Analyt. Monitoring	Not indicated
Exposure period	48 hours
Statist. Methods	Not specified
Remarks on Test Conditions	Limited experimental information given. An emulsifier (ethoxylated castor oil [40 EO] was added (90 mg/L) to test solution to help solubilize the test material.
Result/Conclusion	48-hr EC ₅₀ was reported to be 9.1 mg/L as cited in IUCLID dataset (1996) 48-hr EC ₀ was cited as 2.5 mg/L. The 24-hr EC ₅₀ was 24.3 mg/L.
Data Quality	Not assignable [Klimisch reliability 4]. Limited experimental information given. Cited in IUCLID dataset for CAS No. 7434-40-4. Data were unpublished proprietary information reported by business company to ECB for inclusion into IUCLID database.
References	IUCLID (1996). ECB Existing Chemicals Datasheet for Ethane-1,2-diylbis(oxyethane-2,1-diyl) bisheptanoate, CAS No. 7434-40-4. 14 pages. October 23, 1995. Information from IUCLID CD-ROM (version 1996).
Other	Date: December 3, 2003

Acute toxicity to aquatic plants (e.g., algae) (CAS No. 7434-40-4)

Test Substance	Triethylene glycol, diheptanoate
CAS Number	7434-40-4
Remarks	Purity not indicated
Method/guideline	Other, 88/302/EWG
Type (test type)	Algae, growth inhibition test
Test System	Aquatic plant (e.g., algae)
GLP	Yes
Year	Not specified
Species/Strain	Algae / <i>Scenedesmus subspicatus</i>
Analyt. Monitoring	Not indicated
Exposure period	72 hours
Statist. Methods	Not specified
Remarks on Test Conditions	Limited experimental information given. Biomass and growth rate were the toxicity endpoints monitored for algae growth inhibition.

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Results/ Conclusions	72-hr EC ₅₀ was reported to be 559 mg/L (biomass) and >712 mg/L (growth rate) as cited in IUCLID dataset (1996). The EC ₁₀ was cited as 253 mg/L and 318 mg/L, for biomass and growth rate, respectively. Data would suggest that test substance did not cause algae growth inhibition at or close to its water saturation levels or water solubility limits (WSL).
Data Quality	Not assignable [Klimisch reliability 4]. Limited experimental information given. Cited in IUCLID dataset for CAS No. 7434-40-4. Data were unpublished proprietary information reported by business company to ECB for inclusion into IUCLID database.
References	IUCLID (1996). ECB Existing Chemicals Datasheet for Ethane-1,2-diylbis(oxyethane-2,1-diyl) bisheptanoate, CAS No. 7434-40-4. 14 pages. October 23, 1995. Information from IUCLID CD-ROM (version 1996).
Other	Date: December 3, 2003

Biodegradation (CAS No. 7434-40-4)

Test Substance CAS Number Remarks	Triethylene glycol, diheptanoate 7434-40-4 Purity not specified
Method/guideline Test type GLP Year	OECD 301B Closed Bottle Test Aerobic Ready Biodegradability test Yes 1981
Test system	Exposure Period: 28 Days Inoculum: Predominantly domestic sewage Kinetics: Not Reported Monitoring: CO ₂ evolution
Test Conditions	Limited experimental information on aerobic biodegradation study was given.
Results/ Conclusions	Biodegradation was reported to be 65% in 28 days. Information regarding positive controls and blanks was not reported. No data given on whether test material met readily biodegradable classification.
Data Quality	Not assignable [Klimisch reliability 4]. Cited in IUCLID dataset for CAS No. 7434-40-4
References	IUCLID (1996). ECB Existing Chemicals Datasheet for Ethane-1,2-diylbis(oxyethane-2,1-diyl) bisheptanoate, CAS No. 7434-40-4. 14 pages. October 23, 1995. Information from IUCLID CD-ROM (version 1996).
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Acute Oral Toxicity (CAS No. 1323-39-3)

Test Substance CAS Number Remarks	Propylene glycol, monostearate 1323-39-3 Purity not specified
Method/guideline Test type GLP Year	Not indicated Acute oral toxicity Not specified Not specified
Test system	Species (Strain) Rat (strain not specified) Sex: Not specified No. of animals: 5 rats/treatment dose Route: Oral Gavage Dosage: 1.0, 2.0, 4.0, 8.0, 16.0, 20.0 25.0 and 32.0 g/kg
Test conditions	Remarks: Test material was administered by oral gavage to group of 5 rats per each of the eight dose levels. The animals were fasted overnight and administered a single oral dose of the test material by gastric intubation. Animals were observed for mortality and clinical signs daily for 14-day period. Statistical methods were not specified.
Results/Remarks	Elder (1983) reported that the acute oral LD ₅₀ was 25.8 g/kg. No effects were reported for the 1.0 and 2.0 g/kg dose group of animals. Animals in the 4.0 and 8.0 g/kg dose groups were observed to have unkempt coats for 12-16 hrs. Lethargy, staggering gait, impaired locomotion and unkempt coats were seen in animals of the 16.0, 20.0, 25.0 and 32.0 g/kg dose groups. Two animals died on day 2 at 25.0 g/kg and all five animals died on day 1 at 32.0 g/kg. Survivors at 25.0 g/kg appeared normal by day 4.
Conclusions	The acute oral LD ₅₀ was 25.8 g/kg for propylene glycol monostearate.
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature. Limited experimental information.
References	1) Elder RL (1983). Final report on the safety assessment of propylene glycol stearate and propylene glycol stearate self-emulsifying. J. Amer. Coll. Toxicol. 2(5) : 101-123. 2) Andersen FA (1999). Final report on the safety assessment of propylene glycol (PG) dicaprylate, PG dicaprylate/dicaprate, PG dicocoate, PG dipelargonate, PG isostearate, PG laurate, PG myristate, PG oleate, PG oleate SE, PG dioleate, PG dicaprate, PG diisostearate and PG dilaurate. Internat. J. Toxicol. 18 (Suppl. 2) : 35-52.
Other	Date: December 3, 2003

Repeated-Dose Toxicity (CAS No. 1323-39-3)

Test Substance CAS Number Remarks	Propylene glycol, monostearate 1323-39-3 Purity not specified. Propylene glycol stearate comprised 17% of a propylene glycol ester mixture which also contained 50% stearyl propylene glycol hydrogen succinate and lesser amounts of other propylene glycol derivatives.
Method/guideline Test type GLP Year	Not specified Six month oral feeding toxicity study Not indicated Not indicated

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Species/strain	Rats / Strain not indicated
Route of Administ.	Diet containing 2.5%, 5% and 10% propylene glycol ester mixture (containing 17% propylene glycol stearate).
Duration of test	Six months
No. of animals	30 rats, 10 per group
Dose/Conc. Levels	0.425%, 0.85% and 1.7% propylene glycol stearate in diet
Sex	Not specified
Frequency of treatment	Daily administration in diet
Control Group	Not specified
Post-exposure observat.	Limited experimental information was specified in secondary literature. Gross and histopathological observations were performed.
Statist. Methods	Not specified.
Results/Conclusions	Elder (1983) and Andersen (1999) reported that rats feed for 6 months on diets containing up to 1.7% of propylene glycol stearate (highest dose level) showed no evidence of gross or histological pathology. The same mixture containing 17% propylene glycol stearate was fed at levels of 5% and 10% in the diet to groups of four dogs for six months did not produced any reported signs of toxicity.
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature.
References	1) Elder RL (1983). Final report on the safety assessment of propylene glycol stearate and propylene glycol stearate self-emulsifying. J. Amer. Coll. Toxicol. 2(5) : 101-123. 2) Andersen FA (1999). Final report on the safety assessment of propylene glycol (PG) dicaprylate, PG dicaprylate/dicaprate, PG dicocoate, PG dipelargonate, PG isostearate, PG laurate, PG myristate, PG oleate, PG oleate SE, PG dioleate, PG dicaprate, PG diisostearate and PG dilaurate. Internat. J. Toxicol. 18 (Suppl. 2) : 35-52.
Other	Date: December 3, 2003.

Repeated-Dose Toxicity/Reproductive Toxicity (CAS No. 1323-39-3)

Test Substance	Propylene glycol, monostearate
CAS Number	1323-39-3
Remarks	Purity not specified for propylene glycol stearate
Method/guideline	Not specified
Test type	13 week oral feeding toxicity study
GLP	Not indicated
Year	Not indicated
Species/strain	Rats / Strain not indicated
Route of Administ.	Diet containing 0%, 1.5%, 3.36% or 7.52% propylene glycol stearate and supplemented with additional mono- and diglycerides if necessary to bring total fat content to 7.52%.
Duration of test	13 weeks
No. of animals	Groups of 48 rats
Dose/Conc. Levels	0%, 1.5%, 3.36% or 7.52% propylene glycol stearate in diet
Sex	Not specified
Frequency of treatment	Daily administration in diet for 13 weeks
Control Group	Yes, control group of animals
Post-exposure observat.	Limited experimental information was specified but it appears that mortality, clinical signs, body weight gain, hematology, clinical chemistry, urinalysis, coagulation, necropsy, organ weights, gross and histopathology were performed.
Statist. Methods	Not specified.

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Results/Conclusions	Elder (1983) reported that rats feed diet containing 1.5%, 3.36% or 7.52% of test material for 13 weeks showed no significant differences (compared to controls) with respect to growth, relative organ weights (e.g., adrenals, gonads, heart, kidneys, liver, spleen, brain), histopathology, blood glucose, BUN, plasma cholesterol, plasma glutamate pyruvate transaminase, hemoglobin, hematocrit, white cell count, white cell differential count, clotting times or urinalysis. Repeated dose oral exposure did not show signs of systemic toxicity in rats and has not been reported to adversely affect the reproductive organs in rats.
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature.
References	Elder RL (1983). Final report on the safety assessment of propylene glycol stearate and propylene glycol stearate self-emulsifying. J. Amer. Coll. Toxicol. 2(5) : 101-123.
Other	Date: December 3, 2003.

Genetic Toxicity In vitro (CAS No. 1323-39-3)

Test Substance	Propylene glycol, monostearate
CAS Number	1323-39-3
Remarks	Purity not specified for propylene glycol stearate
Method/guideline	Not specified
Type of Study	Ames <i>Salmonella</i> - <i>Saccharomyces</i> Reverse Mutation Assay
Test System	Bacterial
GLP	Not specified
Year	1975
Species/Strain	<i>Salmonella typhimurium</i> / TA1535, TA 1537, TA 1538 <i>Saccharomyces cerevisiae</i> (strain D4)
Metab. Activation	Yes. Metabolic activation system used but specific information not given.
Concentrations	Not indicated
Statist. Methods	Not specified
Remarks on Test Conditions	Limited experimental information given but study presumably followed reverse mutation assay procedures, with and without metabolic activation.
Conclusions	Elder (1983) and Litton Bionetics (1975) reported that the test substance was negative for mutagenic activity in the <i>Salmonella typhimurium</i> and <i>Saccharomyces cerevisiae</i> (strain D4) mutation assays, with and without metabolic activation.
Data Quality	Not assignable [Klimisch reliability 4]. Secondary literature. Limited information and experimental details.
References	1) Elder RL (1983). Final report on the safety assessment of propylene glycol stearate and propylene glycol stearate self-emulsifying. J. Amer. Coll. Toxicol. 2(5) : 101-123. 2) Litton Bionetics (1975). Mutagenic evaluation of compound FDA 73-57, propylene glycol monostearate. U.S. NTIS PB-245 499
Other	Date: December 3, 2003.

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Acute Oral Toxicity (CAS No. 22788-19-8)

Test Substance	Propylene glycol dilaurate
CAS Number	22788-19-8
Remarks	Purity not specified
Method/guideline	Not indicated
Test type	Acute oral toxicity
GLP	Not indicated
Year	Not indicated
Test system	Species (Strain) Rat (not specified) Sex: Not specified No. of animals: Not specified Route: Oral gavage Dosage: Not specified
Remarks	Acute oral toxicity studies have not been reported for propylene glycol dilaurate. However, Andersen (1999) has reported that the rat oral LD50 value was greater than 34.6 g/kg for propylene glycol laurate (CAS 142-55-2) which is the corresponding propylene glycol monolaurate ester.
Conclusions	Based on structural similarity of the dilaurate ester to the corresponding monolaurate and the fact that the dilaurate is higher in molecular weight and probably similarly or less likely to be absorbed orally than the monolaurate, it would not be unexpected for the dilaurate ester to have a similar oral LD50 value to that for the monolaurate. Hence, the likely oral LD50 for propylene glycol dilaurate is estimated to be ≥ 34.6 g/kg, based on "read-across" data for the corresponding monolaurate ester.
Data Quality	Not assignable [Klimisch reliability 4]. Rat oral LD50 value based "read-across" data reported for propylene glycol monolaurate ester. Secondary literature.
References	Andersen FA (1999). Final report on the safety assessment of propylene glycol (PG) dicaprylate, PG dicaprylate/dicaprate, PG dicocoate, PG dipelargonate, PG isostearate, PG laurate, PG myristate, PG oleate, PG oleate SE, PG dioleate, PG dicaprate, PG diisostearate and PG dilaurate. Internat. J. Toxicol. 18 (Suppl. 2) : 35-52.
Other	Date: December 3, 2003

Acute Oral Toxicity (CAS No. 68958-54-3)

Test Substance	Propylene glycol diisostearate
CAS Number	68958-54-3
Remarks	Purity not specified
Method/guideline	Not indicated
Test type	Acute oral toxicity
GLP	Not indicated
Year	Not indicated
Test system	Species (Strain) Rat (not specified) Sex: Not specified No. of animals: Not specified Route: Oral gavage

Appendix -Robust Summaries for Aliphatic Esters - Glycol Esters HPV Test Plan

<p>Remarks</p> <p>Conclusions</p> <p>Data Quality</p> <p>References</p> <p>Other</p>	<p>Dosage: Not specified</p> <p>Acute oral toxicity studies have not been reported for propylene glycol diisostearate. However, Elder (1983) has reported that the rat oral LD50 value was 25.8 g/kg for propylene glycol stearate (CAS 1323-39-3) which is the corresponding propylene glycol monostearate ester.</p> <p>Based on carbon number (C18) structural similarity of the diisostearate ester to the corresponding monostearate (C18) and the fact that the diisostearate is higher in molecular weight and probably similarly or less likely to be absorbed orally than the monostearate, it would not be unexpected for the diisostearate ester to have a similar oral LD50 value to that for the monostearate. Hence, likely oral LD50 for propylene glycol diisostearate is estimated to be 25.8 g/kg, based on "read-across" data for the corresponding monostearate ester. See robust summary for CAS No. 1323-39-3 (propylene glycol monostearate) within this appendix.</p> <p>Not assignable [Klimisch reliability 4]. Rat oral LD50 value based "read-across" data reported for propylene glycol monostearate. Secondary literature.</p> <p>Elder RL (1983). Final report on the safety assessment of propylene glycol stearate and propylene glycol stearate self-emulsifying. J. Amer. Coll. Toxicol. 2(5): 101-123.</p> <p>Date: December 3, 2003</p>
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