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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Component 2 in CYCOM 5250-4 RTM Resin

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 the Environment, Water, Heritage and the Arts.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

This Full 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:

Street Address:	334 - 336 Illawarra Road MARRICKVILLE NSW 2204, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Cytec Australia Holdings Pty Ltd (ABN: 45 081 148 629)
Suite 1, Level 1 Norwest Quay
21 Solent Circuit
Norwest Business Park
Baulkham Hills NSW 2153

Boeing Aerostructures Australia Pty Limited (ABN: 15 103 165 466)
226 Lorimer Street
Port Melbourne VIC 3207

NOTIFICATION CATEGORY
Limited-small volume: Chemical other than polymer (1 tonne or less per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, purity, impurities and use details.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: melting point, boiling point, density, vapour pressure, hydrolysis as a function of pH, partition coefficient, adsorption/desorption, dissociation constant, flash point, flammability and autoignition temperature.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
CEC/682
CER/19

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
CYCOM 5250-4 RTM Resin (contains 10-30% of the notified chemical)

OTHER NAME(S)
TDAB

MOLECULAR WEIGHT
< 500 Da

ANALYTICAL DATA
Reference IR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY > 95%

ADDITIVES/ADJUVANTS None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Yellow powder

Property	Value	Data Source/Justification
Melting Point	175°C	MSDS
Boiling Point	511°C at 101.3 kPa	Calculated
Density	620 kg/m^3 (bulk density)	MSDS
Vapour Pressure	1.33×10^{-11} kPa	Calculated
Water Solubility	0.060 g/L at 20°C	Measured
Hydrolysis as a Function of pH	Not determined.	The notified chemical contains groups that can undergo hydrolysis, but typically only under conditions of extreme temperature and pH.
Partition Coefficient (n-octanol/water)	log P_{ow} =-0.0036	Estimated using KOWWIN (v1.67)
Adsorption/Desorption	log K_{oc} = 0.8743 – 2.7051	Estimated using KOCWIN (v2.00)
Dissociation Constant	Not determined	The notified chemical does not have any groups that can dissociate in water.
Particle Size	Inhalable fraction (<100 μm): 100% Respirable fraction (<10 μm): > 85% MMAD* = 1.8 -3.1 μm	Measured
Flash Point	Not determined	Given the physical state and low vapour pressure the flash point is likely to be high.
Flammability	Not highly flammable	Measured
Autoignition Temperature	Not determined	Expected to be high based on the lack of flammability.
Explosive Properties	Not expected to be explosive	The structural formula contains no explosophores.

* MMAD = Mass Median Aerodynamic Diameter

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties, refer to Appendix A.

Reactivity
The notified chemical is not expected to be stable at temperatures significantly above room temperature based on its use in the manufacture of heat-cured composite structures. The notified chemical also appears to undergo reactions in water that may involve hydrolysis.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured within Australia.
The notified chemical will be imported as a resin (CYCOM 5250-4RTM) at up to 30% concentration.

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

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

PORT OF ENTRY
Sydney and Melbourne.

IDENTITY OF MANUFACTURER/RECIPIENTS
Cytec Australia Holdings Pty Ltd

Suite 1, Level 1 Norwest Quay
21 Solent Circuit
Norwest Business Park
Baulkham Hills NSW 2153

Boeing Aerostructures Australia Pty Limited
226 Lorimer Street
Port Melbourne VIC 3207

TRANSPORTATION AND PACKAGING
The notified chemical will be imported in 20 L sealed pails as a resin. It is anticipated that it may also be introduced in 4 L pails. The pails will be transported by road from the wharf to the customer's warehouse.

USE
The notified chemical will be imported as a component of resin (up to 30%) for the manufacture of composite materials.

OPERATION DESCRIPTION
The notified chemical will not be manufactured or reformulated within Australia.

Truck drivers will transport the sealed CYCOM 5250-4 RTM resin (10-30% notified chemical) containers by road from the wharf to the customer's warehouse and then used as needed. Two incoming goods receiving personnel will unload the containers of CYCOM 5250-4 RTM resin for storage in designated refrigeration equipment.

The CYCOM 5250-4 RTM resin containing the notified chemical will be moulded into articles at the customer's manufacturing site. CYCOM 5250-4 RTM resin will be used in a closed mould process known to the aerospace industry as Resin Transfer Moulding (RTM). In this process the resin will be removed from refrigeration (the resin is a one part, self catalysed system and will undergo slow, non facile curing at room temperature and above, thus requiring cold temperature storage) and allowed to warm to room temperature. The resin, in a solid state after refrigerated storage, will be transferred manually to a sealed pressure pot (4 L capacity) of the injection moulding system, which extrudes the resin into the mould under heat and pressure conditions. The resin will be then injected into the mould at a temperature range of 90°C – 120°C. The mould will be sealed from atmosphere and internal pressure maintained while the temperature is elevated to a cure temperature of 190ºC for 3 hours. After this initial cure process the matrix is near fully cross-linked. An in-situ post cure is then performed at 210ºC for 4 hours. The post cure stage increases the glass transition temperature (Tg) of the polymer matrix to allow continuous service of the finished part in operating temperatures of 180°C. The above processes will be carried out under local exhaust ventilation.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storage			
Transporting from dock to customer's site for warehousing	2	2 – 3	10 – 15
Manufacture of parts			
Workers involved in introducing CYCOM® 5259-4 RTM resin to resin moulding machine	2-4	0.5 – 6	30
Quality control/chemists and technical service	4-8	1	30
Workers involved in packaging of parts	4	3	30
End-use in Aerospace industry			
Assembly of aircrafts	10-15	6 – 8	50

EXPOSURE DETAILS

Transport and Storage

Waterfront, transport and warehouse workers will not be exposed to the notified chemical (10-30% in CYCOM 5250-4 RTM resin) except in an accident.

Manufacture of parts

Dermal and ocular exposure to the notified chemical will be possible when manually transferring the resin (10-30% notified chemical) to the pressure pot, during equipment maintenance or quality control testing. Exposure is expected to be minimised by the use of PPE including coveralls, goggles and gloves. Inhalation exposure to the notified chemical is likely to be negligible due to the very low vapour pressure (1.33×10^{-11} kPa) of the notified chemical, the form of the resin in which it will be introduced, the enclosed systems and the use of exhaust ventilation.

End use -in aerospace parts

Exposure to notified chemical during end use is expected to be negligible. Once cured the notified chemical will be bound within a polymer matrix and will not be bioavailable.

6.1.2. Public exposure

There is negligible potential for public exposure to the notified chemical as it will only be used within the aerospace industry and once cured the notified chemical will be bound within a polymer matrix and will not be bioavailable.

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	oral LD50 > 2000 mg/kg bw low toxicity
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw low toxicity
Rat, acute inhalation toxicity	LC50 0.09 mg/L/4 hour very toxic
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	severely irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence
Guinea pig, skin sensitisation – adjuvant test	evidence of sensitisation
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution.

Based on the low molecular weight (< 500 Da) and the low lipophilicity of the notified chemical (water solubility 0.060 g/L at 20ºC; log Pow = log P_{ow} =-0.0036) dermal absorption may occur, but the transfer from the stratum corneum into the epidermis is expected to be slow.

Acute toxicity.
The notified chemical is considered to be of low acute toxicity via the oral and dermal routes based on tests conducted in rats. The notified chemical is very toxic via inhalation based on a test conducted in rats.

Irritation and Sensitisation.
Based on tests conducted in rabbits the notified chemical is considered to be non-irritating to the skin and severely irritating to the eye.

The notified chemical was found to be a non-sensitiser in one maximisation test involving guinea pigs where a 25% topical application was used at challenge. In second maximisation test involving guinea pigs where a 10% topical application was used at challenge, 70% of the guinea pigs in the test group exhibited a reaction significantly greater than in the control animals. In 4 separate local lymph node assays conducted using mice the notified chemical was found to be a strong sensitiser (J. Appl. Toxicol., 1992). Therefore, based on the weight of evidence the notified chemical is considered to be a sensitiser.

Mutagenicity.
The notified chemical was found to be non mutagenic using a bacterial reverse mutation test.

Health hazard classification
Based on the acute inhalation, eye irritation and sensitisation tests the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrases:
T^+: R26 Very toxic by inhalation
Xi: R41 Risk of serious damage to eyes
Xi: R43 May cause sensitisation by skin contact

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
Dermal and ocular exposure to the notified chemical (up to 30%) will be possible during the manufacture of articles. The notified chemical is severely irritating to the eyes and a sensitiser and as such, good hygiene practices should be maintained and exposure to the skin and eyes minimised by the use of impervious gloves, safety glasses and protective clothing.

The notified chemical is very toxic by inhalation. Inhalation exposure to the notified chemical is likely to be negligible due to the very low vapour pressure (1.33×10^{-11} kPa) of the notified chemical and the form of the resin in which it will be introduced. Inhalation exposure will be further minimised by the enclosed systems and the use of exhaust ventilation. Therefore, the risk to workers from inhalation exposure to the notified chemical is not considered to be unacceptable.

Given the risk of causing skin sensitisation and eye irritation, the risk to workers is likely to only be acceptable when used under controlled conditions with the appropriate PPE.

6.3.2. Public health
There is negligible potential for public exposure to the notified chemical as it will only be used within the aerospace industry and once cured the notified chemical will not be bioavailable, as it will be bound in an inert polyurethane matrix. Therefore, the risk to public health is considered to be low, due to the expected negligible exposure.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The imported resin, in the end-use formulation, will be transported directly to customer's site for storage and use. Release of notified chemical would only arise if accidental spills occur during transport and handling operations.

RELEASE OF CHEMICAL FROM USE
Very little release of the notified chemical is anticipated during manufacture of parts for the aerospace industry. The closed mould process known as Resin Transfer Moulding (RTM) has a dedicated dispensing system and ≤0.5% of the annual introduction volume is expected to be released as a result of cleaning and maintenance operations. Spillage from pails during transfer operations is expected to account for ≤1% of the annual introduction volume. Residual within import containers may also account for ≤1% of the annual introduction volume. Any notified chemical that is not consumed in the manufacturing process is expected to react with other ingredients in the residual end-use formulation and cure under ambient environmental conditions prior to disposal.

RELEASE OF CHEMICAL FROM DISPOSAL
Resin collected from spillages, cleaning and maintenance operations and from residual within import containers is expected to be disposed of to landfill after curing, through reactions with other ingredients in the end-use formulation.

The majority of the notified chemical will share the fate of the manufactured composite components. Given their use in aircraft, it is expected that this will entail eventual disposal to landfill.

7.1.2 Environmental fate

A single Ready Biodegradability test report was submitted which concluded that the notified chemical is not "ready biodegradable". For the details of the environmental fate studies refer to Appendix C.

7.1.3 Predicted Environmental Concentration (PEC)

Release of the notified chemical to the aquatic environment is not expected to occur in any significant quantities at any stage in its lifecycle. Therefore, a Predicted Environmental Concentration cannot be estimated.

7.2. Environmental effects assessment

The results from the single ecotoxicological investigation conducted on the notified chemical is summarised in the table below. Details of this study can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Daphnia Toxicity	48 h EC50 = 0.59 mg/L (95% C.I. = 0.52 – 0.72 mg/L)	Very toxic to aquatic invertebrates.

7.2.1 Predicted No-Effect Concentration

Based on the single ecotoxicity study submitted, the Predicted No-Effect Concentration has been calculated using a conservative assessment factor of 1000, as shown below.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Invertebrates)	0.59	mg/L
Assessment Factor	1,000	
PNEC:	0.59	µg/L

7.3. Environmental risk assessment

The notified chemical will be imported into Australia in the end-use formulation. The notified chemical is expected to react with other ingredients in the end-use formulation and cross-link under ambient environmental conditions. During the reaction, the notified chemical will be consumed in the formation of an inherently stable cross-linked matrix. Due to the combination of its high toxicity to aquatic invertebrates and low biodegradability, releases of the notified chemical to the aquatic environment could have long-lasting harmful effects. However, release of the notified chemical into water is not expected under the proposed use pattern. Release of the notified chemical to atmosphere will not be significant due to its low vapour pressure, and the specific engineering practices employed. In landfill, cross-linked polymer matrix containing the notified chemical is expected to be stable, immobile and inert. Ultimately, it is expected that this will degrade via abiotic and biotic process to form simple organic compounds and water.

Therefore, the notified chemical is not considered to pose a risk to the aquatic environment under the proposed use and introduction volume.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

Based on the provided data the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)]. The following risk phrases apply to the notified chemical:

- T^+: R26 Very toxic by inhalation
- Xi: R41 Risk of serious damage to eyes
- Xi: 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 2009) 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	Category 2	Fatal if inhaled
Serious Eye Damage/Eye Irritation	Category 1	Causes serious eye damage
Skin Sensitisation	Category 1A	May cause an allergic skin reaction
Environment	Acute Category 1	Very toxic to aquatic life
Environment	Chronic Category 1	Very toxic to aquatic life with long lasting effects

Human health risk assessment

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

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

Environmental risk assessment

On the basis of the reported use pattern, the notified chemical is not expected to pose a risk to the environment.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia should consider the following health hazard classifications for the notified chemical:
  - T^+: R26 Very toxic by inhalation
  - Xi: R41 Risk of serious damage to eyes
  - Xi: R43 May cause sensitisation by skin contact

- Use the following cut-off concentrations and risk phrases for products/mixtures containing the notified chemical:
  - Conc ≥ 10%: R26; R41; R43
  - ≥ 7% Conc < 10%: R26; R36; R43
  - ≥ 5% Conc < 7%: R23; R36; R43
  - ≥ 1% Conc < 5%: R23; R43
  - ≥ 0.1% Conc < 1%: R20

Health Surveillance

- As the notified chemical is a sensitiser and very toxic by inhalation, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of sensitisation or inhalation exposure to the notified chemical.

CONTROL MEASURES
Occupational Health and Safety

- Employers should ensure that the facilities are equipped such that operations involving the notified polymer are performed in a controlled manner. The following isolation and engineering controls should be in place to minimise occupational exposure to the notified polymer:
  - Automated processes
  - Local exhaust ventillation
  - Sealed equipment

- Employers should implement the following safe work practices to minimise occupational exposure during handling of products containing the notified polymer:
  - Avoid inhalation of aerosols/particles
  - Avoid contact with skin and eyes
  - Clean spills immediately, taking care to avoid inhalation

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical in the product CYCOM 5250-4 RTM resin:
  - impervious gloves
  - safety glasses
  - protective clothing
  - respirator

  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 *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified chemical should be disposed of to landfill.

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(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the notified chemical is introduced in a powdered form instead of a resin.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of resin (up to 30%) for the manufacture of composite materials, or is likely to change significantly;
- the amount of chemical being introduced has increased from 1 tonne, 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.

Material Safety Data Sheet
The MSDS 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 MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility 0.060 g/L at 20°C

Method EC Directive 92/69/EEC A.6 Water Solubility.
Remarks Flask Method, with HPLC/UV analysis. The chromatographic analysis apparently shows that the test item isn't stable in water. Additional peaks in the chromatogram of the notified chemical were attributed to hydrolysis products, although they were not identified.
Test Facility Kesla Forschung and Service GmbH, Greppin, Germany (2006)

Particle Size

Inhalable fraction (<100 µm): 100%
Respirable fraction (<10 µm): > 85%
MMAD = 1.8 -3.1 µm

Method OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions.

Range (µm)	*Mass (%)*
29.5	1.8 – 2.4
18.2	1.7 – 3.4
8.5	3.2 – 9.3
5.5	3.7 – 9.3
2.8	23.9 – 35.9
1.2	25.7 – 33.4
< 1.2	16.1 – 32.3

Remarks The particle size was measured as part of the acute inhalation toxicity test. A sample for particle size testing was taken from each of the 4 dose groups.
Test Facility BASF (1990)

Flammability Not highly flammable

Method EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks The test substance could not be ignited although it did melt and emit sparks while in contact with the ignition source.
Test Facility NOTOX (2003a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 401 Acute Oral Toxicity. EC Directive 92/69/EEC B.1 Acute Toxicity (Oral).
Species/Strain	Rat/Wistar
Vehicle	Distilled water
Remarks - Method	The test substance was administered via gavage. No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	5 per sex	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity	There were no deaths from the test material. Ruffled fur (5 animals) and a hunched posture (1 male) were observed during the course of the study.
Effects in Organs	Discolouration of the liver and lungs was noted in 1 male animal.
Remarks - Results	Body weight gains were as expected.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	RCC (1990a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal).
Species/Strain	Rat/Wistar
Vehicle	Distilled water
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
I	5 per sex	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	Scales and yellow discolouration of the skin was seen in all animals.
Signs of Toxicity - Systemic	There were no deaths or test-substance related clinical signs.
Effects in Organs	Discolouration of the lungs was seen in 1 animal per sex.
Remarks - Results	Body weight gains were as expected.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	RCC (1990b)

B.3. Acute toxicity – inhalation

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 403 Acute Inhalation Toxicity.
Species/Strain	Rat/Wistar
Vehicle	Test substance administered as supplied
Method of Exposure	Oro-nasal exposure.
Exposure Period	4 hours
Physical Form	solid aerosol (particulate).
Particle Size	Inhalable fraction (<100 μm): 100% Respirable fraction (<10 μm): > 85% MMAD = 1.8 -3.1 μm
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Concentration mg/L*		*Mortality*
		Nominal	*Actual*	
I	5 per sex	0.021	0.016	0/10
II	5 per sex	5.77	0.13	7/10 (5 male, 2 female)
III	5 per sex	15.5	0.52	10/10
IV	5 per sex	28.1	5.0	10/10

LC50	0.09 mg/L/4 hours both sexes combined > 0.016 and < 0.13 mg/L/4 hours male rats Approximately 0.13 mg/L/4 hours female rats
Signs of Toxicity	The only sign of toxicity noted in the lowest dose group was accelerated respiration. In the higher dose groups a range of respiration difficulties were observed as well as eyelid closure, nasal discharge, restlessness during the first few hours and apathy at later stages. All recorded deaths occurred on day 1 of study, except for group III, where 3 deaths occurred on day 2.
Effects in Organs	In animals dying during study, main effects were hyperaemia, oedema and emphysema of lung and hydrothorax. No adverse effects were seen in animals surviving to end of study.
Remarks - Results	Body weight gains of surviving animals in groups I and II were retarded compared to control animals.
CONCLUSION	The notified chemical is very toxic via inhalation.
TEST FACILITY	BASF (1990)

B.4. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Directive 84/449/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 (1male, 2 female)
Vehicle	The test substance was moistened with distilled water prior to application.
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	Study terminated after 72 hrs as no irritant effects were seen.

RESULTS

Remarks - Results	No acute clinical symptoms were observed in animals during the test

period, and no mortality occurred. No effect on bodyweight gain was seen.

CONCLUSION The notified chemical is non-irritating to the skin.

TEST FACILITY RCC (1989a)

B.5. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 84/449/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain Rabbit/New Zealand White
Number of Animals 3 (1male, 2 female)
Observation Period 21 days
Remarks - Method No significant protocol deviations

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	2	2	2	2	21 days	1
Conjunctiva: chemosis	3	3	3	3	14 days	0
Conjunctiva: discharge	**	**	**	**	14 days	0
Corneal opacity	2.7	2.7	2.7	4	21 days	3
Iridial inflammation	1	1	1	2	21 days	1

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.
** No score assigned, but described as severe at all observation times up to 14 days.

Remarks - Results Corneal opacity was seen in all animals from 1 hour to 21 days. Corrosion (partial) of the conjunctiva was observed in all animals from 24 or 48 hours to 7 days post treatment. Conjunctiva chemosis and discharge had resolved in all animals by day 14.
No acute clinical effects or effects on bodyweight gains were seen.

CONCLUSION Considering that severe ocular lesions were still present at the end of the observation period, the notified chemical is severely irritating to the eye.

TEST FACILITY RCC (1990c)

B.6. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD TG 406 Skin Sensitisation - Maximisation test (Magnusson and Kligman method)
EC Directive 84/449/EC B.6 Skin Sensitisation - Maximisation test (Magnusson and Kligman method)

Species/Strain Guinea pig/albino (Himalayan spotted)
PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: 3% (test substance in ethanol)
topical: 25% (test substance in ethanol)
MAIN STUDY
Number of Animals Test Group: 20 (10 animals per sex)
Control Group: 10 (5 animals per sex)

INDUCTION PHASE	Induction Concentration: intradermal: 3% (test substance in ethanol) topical: 25% (test substance in ethanol)
Signs of Irritation	Slight to well defined erythema was seen in all test group animals immediately after induction along with slight oedema in 3 animals. Slight oedema was still present in 3 animals after 24 hours but erythema was observed in half of the test animals. At the 48 hour observation no oedema was observed with slight to well defined erythema present in 4 animals.
CHALLENGE PHASE	
1st challenge	topical: 25% (test substance in ethanol)
Remarks - Method	No significant protocol deviations.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after: 1st challenge*	
		24 h	*48 h*
Test Group	0% (ethanol only)	0/19	0/19
	25%(test substance in ethanol)	0/19	0/19
Control Group	0% (ethanol only)	0/10	0/10
	25%(test substance in ethanol)	0/10	0/10

Remarks - Results	One female died spontaneously (on day 3 of study). No systemic effects were observed during the study. No effect on bodyweight gain was seen. At 24 and 48 hours after the challenge procedure, all irritation scores in test and control animals were zero. The positive control induced a marked sensitisation response confirming the sensitivity of the test.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	RCC (1990d)

B.7. Skin sensitisation

TEST SUBSTANCE	Notified chemical
METHOD	The method was based on that described in the following 2 references. Magnusson and Kligman (1969) Magnusson and Kligman (1970)
Species/Strain	Guinea pig/Dunkin Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: 0.1% (test substance in ethanol)
MAIN STUDY	
Number of Animals	Test Group: 10 Control Group: 4
INDUCTION PHASE	Induction Concentration: topical: 25%
Signs of Irritation	The paper mentions that intradermal injections of a slightly irritating concentration were applied.
CHALLENGE PHASE	
1st challenge	topical: 10%
Remarks - Method	Freund's complete adjuvant was injected along with the notified chemical during the preliminary stage. An occluded dressing was applied for 48 hours during the induction phase.

The potential of the test substance to cause skin sensitisation was determined by assessment of the erythema at 24 and 48 hours after the challenge procedure.
The use of a positive control was not reported.

RESULTS

Remarks - Results
No deaths or signs of toxicity were reported.

The percentage of guinea pigs exhibiting a reaction significantly greater than in the control animals was 70%.

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

TEST FACILITY
J. Appl. Toxicol. (1992)

B.8. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE
Notified chemical

METHOD
The method was based on that described in the following 3 references:
Kimber et al. (1989)
Kimber et al. (1991)
Basketter et al. (1991)
Species/Strain
Mouse/CBA/Ca female
Vehicle
Dimethylfomamide and dimethyl sulfoxide
Remarks - Method
The study was carried out in four different laboratories, 3 used dimethylfomamide as the vehicle and 1 used dimethyl sulfoxide (Lab A).
The proliferative response values were not reported in the paper.
The study differed from the test methods above with the modification that the test subjects received topical applications of the test substance on 3 consecutive days and the assay was terminated after 5 days.
Whether a positive control was used was not reported in the paper.

RESULTS

Concentration of test substance (% w/w)	*Stimulation Index (Test/Control Ratio)*			
	Lab A	*Lab B*	*Lab C*	*Lab D*
0 (vehicle control)				
2.5	-	-	-	18.4
5.0	11.9	13.8	16.3	29.6
10.0	12.2	19.1	25.3	35.3
25.0	11.8	15.5	25.7	-

Remarks - Results
No information on test subject deaths or signs of systemic toxicity was reported in the paper.
A stimulation index of greater than 3 was observed for all concentrations of the test substance.

CONCLUSION
There was evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical.

TEST FACILITY
J. Appl. Toxicol. (1992)

B.9. 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	Rat S9 fraction from phenobarbitone/β-napthoflavone induced rat liver
Concentration Range in Main Test	*Test 1* TA100 and WP2uvrA a) With metabolic activation: 3 – 5000 µg/plate b) Without metabolic activation: 3 – 5000 µg/plate TA1535, TA1537 and TA98 a) With metabolic activation: 3 – 1000 µg/plate b) Without metabolic activation: 3 – 1000 µg/plate *Test 2* TA1535 and TA100 a) With metabolic activation: 3 – 333 µg/plate b) Without metabolic activation: 3 – 333 µg/plate TA1537 and TA98 a) With metabolic activation: 3 – 333 µg/plate b) Without metabolic activation: 1 – 100 µg/plate WP2uvrA a) With metabolic activation: 10 – 1000 µg/plate b) Without metabolic activation: 10 – 1000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	5% v/v of S9 was used in experiment 1 and 10% v/v S9 was used in experiment 2. No significant protocol deviations. The positive control chemical for all strains with metabolic activation was 2-aminoanthracene. Positive control chemicals without activation: TA 1535: sodium azide; TA1537: 9-aminoacridine; TA98: 2-nitrofluorene; TA100: MMS; Negative control: solvent (dimethyl sulfoxide).

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	333	100	> 5000	negative
Test 2		100	> 1000	negative
Present				
Test 1	333	100	> 5000	negative
Test 2		100	> 1000	negative

Remarks - Results	No toxicologically significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test material, either with or without metabolic activation. Moderate reduction in the background lawn seen at a concentration of 100 µg/plate in both tests with and without the presence of metabolic activation. Negative controls were within historical limits. All the positive control chemicals used in the test induced marked increases in the frequency of revertant colonies thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.

CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	NOTOX (2008)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test. EC Directive 92/69/EEC C.4-C Biodegradation: Determination of the "Ready" Biodegradability: Carbon Dioxide Evolution Test
Inoculum	Activated sludge from a municipal STP.
Exposure Period	29 days
Auxiliary Solvent	Water
Analytical Monitoring	None.
Remarks - Method	No significant protocol deviations. Since the notified chemical was not sufficiently soluble, test solutions were continuously stirred during the test to ensure optimal contact between the test substance and the test organisms.

RESULTS

Test substance		*Sodium acetate*	
Day	*% Degradation (Avg)*	*Day*	*% Degradation*
0	0	0	0
2	3.5	2	9
5	7.5	5	43
7	8	7	59
9	8	9	68
14	8	14	75
19	10	19	83
23	12	23	86
27	14	27	86
29	16	29	88

Remarks - Results	Since all criteria for acceptability of the test were met, this study was considered to be valid.
CONCLUSION	The notified chemical cannot be classed as ready biodegradable.
TEST FACILITY	NOTOX (2003b)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	ISO International Standard 6341 – Water Quality – Determination of the inhibition of the mobility of *Daphnia magna Straus* – Acute Toxicity Test, Third Edition (1996). OECD TG 202 *Daphnia sp* Acute Immobilisation Test and Reproduction Test – 48 hr flow-through (1994). EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia.
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Dimethylsulphoxide
Water Hardness	250 mg $CaCO_3$/L

Analytical Monitoring	Temperature was recorded continuously. Dissolved oxygen and pH were recorded before and after study. The concentrations of the test solutions were verified by chemical analysis at 0 hr, 24 h and 48 h using a validated HPLC analytical method.
Remarks - Method	No significant protocol deviations. Target concentrations were within 30-60% of nominal concentrations for the definitive flow-through test. Concentrations remained within 20% variance during the study period. Flow through rate 6 L/h. The sensitivity of *Daphnia* was checked by a reference test with potassium dichromate (48 h EC50 = 0.60 mg/L).

RESULTS

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual (mean*)*		*24 h*	*48 h*
0**	0	20	0	0
0.10	0.059	20	0	0
0.22	0.085	20	0	0
0.46	0.19	20	0	0
1.0	0.31	20	0	0
2.2	0.82	19	12	16

*mean of 0 hr and 48 hr analyses. **DMSO

EC50	0.71mg/L at 24 hours (95% C.I. = 0.60 – 0.94 mg/L) 0.59 mg/L at 48 hours (95% C.I. = 0.52 – 0.72 mg/L)
NOEC	0.31 mg/L at 48 hours
Remarks – Results	The study met the acceptability criteria prescribed by the protocols and was considered valid.

CONCLUSION The notified chemical is very toxic to aquatic invertebrates.

TEST FACILITY NOTOX (2003c)

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