File No: STD/1601

March 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Carbamo(dithioperoxo)thioic acid, *N*,*N*-bis(phenylmethyl)-, *C*,*C*'-1,6-hexanediyl ester

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (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 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 and Energy.

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

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Director
NICNAS

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SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1601	Lanxess Pty Ltd	Carbamo(dithioperoxo)thioic acid, *N*,*N*-bis(phenylmethyl)-, *C*,*C*'-1,6-hexanediyl ester	No	≤ 10 tonnes per annum	Rubber crosslinking agent

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

Human health risk assessment
Provided that the recommended controls are being adhered to, under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

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

Environmental risk assessment
On the basis of the low expected aquatic release and the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical:
  - Local exhaust ventilation if dust/aerosols are generated

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid inhalation of dust/mist/fumes

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Safety glasses
  - Respiratory protection if inhalation exposure may occur

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)*

as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

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 rubber containing the notified chemical is used in articles intended to come in contact with potable water

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from rubber crosslinking agent, or is likely to change significantly;
  - the amount of chemical being introduced has increased, 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 (M)SDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT
Lanxess Pty Ltd (ABN: 58 071 919 116)
Unit 1, 31 Hill Road
HOMEBUSH BAY NSW 2127

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: analytical data, degree of purity, impurities, use details, import volume and site of reformulation.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: Vapour pressure, Adsorption/Desorption, and Dissociation constant

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA, China, EU and Korea

2. IDENTITY OF CHEMICAL

MARKETING NAME
Vulcuren® VP KA 9188

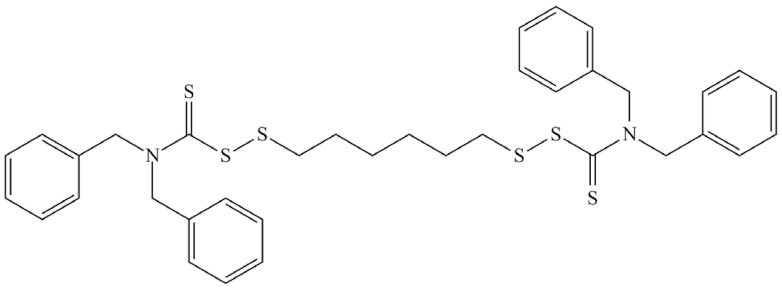
CAS NUMBER
151900-44-6

CHEMICAL NAME
Carbamo(dithioperoxo)thioic acid, *N*,*N*-bis(phenylmethyl)-, *C*,*C*'-1,6-hexanediyl ester

OTHER NAMES
1,6-Bis(*N,N*-dibenzylthiocarbamoyldithio)hexane
1,6-Bis(*N,N'*-dibenzylthiocarbamoyldithio)hexane
KA 9188
Vulcuren
VP-KA 9188
Vulcuren KA 9188
Vulcuren Trial Product KA 9188
Vulcuren VP-KA 9188

MOLECULAR FORMULA
$C_{36}H_{40}N_2S_6$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
693.12 Da

ANALYTICAL DATA
Reference NMR, IR, HPLC and UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 87 %

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: colourless to pale yellow powder

Property	Value	Data Source/Justification
Melting Point/Freezing Point	90.9 °C	Measured
Boiling Point	Not determined	Measured. Decomposes at 145°C before boiling
Relative Density	1.299 at 20 °C	Measured
Vapour Pressure	3.73×10^{-18} kPa at 25 °C	Calculated using MPBPVP v1.43 (US EPA, 2011)
Water Solubility	$< 5 \times 10^{-5}$ g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Not expected to hydrolyse based on low water solubility
Partition Coefficient (n-octanol/water)	Log P_{OW} = 10.4	Measured
Adsorption/Desorption	Log K_{OC} = 7.866	Calculated using KOCWIN v2.00 (US EPA, 2011)
Dissociation Constant	Not determined	Contains no dissociable functionalities
Particle Size*	1.14-830 µm fraction: 6.6% 830-5900 µm fraction: 93.4% MMD# 1.14 – 5900 µm	Measured. Oil is added to the powder to prevent dust formation
Solid Flammability	Not highly flammable	Measured
Autoignition Temperature*	> 420 °C	Measured
Explosive Properties	Not determined	Contains no functional group that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional group that would imply oxidising properties

* – study summary only provided in English
# – MMAD = Mass Median Diameter

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

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

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

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported in neat form for use under industrial settings.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 10	< 10	< 10	< 10	< 10

PORT OF ENTRY
Melbourne and Sydney

TRANSPORTATION AND PACKAGING
The notified chemical at concentration > 87% will be imported into Australia in 20.3 kg lined paper bags stacked on pallets and shrink wrapped. From the port of entry, the notified chemical will be transported by road to the warehouse and /or site of end-use.

USE
The notified chemical is a crosslinking agent used in manufacture of rubber. The notified chemical will be added at a rate of 0.5 – 3% during the manufacture of rubber.

OPERATION DESCRIPTION
The notified chemical will initially be compounded into rubber using a two-roll mill, which flattens and draws out the rubber into thin sheets. The milling workers will manually weigh and add the notified chemical onto the rubber sheet surface as the sheet transverses between the two rollers.

During the moulding process, the rolls of milled rubber will be manually placed into the barrel of an extruder. The rubber sheet is then made to the required shape using compression moulding, in an automatic process with exhaust ventilation. Heat will be applied during moulding to cure the rubber containing the notified chemical. The moulding process is expected to be carried out in an enclosed system and the moulded articles will only be handled after they cool down. The rubber may be cut to size using mechanical methods. The moulded articles and the moulds will be cleaned mechanically. The rubber waste generated during moulding and from cleaning of the moulding machine will be collected for re-use.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and warehouse	0.5-1	12-24
Milling	4-8	200
Moulding/extrusion	4-8	200

EXPOSURE DETAILS
Transport and warehouse workers are not expected to be exposed to the notified chemical except in the unlikely event of an accident where the container is breached. Spills will be cleaned by workers using an industrial vacuum cleaner. According to the notifier, the cleaners are expected to wear proper personal protective equipment (PPE) including dust masks to reduce exposure to the notified chemical.

Mill workers may be exposed to the notified chemical at up to 87% concentration via the dermal, ocular and perhaps inhalation route during the manual weighing and addition of the notified chemical to the rubber while the rubber transits between the rollers. According to the notifier, the workers are expected to wear PPE such as coveralls, safety boots, impervious gloves, safety goggles and respiratory protection (dust mask) to reduce exposure. The notified chemical is proposed to be supplied in an anti-dusting form, which would reduce the likelihood of inhalation exposure.

Extrusion and moulding workers may be exposed to the notified chemical at concentration up to 3% via the dermal and ocular route during transfer of the milled rubber into the moulding and/or extrusion machine. The moulding/extrusion is expected to be carried out in enclosed equipment with local exhaust ventilation. The

notifier advised that workers are expected to wear PPE such as coveralls, safety boots, impervious gloves and safety goggles to reduce exposure.

After extrusion and/or moulding, the notified chemical is expected to be cross-linked within the moulded rubber. This will trap the notified chemical into the rubber matrix and hence the notified chemical is not expected to be available for exposure after the moulding stage.

6.1.2. Public Exposure

The notified chemical is for industrial use only. The rubber products containing the notified chemical are also intended for use under industrial settings only and thus the general public is not expected come into contact with the notified chemical.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation*	non-irritating
Rabbit, eye irritation	slightly irritating
Rabbit, eye irritation*	irritating
Guinea pig, skin sensitisation – adjuvant test (GPMT)	no evidence of sensitisation
Guinea pig, skin sensitisation – non-adjuvant test (Buehler)*	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOAEL 1,000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian chromosome aberration test	clastogenic
Genotoxicity – *in vivo* mammalian erythrocyte micronucleus test	non clastogenic
Genotoxicity – *in vivo* alkaline comet assay	non genotoxic
Rat developmental toxicity	NOAEL 1,000 mg/kg bw/day NOEL 300 mg/kg bw/day

* – study summary only provided in English

Toxicokinetics, metabolism and distribution

No information on toxicokinetics, metabolism and distribution of the notified chemical was available. The molecular weight (693 Da), very low solubility in water (< 0.05 mg/L) and partition coefficient (Log P_{OW} = 10.4) would limit transport of the notified chemical across biological membranes. According to a study, approximately 6.6 % of the notified chemical has particle size < 830 µm.

Acute toxicity

The notified chemical was found to be of low toxicity via the oral and dermal routes with LD > 2,000 mg/kg body weight. No information on inhalation toxicity was provided. However, based on the calculated vapour pressure (3.73×10^{-18} kPa at 25 °C), the notified chemical, inhalation exposure is not likely unless dusts or aerosols are generated.

Irritation and sensitisation

The notified chemical was non-irritating to the skin and slightly irritating to the eyes with corneal effects in studies in rabbits carried out to OECD guidelines. A second eye irritation study was disregarded in the REACH dossier as purity was lower than usual. This study showed some conjunctival effects as well as corneal effects.

A guinea pig maximisation and Buehler test on the notified chemical reported the test substance to be non-sensitising.

Repeated dose toxicity

A 28-day repeated dose oral toxicity study with a 14 day recovery period was carried out on the notified chemical. The test animals were fed the test substance at concentrations of 40, 200 and 1,000 mg/kg bw/day. No deaths or signs of toxicological relevance were reported by the study authors, with minor reversible effects observed in clinical chemistry, haematology and organ weights. A No Observed Adverse Effect Level (NOAEL) of 1,000 mg/kg bw/day was established by the study authors.

Mutagenicity/Genotoxicity
Two *in vitro* and two *in vivo* genotoxicity studies were conducted using the notified chemical.

The notified chemical was found to be clastogenic in an *in vitro* mammalian chromosome aberration test conducted using Chinese Hamster V79 cell lines, in the presence of metabolic activation system (S9 mix) and at an 18 h harvest time. In the remainder of the studies for genotoxicity (one *in vitro* and two *in vivo* tests), the notified chemical did not induce any mutation or chromosome aberrations.

Considering the negative results in 3 of 4 studies, including both *in vivo* studies, on a weight of evidence the notified chemical is not expected to be genotoxic.

Developmental Toxicity
A prenatal developmental study was conducted using the notified chemical at 100, 300 and 1000 mg/kg bw/day concentrations. The test substance was administered by oral gavage from day 6 to day 20 of gestation. A NOAEL of 1000 mg/kg bw/day was established by the study authors, and a NOEL of 300 mg/kg bw/day was set, based on the increased incidence of engorged placentas observed at 1000 mg/kg bw/day.

Health hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the provided toxicological information, the notified chemical is slightly irritating to the eyes. Workers handling the notified chemical during rubber production may be exposed to the notified chemical at up to 87% concentration via the dermal, ocular and inhalation routes. Exposure would be reduced by the use of engineering controls for some processing steps, including local exhaust ventilation. The proposed use of PPE including coveralls, impervious gloves, safety boots, safety goggles and respiratory protection if required will also reduce exposure to the notified chemical during processing. Once bound in the rubber, the notified chemical is not expected to be significantly bioavailable. Overall, the risk to the occupational health and safety of workers is not considered unreasonable.

6.3.2. Public Health
The notified chemical will not be available to the public. The public is unlikely to come in contact with the rubber material which contains the notified chemical due to its limited use in industry only. Once incorporated into the rubber, the notified chemical will be bound into the rubber matrix and is not expected to be significantly available for exposure, hence the risk to the public is not considered unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified chemical will be imported neat into Australia for use as a crosslinking agent in the manufacture of rubber products. There is unlikely to be any significant release to the environment from transport and storage, except in the case of accidental spills and leaks. In the event of spills, the notified chemical is expected to be collected and disposed of to landfill in accordance with local government regulations.

During the rubber manufacturing process, the notified chemical will be manually applied between rubber sheets, followed by compounding and curing of the finished rubber. The compounding and curing process will involve operations that will be highly automated, and is expected to occur within a fully enclosed environment. The finished rubber will then be moulded or extruded into finished articles within the enclosed system. Therefore, significant release of the notified chemical from this process to the environment is not expected. Wastes containing the notified chemical generated during rubber manufacture include equipment cleaning wastes, residues in import containers, excess rubber trimmings and spilt materials. It is estimated by the notifier that up to 2.1% of the import volume of the notified chemical (or up to 210 kg) may be released as wastes and spilt material during rubber manufacturing processes. These are expected to be collected and recycled during

subsequent manufacturing batches, or disposed of to landfill in accordance with local government regulations. Empty import containers will be collected for disposal to landfill.

RELEASE OF CHEMICAL FROM USE
The majority of the notified chemical is expected to be cured within an inert rubber matrix in rubber articles. A small proportion of the rubber containing the notified chemical may be released to the environment as a result of mechanical wear of rubber articles during use. It is estimated by the notifier that up to 2% of the import volume of the notified chemical (or up to 200 kg) may be released from mechanical wear of rubber articles.

RELEASE OF CHEMICAL FROM DISPOSAL
The majority of the notified chemical will be cured within rubber articles, and is expected to share the fate of the rubber articles. These are expected to be disposed of to landfill at the end of their useful life.

7.1.2. Environmental Fate
The majority of the notified chemical will be cured within an inert rubber matrix, and will share the fate of the rubber articles. Therefore, the notified chemical in this form is not expected to be mobile or bioavailable. Based on the results of a ready biodegradability study and an inherent biodegradability study, the notified chemical is not considered to be readily biodegradable (showing 14% in 28 days) or inherently biodegradable (showing 0% degradation in 56 days). For details of the environmental fate studies, please refer to Appendix C. Although the measured partition coefficient of the notified chemical is high (log P_{OW} = 10.4), it is not expected to be bioaccumulative based on the results of a bioaccumulation study (notified chemical was below the limit of quantitation). Based on its low water solubility and calculated adsorption coefficient, the notified chemical is expected to bind strongly to soil and sediment, and is therefore not expected to be mobile. In landfill, the notified chemical is expected to eventually degrade through biotic and abiotic processes to form water and oxides of carbon, sulphur and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)
The predicted environmental concentration (PEC) has not been calculated, as significant release of the notified chemical to the aquatic environment is not expected, based on its reported use pattern as a crosslinking agent in rubber manufacture.

7.2. Environmental Effects Assessment
The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h LL50 > 1 mg/L (WAF*)	Not harmful to fish up to water solubility limit
Daphnia Toxicity	48 h EL50 > 7.6 mg/L (WAF*)	Not harmful to aquatic invertebrates up to water solubility limit
	21 d NOEL = 0.024mg/L (WAF*)	Not harmful to aquatic invertebrates up to water solubility limit (chronic)
Algal Toxicity	72 h EL50 > 24.9 mg/L (WAF*)	Not harmful to algae up to water solubility limit
Inhibition of Bacterial Respiration	3 h IC50 > 10,000 mg/L	Not inhibitory to microbial respiration

* Water accommodated fraction

The notified chemical is determined to be not harmful to aquatic life up to the water solubility limit on acute basis. Therefore, the notified chemical is not formally classified under the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* (United Nations 2009).

The notified chemical is poorly soluble in the testing medium, reaching 0.024 mg/L in a chronic study. The maximum solubility was assumed to be achieved in this study, as it was within the range determined in the water solubility study (< 0.05 mg/L). No long term toxic effects to aquatic invertebrates were observed in the study at the limit of its water solubility. Therefore, the notified chemical is not formally classified for its long term hazard under the GHS.

7.2.1. Predicted No-Effect Concentration
A predicted no-effect concentration (PNEC) for the aquatic compartment has not been calculated, since the notified chemical is not harmful to aquatic life up to the limit of its solubility in water. There is also no significant release of the notified chemical to the aquatic environment expected.

7.3. Environmental Risk Assessment

The Risk Quotient (Q = PEC/PNEC) has not been calculated, since neither the PEC nor PNEC are available. Although the notified chemical is not considered readily biodegradable, it is expected to have a low potential for bioaccumulation. On the basis of the low expected aquatic release and assessed use pattern as a crosslinking agent in rubber manufacture, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point 90.9 °C

Method	EC Council Regulation No 92/69 A.1 Melting/Freezing Temperature.
Remarks	Differential thermal analysis method. Two samples were tested. A study summary only was provided.
Test Facility	Bayer AG (1999a)

Boiling Point Not determined

Method	EC Council Regulation No 92/69 A.2 Boiling Temperature.
Remarks	Differential thermal analysis (DTA) and Isothermal Step Thermal Analysis (ISTA) methods. In the first run the DTA system was used. In the second run the ISTA method with a slower heating rate was used. The test substance decomposed at 145 °C before boiling. A study summary only was provided.
Test Facility	Bayer AG (1999a)

Relative Density 1.299 at 20 °C

Method	EC Council Regulation No 92/69 A.3 Relative Density.
Remarks	Pycnometer method. Two samples were tested. Study summary only was provided
Test Facility	Bayer AG (1999a)

Water Solubility $< 5 \times 10^{-5}$ g/L at 20 °C

Method	EC Council Regulation No 92/69 A.6 Water Solubility.
Remarks	Column Elution Method
Test Facility	Bayer AG (1999b)

Partition Coefficient (n-octanol/water) log Pow = 10.4

Method	EC Council Regulation No 92/69 A.8 Partition Coefficient.
Remarks	Reverse Phase HPLC Method
Test Facility	Bayer AG (1999c)

Flammability Not highly flammable

Method	EC Council Regulation No 440/2008 A.10 Flammability (Solids).
Remarks	In the preliminary test, the test substance melted when approached by the ignition flame. The test substance did not burn down or burn up. Therefore no further testing was required.
Test Facility	Bayer AG (1999d)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 401 Acute Oral Toxicity – Limit Test (1987).
- Species/Strain: Rat/Bor: WISW (SPF Cpb)
- Vehicle: Corn Oil MEH 56
- Remarks - Method: No significant variations from the OECD guideline. The test substance was finely crushed and suspended in corn oil. A preliminary test was conducted on 2 male and 2 female rats followed by a limit test consisting 3 rats of each sex. The combined results are presented below.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
A	5 F / 5 M	2,000	0/10

- LD50: > 2,000 mg/kg bw
- Signs of Toxicity: Five to six afters after administration 3 male rats had diarrhoea. One female rat showed squatting position and rough coat. These effects had resolved by 72 h. No signs of toxicity were noted in other test animals.
- Effects in Organs: None reported
- Remarks - Results: No deaths were observed. No significant changes in body weight and weight gains were observed. Necropsies and gross pathological examinations of organs showed no evidence of test substance related effects.

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

TEST FACILITY: Hüls AG (1992a)

B.2. Acute toxicity – dermal

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 402 Acute Dermal Toxicity – Limit Test (1987).
- Species/Strain: Rat/Bor: WISW (SPF Cpb)
- Vehicle: Corn Oil MEH 56
- Type of dressing: Semi-occlusive.
- Remarks - Method: No significant deviations from the OECD guideline. The exposure period was 24 hours. The test substance was finely crushed and suspended in corn oil. A preliminary test was conducted on 2 male and 2 female rats followed by a limit test consisting 3 rats of each sex. The combined results are presented below.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
A	5 F / 5 M	2,000	0/10

- LD50: > 2,000 mg/kg bw
- Signs of Toxicity - Local: Scale formation was observed at the site of test substance application in 3 female rats and two of those also displayed redness on day 5. After the scales had been shed on day 7 (2 animals) and day 9 (1 animal) the application surface was normal.

Signs of Toxicity - Systemic	None reported
Effects in Organs	None reported
Remarks - Results	No deaths were observed. Reduction in weight was observed on day 7 in one female rat and no weight gain was observed in another female rat between day 7 and 14. The changes in body weights were considered by the study authors to be due to physiological reasons. No other significant changes in body weight or weight gains were observed. Necropsies and gross pathological examinations of organs showed no evidence of test substance related effects.

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

TEST FACILITY Hüls AG (1992b)

B.3. Irritation – eye

TEST SUBSTANCE Notified chemical

METHOD	OECD TG 405 Acute Eye Irritation/Corrosion (1987).
Species/Strain	Rabbit/Himalayan
Number of Animals	3 (male)
Observation Period	72 hours
Remarks - Method	No significant deviations from the OECD guideline. A single instillation of 100 mg test substance was done into the conjunctival sac. 24 hours after application, the eyes were treated with fluorescein for examination.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0	0	0	0	-	0
Conjunctiva: chemosis	0	0	0	0	-	0
Conjunctiva: discharge	0	0	0	0	-	0
Corneal opacity	0.33	0.33	0	1	< 48	0
Iridial inflammation	0	0	0	0	-	0

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

Remarks - Results	Whitish deposit (probably pus) was noted in the conjunctival sac of 2 test animals at 24 and 48 hour observations, which had resolved by 72 h. Two animals showed corneal effects at 1 h and 24 h after treatment. This was confirmed by fluorescein staining at 24 h (1/4 of the surface).

CONCLUSION The notified chemical is slightly irritating to the eye.

TEST FACILITY LPT (1999)

B.4. Skin sensitisation

TEST SUBSTANCE Notified chemical

METHOD	OECD TG 406 Skin Sensitisation – Guinea Pig Maximisation Test.	
Species/Strain	Guinea pig/Hsd Poc:DH	
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: 0% topical: 25%	
MAIN STUDY		
Number of Animals	Test Group: 10 F	Control Group: 5 F
Vehicle	Polyethylene glycol 400	

Positive control	Not conducted in parallel. The laboratory had done a GPMT and a Buehler test using α-hexylcinnamaldehyde in same year. The tests were positive.
INDUCTION PHASE	Induction Concentration: intradermal: 2.5% topical: 25%
Signs of Irritation	Strong irritation effects were observed 7 days after the intradermal injection in both test and control groups. Local effects at the site of injection were observed 48 hours after injection in control and test group animals. The effects included white wheals with red surrounding, red wheals or red surrounding. The control animals showed wheals or encrustation after 7 days. At day 9, 48 hours after dermal induction, the treatment area showed grade 1 skin irritation effects in 3 test animals from test group. No effects were observed in control groups.
CHALLENGE PHASE	
challenge	topical: 25%
Remarks - Method	There were no significant deviations from the OECD guideline. Three dose range finding studies were conducted to determine the intradermal and topical induction concentrations and the challenge concentration.

RESULTS

Group	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after patch removal:*	
		24 h	*48 h*
Test	25%	0	0
Control	25%	0	0

Remarks - Results	No skin reactions were observed at the challenge site. No change in weight gain was noted in test animals compared to controls.

CONCLUSION There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY Bayer AG (1999e)

B.5. Repeat dose toxicity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents (1995).

Species/Strain	Rats/HsdCpb:WU
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: Test group – 31 days (males) and 31 days (females) Recovery group – 28 days Dose regimen: 7 days per week Post-exposure observation period: 14 days
Vehicle	Corn oil
Remarks - Method	No significant deviations from the OECD guideline. A separate non guideline dose selection study was conducted. Two female rats were administered the test substance at 1,000 mg/kg bw/day for 5 days.no adverse effects were reported.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5 F / 5 M	0	0/10
low dose	5 F / 5 M	40	0/10

mid dose	5 F / 5 M	200	0/10
high dose	5 F / 5 M	1,000	0/10
control recovery	5 F / 5 M	0	0/10
high dose recovery	5 F / 5 M	1,000	0/10

Mortality and Time to Death
No deaths reported.

Clinical Observations
Discoloration of the faeces was noted in test animals from high dose group during the administration period. No other treatment related changes were reported.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Haematology
Decrease in haemoglobin and haematocrit values were not in males from mid dose group. Decrease in erythrocyte count and mean corpuscular volume was noted in males from high dose group. Decrease in mean corpuscular haemoglobin was observed in high dose recovery group males. Decrease in mean corpuscular haemoglobin concentration was noted in high dose recovery group females. The changes were statistically significant but were within the historical control ranges.

Clinical chemistry
Decrease in creatinine levels were observed in males from mid and high dose groups. Decrease in total bilirubin levels were observed in males from low, mid and high dose groups. Also decrease in albumin levels were observed in males from low dose group and decrease in urea levels were observed in high dose recovery group males. Decrease in sodium levels was observed in females from high dose group. And increase in triiodothyronine (T3) level was noted in females from high dose recovery group. All the changes were statistically significant but were considered by the study authors to be not toxicologically relevant due the lack of dose response or due to the values being within historical control ranges.

Effects in Organs
Statistically significant increase in absolute liver and adrenal weights was observed in females from mid dose (16%) and high dose recovery group (7.4%). Increase in absolute liver weight was also noted in mid dose males (11%) but did not reach statistical significance when compared to control. Increase in absolute ovary weight was observed in high dose recovery group females. No statistically significant changes were observed in relative organ-to-body weights. The absolute weight changes were considered by the study authors to be due to body weight changes and not toxicologically relevant.

No significant changes were noted in histopathological studies. All changes were considered by the study authors to be random.

Remarks – Results
Food intake and body weight changes were not affected in any of the treatment and recovery group animals when compared to controls. No test substance related significant changes in the functional observation battery and the motor activity were noted. The minor changes were considered by the study authors to be random and not toxicologically relevant.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 1,000 mg/kg bw/day by the study authors in this study.

TEST FACILITY Bayer AG (2000a)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical

METHOD OECD TG 471 Bacterial Reverse Mutation Test (1997).
Plate incorporation procedure (Test 1) and Pre incubation procedure (Test 2)

Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100, TA102

Metabolic Activation System	S9 fraction from Aroclor 1254 induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 50-5,000 µg/plate b) Without metabolic activation: 50-5,000 µg/plate
Vehicle	Dimethyl Sulfoxide
Remarks - Method	No significant deviations from the OECD guidelines.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* Cytotoxicity	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,000	≥ 1,581	Negative
Test 2	> 5,000	≥ 1,581	Negative
Present			
Test 1	> 5,000	≥ 1,581	Negative
Test 2	> 5,000	≥ 1,581	Negative

Remarks - Results	The positive controls produced satisfactory results, validating the S9 fraction and the test system.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Bayer AG (2000b)

B.7. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
Species/Strain	*Chinese Hamster*
Cell Type/Cell Line	V79 cells
Metabolic Activation System	S9 fraction from Aroclor 1254 induced rat liver
Vehicle	Dimethyl Sulfoxide
Remarks - Method	No significant deviations from the OECD guideline. A pre-test was conducted to evaluate the toxicity of test substance. Due to strong cytotoxicity effects seen in presence of S9 mix, three additional trials were needed to be performed at test substance concentration ranging from 2 to 32 µg/ml. The result

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	16, 32, 64*, 96*, 128*	4 h	18 h
Test 2	128*	4h	30 h
Present			
Test 1**	6, 12*, 15*, 18*	4 h	18 h
Test 2	18*	4 h	30 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:* Cytotoxicity in Preliminary Test	Cytotoxicity in Main Test	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 128	>128	128	Negative
Test 2		≥96		Negative
Present				
Test 1**	≥ 128	>18	128	Positive
Test 2		≥ 12		Negative

Remarks - Results	Without S9 mix no cytotoxic effects were observed. With S9 mix cytotoxic effects were observed at 12 µg/ml and above, and test 1 was carried out several times, using decreasing concentrations. The results of the last test are reported in the table. Precipitation in the medium occurred at 128 µg/ml and above. In the absence of S9 mix cultures treated with the test substance showed no biologically relevant and statistically significant increased numbers of aberrant metaphases at harvest times of 18 h and 30 h. However in the presence of S9 mix and a harvest time of 18 h, cultures treated with the highest dose of 18 µg/mL test substance showed weakly but biologically relevant and statistically significant increased numbers of aberrant metaphases. In the presence of S9 mix and a harvest time of 30 h, cultures treated with the only dose of 18 µg/mL did not show an increase in aberrant metaphases. No increase in polyploidy metaphases was seen, with or without metabolic activation. The positive controls induced clastogenic effects confirming the validity of the assay and S9 mix.
CONCLUSION	The notified chemical was clastogenic to Chinese Hamster V79 cells treated in vitro under the conditions of the test.
TEST FACILITY	Bayer (2000c)

B.8. Genotoxicity – in vivo

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 474 Mammalian Erythrocyte Micronucleus Test (1997).
Species/Strain	Mice/Hsd/Win:NMRI
Route of Administration	Intraperitoneal
Vehicle	Corn oil
Remarks - Method	No significant deviations from the OECD guideline. A pre-test was conducted for dose selection. The test substance was administered twice, after a 24 h interval. A second high dose group was prepared as a backup, but was not required.

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5 M	0	24
II (low dose)	5 M	1,000	24
III (mid dose)	5 M	2,000	24
IV (high dose)	5 M	4,000	24
V (positive control, CP)	5 M	100	24

CP=cyclophosphamide.

RESULTS	
Doses Producing Toxicity	Test animals exposed to the test substance showing the following signs of toxicity until sacrifice: apathy, roughened fur, spasm and periodically stretching of body which ae symptoms of systemic toxicity. No animal death occurred during the course of the study. The PCE/NCE ratio did not vary significantly between the test and control groups, indicating that bone marrow toxicity did not occur.
Genotoxic Effects	No increase in the incidence of micronucleated polychromatic erythrocytes was seen in the test groups.
Remarks - Results	The clinical signs described above suggest that there was systemic exposure to the test substance.

	The positive control caused the expected increase in micronucleated cells, confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic under the conditions of this *in vivo* micronucleus test.
TEST FACILITY	Bayer AG (2000d)

B.9. Genotoxicity – in vivo

TEST SUBSTANCE	Notified chemical
METHOD	Method similar to OECD TG 489 In Vivo Alkaline Comet Assay. According to an internationally accepted protocol for the comet assay in vivo (Hartmann et al., Mutagenesis vol. 18, no. 1, 45-51, 2003)
Species/Strain	Rat/Wistar
Route of Administration	Oral – gavage
Vehicle	Corn oil
Remarks - Method	Similar to the OECD guideline, except that the recommended three dose levels were not tested. The tissues tested were liver and stomach cells. Five male rats treated once via gavage with 2,000 mg/kg test substance. As vehicle control 5 male rats were treated with corn oil and as positive control 400 mg/kg Ethylmethanesulfonate (EMS) in corn oil was administered once via gavage to 5 male rats. All rats were sacrificed 3 hours after administration. The dose of test substance was selected based on the results of a dose range finding study, demonstrating no tissue toxicity.
RESULTS	
Systemic Toxicity	None reported. No toxicity was evident in stomach and liver cells.
Genotoxic Effects	Negative. The tail lengths of liver and stomach cells revealed no biologically relevant differences to the vehicle control. Although the mean tail length of the stomach cells was higher than the control, with statistical significance $p < 0.01$), it was within the range of historical controls and the difference was not considered by the study authors to be biologically relevant. As one concentration only was tested, it was not possible to see if there was a dose-response.
Remarks - Results	The tail length of positive control was clearly increased as compared to the vehicle control, demonstrating the sensitivity of the test system for the detection of genotoxic effect.
CONCLUSION	The notified chemical was non genotoxic under the conditions of this in vivo comet assay.
TEST FACILITY	Bayer AG (2005)

B.10. Developmental toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 414 Prenatal Developmental Toxicity Study (2001).
Species/Strain	Rat/Wistar Hsd Cpb:WU
Route of Administration	Oral – gavage
Exposure Information	Exposure days: 15 (day 6 to day 20 of gestation)
Vehicle	Corn oil
Remarks - Method	No significant deviations from the OECD guideline. The dose levels were selected based on the results of a previous pilot prenatal developmental study.

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
Control	25	0	0/25
Low	25	100	0/25
Medium	24*	300	0/24
High	25	1,000	0/25

* – one test animal died before the start of the treatment.

Mortality and Time to Death

One female from mid dose group was found dead on day 4 post conception. The death was not test substance related as it occurred before starting the treatment. All animals survived to the scheduled necropsies.

Effects on Dams

No signs of toxicological significance were noted. A statistically significant increased incidence of engorged placentas occurred in high dose group test animals, for which a treatment related effect cannot be ruled out.

One female from high dose group showed unilateral dilation of renal pelvis and one female from low and mid dose groups showed revealed a uterus filled with brownish or clear fluid. These effects were considered by the study authors to be not test substance related due to its presence in controls or lack of dose response respectively.

Total resorption was seen one female from low dose group. Fertility rate, the mean numbers of corpora lutea, preimplantation losses, and implantations sites in the treated groups did not differ to a meaningful extent from the control group values indicating a homogenous distribution regarding these parameters.

Effects on Foetus

Intrauterine development was not affected. The overall incidence of foetuses or litter with malformations lay within the range of historical control data, revealed no statistical significance, and were thus unaffected by treatment.

Remarks - Results

The food consumption and body weights and weight gains were not affected.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 1,000 mg/kg bw/day for maternal toxicity and developmental toxicity in this study. The No Observed Effect Level (NOEL) was set at 300 mg/kg bw/day based on an increased incidence of engorged placenta seen in 1000 mg/kg bw/day animals.

TEST FACILITY Bayer AG (2013)

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: CO2 Evolution Test.

Inoculum	Activated sewage sludge
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Carbon Dioxide ($ThCO_2$)
Remarks - Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	0	7	82
12	4	12	82
21	9	21	88
28	14	28	87

Remarks - Results: All validity criteria for the test were satisfied. The percentage degradation of the reference compound reached the threshold level of 60% by day 4. Therefore, the tests indicate the suitability of the inoculum. The degree of degradation of the test substance after 28 days was 14%. Therefore, the test substance is not considered to be readily biodegradable according to the OECD (301 B) guideline.

CONCLUSION: The notified chemical is not readily biodegradable.

TEST FACILITY: Hüls AG (1992c)

C.1.2. Bioaccumulation

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 305 Bioconcentration: Flow-through Fish Test.

Species	*Danio rerio* (zebra fish)
Exposure Period	Exposure: 11 days Depuration: None
Auxiliary Solvent	None
Dietary Concentration Range	100 µg/g and 1000 µg/g
Analytical Monitoring	HPLC
Remarks - Method	The test was conducted under continuous flow-through conditions, using synthetic fresh water prepared in accordance with ISO 7346-1. Fish were fed daily at 3% wet body weight per day. Hexachlorobenzene was used as the reference compound. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Bioconcentration Factor	The test substance was not detectable in fish after the feeding phase at both concentrations tested. It was concluded that the test substance is not expected to have significant bioaccumulation potential.
CT50	Not determined
Remarks - Results	All validity criteria for the test were satisfied. As the concentration of the test substance was below the limit of quantitation after the exposure period, the test was ended without a depuration phase. No mortality or abnormal

behaviours were observed at both concentrations tested.

CONCLUSION The notified chemical is not considered to be bioaccumulative.

TEST FACILITY Bayer Industry Services (2007)

C.1.3. Inherent biodegradability

TEST SUBSTANCE Notified chemical

METHOD OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test
OECD TG 302 C Inherent Biodegradability: Modified MITI Test (II)

Inoculum	Activated sewage sludge
Exposure Period	56 days
Auxiliary Solvent	None
Analytical Monitoring	Theoretical Oxygen Demand (ThOD)
Remarks – Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Test substance		*Toxicity control*		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*	*Day*	*% Degradation*
6	0	6	29	6	74
14	0	14	33	14	81
20	0	20	34	20	83
28	1	28	35	28	85
34	1	34	35	34	85
42	3	42	36	42	89
48	3	48	36	48	90
56	0	56	36	56	90

Remarks – Results All validity criteria for the test were satisfied. The percentage degradation of the reference compound surpassed the threshold level of 60% by 6 days (74%). Therefore, the tests indicate the suitability of the inoculum. The percentage degradation of the toxicity control surpassed the threshold level of 25% by 6 days (29%; 35% in 28 days), showing that toxicity was not a factor inhibiting the biodegradability of the test substance.
The degree of degradation of the test substance after 56 days was 0%. Therefore, the test substance is not considered to be inherently biodegradable according to the OECD (302 C) guideline.

CONCLUSION The notified chemical is not inherently biodegradable.

TEST FACILITY Bayer Industry Services (2006)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE Notified chemical

METHOD EC Council Regulation No 92/69 C.1 Acute Toxicity for Fish – Static.

Species	*Brachydanio rerio* (zebra fish)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	255 mg $CaCO_3$/L
Analytical Monitoring	None reported
Remarks – Method	The test substance was prepared as a Water Accommodated Fraction (WAF) due to its low water solubility. A stock solution with a nominal

loading rate of 1 mg/L was prepared by treating the solution of the test substance in an ultrasonic bath for 1 h then stirring the solution for 24 h. Any undissolved material removed by filtration. As no effects were observed at the highest concentration tested, the test was only conducted at the nominal loading rate of 1 mg/L of the test substance. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Nominal Concentration mg/L	*Number of Fish*	*Mortality (%)*				
		2 h	*24 h*	*48 h*	*72 h*	*96 h*
Control	10	0	0	0	0	0
1	10	0	0	0	0	0

LL50	> 1 mg/L (WAF) at 96 hours.
NOEL	1 mg/L (WAF) at 96 hours.
Remarks – Results	All validity criteria for the test were satisfied. The test solutions were not renewed during the 96 h test period. As no effects were observed at the highest concentration tested, the actual concentrations of the test substance were not measured during the 96 h test period. The 96 h LL50 and NOEL for fish were determined to be > 1 mg/L (WAF) and 1 mg/L (WAF), respectively, based on nominal concentrations.

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

TEST FACILITY Bayer AG (1999f)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – Static.

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	2.5 mmol Ca^{2+} + Mg^{2+}
Analytical Monitoring	None reported
Remarks - Method	The test substance was prepared as a Water Accommodated Fraction (WAF) due to its low water solubility. A stock solution with a nominal loading rate of 1,000 mg/L was prepared by stirring the test substance in water for 18 h. Any undissolved material was removed by filtration. The actual concentration of the test substance in the stock solution was calculated to be 8.4 mg/L, based Total Organic Carbon (TOC). The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Nominal Concentration mg/L	*Number of D. magna*	*Cumulative Immobilised (%)*	
		24 h	*48 h*
Control	20	0	0
0.7	20	0	10
0.9	20	0	0
1.3	20	0	0
1.8	20	0	0
2.7	20	0	0
3.8	20	10	10

5.5	20	0	5
7.6	20	10	15

EL50	> 7.6 mg/L (WAF) at 48 hours
NOEL	5.5 mg/L (WAF) at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. The test solutions were not renewed during the 48 h test period. The actual concentrations of the test substance were not measured during the 48 h test period. The 48 h EL50 and NOEL for daphnids were determined to be > 7.6 mg/L (WAF) and 5.5 mg/L (WAF), respectively, based on nominal concentrations.
CONCLUSION	The notified chemical is not considered to be harmful to aquatic invertebrates up to the limit of its solubility in water.
TEST FACILITY	Hüls AG (1992d)

C.2.3. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 211 *Daphnia magna* Reproduction Test – Semi-static.
Species	*Daphnia magna.*
Exposure Period	21 days.
Auxiliary Solvent	None
Water Hardness	252-271 mg $CaCO_3$/L
Analytical Monitoring	HPLC
Remarks - Method	The test substance was prepared as a Water Accommodated Fraction (WAF) due to its low water solubility. A stock solution with a nominal loading rate of 1 mg/L was prepared by treating the solution of the test substance in an ultrasonic bath for 1 h then stirring the solution for 24 h. Any undissolved material removed by filtration. The definitive test was conducted at the nominal loading rates of 1.736, 4.167, and 10 mg/L of the test substance. The maximum time-weighted mean measured concentration of the test substance in solution was < 0.024 mg/L. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

	Test Concentration (nominal; mg/L)			
	Control	1.736	*4.617*	*10*
Total No. of Offspring Released by Survived *Daphnia*	87.0	82.9	85.0	101.9
Survival (%)	100	100	100	100

NOEL	0.024 mg/L (WAF) at 21 days
Remarks - Results	All validity criteria for the test were satisfied. The test solutions were renewed three times a week during the 21 d test period. The actual concentrations of the test substance were measured every 2-5 days during the 21 d test period. The 21 d NOEL for daphnids was determined to be 0.024mg/L (WAF), based on the time-weighted mean measured concentrations.
CONCLUSION	Notified chemical is not harmful to aquatic invertebrates up to the limit of its solubility in water.
TEST FACILITY	Currenta (2014)

C.2.4. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical

METHOD	OECD TG 201 Freshwater Alga and Cyanobacteria, Growth Inhibition Test.
Species	*Scenedesmus subspicatus* (green alga)
Exposure Period	72 hours
Concentration Range	Nominal: 0.97-24.93 mg/L Actual: Not determined
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	None reported
Remarks - Method	The test substance was prepared as a Water Accommodated Fraction (WAF) due to its low water solubility. A stock solution with a nominal loading rate of 1,000 mg/L was prepared by stirring the test substance in water for 18 h. Any undissolved material was removed by filtration. The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported.

RESULTS

Biomass		*Growth*	
EL50 *mg/L at 72 h*	*NOEL* *mg/L*	*EL50* *mg/L at 72 h*	*NOEL* *mg/L*
> 24.9	8.3	> 24.9	8.3

Remarks - Results	All validity criteria for the test were satisfied. Renewal of the test solutions was not specified. The actual concentrations of the test substance were not measured during the 72 h test period. The 72 h EL50 and NOEL for algae were determined to be > 24.9 mg/L (WAF) and 8.3 mg/L (WAF), respectively, based on nominal concentrations.
CONCLUSION	The notified chemical is not considered to be harmful to algae up to the limit of its solubility in water.
TEST FACILITY	Hüls AG (1992e)

C.2.5. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Activated sewage sludge
Exposure Period	3 hours
Concentration Range	Nominal: 10-10,000 mg/L Actual: Not determined
Remarks – Method	The test was conducted in accordance with the test guideline above, with no significant deviation in protocol reported. 3,5-Dichlorophenol was used as the reference control. The respiration rate was determined by measurement of Biochemical Oxygen Demand during the test after 3 hours of exposure.
RESULTS	
IC50	> 10,000 mg/L at 3 hours
NOEC	Not determined
Remarks – Results	All validity criteria for the test were satisfied. The 3 h IC50 was determined to be > 10,000 mg/L, based on nominal concentrations.
CONCLUSION	The notified chemical is not inhibitory to microbial respiration.
TEST FACILITY	Bayer AG (2000e)

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