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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Flotinor V 4085-1 Intermediate

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Director
Chemicals Notification and Assessment

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Component of Flotinor V 4085-1 Intermediate

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Clariant (Australia) Pty Ltd (ABN 30 069 435 552)
675 Warrigal Road
Chadstone, VIC 3148

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:

Chemical Name
Other Name(s)
CAS Number
Molecular Formula
Structural Formula
Molecular Weight
Spectral Data
Composition
Maximum Introduction Volume
Use
Operation Description
Identity of Analogues used for Toxicological Studies

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:

Methods of Detection and Determination
Vapour Pressure
Adsorption/Desorption
Dissociation Constant
Flammability
Autoignition
Acute toxicity – dermal (analogue data)
Acute toxicity – inhalation (analogue data)
Irritation (analogue data)
Sensitisation (analogue data)
Chronic toxicity – oral (analogue data)
Genetic toxicity (analogue data)
Ready biodegradability (analogue data)
Acute toxicity – fish (analogue data)
Acute toxicity – *Daphnia magna* (analogue data)
Acute toxicity – microbial inhibition (analogue data)

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Component of Flotinor V 4085-1 Intermediate
Component of Flotinor V 4085-1 Vorprodukt
Component of Flotinor V 4085-1 Prestage

3. COMPOSITION

DEGREE OF PURITY
<20% of the imported product Flotinor V 4085-1 Intermediate

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
The notified chemical is not separated during manufacture of Flotinor V 4085-1 Intermediate. All impurities are components of the imported formulation Flotinor V 4085-1 Intermediate, which has an acute oral LD50 > 2000 mg/kg bw in S-D rats. The other major component of Flotinor V 4085-1 Intermediate is acutely toxic by inhalation to rats, with LC50 >1.22 mg/L.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical is to be imported as a component (<20%) of the product Flotinor V 4085-1 Intermediate. The notified chemical will not be manufactured in Australia.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	50	50	50	50	50

USE
For manufacture of a corrosion inhibitor for metalworking.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Melbourne or Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
Clariant (Australia) Pty Ltd
100 Heales Road
Lara VIC 3212

TRANSPORTATION AND PACKAGING
The product Flotinor V 4085-1 Intermediate will be packaged in 1000 L Schutz containers (1000 L plastic container in a steel frame on a metal or timber pallet) and can be transported as Non-Dangerous Goods. Transport will be by road from port of entry to Clariant (Australia) Pty Ltd, Lara, Victoria. No exposure to the environment is expected during normal transportation of unopened drums.

5.2. Operation description

Chemical Transfer
After weighing, Flotinor V 4085-1 Intermediate is pumped from original import packaging into the reaction vessel.

Reaction
Flotinor V 4085-1 Intermediate is combined with other reactants in a closed vessel. Chemical reaction between starting components takes place at 50˚C. The notified chemical is completely consumed during the reaction process.

After the reaction process, the final product is pumped from the vessel to the packaging area. The final product is not expected to contain any notified chemical.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Forklift/Truck drivers	3	1 hr/day	20 days/year
Storemen	2	1 hr/day	20 days/year
Plant operators	8	6 hrs/day	30 days/year
Q.C. Technicians/Laboratory staff	8	1 hr/day	30 days/year
Development chemists	3	40-75 hrs/year	
Maintenance Personnel	2	1 hr/day	10 days/year

Exposure Details
The notified chemical will be imported into Australia as a component of the product Flotinor V 4085-1 Intermediate for manufacture of a product for end use in metalworking operations. For each of the worker categories, the nature of the work to be carried out with the chemical is described below:

Forklift Operators/Truck Drivers/Storemen
Transportation and warehouse picking of drummed chemical only, no direct contact with Flotinor V 4085-1 Intermediate, except in case of spillage. Potential contact during loading/unloading of vehicles and picking of stock.
Personal Protective Equipment – Industrial standard coveralls.

Plant Operators
Weighing reactants, pumping Flotinor V 4085-1 Intermediate into reaction vessel and drumming off final product. Supervision of reaction process while product is held in vessel.
Personal Protective Equipment – Safety goggles, rubber safety gloves, industrial standard overalls.

Q.C. Technicians/Laboratory Staff
Potential contact whilst analysing reaction product for quality approval. Tests to include acid value, base nitrogen, infra-red analysis, water content. Appropriate laboratory technique and care maintained.
Personal Protective Equipment: safety glasses, PVC or rubber safety gloves, laboratory dust coat.

Development Chemist
Potential contact during formulation and evaluation of finished product based on notified chemical.
Personal Protective Equipment: safety glasses, PVC or rubber safety gloves, laboratory dust coat.

Maintenance Personnel
Involved in maintenance of production and packaging equipment after equipment washed.
Personal Protective Equipment: industrial standard coveralls.

The operations of weighing, chemical transfer and reaction, and the general workplace activities, are carried out under exhaust ventilation. Venting of workplace air will take place at the weighing and packaging stages, for capture of vapours escaping the reaction vessel, and throughout the general workplace.

5.4. Release

RELEASE OF CHEMICAL AT SITE
The possible points of release when the notified chemicals is used during production are:

a) Atmospheric release during mixing, reaction and transfer. All of these stages will be maintained under negative atmosphere. Any fumes that may be released will be captured and

passed through a water jet scrubber, a carbon absorber and a second water scrubber before discharge to atmosphere. All contaminants will be discharged to the effluent pit/plant in the scrubber water. Here they will be passed through a triple interceptor pit and neutralised before discharge to the Melbourne Water sewerage system. It is assumed that less than 1% (less than 500 kg annually) of notified chemical will be released via this means.

b) Residues in the import containers after draining of the contents will account for less than 1% of the annual import volume (500 kg annually). Some of the 1000 L Schutz containers will be re-used for the end use product without cleaning. Licensed waste contractors will collect the empty import containers and either prepare them for reuse by cleaning them and treating the resultant effluent, or dispose of them to landfill. Some container cleaning rinsate may enter the onsite effluent pit/plant.

c) All production raw materials and finished goods are stored in bunded stores. Consequently, any minor spillages in stores and in the manufacturing area will be able to be rinsed and discharged to effluent pits. It is presumed that less than 1% (less than 500 kg annually) of the imported notified chemical will be released via this route.

Since during the manufacturing process the notified chemical undergoes complete reaction, there will be none present in the equipment cleaning effluent. Thus there is no release due to process equipment cleaning.

RELEASE OF CHEMICAL FROM USE
Due to the complete conversion of the notified chemical during the reaction process, there will be no release of the notified chemical during use of the end-use product.

5.5. Disposal

It is intended that all of the notified chemical will be used as a starting reactant in the production of the end use product. The need for disposal of the substance will be limited and would only be required if spillage occurred. Disposal should be by a licensed waste disposal contractor to either a regulated landfill or by incineration.

5.6. Public exposure

Flotinor V 4085-1 Intermediate, containing <20% notified chemical, is to be imported for use in the production of an emulsifier/corrosion inhibitor that is incorporated in products which act as coolant/lubricant during metal working. The coolant/lubricant products are to be used industrially to assist metal working operations such as required during motor vehicle and whitegoods manufacture.

The notified chemical will not be available for use by the public. Flotinor V 4085-1 Intermediate and the final reaction product based on the notified chemical will be packaged in 1000 L Schutz containers for large scale industrial use and will not be available in smaller packages or to the general public.

The packaging used for the notified chemical and the manufactured product will protect the contents from being released during normal storage, handling and transportation. Only in extreme cases of inappropriate handling or accidents during transportation would there be any likelihood of the notified chemical being released from the packaging and the public being exposed.

Flotinor V-4085-1 Intermediate will only be used in manufacturing processes in Australia at one location at the Clariant (Australia) Pty Ltd, Lara, Victoria site. At this site atmospheric release of the new substance would be virtually zero, because of the reflux production process that cycles vapours back into the reaction.

Appropriate disposal is required of all waste quantities of Flotinor V 4085-1 Intermediate to ensure members of the public are protected from any exposure.

Based on the expected use of the notified chemical, members of the public will not be exposed to the new chemical; therefore no hazards to public health are expected.

6. PHYSICAL AND CHEMICAL PROPERTIES

The notified chemical is not isolated but manufactured as a component (<20%) of the product Flotinor V 4085-1 Intermediate. Data presented below apply to this product, except where specified otherwise.

Appearance at 20ºC and 101.3 kPa Viscous, yellowish to brownish liquid, acid-like odour

Pour Point (1) -21ºC

METHOD A pour point cylinder is cooled by liquid nitrogen-cooled methanol. The pour point is the lowest recorded temperature at which the sample still pours when the cylinder is tilted.
Remarks
TEST FACILITY Clariant Functional Chemicals (2004a)

Pour Point (2) -21ºC

METHOD An automatic pour point tester Herzog MP 852 Combi (Walter Herzog GmbH) is used as specified in the document ISO 3016 for determining the pour point of mineral oil and petroleum products.
A preheated test sample is cooled in steps of 3 K. After each cooling step the testing tube is removed from the cooling bath and bent to 90˚. The surface of test substance is observed for movement by video camera. The pour point is the temperature at which no movement can be observed at a bend angle of 90˚C over a period of 5 seconds.
Remarks
TEST FACILITY Clariant GmbH, Germany (2004)

Boiling Point >216˚C

METHOD Lowest case value obtained by several test methods.
1) Boiling point (BP) of the test material was extrapolated from calculated data of the main active components. The calculated BP = 352˚C
2) BP of residual raw materials was obtained from public literature. BP for raw materials = 251˚C and 216˚C.
3) Decomposition temperature for the test material was determined by differential scanning calorimetry. No endothermic effect (indicative of phase transfer) was observed before decomposition began at 352˚C.

Remarks
TEST FACILITY Clariant GmbH, Germany (2004)

Density (1) 1003 kg/m^3 at 20ºC

METHOD Pycnometer method
Remarks
TEST FACILITY Clariant Functional Chemicals (2004b)

Density (2) 990 kg/m^3 at 20ºC

METHOD Oscillation frequency measurement. Density is determined by measuring the frequency change, which is a function of mass, of an oscillating U-tube, calibrated to a defined filling volume.
Remarks
TEST FACILITY Clariant GmbH, Germany (2004)

Vapour Pressure (1) 0.0014 Pa at 25ºC ($1.08x10^{-5}$ mm Hg)

METHOD EPI Suite model software ver. 3.10 - Modified Grain method.
Remarks Model used the structure of the notified chemical.
TEST FACILITY In-house during the assessment process.

Vapour Pressure (2) Determined for close analogue of the notified chemical.

METHOD Measured (method not specified)
Remarks For a close analogue, the vapour pressure is <0.133 kPa at 20ºC from IUCLID database. The notified chemical is likely to be more volatile than the analogue, thus it would be moderately volatile.
TEST FACILITY IUCLID (2004)

Water Solubility (1) $6x10^{-6}$ g/L at 25ºC (6 µg/L)

METHOD EPI Suite model software ver. 3.10 - Modified Grain method.
Remarks Model used the structure of the notified chemical.
TEST FACILITY In-house during the assessment process.

Water Solubility (2) 0.08 g/L at 25ºC

METHOD An in-house protocol was used whereby 0.5, 1.0 and 2.0 g of sample was added to 200 mL distilled water in a stoppered flask. The mixtures were shaken for 24 hours, then centrifuged for 1 hour at 3000 rpm. The concentration in the sample was determined by HPLC.
Remarks The result for this test indicates that the notified chemical is moderately water soluble (Mensink 1996).
TEST FACILITY Clariant Functional Chemicals (2004c)

Water Solubility (3) <0.1 g/L at 21ºC and pH 7

METHOD OECD Guideline for the Testing of Chemicals 105, Preliminary Test Method
Remarks Test material was mixed with buffer at pH 7. After stirring, the solutions were checked for undissolved particles or phase separation.
Water solubility at pH 1 and 11 were not determined, as the test material hydrolyses to form more water soluble products.
TEST FACILITY Clariant GmbH, Germany (2004)

Hydrolysis as a Function of pH Not determined

Remarks Due to the low water solubility of the test material it was impractical to determine the hydrolysis as a function of pH. In the environmental pH range it is likely that the notified chemical will undergo slow hydrolysis under neutral or alkaline conditions.
TEST FACILITY Clariant Functional Chemicals Pty Ltd (2004c)

Partition Coefficient (n-octanol/water) (1) Log P_{ow} = 7.4

METHOD EPI Suite model software ver. 3.10 - Modified Grain method.
Remarks Model used the structure of the notified chemical.
TEST FACILITY In-house during the assessment process.

Partition Coefficient (n-octanol/water) (2) log Pow > 4 at 20ºC

METHOD Calculation based on the following information:
- Water solubility for the sample = 0.08 g/L
- Sample is miscible in n-octanol in all proportions
- $P_{ow} = C_{n\text{-}octanol} / C_{water}$

Remarks
TEST FACILITY Clariant Functional Chemicals (2004d)

Partition Coefficient (n-octanol/water) (3) log Pow = 7.02

METHOD Modelled data based on weighted average logP for major active components.
Remarks
TEST FACILITY Clariant GmbH, Germany (2004)

Adsorption/Desorption Not determined

Remarks Variation requested on the grounds that the notified chemical will not be released to the aqueous or soil compartments of the environment. On the basis of the data for partition coefficient, the notified chemical would adsorb onto soil or sediment and be immobile (McCall et al 1981).

Dissociation Constant Not determined

Remarks Variation requested on the basis of very low water solubility, and expected pattern of use, which will not involve release of the notified chemical to the aqueous environment. It is expected that the notified chemical would remain neutral unless it is hydrolysed.

Particle Size Not applicable

Remarks Notified chemical not isolated

Flash Point (1) 130ºC at 101.3 kPa

METHOD Cleveland open cup method
Remarks
TEST FACILITY Clariant Functional Chemicals (2004e)

Flash Point (2) 108ºC

METHOD Pensky-Martens closed cup method
Remarks Test material heated in a closed metal cup with a constant heating rate of 3-4 K/minute. An ignition flame is moved in and out of the cup after each rise of 1 K. The surface of test material is continuously checked for ignition.
TEST FACILITY Clariant GmbH, Germany (2004)

Flammability Fire point 170˚C

METHOD Variation requested to substitute alternate methodology.
Remarks Fire point was determined as the lowest temperature at which the sample will sustain burning for 5 seconds.
TEST FACILITY Clariant Functional Chemicals (2004e)

Autoignition Temperature Not determined

Remarks Variation requested on the basis of flash point and fire point results.

Explosive Properties None expected

Remarks The imported product containing <20% notified chemical is classified as a Combustible Liquid Class C1. Under proposed reaction temperature (50˚C) and in a closed reaction system with vapours cycled back into the reaction, conditions for ignition or explosion will not occur.

Reactivity with Water

Remarks The notified chemical is expected to hydrolyse to its acid form.

Comments on Physical and Chemical Properties

Remarks

A US High Production Volume Test Plan report on this class of chemicals concluded that, as these chemicals hydrolyse to the acid form in aqueous solutions, water solubility and octanol-water partition coefficient data should be based on the acid form. Water solubility for the acid form of an analogue chemical was calculated (modelled) as 3.2 mg/L (i.e. sparingly soluble in water), while log K_{ow} was calculated as 4.8.

The HPV report also stated that members of this category of chemical are characterised by low vapour pressure, with modelled data indicating vapour pressure for analogue chemicals to be no more than $3x10^{-7}$ kPa at 25˚C.

7. TOXICOLOGICAL INVESTIGATIONS

Analogue data

Variations to Schedule requirements for toxicological data were requested. Data from acceptable analogue chemicals are summarised below. Six analogues were used, of the same chemical class as the notified chemical. AA1, AA2, AA3, AA4 and AA5 are very similar to the notified chemical, while succinic anhydride is of the same class but has a much lower molecular weight. The chemical identity of analogues AA1-AA5 is exempt information. The identity of succinic anhydride is disclosed in order to provide some information as to chemical class and likely behaviour and effects of the notified chemical.

Acceptable analogue	*Endpoint*	*Results and Conclusion*
AA1	Rat, acute oral toxicity	LD50 = 2550 mg/kg bw
	Rabbit, acute dermal toxicity	LD50 = 6200-7500 mg/kg bw
AA2	Rat, acute oral toxicity	LD50 = 940 (610-1440) mg/kg bw
	Rabbit, acute dermal toxicity	LD50 = 890 (550-1440) mg/kg bw
AA3	Rat, acute inhalation toxicity	LC50 > 1.22 mg/L 4/10 animals died after 4 hours exposure at 1.22 mg/L
AA4	Rabbit, skin irritation	Slightly irritating to skin
	Rabbit, skin irritation	Severely irritating to skin
	Rabbit, mucous membrane (eye) irritation	Irritating to the eye
AA5	Rabbit, skin irritation	Irritating to skin
	Rabbit, eye irritation	Slightly irritating to the eye
	Guinea pig, sensitisation (modified Ritz and Buehler test)	Evidence of sensitisation
	Guinea pig, sensitisation (maximisation test)	Evidence of sensitisation
Succinic anhydride*	Rat, acute oral toxicity	LD50 = 2160 mg/kg bw in males LD50 = 1510 mg/kg bw in females
	Rabbit, eye irritation	Irritating to the eye
	Rat, repeat dose oral toxicity-20 days	NO(A)EL = 94 mg/kg bw/day
	Rat, repeat dose oral toxicity-13 weeks	NO(A)EL = 50 mg/kg bw/day
	Mouse, repeat dose oral toxicity-16 days	NO(A)EL = 219 mg/kg bw/day
	Mouse, repeat dose oral toxicity-13 weeks	NO(A)EL = 75 mg/kg bw/day
	Rat and mouse, carcinogenicity-2 years	No evidence of carcinogenicity
	Genotoxicity-bacterial reverse mutation	Non mutagenic
	Genotoxicity-in vitro chromosomal aberration and sister chromatid exchange	Non genotoxic
	Mouse, developmental effects	Minimum teratogenic dose = 25 mg/kg bw/day

* Data regarding succinic anhydride were obtained from a US National Toxicology Program report on toxicology and carcinogenesis.

Data on the notified chemical

The following data were obtained using Flotinor V 4085-1 Intermediate, the imported product containing <20% notified chemical.

Endpoint	*Result and Conclusion*
Rat, acute oral toxicity	low toxicity LD50 > 2000 mg/kg bw

7.1.1. Acute toxicity – oral

TEST SUBSTANCE	Flotinor V 4085-1 Intermediate, containing < 20% notified chemical.
METHOD	OECD TG 401 Acute Oral Toxicity – Limit Test
Species/Strain	Rat/S-D

Vehicle None
Remarks - Method

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	2000	None

LD50 >2000 mg/kg bw
Signs of Toxicity
Effects in Organs Isolated white foci (approximately 0.5 x 0.5 mm) over 75% of the non-glandular region of the stomach in all animals treated.
Remarks - Results

CONCLUSION The notified chemical is of low toxicity via the oral route.

TEST FACILITY SafePharm Laboratories, Derby, UK (1989)

7.1.2. Acute oral toxicity of analogues

The acute oral LD50s of acceptable analogues of the notified chemical are as follows:

Analogue	Species/Strain	LD50 (mg/kg bw)	Reference
AA1	Rat	2550	Deichmann & Gerarde (1969)
AA2	Rat	940 (610-1440)	Smyth et al (1969)
Succinic anhydride	Rat/S-D	Males: 2160 Females: 1510	

7.2 Acute dermal toxicity of analogues

The acute dermal LD50s of acceptable analogues of the notified chemical are as follows:

Analogue	Species/Strain	LD50 (mg/kg bw)	Reference
AA1	Rat	6200-7500	Deichmann & Gerarde (1969)
AA2	Rabbit	890 (550-1440)	Smyth et al (1969)

7.3. Acute toxicity – inhalation

TEST SUBSTANCE Acceptable analogue AA3

METHOD
Species/Strain Rat/S-D
Vehicle Not reported
Method of Exposure Not specified
Exposure Period 4 hours
Physical Form Not specified
Particle Size Not specified
Remarks - Method

RESULTS

Group	*Number and Sex of Animals*	*Concentration (mg/L)*		*Mortality*
		Nominal	*Actual*	
1	5 male	5.3	1.22	2/5
	5 female	5.3	1.22	2/5

LC50 >1.22 mg/L/4 hours

Signs of Toxicity	Laboured breathing, transient urinary incontinence, alopecia, eye irritation and body weight loss.
Effects in Organs	Gross necropsy revealed colour alterations that were not considered treatment related.
Remarks - Results	

CONCLUSION The notified chemical is harmful via inhalation.

TEST FACILITY Food & Drug Research Labs Inc (1981)

7.4.1. Irritation – skin

TEST SUBSTANCE Acceptable analogue AA4

METHOD

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive.
Remarks - Method	Volume of test substance: 0.5 mL Exposure period: 4 hours

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	2	1.7	1	2	7 days	0
Oedema	1.7	0.3	1.3	3	3 days	0

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

Remarks - Results	Dry, rough, flaky skin was observed at the end of the observation period.

CONCLUSION The test analogue is slightly irritating to the skin.

TEST FACILITY Hoechst AG (1984).

7.4.2. Irritation – skin

TEST SUBSTANCE Acceptable analogue AA4

METHOD

Species/Strain	Rabbit/Himalayan White
Number of Animals	2/group
Vehicle	Polyethylene glycol 400
Observation Period	72 hours
Type of Dressing	Occlusive
Remarks - Method	The exposure time was 24 hours, instead of the usual 4 hours specified in OECD Test Guideline 404. 0.5 mL of the test substance was tested undiluted and diluted to 10% and 1%. Half of the exposed skin area was scarified. Observation period was up to 48 hours after exposure period.

RESULTS Moderate to severe erythema and distinct to severe oedema going beyond the borders of application were observed with both intact and scarified skin using the undiluted test substance. With both the 1% and 10% dilutions, very light, barely visible traces of erythema were evident on the scarified skin and intact skin. Very light, barely visible oedema was observed only on the scarified skin.

Remarks - Results	Data for individual animals not available.
CONCLUSION	The test analogue is severely irritating to the skin under the conditions of the test.
TEST FACILITY	Hoechst AG (1981).

7.4.3. Irritation – skin

TEST SUBSTANCE	Acceptable analogue AA5
METHOD	Skin irritation test (no reference to a specific test guideline)
Species/Strain	Rabbit/New Zealand White
Number of Animals	6
Vehicle	Not specified
Observation Period	48 hours after exposure period
Type of Dressing	Not specified
Remarks - Method	Skin sites were clipped, and 2 intact and 2 abraded skin sites prepared on each rabbit. 0.5 mL of test substance was applied to each site, and left in contact for 24 hours, rather than the usual 4 hours specified in OECD Test Guideline 404. Skin sites were evaluated for redness and oedema at 24 and 72 hours, then until all sites returned to normal (day 7).
RESULTS	
Remarks - Results	Slight to moderate erythema was visible at 24 and 72 hours and on day 4 after treatment. Slight oedema was visible at 24 and 72 hours and persisted until day 6. Four animals had scores of 2 for redness and oedema at 24 hours. Three animals had positive scores for oedema at 72 hours and one had a positive score for redness at 72 hours. Primary Irritation Index was 2.65 out of 8.
CONCLUSION	The test analogue is irritating to the skin under the conditions of the test.
TEST FACILITY	IUCLID (2000)

7.5.1. Irritation – eye

TEST SUBSTANCE	Acceptable analogue AA4
METHOD	Mucous membrane compatibility (internal protocol)
Species/Strain	Rabbit/Himalayan White
Number of Animals	2/group
Observation Period	48 hours after exposure period
Remarks - Method	0.1 mL of undiluted, 10% or 1% test substance (diluted in polyethylene glycol 400) was applied to the conjunctival membrane of the left eye. The right eye served as the untreated control. After 24 hours of exposure, the eyes were rinsed with saline. Eyes were examined with a magnifying glass 1, 7, 24, 48 and 72 hours after application. 48 and 72 hour examinations were done after instillation of one drop of 0.01% sodium fluorescein.
RESULTS	After application of the undiluted substance, slight corneal clouding was exhibited over the whole eye. The conjunctiva of the treated animals showed a diffuse dark red to meat-like colour as well as a clear swelling with parts of the lid raised. The treated eyes also showed severe discharges. After application of 10% test substance, slight corneal clouding was observed. The treated eyes also showed severe discharge. These effects

	were reversible, except for slight reddening and swelling. After application of 1% test substance, slight discharge was observed in treated eyes. These effects were reversible 24 hours after the exposure period.
Remarks - Results	Data for individual animals not available.
CONCLUSION	The test analogue is irritating to the eye.
TEST FACILITY	Hoechst AG (1981).

7.5.2. Irritation – eye

TEST SUBSTANCE	Acceptable analogue AA5
METHOD	Eye irritation test (no reference to a specific test guideline)
Species/Strain	Rabbit/New Zealand White
Number of Animals	6
Observation Period	7 days
Remarks - Method	Exposure period not specified 0.1 mL of test substance was applied to the right eye of each animal. Observations were made 1, 24, 48 and 72 hours and 7 days after exposure.
RESULTS	At 1 hour, five animals had a score of one for the iris, and one animal had a positive score for conjunctival swelling. At 24 hours, one animal had a chemosis score of one. At 48 hours and 7 days all scores were zero.
Remarks - Results	
CONCLUSION	The test analogue is slightly irritating to the eye.
TEST FACILITY	IUCLID (2000)

7.5.3. Irritation – eye

TEST SUBSTANCE	Succinic anhydride
METHOD	Eye irritation test (no reference to a specific test guideline)
Species/Strain	Rabbit/strain not specified
Number of Animals	1
Observation Period	24 hours
Remarks - Method	5 µL of a 15% solution of succinic anhydride in propylene glycol was applied to the centre of the cornea while the lids were retracted.
RESULTS	This caused necrosis that covered approximately 75% of the cornea. On a grading system of 1 (least severe) to 10 (most severe), the severity was rated 8.
Remarks - Results	
CONCLUSION	The test analogue is irritating to the eye.
TEST FACILITY	National Toxicology Program (1990)

7.6. Skin sensitisation

TEST SUBSTANCE	Acceptable analogue AA5
METHOD	Modified Ritz and Buehler test

Species/Strain	Guinea pig/Hartley albino
PRELIMINARY STUDY	Maximum Non-irritating Concentration: Information not available
MAIN STUDY	
Number of Animals	Test Group: 10F + 10M Control Group: 5F + 5M
INDUCTION PHASE	Induction Concentration: topical: 50% w/v test substance in acetone
Signs of Irritation	Information not available
CHALLENGE PHASE	
1st challenge	topical: 10% w/v test substance in acetone
2nd challenge	topical: 3% w/v test substance in acetone
Remarks - Method	For induction, patches were applied to sites once weekly for 3 applications. For challenge, challenge patches were applied for six hours. Appearance of the challenge sites was scored 24 and 48 hours after the challenge period. For rechallenge, the original test animals were used seven days after challenge. A single patch was applied to a new test site. Sites were scored 24 and 48 hours after patch removal.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*	
		1st challenge	*2nd challenge*
Test Group	10% w/v	11/20	
	3% w/v		12/20
Control Group	10% w/v	0/10	
	3% w/v		0/10

Remarks - Results	Not clear whether reported reactions were observed at the 24 or 48 hour time point.

CONCLUSION There was evidence of reactions indicative of skin sensitisation to the test analogue under the conditions of the test.

TEST FACILITY IUCLID (2000)

7.6. Skin sensitisation

TEST SUBSTANCE Acceptable analogue AA5

METHOD Guinea pig maximisation test (no reference to a specific test guideline)

Species/Strain	Guinea pig/Hartley albino
PRELIMINARY STUDY	Maximum Non-irritating Concentration: Information not available
MAIN STUDY	
Number of Animals	Test Group: 10F + 10M Vehicle control: 2F + 2M Saline control: 2F + 2M Positive Control: 3F + 3M Test substance for positive control: 0.1% 1-chloro-2,4 dinitrobenzene
INDUCTION PHASE	Induction Concentration: intradermal: 1% in 80% ethanol topical: 5% in 80% ethanol
Signs of Irritation	Information not available
CHALLENGE PHASE	
1st challenge	topical: 1% in 80% ethanol
2nd challenge	topical: 0.5% in 80% ethanol
Remarks - Method	For induction, all animals were intradermally injected in 6 sites: 2 with 0.1 mL Freund's complete adjuvant, 2 with 0.1 mL test substance, and 2 with test substance emulsified with Freund's adjuvant. One week after intradermal injection, test substance was applied topically on the intradermal sites for 48 hours. 14 days after induction, challenge patches were applied to fresh sites for 24

hours. Sites were cleaned 21 hours after wrappings were removed. Sites were examined 24 and 48 hours after removal of wrappings.
Re-challenge was made 6 days after the challenge period.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*		
		1st challenge		*2nd challenge*
		24 h	*48 h*	
Test Group	1%	7/20	7/20	Information not available
	0.5%	Information not available		3/20
Control Group	Vehicle only	0/4	0/4	Information not available
	Positive control (DCNB)	6/6	6/6	Information not available

Remarks - Results: Not clear whether reported reactions after re-challenge were observed at the 24 or 48 hour time point.

CONCLUSION: There was evidence of reactions indicative of skin sensitisation to the test analogue under the conditions of the test.

TEST FACILITY: IUCLID (2000)

7.7.1. 20 day repeat dose oral toxicity

TEST SUBSTANCE: Succinic anhydride

METHOD: Repeated Dose 20-day Oral Toxicity Study in Rats
Species/Strain: Rat/F344/N (Charles River)
Route of Administration: Oral – gavage
Exposure Information: Total exposure days: 20 days
Dose regimen: 5 days per week (14 doses in 20 days)
Post-exposure observation period: None
Vehicle: Corn oil
Remarks - Method: Necropsy was performed on all rats. Histologic examination was performed on vehicle controls, animals in the 375 and 750 mg/kg groups, and those in the 187 mg/kg groups that died before the end of the study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (vehicle control)	10F + 10M	0	0/20
II	10F + 10M	47	0/20
III	10F + 10M	94	0/20
IV	10F + 10M	187	3/10 females 0/10 males
V	10F + 10M	375	3/10 females 1/10 males
VI	10F + 10M	750	4/10 females 5/10 males

Mortality and Time to Death
No mortality was observed in the vehicle control, 47 mg/kg and 94 mg/kg groups. In the female 187 mg/kg group, 2 treatment related deaths occurred on days 6 and 7; a further death was related to gavage trauma. Among animals that received 375 mg/kg, 3 females died on day 9, and 1 male died on day 6. Four females receiving the highest dose of 750 mg/kg died, on days 6, 8, 9 and 20; five high dose males also died, on days 1, 2 (two deaths), 8 and 9.

Clinical Observations
Compound-related clinical observations included laboured breathing, lethargy, distended abdomens and rough

hair coats. The report does not make clear with which dose groups these observations were associated.
Final mean body weights of male rats were not clearly related to treatment dose. Final mean body weight of female rats in the 750 mg/kg group was 11% lower than that of vehicle controls.

Pathology
Necrosis and inflammation of the upper respiratory tract were seen in 3/10 males and 3/10 females in the highest dose group, and in 2/10 females in the 375 mg/kg group.

Remarks – Results
Detailed pathology and histopathology results unavailable.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established as 94 mg/kg bw/day in this study, based on mortality in the female 187 mg/kg bw group and all higher dose groups.

TEST FACILITY National Toxicology Program (1990)

7.7.2. 13 week repeat dose oral toxicity

TEST SUBSTANCE Succinic anhydride

METHOD Repeated Dose 13-week Oral Toxicity Study in Rats
Species/Strain Rat/F344/N (Charles River)
Route of Administration Oral – gavage
Exposure Information Total exposure days: 13 weeks
Dose regimen: 5 days per week
Post-exposure observation period: None
Vehicle Corn oil
Remarks - Method Necropsy was performed on all rats. Histologic examination was performed on vehicle controls, females in the 100 and 200 mg/kg groups, males in the 200 and 400 mg/kg groups, and all animals that died before the end of the study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (vehicle control)	10F + 10M	0	0/20
II	10F	12.5	0/10
III	10F + 10M	25	2/20
IV	10F + 10M	50	3/20
V	10F + 10M	100	2/20
VI	10F + 10M	200	7/10 females 4/10 males
VII	10M	400	8/10

Mortality and Time to Death
No mortality was observed in the vehicle control and 12.5 mg/kg groups. Deaths of 8/10 males that received 400 mg/kg, and 5/10 females and 4/10 males that received 200 mg/kg, were considered treatment related. Other deaths, in lower dose groups, were reported to be the result of gavage error.

Clinical Observations
Lethargy and distended abdomens were observed at the two highest doses. Mean final body weights of dosed females were similar to vehicle controls. Mean final body weights of males in the 200 and 400 mg/kg groups were 9% and 15% lower than that of vehicle controls.

Pathology
Relative liver weights for females in the 100 and 200 mg/kg groups were significantly higher compared to vehicle controls. No treatment-related lesions were seen microscopically.

Remarks – Results
Detailed pathology and histopathology results unavailable.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established as 50 mg/kg bw/day in this study, based on increased relative liver weights in females dosed with 100 mg/kg bw, and treatment-related mortality in all higher dose groups.

TEST FACILITY National Toxicology Program (1990)

7.7.3. 16 day repeat dose oral toxicity

TEST SUBSTANCE Succinic anhydride

METHOD Repeated Dose 20-day Oral Toxicity Study in Mice
Species/Strain Mouse/B6C3
Route of Administration Oral – gavage
Exposure Information Total exposure days: 16 days
Dose regimen: 5 days per week (12 doses over 16 days)
Post-exposure observation period: None
Vehicle Corn oil
Remarks - Method Necropsy was performed on all animals that died before the end of the study. Histologic examination was conducted on 2 females and 4 males from the 438 mg/kg group.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (vehicle control)	5F + 5M	0	0/10
II	5F + 5M	219	0/10
III	5F + 5M	438	1/5 males
IV	5F + 5M	875	10/10
V	5F + 5M	1750	10/10
VI	5F + 5M	3500	10/10

Mortality and Time to Death
All mice that received 875 mg/kg or more died before the end of the study. One male died from the 438 mg/kg group (day not specified in report).

Clinical Observations
Body weight data was not useable due to equipment malfunction. Treatment-related clinical signs included lethargy, distended abdomens and rough coats. Report does not specify which groups these signs were observed in.

Pathology
No treatment-related lesions were seen in the 2 females and 4 males from the 438 mg/kg groups examined histopathologically.

Remarks – Results

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) was established as 219 mg/kg bw/day in this study, based on mortality in all higher dose groups.

TEST FACILITY National Toxicology Program (1990)

7.7.4. 13 week repeat dose oral toxicity

TEST SUBSTANCE	Succinic anhydride
METHOD	Repeated Dose 13-week Oral Toxicity Study in Mice
Species/Strain	Mouse/B6C3
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 13 weeks Dose regimen: 5 days per week Post-exposure observation period: None
Vehicle	Corn oil
Remarks - Method	Necropsy was performed on all animals. Histologic examination was conducted on all animals in vehicle control and high dose groups.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (vehicle control)	10F + 10M	0	0/20
II	10F + 10M	37	0/20
III	10F + 10M	75	0/20
IV	10F + 10M	150	0/20
V	10F + 10M	300	2/10 females 2/10 males
VI	10F + 10M	600	8/10 females 10/10 males

Mortality and Time to Death

8 females and all 10 males in the highest dose group died before the end of the study. Of these deaths, 9 occurred in the first week, and the remainder in weeks 2, 3, 5 (four deaths), 6, 7 and 8. 2 females and 2 males in the 300 mg/kg group died before the end of the study, in weeks 1 (3 deaths) and 4.

Clinical Observations

Final mean body weights of the 2 females in the highest dose group that survived to the end of the study were lower than their initial weights. Final body weights for female and male mice in the 300 mg/kg groups were 9% and 7% lower, respectively, compared to vehicle controls; and in the 150 mg/kg groups were 8% and 13% lower, respectively, compared to vehicle controls.

Clinical observations included rough coats and lethargy in the 600 mg/kg groups, and rough hair coats in the 300 mg/kg groups.

Pathology

The incidence of inflammation of the stomach was higher in male mice that received 150 or 300 mg/kg compared to vehicle controls.

Remarks – Results

CONCLUSION

The No Observed (Adverse) Effect Level (NO(A)EL) was established as 75 mg/kg bw/day in this study, based on the incidence of stomach inflammation in male mice that received 150 mg/kg bw/day.

TEST FACILITY National Toxicology Program (1990)

7.8. Genotoxicity – bacteria

TEST SUBSTANCE	Succinic anhydride
METHOD	Similar to OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100, TA97
Metabolic Activation System	Aroclor 1254-induced S9 fraction from S-D rat or Syrian hamster liver
Concentration Range in	a) With metabolic activation: 0-10,000 µg/plate

Main Test	b) Without metabolic activation: 0-10,000 µg/plate
Vehicle	Dimethylsulfoxide
Remarks - Method	Positive controls: 2-aminoanthracene on all strains in the presence of S9; in the absence of S9 4-nitro-o-pheylenediamine was used with TA98, sodium azide with TA100 and TA1535, and 9-aminoacridine with TA 1537 and TA97.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	Not reported		Not reported	
Test 1		333		None
Test 2		333		None
Present			Not reported	
Test 1		3,333		None
Test 2		3,333		None

Remarks - Results

CONCLUSION	The test analogue was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	SRI International and Microbiological Associates, Inc. in National Toxicology Program (1990)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE	Succinic anhydride
METHOD	Chinese Hamster Ovary cytogenetics assay
Cell Type/Cell Line	Chinese Hamster Ovary cells
Metabolic Activation System	Aroclor 1254-induced S9 fraction from male S-D rat liver
Vehicle	Dimethylsulfoxide
Positive controls	Mitomycin C and cyclophosphamide
Remarks - Method	Cells were tested for induction of sister chromatid exchanges (SCEs) and chromosomal aberration. In the SCE test without S9, cells were incubated for 26 hours with the test substance in medium supplemented with 10% foetal bovine serum. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 26 hours medium was removed and fresh medium containing BrdU and colcemid was added for a further 2 hour incubation. In the SCE test with S9, cells were incubated with the test substance in serum-free medium with S9 for 2 hours, then fresh medium containing BrdU for a further 26 hour incubation, including a final 2 hours with colcemid added. In the chromosomal aberration test without S9, cells were incubated in medium with the test substance for 8 hours, then colcemid was added for a further 2 hour incubation. For the test with S9, cells were treated with the test substance and S9 for 2 hours, then incubated with fresh medium for 10 hours, including addition of colcemid for the final 2 hours. Cells were harvested by mitotic shake-off, dried, fixed and stained for quantitation of SCEs and chromosomal aberrations.

Sister Chromatid Exchange Test				
Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent	50, 166.5 and 500	26 hours	24 hours	2 hours

Present	50, 166.5 and 500	2 hours	24 hours	2 hours

*All cultures harvested for metaphase analysis.

Chromosomal Aberration Test				
Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent	500, 750 and 1000	8 hours		2 hours
Present	500, 750 and 1000	2 hours	10 hours	2 hours

*All cultures harvested for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in SCE Test	*Cytotoxicity in Chromosomal Aberration Test*	*Precipitation*	*Genotoxic Effect*
Absent	No cytotoxicity up to 500	No cytotoxicity up to 1000	None reported up to 1000	None observed
Present	No cytotoxicity up to 500	No cytotoxicity up to 1000	None reported up to 1000	None observed

Remarks - Results

CONCLUSION The test analogue was not clastogenic to Chinese Hamster Ovary cells treated in vitro under the conditions of the test.

TEST FACILITY Litton Bionetics, Inc. in National Toxicology Program (1990)

ADDITIONAL INVESTIGATIONS

7.14T. Developmental toxicity

TEST SUBSTANCE Succinic anhydride

REMARKS
Three studies have assessed developmental toxicity of succinic anhydride, delivered intraperitoneally in CD-1 mice.
In Study I, 50 mg/kg bw administered on days 8-10 of gestation resulted in 23% of viable pups exhibiting branched ribs, fused vertebrae, or cleft palate. No increases in resorptions or decreases in birth weight were observed.
In Study II, the minimally effective dose that produced a significant rise in defects after administration on gestational days 11-13 was 25 mg/kg bw.
In Study III, the median effective teratogenic dose was 80 mg/kg bw/day, while the minimum teratogenic dose was 30 mg/kg bw/day.
In all three studies, no dam mortality was reported; all reported teratogenic doses reported were sub-lethal. No other adverse effects on the dams were reported.

TEST FACILITY National Toxicology Program (1990)

7.17T. Carcinogenicity

TEST SUBSTANCE Succinic anhydride

METHOD Two year carcinogenicity study
Species/Strain Rat/F344/N (Charles River)
Mouse/B6C3
Route of Administration Oral – gavage
Exposure Information Total exposure: 103 weeks
Dose regimen: 5 days per week
Vehicle Corn oil
Remarks - Method Both rats and mice received the same lot of test substance. Necropsy was performed on all animals. Histologic examination was performed on all animals in vehicle control and high dose groups; all rats that died before the end of the study; all mice that died before week 92; and all animals with gross lesions.

RESULTS

Rats

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality (at day 729)*
I (vehicle control)	60F + 60M	0	Females: 29/60 Males: 24/60
II	60F + 60M	50	Females: 33/60 Males: 27/60
III	60F + 60M	100	Females: 33/60 Males: 28/60

Mice

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality (at week 103)*
I (vehicle control)	50F + 50M	0	Females: 13/50 Males: 23/50
II	50M	38	20/50
III	50F + 50M	75	Females: 12/50 Males: 8/50
IV	50F	150	9/50

Mortality and Time to Death

No significant differences in survival were observed between any groups of rats of either sex. The survival of vehicle control male mice was significantly lower than high dose male mice at week 77. No other significant differences in survival were observed between any groups of mice of either sex.

Clinical Observations

Mean body weights of high dose (100 mg/kg) rats were 8% and 6% lower than vehicle controls for females and males, respectively. No other adverse clinical signs were reported.

Mean body weights of high dose (150 mg/kg) female mice were 10-32% lower than vehicle controls from week 28. Mean body weights of high dose (75 mg/kg) male mice were 5-12% lower than vehicle controls after week 11. During months 8-12, all treated groups of mice showed arched posture and lethargy, and were observed to rub their faces and burrow in bedding, for up to 15 minutes post-dosing. High dose female mice occasionally wheezed and had rough coats.

Effects in Organs – Non-neoplastic

Treated mice showed increased incidence of acute inflammation in the nasal cavity. Squamous metaplasia, secondary to inflammation, was observed in 4 high dose male mice. Renal mineralisation was observed with a negative dose-related trend in male mice.

Effects in Organs – Tumours

In treated rats, marginal increases in the incidence of neoplastic lesions was observed for the skin and mammary gland. Keratoacanthomas occurred in high dose rats, but the incidence was not significantly greater compared to vehicle controls (vehicle: 2/60, high dose: 6/60), and was within the range of historical corn oil controls. Fibroadenomas of the mammary gland occurred in female rats with a negative trend: the incidence in high dose animals was lower than vehicle controls.

No significant increases in the incidences of neoplastic lesions were observed in treated mice.

Remarks – Results

Retrospective detection of oil in the lung of some animals (both rats and mice) that died early (or were killed moribund) indicated that some deaths may have been related to gavage error.

CONCLUSION

There was no evidence of carcinogenic activity of the test analogue under the conditions of the study.

TEST FACILITY National Toxicology Program (1990)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

8.1.1.1.

TEST SUBSTANCE: Acceptable analogue AA4

METHOD: OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.

- Inoculum: Activated sludge from STP Frankfurt-Niederrad
- Exposure Period: 28 days
- Auxiliary Solvent: Not specified
- Analytical Monitoring: Titration of barium hydroxide
- Remarks - Method: Tests were done in duplicate before and after alkaline hydrolysis.
  Reference Substance – sodium benzoate
  Treatments: C1 and C2, inoculum control,
  S1 and S2, test substance at 34.4 and 35.4 mg/L respectively, before hydrolysis, with inoculum,
  S3 and S4, test substance 32.8 and 33.9 mg/L respectively, after hydrolysis, with inoculum,
  R, reference substance at 22.1 mg/L

RESULTS

Test substance (before hydrolysis)		*Test substance (after hydrolysis)*		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*	*Day*	*% Degradation*
1	0	1	0	1	0
2	0.5	2	0.5	2	14
5	1	5	1	5	43
9	1	9	1	9	65
12	1	12	2	12	76
16	1.5	16	2	16	81
21	2	21	2	21	83
28	2.5	28	2.5	28	84

- Remarks - Results: Since the CO_2 evolution from the inoculum controls did not exceed 40 mg/L and the degradation of the reference substance exceeded 60% by day 14, the study conditions were validated.
  The test substance and its hydrolysis product both had a degradation of 2.5% by the end of the study and did not satisfy the 10 day window.

CONCLUSION: Under the test conditions, the test analogue cannot be classified as readily biodegradable.

TEST FACILITY: Clariant GmbH (2002)

8.1.1.2

TEST SUBSTANCE: Acceptable analogue AA7

METHOD: OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.

- Inoculum: Supernatant from homogenised activated sludge.
- Exposure Period: 28 days
- Auxiliary Solvent: Not specified
- Analytical Monitoring: BI-1000 electrolytic respirometer system
- Remarks - Method: Tests were done in duplicate at 23°C.
  Treatments: Controls: blank
  Test substance at 107.2 and 110.2 mg/L
  Reference Substance: sodium benzoate

RESULTS

Remarks - Results	Test substance: 18.3% after 28 days Positive Substance: >60% (3 d). All validity criteria met. The CO_2 evolution from the inoculum controls did not exceed 40 mg/L and the degradation of the reference substance exceeded 60% by day 14.
CONCLUSION	Under the test conditions, the test analogue cannot be classified as readily biodegradable.
TEST FACILITY	Health, Environmental and Regulatory Task Group (2002)

8.1.2. Bioaccumulation

REMARKS	A bioaccumulation study using the notified chemical was not conducted. Due to its low water solubility and high partition coefficient, the notified chemical has the potential to bioaccumulate.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

8.2.1.1

TEST SUBSTANCE	Acceptable analogue AA4
METHOD	Unclear
Species	Goldorfen (*Leuciscus idus f. melonatus*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	114.3 mg $CaCO_3$/L (6.4° d)
Analytical Monitoring	None
Remarks – Method	The glass study tanks were filled with 20 L of test water. The water temperature was maintained at 20±1°C and the tanks were constantly aerated at 100 mL/min, thus giving an oxygen concentration above 8.4 mg/L. The tanks were maintained under a 12 hour day/night photoperiod at 700 Lux. Fish were placed in the tanks approximately 65 hours prior to the addition of the test substance. Due to the test substance's low water solubility, it was emulsified in the test water by Ultra Turrax for 5 minutes at high rotation, then added to the tanks and mixed with a glass rod to achieve even distribution. Note: The concentration is the total amount of substance added to the tanks. While not stated, it is likely that the test solutions were cloudy due to precipitated or undissolved material. Prior to adding the test substance, and at 2, 24, 48 72 and 96 hours, the parameters pH, O_2 and temperature were measured in all tanks. Regular fish observations were taken with behaviour and mortality recorded. Dead fish were immediately removed.

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality %*	
Nominal	*Actual*		*48 h*	*96 h*
0		10	0	0
1		10	0	0
10		10	0	0
100		10	100	100

500	10	100	100

LC50	10-100 mg/L at 96 hours.
NOEC	100 mg/L at 96 hours.
Remarks – Results	The fish died between 20 and 100 minutes after the test substance was added. In the 100 mg/L test concentration the pH dropped to 7.2 and in the 500 mg/L test concentration it dropped to 5.1, which may have affected the results. In the other concentrations the pH remained in the range 7.9 and 8.3. The oxygen concentration ranged from 8.4 and 8.9 mg/L.
CONCLUSION	Under the test conditions, the test analogue may be harmful to fish (Mensink 1995).
TEST FACILITY	Hoechst (1981)

8.2.1.2

TEST SUBSTANCE	Acceptable analogue AA8
METHOD	US FIFA Pesticide Assessment guidelines for Aquatic Organisms and ASTM Standard E 729-88 – semi static.
Species	Sheepshead minnow (*Cyprinodon variegates*)
Exposure Period	96 hours
Auxiliary Solvent	Unknown
Water Hardness	Unknown
Analytical Monitoring	Unknown
Remarks – Method	Fish were exposed either to saltwater control or to the water soluble fraction (WSF) generated from 100, 300 or 1000 mg/L. Salinity was 26 0/00 and pH was 8.2. Total organic carbon (TOC) samples were taken at the start and at 24 hours – the TOC for the control and the three test concentrations were 2.3, 2.5, 3.0 and 3.5 mg TOC/L respectively.
RESULTS	
LC50	>1000 mg/L (WSF) at 96 hours.
NOEC	>1000 mg/L (WSF)
Remarks – Results	No mortality was observed.
CONCLUSION	Under the test conditions, the test analogue is not toxic to sheepshead minnow, to the limit of its water solubility (Mensink 1995).
TEST FACILITY	IUCLID (2004)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Acceptable analogue AA8
METHOD	US FIFA Pesticide Assessment guidelines for Aquatic Organisms and ASTM Standard E 729-88
Species	*Mysidopsis bahia*
Exposure Period	96 hours
Auxiliary Solvent	Unknown
Water Hardness	Unknown
Analytical Monitoring	Unknown
Remarks - Method	Organisms exposed to saltwater control or to the WSF generated from 8.1, 27, 90, 300 or 1000 mg/L. Salinity was 24 0/00 and pH was 8.2. TOC samples were taken at the start and at 24 hours.
RESULTS	

LC50	169 mg/L (WSF) at 96 hours
NOEC (or LOEC)	8.1 mg/L (WSF) at 96 hours
Remarks - Results	All organisms died at 1000 mg/L (WSF).

CONCLUSION Under the test conditions, the test analogue appears to show some toxicity to *Mysidopsis bahia* below its water solubility limit.

TEST FACILITY IUCLID (2004)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE Acceptable analogue AA7

METHOD OECD TG 201 Alga, Growth Inhibition Test – static.

Species	Fresh water (*Pseudokirchneriella subcapitata* formerly *Selenastrum capricornutum*)
Exposure Period	96 hours
Concentration Range	Nominal: 0, 0.3, 3.0, 33, 330 and 3300 mg/L WAF
Auxiliary Solvent	None
Water Hardness	Not specified
Analytical Monitoring	None
Remarks - Method	A measured amount of the test substance was added to a measured amount of dilution water and stirred with a magnetic stirrer for 20 hours and then allowed to stand for 4 hours. After this the water phase (WAF) was siphoned off and used for the aquatic test. Insoluble material was observed at 330 and 3300 mg/L at 24, 48 and 96 hours. Test media pH at 0 hours was 7.4 and 10.2 at 96 hours, in test concentration 330 mg/L pH was 4.3-4.4 and in 3300 mg/L it was 3.9-4.0. This was possibly due to hydrolysis of the test substance.

RESULTS

Biomass		*Growth*	
E_bC_{50} *mg/L(WAF) at 96 h*	NOEC *mg/L (WAF)*	E_rC_{50} *mg/L (WAF) at 96 h*	NOEC *mg/L*
93	33	100	-
(95% C.I. 33-330 mg/L)		(95% C.I. 33-330 mg/L)	-

Remarks - Results No unusual observations were made. Good algal growth was observed in the control.

An aliquot of cells from the 330 mg/L test concentration were cultured in fresh control media and showed rapid regrowth, thus the observed toxic effects were concluded to be algistatic.

CONCLUSION Under the study conditions the analogue was harmful to aquatic life (United Nations, 2003)

TEST FACILITY Health, Environmental and Regulatory Task Group (2002)

8.5E. Toxicity to bacteria

TEST SUBSTANCE Acceptable analogue AA3

METHOD Fermentation Test tube – No other details given

Remarks - Method	Duration – 24 hours

RESULTS

Remarks - Results	EC_0 > 2500 mg/L

CONCLUSION

TEST FACILITY	Hoechst (1987)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

During manufacture of the end use product, the notified chemical will be consumed, therefore the only sites of release will be import container residues (up to 1%), atmospheric release from transfers and mixing vessels (up to 1%), and spills (up to 1%). Thus a maximum of up to 3% will be lost and 97% will undergo reaction during the manufacturing process.

Spilt material will be contained, collected and placed in a sealable container and then disposed of to landfill, or, possibly for small spills, washed into drains that go to the onsite effluent treatment plant. The container rinsate, containing any residues, will also go to the onsite effluent treatment plant, as will the scrubber water with any contaminants.

If, as a worst case scenario, released notified chemical remains in the effluent, and is not removed to sludge or degraded, then the following Predicted Environmental Concentration (PEC) can be estimated, based on the effluent going to the Western Treatment Plant, Werribee:

Maximum amount entering Effluent treatment plant	1500 kg
Maximum amount entering Sewage treatment plant	1500 kg
Daily influent volume to STP	500 ML
Number of days notified chemical used	30 days
PEC_{STP}	0.1 mg/L/day used

Since the Werribee STP consists of a series of long term retention ponds and grass filtration system, it is unlikely that the notified chemical would be released into the natural aquatic environment. The notified chemical will adsorb to grass, sediment etc, and, within the ponds, the notified chemical would undergo biotic and abiotic degradation.

9.1.2. Environment – effects assessment

The results of the acute aquatic toxicity tests for the analogues provided are listed below.

Analogue	*Organism*	*Duration*	*End Point*	*mg/L*
AA4	Fish	96 h	LC_{50}	10-100
AA8	Fish	96 h	LC_{50}	>1000 (WSF)
AA8	Crustacean	96 h	EC_{50}	169 (WSF)
AA7	Algae	96 h	E_BC_{50}	93 (WAF)
AA3	Bacteria	24 h	EC_0	>2500

Using the lowest EC_{50} of 10 (10-100 mg/L) for fish and a safety factor of 1000 (OECD), a predicted no effect concentration (PNEC) for aquatic ecosystems of 0.01 mg/L has been estimated (10/1000). The safety factor of 1000 is chosen as the toxicity data are for analogues and details of the tests are brief, even though data for 3 trophic levels are available.

9.1.3. Environment – risk characterisation

Since very little of the notified chemical will actually reach the aquatic environment, a $PEC_{aquatic}$ and risk quotient cannot be determined. While the PEC entering Werribee STP is 0.1 mg/L, this does not take into account adsorption or hydrolysis during treatment at the use site and similar processes in the extensive treatment at Werribee. Hence, it is unlikely that the notified chemical will pose a risk to the aquatic environment.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Transport & Storage

Occupational exposure to the notified chemical during transport and storage of Flotinor V 4085-1 Intermediate containing less than 20% of the notified chemical is only likely in the event of accidental container breakage and/or spillage. Exposure in these circumstances is expected to be infrequent and acute, and can be limited by use of respiratory, skin and eye protection (including masks, goggles and protective clothing) during clean-up operations.

Production Operations

During use of Flotinor V 4085-1 Intermediate as a wholly consumed reactant in the production of corrosion inhibitor, dermal and inhalation exposure are the most likely routes. Ocular exposure may occur as a result of accidental splashes. All routes of exposure may occur when workers open drums containing the imported product and when weighing and transferring the imported product into the reactant vessel. Inhalation exposure may also occur during the reaction process. Exposure to the notified chemical may occur during QC sampling, and during laboratory analysis and development work. No exposure is anticipated after the reaction process is complete, as the notified chemical is expected to be completely consumed in the reaction.

Dermal exposure during formulation was estimated using the EASE model (HSE, 1994). Assuming non-dispersive use and intermittent direct handling, the estimated dermal exposure during formulation is 0.1-1 mg/cm^2/day of imported product containing less than 20% of the notified chemical. This equates to 0.02-0.2 mg/cm^2/day of the notified chemical. Absorption of the notified chemical may be significant, as the substance has a high Log P_{ow} and fat solubility so ready diffusion across membranes would be expected. Therefore, for a 70 kg worker with surface area for hands at 820 cm^2 and forearms at 1140 cm^2, and assuming 100% absorption, systemic exposure is estimated to be 2.8-28 mg/kg bw/day of the notified chemical. This exposure would be substantially reduced by the use of protective clothing and gloves.

The vapour pressure of the notified chemical is not known. Therefore it is not possible quantitatively to estimate the atmospheric concentration of notified chemical during production operations. As the reaction takes place in a closed vessel, with reflux of vapours in the reaction system and exhaust ventilation of the reaction vessel, the reaction process is not expected to generate significant inhalation exposure for workers. Inhalation exposure may, however, occur during weighing of reactants, pumping reactants into the reaction vessel, quality control sampling and laboratory analysis. Exposure will be reduced by the use of exhaust ventilation for all weighing and chemical transfer operations.

9.2.2. Public health – exposure assessment

It is expected that during import, transport and storage of Flotinor V 4085-1 Intermediate containing up to 20% notified chemical, exposure of the general public will only occur in the event of an accident involving breach of import containers. No special storage facilities will be required for safe storage of Flotinor V 4085-1 Intermediate. The notified chemical is not classified as dangerous goods or as a scheduled poison. Consequently, storage in general industrial chemical stores in 1000 L Schutz containers will provide satisfactory protection from exposure to the general public. The only possibility of exposure to the public during normal storage and transport of unopened drums would be by accidental spillage.

Flotinor V 4085-1 Intermediate will not be available to the public. It will be used entirely in manufacturing processes, as a reactant that is completely consumed to form the final product. The final product will be packaged for large scale industrial use and will also not be available to the public.

Based on this use pattern, members of the public will not be exposed to the notified chemical.

9.2.3. Human health – effects assessment

Almost all health effects have been assessed using analogues of the notified chemical that have been accepted for toxicological purposes. Six analogues were used. All six analogues are of the same chemical class as the notified chemical. Five analogues, designated AA1, AA2, AA3, AA4 and AA5 for this report, are very similar to the notified chemical, while the sixth analogue, succinic anhydride, is of the same class but has a much lower molecular weight. It is therefore considered that test results from analogues AA1-5 are of most relevance to this assessment, while results for succinic anhydride are also useful, but likely to provide a more conservative estimate of the effects of the notified chemical.

In the only toxicity study available on the notified chemical, the imported product Flotinor V 4085-1 Intermediate, containing <20% notified chemical, was of low acute oral toxicity in rats, with LD50 >2000 mg/kg bw. Similar studies using analogues of the notified chemical gave LD50 values of 2550 and 940 mg/kg bw for analogues AA1 and AA2, respectively. Acute oral

LD50 for succinic anhydride in rats is 2160 mg/kg bw for males and 1510 mg/kg bw for females.

All remaining toxicological endpoints are informed by data from analogue chemicals.

Acute dermal LD50 was shown to be >6000 mg/kg bw for AA1, and 890 mg/kg bw for AA2. (However, literature values only were available, not full studies.)

AA3 is acutely toxic by inhalation in rats. (Abstract provided.)

Sub-chronic toxicity was measured in several repeat dose oral studies using succinic anhydride. The NO(A)EL observed in 20 day and 13 week studies in rats was 94 and 50 mg/kg bw/day, respectively, while the NO(A)EL observed in 16 day and 13 week studies in mice was 219 and 75 mg/kg bw/day, respectively, based on mortality at the higher doses.

No evidence of carcinogenicity was observed in a 2 year study of succinic anhydride in mice and rats.

Irritation effects have been demonstrated with several different analogue chemicals. AA4 has shown irritant effects in two studies. In a study conducted according to OECD Test Guideline 404, AA4 was slightly irritating. In a second study, in which the exposure time was 24 hours rather than the usual 4 hours specified in OECD Test Guideline 404, AA4 had severe irritant effects. AA5 was also shown to be irritating to rabbit skin; however this study also used a 24 hour exposure period, rather than the usual 4 hours specified in OECD Test Guideline 404.

AA4, AA5 and succinic anhydride are irritating to the eye in rabbits.

AA5 provided evidence of sensitisation in two different Guinea pig tests.

Succinic anhydride was not genotoxic in bacterial reverse mutation tests and *in vitro* mammalian chromosomal aberration and sister chromatid exchange tests.

Succinic anhydride has been shown to have adverse developmental effects in mice, with a minimum teratogenic dose of 25 mg/kg bw/day. However, these results were not available in sufficient detail to enable a definitive assessment to be made, taking into account possible maternal toxicity.

Based on limited analogue data, it is predicted that the notified chemical may be acutely toxic by the oral or dermal route, and is likely to be toxic by inhalation. The only irritancy study conducted according to the relevant OECD Test Guideline showed only slight evidence of skin irritation; however, when the other studies are taken into account, the notified chemical may be irritating to skin. The notified chemical is likely to be irritating to eyes, and may be a skin sensitiser. It is not likely that the notified chemical will be genotoxic. Although there was some evidence of developmental toxicity for succinic anhydride, these studies did not provide sufficient data to conclude that the notified chemical may have adverse developmental effects.

Based on the available data, the notified chemical is classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2002), with the following risk phrases:

R20 Harmful by inhalation
R21 Harmful in contact with skin
R22 Harmful if swallowed
R38 Irritating to skin
R41 Risk of serious damage to eyes
R43 May cause sensitisation by skin contact

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is of low acute toxicity via dermal routes (LD50 >6000 mg/kg for an

analogue of the notified chemical). Analogue data suggest that the notified chemical may be harmful if swallowed; however, this route of exposure is extremely unlikely in the workplace.
Data on another analogue suggest that the notified chemical is acutely toxic by inhalation. Although it is expected that the notified chemical will have a low vapour pressure, all open operations during drum opening, weighing, chemical transfer and sampling should be conducted under local exhaust ventilation (LEV). Any workers subject to prolonged exposure to the notified chemical in the absence of LEV will require personal respiratory protection.
Based on analogue data, the notified chemical is expected to be a skin and eye irritant, with the risk of serious damage to the eyes, and may cause sensitisation by skin contact. Therefore all workers potentially exposed to the notified chemical should wear PPE including protective clothing, gloves and safety goggles.
During manufacturing operations, a reasonable worst-case dermal exposure to the notified chemical was estimated to be 2.8-28 mg/kg bw/day of the notified chemical, assuming 100% skin absorption. The margin of exposure (MOE) for chronic toxicity is based on a NOAEL of 50 mg/kg bw/day (the lowest NOAEL determined in studies on analogue chemicals). MOE greater than or equal to 100 are considered acceptable to account for intra- and inter-species differences. For dermal exposure, the MOE is calculated as 1.8-18. Therefore, the risk of chronic systemic toxicity using modelled worker data is unacceptable for manufacturing workers handling the notified chemical in the form of Flotinor V 4085-1 Intermediate directly. All workers handling this product will therefore require extensive PPE including protective clothing, gloves and safety goggles, in order to minimise dermal exposure.

9.2.5. Public health – risk characterisation

It is expected that public exposure to the imported industrial product Flotinor V 4085-1 Intermediate containing less than 20% notified chemical will be negligible except in the event of serious accidental spill during import or transport. Consequently the public risk from exposure to the notified chemical through all phases of its life cycle is considered to be low.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances*. The classification and labelling details are:
R20 Harmful by inhalation
R21 Harmful in contact with skin
R22 Harmful if swallowed
R38 Irritating to skin
R41 Risk of serious damage to eyes
R43 May cause sensitisation by skin contact

and

As a comparison only, the classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	***Hazard statement***
Acute toxicity	4	Harmful if swallowed
		Harmful if inhaled
	3	Toxic in contact with skin
Skin corrosion/irritation	3	Causes mild skin irritation
Serious eye damage/eye irritation	1	Causes serious eye damage
Skin sensitiser	1	May cause allergic skin reaction

*Since no actual environmental data for the notified chemical have been provided, an environmental classification cannot be given.

10.2. Environmental risk assessment

On the basis of the proposed use of the chemical, it is not considered to pose a risk to the environment.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described, providing all the control measures described are employed.

10.3.2. Public health

There is No Significant Concern to public health when used as a reactant for manufacture of a corrosion inhibitor for metal working as described in the notification.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS for the imported product containing the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for the imported product containing the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC 1994). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

REGULATORY CONTROLS
Hazard Classification and Labelling

- The NOHSC Chemicals Standards Sub-committee should consider the following hazard classification for the notified chemical:
  - R20 Harmful by inhalation
  - R21 Harmful in contact with skin
  - R22 Harmful if swallowed
  - R38 Irritating to skin
  - R41 Risk of serious damage to eyes
  - S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
  - S28 After contact with skin, wash immediately with plenty of water
  - S36/37/39 Wear suitable protective clothing, gloves and eye/face protection

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - >= 1% w/w:
    - R43 May cause sensitisation by skin contact
  - 5-10% w/w:
    - R36 Irritating to eyes
    - R43 May cause sensitisation by skin contact
  - 10-20% w/w:
    - R41 Risk of serious damage to eyes
    - R43 May cause sensitisation by skin contact
  - >= 20% w/w:

- R38 Irritating to skin
- R41 Risk of serious damage to eyes
- R43 May cause sensitisation by skin contact

– >= 25% w/w:
  - R20 Harmful by inhalation
  - R21 Harmful in contact with skin
  - R22 Harmful if swallowed
  - R38 Irritating to skin
  - R41 Risk of serious damage to eyes
  - R43 May cause sensitisation by skin contact

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced:
  – Local exhaust ventilation (LEV) for all open operations during drum opening, weighing, transfer and sampling.

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced:
  – Avoid direct handling.
  – Avoid skin and eye contact.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced:
  – Protective clothing, gloves and safety goggles.
  – Personal respiratory protection for any worker subject to prolonged exposure in the absence of LEV.

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

- A copy of the MSDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances*, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Environment

- The following control measures should be implemented by manufacturers of the end product to minimise environmental exposure during use of the notified chemical:
  – All drains in process areas must go to an on-site treatment plant.

Disposal

- Disposal procedures should be in accordance with State and local Government regulations. It is recommended that waste liquids be collected with a liquid binding substance, and all waste materials should be disposed of either through a licensed waste disposal contractor to a regulated landfill or incinerated in an approved incinerator.

Emergency procedures

- Spills/release of the notified chemical should be handled by containment and collection with absorbent material and then stored in a labelled container ready for disposal.

12.1. Secondary notification

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- There are any changes in use of the notified chemical that may lead to a significant increase in the release of the notified chemical to the aquatic environment.

or

(2) Under Section 64(2) of the Act:
- If any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

Should secondary notification proceed, aquatic data for the notified chemical itself will be required, and a reviewed risk assessment undertaken.

13. BIBLIOGRAPHY

Clariant Functional Chemicals (2004a) Technical Report: Pour Point/Melting Point of Flotinor V 4085-1 Intermediate. Clariant (Australia) Pty Ltd, Chadstone VIC (Unpublished report provided by the notifier)

Clariant Functional Chemicals (2004b) Technical Report: Density of Flotinor V 4085-1 Intermediate. Clariant (Australia) Pty Ltd, Chadstone VIC (Unpublished report provided by the notifier)

Clariant Functional Chemicals (2004c) Technical Report: Solubility and Hydrolysis as a Function of pH of Flotinor V 4085-1 Intermediate. Clariant (Australia) Pty Ltd, Chadstone VIC (Unpublished report provided by the notifier)

Clariant Functional Chemicals (2004d) Technical Report: Partition Coefficient of Flotinor V 4085-1 Intermediate. Clariant (Australia) Pty Ltd, Chadstone VIC (Unpublished report provided by the notifier)

Clariant Functional Chemicals (2004e) Technical Report: Flash & Fire Points of Flotinor V 4085-1 Intermediate. Clariant (Australia) Pty Ltd, Chadstone VIC (Unpublished report provided by the notifier)

Clariant GmbH (2002) [Analogue] Ready Biodegradability in the OECD 301B "CO2 Evolution Test (Modified Sturm Test)", Report No. H821. Clariant GmbH Division Function Chemicals, Frankfurt, Germany (Unpublished report provided by the notifier)

Clariant GmbH (2004) Flotinor V 4085-1 Prestage: Chem-Physical Data (Melting Point, Boiling Point, Density, Water Solubility, Partition Coefficient, Flash Point), Report No. 2004-H01. Clariant GmbH Division Function Chemicals, Frankfurt, Germany (Unpublished report provided by the notifier)

Deichmann, W.B. and Gerarde, H.W. (1969) Toxicology of Drugs and Chemicals.

European Commission (2003) Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances - Parts II and III.

Food & Drugs Research Labs Inc. (1981) Acute Inhalation Toxicity of [Analogue] in Sprague-Dawley Rats

Health, Environmental and Regulatory Task Force (2002) Robust summary number [Report Number] in High Production Volume (HPV) Challenge Program. Test Plan for [Chemical Class] Category. The American Chemistry Council.

Hoechst AG (1984) [Analogue] Test for Acute Dermal Irritation/Corrosion in the Rabbit, Report No. 84.0687. Pharma Research Toxicology, Hoechst AG, Frankfurt, Germany (Unpublished report provided by the notifier)

Hoechst AG (1981) Targeted Test for Dermal and Mucous Membrane Compatibility of [Analogue] with the Rabbit, Report No. 79/81. Pharma Research Toxicology, Hoechst AG, Frankfurt, Germany (Unpublished report provided by the notifier)

Hoechst (1981) Acute toxicity of [Analogue] in Goldorfen (*Leuciscus idus f. melanotus*), Report No. 13/81. Pharma Research Toxicology, Hoechst AG, Frankfurt, Germany (Unpublished report provided by the notifier)

IUCLID (2004) Data Set for [Analogue]. European Commission – European Chemicals Bureau

IUCLID (2000) Data Set for [Analogue]. European Commission – European Chemicals Bureau

McCall PJ, Laskowski DA, Swann RL and Dishburger HJ (1981) Measurement of sorption coefficients of organic chemicals and their use on environmental fate analysis. In *Test Protocols of Environmental Fate and Movement Of Toxicants.* Association of Official Analytical Chemists Symposium Proceedings, 94th Annual Meeting, October 21-22 1980, Arlington, Virginia. P 89-109. AOAC, Washington DC.

Mensink BJWG, Montforts M, Wijkhuizen-Maslankiewicz L, Tibosch H and Linders JBHJ (1995) Manual for summarising and evaluating the environmental aspects of pesticides. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

National Toxicology Program (1990) Toxicology and Carcinogenesis Studies of Succinic Anhydride in F344/N Rats and B6C3F1 Mice (Gavage Studies) National Institutes of Health, US Department of Health and Human Services

NOHSC (1994) National Code of Practice for the Labelling of Workplace Substances [NOHSC:2012(1994)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

NOHSC (2002) Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2002)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

NOHSC (2003) National Code of Practice for the Preparation of Material Safety Data Sheets, 2nd edn [NOHSC:2011(2003)]. National Occupational Health and Safety Commission, Canberra, Australian Government Publishing Service.

SafePharm (1989) Acute Oral Toxicity (Limit Test) in the Rat, Project Number 10/464. SafePharm Laboratories Limited, Derby, UK (Unpublished report provided by the notifier)

Smyth, H.F., Carpenter, C.P., Weil, C.S., Pozzani, U.C., Striegel, J.A. and Nycum, J.S. (1969) Range-Finding Toxicity Data: List VII *American Industrial Hygiene Association Journal* 30:470-6

United Nations (2003) Globally Harmonised System of Classification and Labelling of Chemicals (GHS). United Nations Economic Commission for Europe (UN/ECE), New York and Geneva.