File No: STD/1400

March 2013

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in Aeroshell Ascender

This Assessment has been compiled in accordance with the provisions of the Industrial Chemicals (Notification and Assessment) Act 1989 (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health and Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of Sustainability, Environment, Water, Population and Communities.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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SUMMARY

The following details will be published in the NICNAS Chemical Gazette:

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1400	Shell Company of Australia Ltd.	Chemical in Aeroshell Ascender	No	≤ 200 tonnes per annum	Component of engine oil for aviation applications

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS), as adopted for industrial chemicals in Australia, or the Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004).

Human health risk assessment
Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment
On the basis of the assessed use pattern and limited exposure to the aquatic compartment, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES
Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced:
  - Exhaust ventilation if mists or aerosols are generated

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced:
  - Avoid generation of mists or aerosols
  - Avoid eye contact

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  - impervious gloves
  - goggles
  - protective coveralls

Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- A copy of the (M)SDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS), as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

- The notified chemical should be disposed of in accordance with local regulations for recycling, re-use or recovery of calorific content.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the Industrial Chemicals (Notification and Assessment) Act (1989) the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of engine oils for aviation applications, or is likely to change significantly;
  - the amount of chemical being introduced has increased from 200 tonnes per annum, or is likely to increase, significantly;
  - the chemical has begun to be manufactured in Australia;
  - additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

No additional secondary notification conditions are stipulated.

(Material) Safety Data Sheet
The (M)SDSs of the notified chemical and products containing the notified chemical, provided by the notifier, were reviewed by NICNAS. The accuracy of the information on the (M)SDSs remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Shell Company of Australia Ltd (ABN 46 004 610 459)
Level 2, 8 Redfern Road
HAWTHORN EAST VIC 3123

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
No details are claimed exempt from publication.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU (2010)
USA (2003)

2. IDENTITY OF CHEMICAL

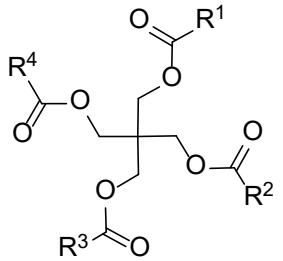
MARKETING NAME(S)
Hatcol 1760 (notified chemical)
Aeroshell Ascender (ingredient of imported product)

CAS NUMBER
156558-98-4

CHEMICAL NAME
Fatty acids, C6-12, mixed tetraesters with heptanoic acid, pentaerythritol, 3,5,5-trimethylhexanoic acid and valeric acid

MOLECULAR FORMULA
Unspecified

STRUCTURAL FORMULA



where R_1, R_2, R_3 and R_4 = any of

$-(CH_2)_nCH_3$ (n = 5-12); or
$-CH_2CH(CH_3)CH_2C(CH_3)_3$

MOLECULAR WEIGHT
Ranging from 472-808 Da

ANALYTICAL DATA
Reference 1H and 13C NMR, IR, GC-MS, HPLC and UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY 99.2%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS None

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% BY WEIGHT)

Chemical Name Partial esters of pentaerythritol
CAS No. Weight % 1

ADDITIVES/ADJUVANTS None

4. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20 ºC and 101.3 kPa: Clear viscous liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	< -20 oC	Measured
Boiling Point	406.0 ± 0.5 oC at 104.54 kPa	Measured
Density	984 kg/m3 at 20 oC	Measured
Vapour Pressure	1.3 × 10-11 kPa at 25 oC	Measured
Water Solubility	< 1.86 × 10-5 g/L at 20 oC	Measured
Hydrolysis as a Function of pH	t1/2 = 96.8 to 360 days at pH 8 t1/2 = 2.65 to 9.85 years at pH 7	Estimated for representative components of the notified chemical (HYDROWIN v1.67) The notified chemical contains hydrolysable functionality however due to its low solubility, it is expected to hydrolyse slowly at environmental pH (4-9).
Partition Coefficient (n-octanol/water)	log Pow > 6.50 at 20 oC	Measured
Adsorption/Desorption	Log Koc > 5.63 at 40 oC	Measured
Dissociation Constant	Not determined	The notified chemical contains no dissociable functional groups
Flash Point	228 ± 2 oC at 101.5 kPa	Measured
Flammability	Not expected to be flammable	Based on measured flash point.
Autoignition Temperature	392 ± 5 oC	Measured
Explosive Properties	Not expected to be explosive	The structure formula contains no explosophers.
Oxidising Properties	Not expected to oxidise	Contains no functional groups that would imply oxidative properties.

Discussion of Properties
For full details of tests on physical and chemical properties, refer to Appendix A.

Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS), as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be introduced as a component of engine oils at concentrations of 90-98%.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	20	50	100	100	< 200

PORT OF ENTRY
Port of Brisbane

IDENTITY OF MANUFACTURER/RECIPIENTS
Recipients are located throughout Australia and include various commercial and military airports.

TRANSPORTATION AND PACKAGING
The finished engine oils containing the notified chemical at 90-98% will be imported in 1 L cans, 20 L drums or 205 L barrels, and transported throughout Australia by road, rail or aircraft.

USE
Component of engine oil for aviation applications

OPERATION DESCRIPTION
The method of decanting the finished engine oils containing the notified chemical at 90-98% concentration will depend on the size of containers and volumes to be transferred. It is expected that larger containers will be manually decanted into 1 L containers for subsequent addition to the aircraft. The 1 L containers will be opened by the aircraft engineer and the finished engine oil will be manually decanted directly into the aircraft.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

Exposure Details
Transport and storage workers may come into contact with the finished engine oils containing the notified chemical at concentrations of 90-98% only in the event of accidental rupture of containers.

Dermal or possibly ocular exposure may occur to the notified chemical at concentrations of 90-98% when aircraft engineers open the containers and manually decant the finished engine oil into the aircraft. Inhalation exposure is not expected given the low vapour pressure of the notified chemical, unless aerosols or mists are generated. Exposure is expected to be minimised through the use of personal protective equipment (PPE) such as coveralls, eye protection and impervious gloves.

Exposure to flight crew is not anticipated except in the unlikely event of an accident where products containing the notified chemical leak into the flight deck and passenger cabin of aircraft.

6.1.2. Public Exposure
The finished engine oils containing the notified chemical (90-98% concentration) are intended for use solely by trained personnel working for commercial and military airlines. The public will not have access to the areas of airports where the engine oils will be used. Exposure to the public is not anticipated except in the unlikely event of an accident where engine oil containing the notified chemical leaks into the passenger cabin of aircraft.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation
Rat, combined repeat dose and reproductive /developmental oral toxicity – 42 days	NOAEL = 250 mg/kg bw/day (repeated dose) = 1000 mg/kg bw/day (reproductive /developmental)
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosome aberration study	non-genotoxic
Genotoxicity – mammalian cell gene mutation assay	non-genotoxic

Toxicokinetics, metabolism and distribution.
No data were available to assess toxicokinetics, metabolism and distribution of the notified chemical. Dermal absorption is expected to be limited by the high log Kow of the notified chemical (>6.5).

Acute toxicity.
The acute oral LD50 was > 2000 mg/kg bw in rats; the notified chemical was considered to be of low toxicity. Acute inhalation and acute dermal toxicity studies were not submitted on the notified chemical. Acute dermal toxicity LD50 was > 2000 mg/kg bw, reported for an analogue chemical (data from MSDS).

Irritation and Sensitisation.
In a skin irritation study in rabbits, the notified chemical was non-irritating to the skin. The notified chemical was slightly irritating to the eye of the rabbit but does not meet the threshold for GHS classification. It was not a skin sensitiser in a local lymph node assay (LLNA).

Repeated Dose Toxicity.
In a 42/54-day combined repeat dose and reproductive/developmental gavage study in rats the NOAEL for repeated dose effects was established as 250 mg/kg bw/day based on histopathological changes in males and females in the high dose group (1000 mg/kg bw/day). Effects seen in male rat kidneys at all dose levels were considered to be α2-microglobulin nephropathy, which is specific to male rats and not considered to be relevant to humans (Alden, 1986).

Mutagenicity.
The notified chemical was found to be negative in a bacterial reverse mutation test. There was no evidence of clastogenicity in a Mammalian Chromosome Aberration Test using Chinese Hamster Lung (CHL) Cells and a Mammalian Cell Gene Mutation test using a Mouse Lymphoma Cell line. Based on these studies, the notified chemical is not expected to be genotoxic.

Toxicity to reproduction
During the combined repeated dose and reproductive/developmental toxicity study, no adverse reproductive or developmental outcomes were noted; the NOAEL for these endpoints was set at 1000 mg/kg bw/day.

Health hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS), as adopted for industrial chemicals in Australia, or the Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

Based on the toxicity data provided the notified chemical may cause slight eye irritation but is not considered a skin irritant or skin sensitiser. Workers at risk of exposure include transportation and warehouse workers, those involved with decanting the finished engine oils containing the notified chemical (90-98%) into smaller containers, and aircraft maintenance workers decanting the oil into the aircraft. The product containing the notified chemical is opened using a device which prevents contamination of the formulated product or splashing. The potential for exposure is greatest during end use where the finished engine oil containing the notified chemical (90-98%) will primarily be manually poured from containers into the engines. Exposure is most likely to occur via the dermal route although ocular and inhalation exposure during oil decanting and aircraft engine maintenance activities is also possible.

Potential dermal and ocular exposure would be minimised by use of personal protective equipment (PPE) such as impervious gloves, goggles and protective coveralls when handling products containing the notified chemical. Exposure to mists or aerosols, if generated, would be controlled by use of local exhaust ventilation. The risk to workers is not considered to be unreasonable provided the above controls are in place.

6.3.2. Public Health

The risk to the public from the notified chemical is not considered to be unreasonable, based on very low potential for exposure, as finished engine oils (90-98% notified chemical) are intended solely for use by trained personnel working for commercial and military airlines.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be manufactured, formulated and packaged into end-use containers overseas. There will be no environmental release of the chemical during these stages of the notified chemical's lifecycle.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be imported as a formulation in 1 L cans, 20 L drums or 205 L barrels and decanted directly into aircraft by a commercial or military aircraft engineer. Empty containers containing the residue of the notified chemical are expected to be recycled by accredited waste management companies or disposed of according to local regulations. Environmental release is therefore expected to be limited to rare occasions of accidental spillage during transport and use. If spillage occurs, the notified chemical is expected to be contained and absorbed using an absorbent material and disposed of according to Local/State/Territory regulations, most likely to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

Empty containers containing the residue of the notified chemical will be recycled by accredited waste management companies or disposed of according to local regulations. Used oils containing the notified chemical will most likely be recycled, thermally decomposed during use or disposed of in landfill in accordance with Local/State/Territory government regulations. If recycled, oils containing the notified chemical are likely to be used as low grade burner fuels.

7.1.2. Environmental Fate

The majority of the notified chemical will be thermally decomposed during use or recycling of waste oil products, and is expected to form water and oxides of carbon. The notified chemical is not readily biodegradable (59% biodegradation after 28 days). However the notified chemical is expected to undergo primary degradation as testing showed that transformation products are formed leaving no detectable notified chemical within 28 days. The notified chemical is not expected to be released to the aquatic environment. If any notified chemical is released to soil or landfill, it is expected to associate strongly with organic matter in soil and remain in situ based on its very low water solubility, and high affinity for organic phases with a high n-octanol/water partition coefficient (log Pow > 6) and high adsorption/desorption coefficient (log Koc > 5). The notified chemical and its transformation products are expected to degrade via biotic and abiotic processes to form simple organic compounds, water and oxides of carbon. Details of the environmental fate studies are in Appendix C.

The notified chemical may bioaccumulate based on its low water solubility and high n-octanol/water partition coefficient (Pow). The notified chemical's potential to biodegrade, although not sufficient to be classified as ready biodegradable, combined with negligible aquatic exposure suggests that it has a low potential for bioaccumulation.

7.1.3. Predicted Environmental Concentration (PEC)

Exposure to the aquatic compartment is not expected during the use and disposal of the notified chemical. It is therefore not possible to calculate a predicted environmental concentration (PEC).

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical using a water accommodated fraction (WAF) are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Acute		
Fish Toxicity (96 hour)	LL50 >100 mg/L (WAF)	Not Harmful
Daphnia Toxicity (48 hour)	EL50 >100 mg/L (WAF)	Not Harmful
Algal Toxicity (72 hour)	ErLR50 >100 mg/L (WAF)	Not Harmful
	NOEL >100 mg/L (WAF)	Not harmful
Inhibition of Bacterial Respiration	EL50 >100 mg/L	Not expected to be inhibitory to microbial activity

The notified chemical is not expected to be acutely harmful to aquatic life, nor harmful to aquatic life with long lasting effects, up to the level of its solubility. Therefore, the notified chemical is not formally classified for acute or long-term hazard under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration (PNEC)

Usually, the endpoint for the most sensitive species from the reported results is used to calculate the predicted no-effect concentration (PNEC), however no adverse effects were observed for any of the submitted ecotoxicity tests. Due to the very low solubility of the notified chemical, the PNEC will be much greater than the notified chemical's worst case aquatic concentration based on its water solubility.

7.3. Environmental Risk Assessment

Based on the lack of aquatic exposure, the potential to biodegrade, the absence of any observed adverse ecotoxicological effects and the proposed use, the notified chemical is not expected to pose an unreasonable risk to the environment.

Appendix A: Physical and Chemical Properties

Melting Point/Freezing Point < -20 oC

METHOD EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks Determined by Differential Scanning Calorimetry.
TEST FACILITY Safepharm (2008a)

Boiling Point 406 oC at 104.54 kPa

METHOD EC Directive 92/69/EEC A.2 Boiling Point.
Remarks Determined by Differential Scanning Calorimetry. The test material was determined to partially boil with decomposition from 406 ± 0.5 oC at 104.54 kPa given a yellow liquid residue remained at the end of the test.
TEST FACILITY Safepharm (2008a)

Density 984 kg/m3 at 20 oC

METHOD EC Directive 92/69/EEC A.3 Relative Density.
Remarks Pycnometer method.
TEST FACILITY Safepharm (2008a)

Vapour Pressure 1.33 × 10-11 kPa at 25 oC

METHOD EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Determined using vapour pressure balance.
TEST FACILITY Safepharm (2008b)

Water Solubility < 1.86 × 10-5 g/L at 20 oC

METHOD EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Flask Method/Analytical Method: GC-MS
TEST FACILITY Safepharm (2008a)

Hydrolysis as a Function of pH Not determined

METHOD EC Directive 92/69/EEC C.7 Hydrolysis as a function of pH.
OECD TG 111 Hydrolysis as a function of pH
Remarks The test was not carried out as the notified chemical is a complex mixture with low water solubility.
HYDROWIN v1.67 was used to estimate the half-life of the test material. Results are reported in the table below. Calculated estimates are based on four of the same alkyl chains per component.

Pentaerythritol tetra-ester component with:-	Estimated half-life at 25 oC pH 7	pH 8
4 × n-pentanoic acid	2.65 years	96.8 days
4 × 3,5,5-trimethylhexanoic acid	9.85 years	360 days
4 × n-decanoic acid	5.83 years	213 days

The notified chemical contains hydrolysable functionality and is expected to eventually hydrolyse at environmental pH (4-9).

TEST FACILITY Safepharm (2008c)

Partition Coefficient (n-octanol/water) log Pow > 6.50 at 20 oC

METHOD EC Directive 92/69/EEC A.8 Partition Coefficient.
Remarks HPLC Method
TEST FACILITY Safepharm (2008a)

Adsorption/Desorption – screening test log Koc > 5.63 at 40 °C

METHOD EC Directive 2001/59/EC C.19 Adsorption Coefficient.
Remarks HPLC Screening method
TEST FACILITY Safepharm (2008a)

Flash Point 228 ± 2 oC at 101.5 kPa

METHOD EC Directive 92/69/EEC A.9 Flash Point.
Remarks Closed cup
TEST FACILITY Safepharm (2008b)

Autoignition Temperature 392 ± 5 oC

METHOD EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
TEST FACILITY Safepharm (2008b)

Explosive Properties

METHOD EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks Based on the chemical structure and oxygen balance the notified chemical was predicted not to have explosive properties.
TEST FACILITY Safepharm (2008b)

Oxidizing Properties

METHOD EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Remarks Based on the chemical structure the notified chemical was predicted not to have oxidising properties.
TEST FACILITY Safepharm (2008b)

Appendix B: Toxicological Investigations

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 420 Acute Oral Toxicity – "Acute Oral Toxicity - Fixed Dose Method". Method B1 bis Acute Toxicity (Oral) of Commission Directive 2004/73/EC.
Species/Strain	Rat/Sprague Dawley CD strain
Vehicle	None
Remarks - Method	

RESULTS

Sighting Study

Dose Mg/kg bw	*Number and Sex of Animals*	*Evident Toxicity*	*Mortality*
2000	1 female	No effects seen	None

Signs of Toxicity	No signs of systemic toxicity.
Effects in Organs	No effects seen at necropsy.

Main Study

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
2000 mg/kg	4 females	2000	None

Signs of Toxicity	No signs of systemic toxicity.
Effects in Organs	No effects seen at necropsy.
Remarks - Results	

CONCLUSION	The notified chemical was of low acute toxicity via oral administration.
TEST FACILITY	Safepharm (2008d)

B.2. Irritation – skin

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	After the exposure period, residual test material was removed from the skin with cotton wool soaked in distilled water.

RESULTS

Remarks - Results	The scores for erythema/eschar and oedema were zero at all observations.
CONCLUSION	The notified chemical is non-irritating to the skin.
TEST FACILITY	Safepharm (2008e)

B.3. Irritation – eye

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Observation Period	72 hours
Remarks - Method	A single application of the test material to the non-irrigated eye of three rabbits.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.33	0.33	0.33	1	24 hours	0
Conjunctiva: chemosis	0.33	0.33	0.33	1	24 hours	0
Conjunctiva: discharge	0.33	0.33	0.33	1	24 hours	0
Corneal opacity	0	0	0	0	No effects seen	0
Iridial inflammation	0	0	0	0	No effects seen	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results: A single application of the test material to the non-irrigated eye of three rabbits produced moderate conjunctival irritation one hour after treatement. All treated eyes appeared normal by the 48-hour observation

CONCLUSION: The notified chemical is slightly irritating to the eye.

TEST FACILITY: Safepharm (2008f)

B.4. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
EC Directive 2004/73/EC B.42 Skin Sensitisation (Local Lymph Node Assay)

Species/Strain	Mouse/CBA/Ca strain
Vehicle	acetone/olive oil 4:1
Remarks - Method	Concentrations were chosen on the basis of a preliminary screening test.

RESULTS

Concentration (% v/v in acetone/olive oil 4:1)	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance		
0 (vehicle control)	976.59 (± 196.39)	N/A
25	1453.95 (± 401.66)	1.49
50	1253.70 (± 451.10)	1.28
100	1679.04 (± 736.95)	1.72
Positive Control		
15	Not reported	10.91

Remarks - Results: No adverse clinical signs or variations in body weight gain were seen in the test animals. The test material was considered to be a non-sensitiser under the conditions of the test. The results of the positive control (non-

	concurrent) confirmed the adequacy of the test.
CONCLUSION	There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.
TEST FACILITY	Safepharm (2008j)

B.5. Repeat dose toxicity

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test.
Species/Strain	Rat/Wistar Han™: HsdRccHan™: WIST strain
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: ≥ 42 days, up to 54 days Dose regimen: 7 days per week Post-exposure observation period: 14 days
Vehicle	Arachis Oil BP
Remarks - Method	Doses for the main study were chosen on the basis of a 14-day preliminary study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	10 males and 10 females	0	None treatment related
low dose	10 males and 10 females	50	None treatment related
mid dose	10 males and 10 females	250	None treatment related
high dose	10 males and 10 females	1000	None treatment related
control recovery	5 males and 5 females	Just vehicle	None treatment related
high dose recovery	5 males and 5 females	1000	None treatment related

Mortality and Time to Death

There were no treatment-related unscheduled deaths during the study.

Clinical Observations

No toxicologically significant clinical signs were evident in terminal kill animals throughout the study.

Laboratory Findings – Clinical Chemistry, Haematology and Urinalysis

No toxicologically significant clinical signs were evident in terminal kill animals and the haematological parameters measured throughout the study. No treatment-related effect was detected in the urinalytical parameters measured.

Effects in Organs

Adrenal Gland: Hypertrophy of the zona glomerulosa was seen in relation to treatment for males only at all treatment levels. The effects were minimal for the low and mid doses, and slight at the high dose. The changes may be adaptive in nature as they reversed in recovery high dose animals following an additional 14 days without treatment. The study authors suggested that the changes may be associated with renal changes (see below), however there is no evidence to confirm this.

Thyroid: Follicular cell hypertrophy was seen in relation to treatment for males treated with 1000 mg/kg/day, but not convincingly at any other treatment level. Females were not similarly affected. There was no difference in incidence or severity of the condition between recovery high dose and recovery control animals following completion of the recovery period.

Thymus: Lymphoid atrophy was observed in high dose females but not at any other treatment level. Males were not similarly affected. The condition was observed to have regressed among recovery group animals following completion of an additional fourteen days without treatment.

Kidneys: Renal changes characterised by globular accumulations of eosinophilic material, tubular basophilia/degeneration, and tubular necrosis, were seen among high dose males only. Globular accumulations of eosinophilic material were also seen in mid dose and low dose males, with tubular necrosis in a few mid dose males. Similar accumulations were also demonstrated by examination of Mallory's Heidenhain stained sections of kidney which assists in the diagnosis of, but which is not diagnostic for alpha-2-Microglobulin. There was regression of globular accumulations of eosinophilic material among recovery high dose males following completion of the 14-day recovery period although residual tubular necrosis remained in four animals, possibly with an associated higher incidence/severity of isolated groups of basophilic tubules.

Liver: Centrilobular hepatocyte enlargement was seen in high dose males, but reversed in the recovery group. Periportal hepatocyte enlargement was seen in high dose recovery males. High dose male and female animals showed increased relative liver weight at the end of dosing, that was not evident in the high dose recovery groups.

Reproductive/developmental Toxicity

No significant changes were noted in reproductive performance, pregnancy or offspring. The offspring body weight gain was slightly reduced from high dose litters, but was considered to be a minor effect.

Remarks – Results

The No Observed Effect Level (NOAEL) for females was established as 250 mg/kg bw/day in this study, based on lymphoid atrophy in the thymus at 1000 mg/kg bw/day.

Histopathological effects were seen in the kidneys of males in all treatment groups and a NOAEL could not be determined for these effects. However the kidney changes identified were consistent with well documented changes that are sex and species specific to the male rat in response to treatment with some hydrocarbons, and are not expected to have human relevance. These effects have been excluded from determination of the NOAEL in male rats. A NOAEL of 250 mg/kg bw/day for males was established at 250 mg/kg bw/day based on the other histopathological effects seen in males at 1000 mg/kg bw/day.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) for repeated dose effects was established as 250 mg/kg bw/day in this study, based on histopathological effects observed in high dose (1000 mg/kg bw/day) animals. The NOAEL for reproductive and developmental outcomes was considered to be 1000 mg/kg bw/day, the highest dose tested.

TEST FACILITY Harlan (2009)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified Chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure
Species/Strain	S. typhimurium: TA1535, TA1537, TA98, TA100 E. coli: WP2uvrA
Metabolic Activation System	Phenobarbitone /β-naphthoflavone induced rat liver S9 mix
Concentration Range in Main Test	a) With metabolic activation: 50 to 5000 µg/plate b) Without metabolic activation: 50 to 5000 µg/plate
Vehicle	Tetrahydrofuran
Physical Form	Slightly viscous liquid
Remarks - Method	Dose levels were chosen on the basis of a preliminary test with two strains.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	>5000		≥ 1500	Negative
Test 2		>5000	≥ 1500	Negative
Present				
Test 1	> 5000		≥ 1500	
Test 2		≥ 1500 µg/plate	> 1500	Negative

Remarks - Results: Precipitate or slight toxicity were noted in some strains and dose levels but did not interfere with scoring. The positive and negative controls confirmed the sensitivity of the test.

CONCLUSION: The notified chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY: SafePharm (2008g)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE: Notified Chemical

METHOD: OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
EC Directive 2000/32/EC B.10 Mutagenicity - In vitro Mammalian Chromosome Aberration Test.

Species/Strain: Hamster
Cell Type/Cell Line: Chinese Hamster Lung (CHL) cell line
Metabolic Activation System: Phenobarbital/beta-naphthoflavone induced, rat liver S9
Vehicle: Acetone
Remarks - Method: Doses were chosen on the basis of precipitation seen in a preliminary cell growth inhibition test.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	78.13, 156.25, 312.5, 625*, 1250*, 2500*	6	24
Test 2	78.13, 156.25, 312.5*, 625*, 1250*, 2500*	24	24
Present			
Test 1	78.13, 156.25, 312.5, 625*, 1250*, 2500	6	24
Test 2	78.13, 156.25, 312.5*, 625*, 1250*, 2500*	6	24

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	No reported effects	> 2500	≥ 78.13	Negative
Test 2			> 156.25	Negative
Present				
Test 1	No reported effects	> 2500	> 156.25	Negative
Test 2			> 156.25	Negative

Remarks - Results: The maximum dose level selected for the main experiments was based on the results of the preliminary study, and was limited to the 2500 µg/ml

dose level for all the exposure groups. The maximum recommended dose of 5000 µg/ml was excluded from the dose range as it was considered to form a precipitate which prevented the cells being exposed fully to the test material.

The test material did not induce any statistically significant increases in the frequency of cells with aberrations in any of the exposure groups. The dose levels of the test material showed some evidence of toxicity to CHL cells in vitro

CONCLUSION The notified chemical was not clastogenic to CHL cells treated in vitro under the conditions of the test.

TEST FACILITY SafePharm (2008h)

B.8. Genotoxicity – in vitro

TEST SUBSTANCE Notified Chemical

METHOD OECD TG 476 In vitro Mammalian Cell Gene Mutation Test.
Species/Strain Mouse
Cell Type/Cell Line Mouse Lymphoma L5178Y TK+/- 3.7.2c cell line
Metabolic Activation System Phenobarbital/beta-naphthoflavone induced, rat liver S9
Vehicle Acetone
Remarks - Method A preliminary toxicity test was performed. The 4-hour exposure with metabolic activation was not repeated. The study authors stated that the justification for this omission was the concurrent chromosome aberration study, also carried out on the notified chemical.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	78.13, 156.25, 312.5, 625, 937.5 and 1250 µg/mL	4 hours	48 hours	14 days
Test 2	78.13, 156.25, 312.5, 625, 937.5 and 1250 µg/mL	24 hours	48 hours	14 days
Present				
Test 1	78.13, 156.25, 312.5, 625, 937.5 and 1250 µg/mL	4 hours	48 hours	14 days

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	None	None	> 1250	None
Test 2	None	None	> 1250	None
Present				
Test 1	None	None	> 1250	None
Test 2	None	None	> 1250	None

Remarks – Results The maximum dose level was limited to 1250 µg/mL due to the onset of an oily precipitate. Whilst precipitate was observed at the end of the exposure periods of the mutagenicity tests, it was not carried over into the maintenance phases of the tests. Mutant frequency values for the control were within the normal range.

CONCLUSION The notified chemical was not clastogenic to Mouse Lymphoma cells treated in vitro, with and without metabolic activation, under the conditions of the test.

TEST FACILITY SafePharm (2008i)

Appendix C: Environmental Fate and Ecotoxicological Investigations

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	Yakushokuhatsu Biodegradability Test corresponding to OECD TG 301 C Ready Biodegradability: Modified MITI Test (I) (1992)
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Degradation product measurement - Reverse phase HPLC Dissolved organic carbon (DOC) – TOC analyser TOC-5000A Biochemical oxygen demand (BOD) – Closed system oxygen consumption measuring apparatus
Remarks - Method	The test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations.

RESULTS

Notified chemical		*Aniline*	
Day	*% Degradation (BOD)*	*Day*	*% Degradation*
28	59	14	>60

Remarks - Results	All relevant test validity criteria were met. The test substance had attained 59% degradation after 28 days based on the BOD. During the test, all of the test substance underwent primary degradation forming 3,5,5-trimethylhexanoic acid and pentaerythritol (see test summary below).
Transformation Products	LC-MS was used to characterise degradation products from the ready biodegradability test. In the LC-MS study, molecular ions of the test substance were not detected indicating none of the test substance remained after degradation. The results indicate that monoesters and diesters of 3,5,5-trimethylhexanoic acid and pentaerythritol were likely to have formed in addition to 3,5,5-trimethylhexanoic acid and pentaerythritol. The notified chemical underwent primary degradation to form monoesters and diesters of 3,5,5-trimethylhexanoic acid and pentaerythritol in addition to 3,5,5-trimethylhexanoic acid and pentaerythritol. These transformation products were present at the end of the biodegradation test. The notified chemical did not completely and ultimately degrade to form CO2. As the judgement of the degradability of the test substance depends on the absence of transformation products, it was concluded in the study that the test substance is not readily biodegradable.
CONCLUSION	The notified chemical cannot be classified as readily biodegradable.
TEST FACILITY	Mitsubishi Chemical Medience Corporation (2010)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test –Semi-static EC Directive 92/69/EEC C.1 Acute Toxicity for Fish – Semi-static
Species	Oncorhynchus mykiss (Rainbow trout)
Exposure Period	96 hours

Auxiliary Solvent	None
Water Hardness	140 mg CaCO3/L
Analytical Monitoring	Test substance measurement - HPLC
Remarks – Method	A limit test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations. A range-finding test determined there were no observed effects at concentrations below the nominal concentration used (100 mg/L nominal loading rate). A filtered water accommodated fraction (WAF) was used due to the test substances low water solubility. Water and the test substance were stirred for up to 95 hours, the aqueous phase was siphoned from the test material phase and filtered through a glass wool plug. The test organisms were exposed to the aqueous phase which may contain dissolved test material or leachates of the test material.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality*					
Nominal	Actual		*3 h*	*6 h*	*24 h*	*48 h*	*72 h*	*96 h*
0	0	14	0	0	0	0	0	0
100	< 0.41 (LOQ*)	14	0	0	0	0	0	0

*Limit of quantification (LOQ) = 0.41 mg/L

LL50	> 100 mg/L (WAF) at 96 hours.
NOEL	100 mg/L (WAF) at 96 hours.
Remarks – Results	All relevant test validity criteria were met. No mortality or sub-lethal effects were observed.

CONCLUSION The notified chemical is not harmful to fish up to the limit of its water solubility

TEST FACILITY Harlan (2009b)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test - Static.
EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia – Static.

Species	Daphnia magna
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg CaCO3/L
Analytical Monitoring	Test substance measurement - HPLC
Remarks - Method	A limit test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations. A range-finding test determined there were no observed effects at concentrations below the nominal concentrations used (10 and 100 mg/L nominal loading rates). A filtered water accommodated fraction (WAF) was used due to the test substances low water solubility. Water and the test substance were stirred for up to 95 hours, the aqueous phase was siphoned from the test material phase and filtered through a glass wool plug. The test organisms were exposed to the aqueous phase which may contain dissolved test material or leachates of the test material.

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	0	20	0	0
100	< 0.41 (LOQ)	20	0	0

*Limit of quantification (LOQ) = 0.41 mg/L

EL50	>100 mg/L (WAF) at 48 hours
NOEL	100 mg/L (WAF) at 48 hours
Remarks - Results	All relevant test validity criteria were met. No immobilisation or adverse behaviour was observed.

CONCLUSION The notified chemical is not harmful to aquatic invertebrates up to the limit of its water solubility.

TEST FACILITY Harlan (2008)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE Notified chemical

METHOD OECD TG 201 Alga, Growth Inhibition Test – Static
EC Directive 92/69/EEC C.3 Algal Inhibition Test.

Species	Desmodesmus subspicatus (Green algae)
Exposure Period	72 hours
Concentration Range	Nominal: 100 mg/L Actual: < Limit of quantification (= 0.69 mg/L)
Auxiliary Solvent	None
Analytical Monitoring	Coulter Multisizer Particle Counter Test substance measurement - HPLC
Remarks - Method	The test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations. A range-finding test determined there were no observed effects at concentrations below the nominal concentration used (100 mg/L nominal loading rate). A filtered water accommodated fraction (WAF) was used due to the test substances low water solubility. Water and the test substance were stirred for up to 95 hours, the aqueous phase was siphoned from the test material phase and filtered through a glass wool plug. The test organisms were exposed to the aqueous phase which may contain dissolved test material or leachates of the test material.

RESULTS

Biomass		*Growth*	
EbLR50 mg/L at 72 h	*NOEbL mg/L*	*ErLR50 mg/L at 72 h*	*NOErL mg/L*
> 100 (WAF)	100 (WAF)	> 100 (WAF)	100 (WAF)

Remarks - Results All relevant test validity criteria were met. No inhibitory effects were observed.

CONCLUSION The notified chemical is not harmful to algae up to the limit of its water solubility.

TEST FACILITY Safepharm (2008k)

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test. EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	Activated Sludge
Exposure Period	3 hours
Concentration Range	Nominal: 1000 mg/L
Water Hardness	140 mg CaCO3/L
Remarks – Method	The test was conducted according to test guidelines using good laboratory practice (GLP) with no significant deviations. A range-finding test determined there were no observed effects at concentrations below the nominal concentration used.
RESULTS	
IL50	> 1000 mg/L
NOEL	1000 mg/L
Remarks – Results	All relevant test validity criteria were met. The percent inhibition of microbial activity for the 3,5-dichlorophenol control at nominal concentrations of 3.2 amd 32 mg/L was 21 and 81% respectively, and consequently the effective median concentration of the reference control was within the required range of 3-50 mg/L.
CONCLUSION	The notified chemical is not inhibitory to microbial respiration up to the limit of its water solubility.
TEST FACILITY	Safepharm (2008l)

BIBLIOGRAPHY

Alden CL (1986) A Review of Unique Male Rat Hydrocarbon Nephropathy. Toxicologic Pathology 14(1): 109-111.

Harlan (2008) HATCOL 1760: Acute toxicity to Daphnia magna. (Project No. 2522/0012, December, 2008). Shardlow, Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Harlan (2009a) Oral (Gavage) combined repeat dose toxicity study with reproductive/developmental toxicity screening test in the rat OECD 422 (with recovery groups) Report No. 2522/0013. Shardlow, Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report submitted by notifier).

Harlan (2009b) HATCOL 1760: Acute Toxicity to Rainbow Trout (Oncorhynchus mykiss) (Project No. 2522/0011, February, 2009). Shardlow, Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report submitted by the notifier).

Mitsubishi Chemical Medience Corporation (2010) Ready Biodegradability of HATCOL 1760. (Report number: A080349, March, 2010). Yokohama, Japan, Yokohama, Japan, Environmental Risk Assessment Center, Mitsubishi Chemical Medience Corporation (Unpublished report submitted by the notifier).

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

NTC (National Transport Commission) 2007 Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 7th Edition, Commonwealth of Australia.

Safepharm (2008a) HATCOL 1760: Determination of General Physico-Chemical Properties (Project No. 2522/0001, April, 2008). Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008b) HATCOL 1760: Determination of Hazardous Physico-Chemical Properties (Project No. 2522/0002, April, 2008). Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008c) HATCOL 1760: Hydrolysis as a function of pH. Project No. 2522/0014. Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008d) HATCOL 1760: Acute Oral Toxicity in the Rat – Fixed Dose Method. Project No. 2522/0003. Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008e) HATCOL 1760: Acute dermal irritation in the Rabbit. Project No. 2522/0006. Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm(2008f) HATCOL 1760: Acute Eye Irritation in the Rabbit. Project No. 2522/0007. Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008g) HATCOL 1760: Reverse Mutation Assay "AMES TEST" Using Salmonella Typhimurium and Escherichia Coli. Project No. 2522/0004. Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008h) HATCOL 1760: Chromosome Aberration Test in CHL cells in vitro. Project No. 2522/0010. Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008i) HATCOL 1760 Hatco1760: L5178Y TK +/- Mouse Lymphoma Assay. Project No. 2522/0015. Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008j) HATCOL 1760: Local Lymph Node Assay in the Mouse. Project No. 2522/0008. Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008k) HATCOL 1760: Algal Growth Inhibition Test. (Project No. 2522/0005, May, 2008). Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

Safepharm (2008l) HATCOL 1760: Assessment of the Inhibitory Effect on the Respiration of Activated Sewage Sludge. (Project No. 2522/0013, July, 2008). Shardlow, Derbyshire, UK, Safepharm Laboratories Ltd. (Unpublished report submitted by the notifier).

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), <http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html >.