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STD/1622

August 2017

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in RC-49155 (STD/1608)
Polymer in RC-49155 (STD/1622)

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/1608	Axalta Coating Systems Australia Pty Ltd	Chemical in RC-49155	Yes	≤ 50 tonnes per annum	Components of industrial automotive coatings
STD/1622		Polymer in RC-49155			

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information on an analogue chemical, the notified chemical and polymer, as an inseparable mixture, are recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	*Hazard statement*
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction

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

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

Environmental risk assessment
On the basis of the assessed use pattern, the notified chemical and polymer are not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical and polymer should be classified as follows:
  - Skin sensitisation (Category 1): H317 – May cause an allergic skin reaction

The above should be used for products/mixtures containing the notified chemical/polymer, if applicable, based on the concentration of the notified chemical present and the intended use/exposure scenario.

Health Surveillance

- As the inseparable mixture of the notified chemical and polymer is a skin sensitiser, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of skin sensitisation.

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 and polymer during use:
  - Enclosed and automated mixing systems, where possible

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of mixtures of the notified chemical and polymer:
  - Avoid contact with skin and eyes
  - Avoid breath of aerosols and mists

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of mixtures of the notified chemical and polymer:
  - Protective clothing
  - Goggles
  - Impervious gloves

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

- Spray applications should be carried out in accordance with the Safe Work Australia Code of Practice for *Spray Painting and Powder Coating* (SWA, 2015) or relevant State or Territory Code of Practice.

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

- If products and mixtures containing the notified chemical and polymer 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 and polymer in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Storage

- The handling and storage of the notified chemical and polymer should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

Emergency procedures

- Spills or accidental release of the notified chemical and polymer 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 and polymer are listed on the Australian Inventory of Chemical Substances (AICS).

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

(1) Under Section 64(2) of the Act; if
- the function or use of the chemical and polymer has changed from components of industrial automotive coatings, or is likely to change significantly;
- the amount of the chemical and polymer being introduced has increased, or is likely to increase, significantly;
- the chemical or polymer has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical and polymer on occupational health and safety, public health, or the environment.

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

No additional secondary notification conditions are stipulated.

Safety Data Sheet
The SDS of the products containing the notified chemical and polymer provided by the notifier were reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Axalta Coating Systems Australia Pty Ltd (ABN: 53 158 497 655)
15–23 Melbourne Road
RIVERSTONE NSW 2765

NOTIFICATION CATEGORY
STD/1608:
Standard: Chemical other than polymer (more than 1 tonne per year)

STD/1622:
Standard (Reduced fee notification): Synthetic polymer with Mn < 1,000 Da (more than 1 tonne per year) – Notified at the same time as a similar chemical

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical names, other names, CAS numbers, molecular and structural formulae, molecular weight, analytical data, degree of purity, polymer constituents, residual monomers, impurities, use details, and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for all physico-chemical endpoints, all toxicological endpoints and ecotoxicological endpoints.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
STD/1608: Chemical in RC-49155
STD/1622: Polymer in RC-49155

OTHER NAME(S)
Polymeric aspartate (Generic name in SDS containing the mixture of STD/1608 and STD/1622)

MOLECULAR WEIGHT
STD/1608: < 1,000 Da
STD/1622: Number Average Molecular Weight (Mn) < 1,000 Da

3. COMPOSITION

DEGREE OF PURITY
> 90% (as a combined mixture of STD/1608 and STD/1622)

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Clear colourless liquid[*]

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Not determined	Estimated to be < 0 °C
Boiling Point[*]	125 °C	SDS
Density[*]	1,020 kg/m^3 at 20 °C	SDS
Vapour Pressure[*]	0.43 kPa	SDS
Water Solubility[^]	3.180 g/L at 25 °C[#]	Measured

Hydrolysis as a Function of pH*	Occurs at pH 4, 7 or 9#	Measured
Partition Coefficient* (n-octanol/water)	log Pow = 2.06 at 25 °C#	Measured
Adsorption/Desorption	Not determined	Expected to partially partition to sludge or soil based on the low solubility
Dissociation Constant	Not determined	Contain no dissociable functional groups
Particle Size	Not determined	Imported in solutions
Flash Point*	34 °C	SDS; contain a flammable solvent
Flammability*	Flammable liquid and vapour	Based on flash point
Autoignition Temperature*	415 °C	SDS
Explosive Properties	Not determined	Contain no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contain no functional groups that would imply oxidative properties

* Properties of the product containing the notified chemical and polymer at a combined concentration of ≤ 60% in a flammable solvent
^ Results affected by hydrolysis
# Average values of the product containing the notified chemical and polymer; not expected to reflect the actual environment behaviours of the notified chemical and polymer

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties, refer to Appendix A. Due to the presence of a flammable solvent in the mixture of the notified chemical and polymer, the mixture is considered to be a Category 3 flammable liquid under GHS.

Reactivity
The notified chemical and polymer are expected to be stable in organic solutions under normal conditions of use. However, the notified chemical may undergo hydrolysis in contact with water.

Physical hazard classification
Based on the limited physico-chemical data depicted in the above table, the notified chemical and polymer may not be recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia. However, due to the presence of a flammable solvent, the reaction mixture of the notified chemical and polymer is considered to be a dangerous good under Australian Code for the Transport of Dangerous Goods by Road and Rail (NTC, 2017).

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical and polymer will not be manufacture in Australia. The inseparable mixture of the notified chemical and polymer will be imported as a component of a coating product containing the mixture at < 60% concentration.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	10–50	10–50	10–50	10–50	10–50

PORT OF ENTRY
Sydney

IDENTITY OF RECIPIENTS
Axalta Coating Systems Australia Pty Ltd

TRANSPORTATION AND PACKAGING
The imported coating product containing the mixture of the notified chemical and polymer will be packed in 1 L and 5 L metal cans for distribution. Due to the presence of flammable solvent, the liquid solution containing the notified chemical and polymer has a dangerous goods classification of Class 3, UN1263, Paint or Paint Related

Material. Therefore, the products containing the notified chemical and polymer will be transported, packaged and stored in accordance with the Australian Code for the Transport of Dangerous Goods (NTC, 2017).

USE
The mixture of the notified chemical and polymer will be used as a component of a two-part coating system for automotive body repairs at a final use concentration of < 40% combined.

OPERATION DESCRIPTION
No repackaging and reformulation of the notified chemical and polymer will occur in Australia. The products containing the mixture of the notified chemical and polymer will be transported to the warehouse prior to distribution to end-users.

The products will then be mixed with an activator at 2:1 ratio prior to use, reaching a concentration of < 40% for the mixture of the notified chemical and polymer. The final coatings will be applied to automotive bodies by spraying, with a majority of the spray applications occurring in spray booths. In some smaller automotive repair shops, the spraying process may be applied outside of a spray booth.

Spray painting workers will open the cans containing the mixture of the notified chemical and polymer in a mixing room. If required, the workers may transfer the coating to a separate container for thinning. The coating will then be transferred to a reservoir for the spray equipment, where it will be applied onto required areas of the automotive body.

Excess coating will be disposed of into a hazardous waste container. Spray equipment will be cleaned by an appropriate solvent and collected in the hazardous waste.

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 storage	1–2	20
Spray painting	8	300

EXPOSURE DETAILS
Transport and storage workers will only be handling sealed cans containing of the mixture of the notified chemical and polymer. There will be little potential for exposure to the notified chemical and polymer, unless in the unlikely event of an accident where the containers are breached.

Spray painters may come into contact with the notified chemical and polymer at concentrations < 60% combined through dermal and ocular routes, mainly from direct contact with drips, spills and splashes during the transfer, application, and cleaning of the coating and spray equipment. Inhalation of aerosols at concentrations < 40% may occur during the spray application, but is expected to be limited if the spraying painting is applied in a spray booth or a well-ventilated area. It is proposed by the notifier that workers are expected to use appropriate personal protective equipment (PPE) in accordance with the SDS, including overalls, protective footwear, impervious gloves, eye protection and breathing masks or respirators if the ventilation is inadequate.

After the coating is dried, the notified chemical and polymer will be cured into the coating matrix and no longer available for exposure.

6.1.2. Public Exposure
Products containing the notified chemical and polymer will not be made available for the do-it-yourself (DIY) market. Therefore, direct public exposure to the notified chemical and polymer is not expected. The general public may come into contact with the cured coating on automotive bodies, where the notified chemical and polymer will be trapped within the matrix and not available for exposure.

6.2. Human Health Effects Assessment

No toxicological study reports were provided for the notified chemical and polymer. The results from toxicological investigations conducted on an acceptable analogue 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
Rat, acute inhalation toxicity	LC50 > 4.224 mg/L/4 hour; low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – non-adjuvant test	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 vivo mammalian erythrocyte micronucleus Test	non genotoxic
Rat, reproductive and developmental toxicity	NOAEL (reproduction) = 200 mg/kg

Toxicokinetics, metabolism and distribution
No information on toxicokinetics of the notified chemical and polymer was provided. The notified chemical and polymer have low molecular weights (< 1,000 Da). The mixture of the notified chemical and polymer has a water solubility of 3.180 g/L at 25 °C and a log Pow of 2.06. Therefore absorption of the mixture across biological membranes may occur.

Acute toxicity
The analogue chemical was found to have low acute oral, dermal and inhalation toxicity in rats. The notified chemical and polymer are expected to have similar low acute toxicity.

Irritation and sensitisation
Based on studies conducted in rabbits, the analogue chemical was considered to be slightly irritating to the skin and eyes, and mildly irritating to the respiratory tract. The mixture of the notified chemical and polymer is therefore likely to be irritating.

The analogue chemical was considered to be a skin sensitiser in a guinea pig skin sensitisation test, with skin reactions observed in the challenge phase in animals induced with the chemical at 5% intradermally and 50% topically. Based on the available information on the analogue chemical, the notified chemical and polymer should be considered as sensitisers.

Repeated dose toxicity
A 28-day repeat dose study on the analogue chemical was conducted in rats, with the analogue administered through the diet at dose levels of 0, 40, 200 and 1,000 mg/kg bw/day. The No Observed Adverse Effect Level (NOAEL) was established at the highest dose level tested as 1,000 mg/kg bw/day under the conditions in this study, based on the absence of any adverse treatment related effects, and also considering clinical pathology and pathology parameters.

Mutagenicity/Genotoxicity
The analogue chemical was not mutagenic in a bacterial reverse mutation study and was not considered to be genotoxic in an *in vivo* micronucleus test. There is no specific genotoxicity structural alert found in the notified chemical and polymer.

Toxicity for reproduction
Two parental developmental toxicity studies conducted on the analogue chemical were provided. In one study based on the fact that minor clinical signs observed for systemic toxicity were not considered to be adverse and no treatment-related effects were observed for reproductive toxicity, the NOAEL for both systemic and reproductive toxicity was established at 1,000 mg/ kg bw/day, the highest dose level tested. In the other study, test substance-related effects were noted for a decrease in F2 pup weight gain at 1,000 mg/kg bw and therefore the NOAEL and No Observed Effect Level (NOEL) for reproductive toxicity was established as 200 mg/kg bw/day.

Health hazard classification
Based on the available information on the analogue chemical, the notified chemical and polymer are recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard classification	*Hazard statement*
Skin sensitisation (Category 1)	H317 – May cause an allergic skin reaction

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the information available, the mixture of the notified chemical and polymer may have potential to be an eye, skin and respiratory irritant. The mixture may also cause skin sensitisation. Professional spray painters may come into contact with the mixture of the notified chemical and polymer at < 60% concentration combined when handling products containing the notified chemical and polymer. However, given the products will only be used in industrial settings with appropriate engineering controls and the use of PPE including coveralls, impervious gloves, eye protection and respiratory protection, the risk of irritation and skin sensitisation to workers is not expected to be unreasonable.

Therefore, under the occupational settings described, the risk to the health of workers from use of the notified chemical and polymer is not considered to be unreasonable.

6.3.2. Public Health
Although the public will come into contact with articles or surfaces which have been treated with coatings containing the notified chemical and polymer, the notified chemical and polymer will be bound within an inert matrix and as such direct public exposure to the chemical and polymer is expected to be negligible.

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

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The inseparable mixture of the notified chemical and polymer will be imported to Australia for use in coating system for automotive body repairs. No repackaging and reformulation of the notified chemical and polymer will occur locally. Therefore, significant release of the notified chemical and polymer mixture from these activities is not expected.

It is estimated by the notifier that up to 1% of the total import volume of the notified chemical and polymer mixture may be lost due to accidental spillage. Spills containing the notified chemical and polymer are expected to be absorbed into inert materials (e.g. sand, soil, vermiculite, etc.) and be disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The coating products containing the notified chemical and polymer will be applied by spray onto metal substrates. The majority of these spray applications will occur in spray booths. After the coating is dried, the notified chemical and polymer will be cured into the coating matrix and no longer available for environmental exposure.

The main release will be as overspray (~ 35%) which will typically entail landfill disposal, after interception by spray booth filters. A small amount (<1%) of the mixture of the notified chemical and notified polymer from cleaning of equipment will be collected, treated and disposed of to landfill in accordance with local, State and Federal regulations.

RELEASE OF CHEMICAL FROM DISPOSAL

The surfaces coated with products containing the mixture of the notified chemical and polymer are likely to be either recycled for metal reclamation or be disposed of to landfill at the end of their useful life. During metal reclamation, the notified chemical and polymer would be converted to water vapour and oxides of carbon and nitrogen.

7.1.2. Environmental Fate

The mixture of the notified chemical and polymer were observed to hydrolyse in the hydrolysis test although the hydrolysis half-lives were not recorded. However, the notified chemical is not expected to be ultimately biodegradable based on the analogue data (6% inherent biodegradation in 28 days). The analogue is structurally similar to the notified chemical and they are expected to have similar environmental behaviours.

Although the environmental fate of the notified polymer is unable to be read-across from the analogue directly due to the structural difference between them, the notified polymer is expected to be more stable than the analogue and the notified chemical given the notified polymer is higher molecular weight oligomers of the notified chemical. Therefore, the notified chemical and polymer are considered ultimately stable under environmental conditions. For the details of the inherent biodegradation study please refer to Appendix C.

The majority of the notified chemical and polymer are expected to be bound within an inert matrix as part of their normal use pattern as components in automotive coating system. The notified chemical and polymer bound within the coating matrix are not expected to be bioavailable nor biodegradable. The majority of notified chemical and polymer disposed of to landfill are expected to be in solid cured coatings and they are not expected to be water dispersible or mobile in this form.

Based on its large molecular size, the notified polymer is not likely to cross biological membranes and therefore, bioaccumulation is not expected. Although the notified chemical has a molecular weight < 1,000 Da, significant bioaccumulation of the notified chemical is not expected due to limited bioavailability in its solid form in landfill and its limited release to surface waters. The notified chemical and polymer will eventually degrade in landfill, or by thermal decomposition during metal reclamation processes, to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

A predicted environment concentration (PEC) is not calculated given the low aquatic exposure of the notified chemical and polymer.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the analogue are summarised in the table below. Details of these studies can be found in Appendix C.

Although the ecotoxicological effects of the notified polymer are unable to be read-across from the analogue directly due to the structural difference between them, the notified polymer is expected to be less toxic than the analogue given the notified polymer has no significant ionic functionalities. Therefore, it is scientifically acceptable to use the analogue data to conservatively predict the environmental effects of the notified chemical and polymer for the purpose of risk assessment.

Endpoint	*Result (mg/L)*	*Assessment Conclusion*
Daphnia Toxicity	21 days NOEC = 0.013	Toxic to aquatic invertebrates with long lasting effects
Algal Toxicity	48 hours EC50 > 1.319	Inconclusive
Acute toxicity to earthworm	14 days NOEC ≥ 1,000	Low toxicity to earthworms
Plant toxicity	14 days NOEC > 100	No negative effects on seedling emergence and growth at the tested concentration

As no ecotoxicity data were determined for the notified chemical and polymer and as an inseparable mixture, the notified chemical and polymer are not classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS 2009), as adopted for industrial chemicals in Australia.

7.2.1. Predicted No-Effect Concentration

A predicted no-effect concentration (PNEC) has not been calculated for the notified chemical and polymer as, based on their reported use pattern, ecotoxicologically significant quantities are not expected to be released to the aquatic environment.

7.3. Environmental Risk Assessment

The risk quotient (Q = PEC/PNEC) for the notified chemical and polymer has not been calculated as release to the aquatic environment in ecotoxicologically significant quantities is not expected based on their reported use pattern as a component in automotive coatings for use on metal substrates.

The majority of the environmental release of the notified chemical and polymer will be disposal of as cured paints to landfill. In cured paints the notified chemical and polymer are bound within the inert coating matrix and are unlikely to leach or be bioavailable. Thermal decomposition during metal reclamation of the notified chemical and polymer mixture will produce water and oxides of carbon and nitrogen.

On the basis of the limited aquatic exposure and assessed use pattern, the notified chemical and polymer are not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility 3.18 g/L at 25 °C

Method	OECD TG 105 Water Solubility
Remarks	Shake Flask Method
Test Facility	Intertek, UK (2016a)

Hydrolysis as a Function of pH Hydrolysis half-lives not reported

Method	Non-standard qualitative method
Remarks	Hydrolysis products were observed at pH 4, 7 and 9 when incubating the test substance in water. The molecular weight of all ions formed by hydrolysis was determined by ESI mass spectroscopy, and their molecular structures were predicted based on molecular weight and original chemical structure.
Test Facility	Intertek, UK (2016b)

Partition Coefficient (n-octanol/water) log Pow = 2.06 at 20 °C

Method	OECD TG 107 Partition Coefficient (n-octanol/water)
Remarks	Shake Flask Method
Test Facility	Intertek, UK (2016c)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Analogue chemical
METHOD	OECD TG 401 Acute Oral Toxicity – Limit Test EEC Directive 84/449/EEC (OJ No. L251, 19.09.84)
Species/Strain	Rat/Wistar
Vehicle	Peanut oil
Remarks - Method	GLP Certificate No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5M, 5F	2,000	0/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity	No signs of toxicity were noted.
Effects in Organs	No abnormalities were noted at necropsy.
Remarks - Results	

CONCLUSION	The analogue is of low toxicity via the oral route.
TEST FACILITY	[Test Facility A] (1990)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Analogue chemical
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test EEC Directive 84/449/EEC (OJ No. L251, 19.09.84)
Species/Strain	Rat/Wistar
Vehicle	None. The analogue chemical was directly applied.
Type of dressing	Occlusive
Remarks - Method	GLP Certificate No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose (mg/kg bw)*	*Mortality*
1	5M, 5F	2,000	0/10

LD50	> 2,000 mg/kg bw
Signs of Toxicity - Local	A slight skin reddening at the application site was observed in 2 males and 3 females. Reddening persisted in 1 female until Day 5, for all other animals it appeared only on the day following the treatment.
Signs of Toxicity - Systemic	There were no deaths or test-substance related clinical signs. Body weight gain in females was retarded.
Effects in Organs	No abnormalities were noted at necropsy.
Remarks - Results	

CONCLUSION	The analogue is of low toxicity via the dermal route.
TEST FACILITY	[Test Facility A] (1992a)

B.3. Acute toxicity – inhalation

TEST SUBSTANCE	Analogue chemical (~90%) in *n*-butylacetate
METHOD	OECD TG 403 Acute Inhalation Toxicity EC Directive 92/69/EEC, 93/21/EEC B.2 Acute Toxicity (Inhalation)
Species/Strain	Rat/Wistar
Vehicle	None. The test substance was directly applied
Method of Exposure	Oro-nasal exposure.
Exposure Period	4 hours
Physical Form	Liquid aerosol
Particle Size	MMAD: 1.4 – 1.7 μm Respirable fraction (≤ 3 μm): 83.7-91.4%
Remarks - Method	GLP Certificate Deviation from protocol: only two dose concentrations tested

RESULTS

Group	*Number and Sex of Animals*	*Concentration (mg/L)*		*Mortality*
		Nominal	*Actual*	
1	5M, 5F	0	0	0/10
2	5M, 5F	1	1.436	0/10
3	5M, 5F	5	4.224	0/10

LC50	> 4.224 mg/L/4 hours
Signs of Toxicity	Bradypnea, laboured and irregular breathing pattern, bristled and ungroomed hair-coat, reddened nostrils, reduced motility and hind limbs which were unable to support body weight were observed in the group treated at 4.224 mg/L. These effects were resolved within the first post-exposure week. Rats exposed to the test substance experienced a concentration-dependent decrease in body temperature (hypothermia). There were no appreciable differences in the susceptibility of males and females.
Effects in Organs	No abnormalities were noted at necropsy.
Remarks - Results	The contribution of the n-butyl acetate could not be resolved. The test substance is a respiratory irritant. Inhalation of respiratory irritants is known to induce reflex changes in breathing pattern and cardiac output and have been reported to be associated with the decline in the metabolic rate and body temperature of rodents. Although the actual high dose of 4.224 mg/L/4 hr falls short of 5 mg/L/4 hr, as no mortalities were observed during the study, it is likely that the LC50 would be > 5 mg/L/4 hr.
CONCLUSION	The analogue is of low toxicity via inhalation.
TEST FACILITY	[Test Facility A] (1998)

B.4. Irritation – skin

TEST SUBSTANCE	Analogue chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion
Species/Strain	Rabbit/New Zealand White
Number of Animals	6
Vehicle	None. The analogue chemical was directly applied
Observation Period	14 days
Type of Dressing	Semi-occlusive.
Remarks - Method	GLP Certificate.

No significant protocol deviations.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
Erythema/Eschar	1.2	2	14 days	1
Oedema	0	0	n/a	0

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

Remarks - Results: Well-defined erythema was observed in four of the six animals. Slight to well defined erythema was observed in 3 animals after seven days with the effects fully reversed in all but one animal by day 14.

CONCLUSION: The analogue is slightly to moderately irritating to the skin.

TEST FACILITY: [Test Facility A] (1991a)

B.5. Irritation – eye

TEST SUBSTANCE: Analogue chemical

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion
Species/Strain: Rabbit/New Zealand White
Number of Animals: 3
Observation Period: 21 days
Remarks - Method: GLP Certificate.
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	0.3	0.3	0.3	1	< 48 h	0
Conjunctiva: chemosis	0	0	0	1	< 24 h	0
Conjunctiva: discharge	0	0	0	2	< 24 h	0
Corneal opacity	0	0	0	0	n/a	0
Iridial inflammation	0	0	0	0	n/a	0

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

Remarks - Results

CONCLUSION: The analogue is slightly irritating to the eye.

TEST FACILITY: [Test Facility A] (1991a)

B.6. Skin sensitisation

TEST SUBSTANCE: Analogue chemical

METHOD: OECD TG 406 Skin Sensitisation – Magnusson and Kligman method
EEC Directive 84/449/EEC (OJ No. L251, 19.09.84)
Species/Strain: Guinea pig/Bor:DHPW
PRELIMINARY STUDY: Maximum Non-irritating Concentration:
intradermal: 5 % (w/v) in polyethylene glycol 400
topical: 50% (w/v) in polyethylene glycol 400
MAIN STUDY
Number of Animals: Test Group: 20 Control Group: 2 groups of 10 (one for each challenge)

INDUCTION PHASE	Induction Concentration: intradermal: 5 % (w/v) in polyethylene glycol 400 topical: 50% (w/v) in polyethylene glycol 400
Signs of Irritation	The test sites were pre-treated with 10% sodium lauryl sulphate 24-hours before topical induction. After the topical induction two animals showed an open wound at the application area on day nine. On day 10 the application area of six animals were scabbed over. These scabs stayed up to day 16.
CHALLENGE PHASE	
1st challenge	topical: 50% (w/v) in polyethylene glycol 400
2nd challenge	topical: 25% and 12% (w/v) in polyethylene glycol 400
Remarks - Method	GLP Certificate. Deviation from protocol: A 50% test substance formulation instead of undiluted test substance was used for topical induction in the preliminary test by mistake. This 50% concentration was taken forward to the main study and used where the undiluted test substance may have been more appropriate.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	50%	17/20	9/10	-	-
	25%	-	-	10/20	4/20
	12%	-	-	7/20	4/20
Control Group	50%	0/10	0/10	-	-
	25%	-	-	0/10	0/10
	12%	-	-	0/10	0/10

Remarks - Results	After the first challenge, very mild to clearly visible skin reddening was observed in 85% of the test animals. After the second challenge, very mild to clearly visible skin reddening was observed in 50% and 35% of the test animals challenged with 25% and 12% test substance respectively. A scaly administration site was observed in some animals.
CONCLUSION	There was evidence of reactions indicative of skin sensitisation to the analogue under the conditions of the test.
TEST FACILITY	[Test Facility A] (1992b)

B.7. Repeat dose toxicity

TEST SUBSTANCE	Analogue chemical
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral)
Species/Strain	Rat/Wistar
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period: 14 days
Vehicle	Polyethylene glycol 400
Remarks - Method	GLP Certificate Deviations from protocol: - Sensory reactivity to stimuli was not reported; - The organ weights of epididymis and thymus were not reported; - Histopathological examinations were performed on the heart,

liver, spleen, adrenals and kidneys.

The doses applied (see table below) were based on a purity of 91.6%. As the actual purity was later determined to be 94%, the dosages applied were in fact higher than that stated by about 2.4%.

The doses were selected based on a dose range finding study. No macroscopic lesions were observed in 6 animals dosed with 1,000 mg/kg bw/day for 7 days.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5M, 5F	0	0/10
low dose	5M, 5F	40	0/10
mid dose	5M, 5F	200	0/10
high dose	5M, 5F	1,000	0/10
control recovery	5M, 5F	0	0/10
high dose recovery	5M, 5F	1,000	0/10

Mortality and Time to Death

No mortality was observed during the treatment or recovery phases.

Clinical Observations

No test substance-related clinical signs were observed during the treatment period or the recovery. There was no significant difference in body weight gain and food and water consumption in treated animals when compared to controls.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Clinical Chemistry

Alkaline phosphatase levels were significantly increased in females of the high dose group (30%, $P < 0.05$) and increased but not significantly in males of the high dose group (22%) when compared to controls. Creatine levels were significantly reduced in males of the high dose group (15%, $P < 0.01$) when compared with controls. A similar reduction was not observed in females of the high dose group. Alkaline phosphatase and creatine levels were not significantly different in the high dose recovery animals when compared to controls. All other significant differences in clinical chemistry parameters noted were without relation to dose and therefore not considered by the study authors to be treatment related.

Haematology

The thrombocyte count was significantly increased in animals of the high dose group, both in males (9%, $P < 0.05$) and females (25%, $P < 0.01$), when compared to controls. A similar increase was not observed in high-dose recovery animals. Although mean corpuscular haemoglobin concentration was significantly increased (1.8%, $P < 0.05$) in females of the high dose group, levels found were within the normal range and hence were considered to be incidental. All other haematological parameters did not differ significantly from the control values.

Urinalysis

There were no significant findings in any of the parameters in any of the treated animals.

Effects in Organs

Organ weights

A significant increase in absolute liver weight was observed in animals of the high dose group, both in males (16%, $P < 0.05$) and females (24%, $P < 0.05$). Relative liver weights were also increased in the same group (16% in males and 12% in females) although this was not significant in females. A similar increase was not observed in high-dose recovery animals. All other significant differences in organ weight parameters noted were without relation to dose and therefore not considered by the study authors to be treatment related.

Macroscopic Findings

There were no significant necropsy findings.

Histopathology
There were no significant histopathological findings.

Remarks – Results
Clinical Chemistry
The differences observed in creatine and alkaline phosphatase levels in high dose group animals were not considered by the study authors to be toxicologically relevant as the levels were within the range of historical controls.

Haematology
The increase in thrombocyte count in high dose animals was not considered by the study authors to be toxicologically significant as the differences were not biologically significant in males and the mean value in females was influenced by only one relatively high value.

Organ weight
As the increase in liver weight was not accompanied by any histopathological change and appeared to reverse during the recovery phase, the effects were interpreted as adaptive in nature.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as the highest dose tested at 1,000 mg/kg bw/day in this study, based on the absence of adverse treatment related effects.

TEST FACILITY [Test Facility A] (1992c)

B.8. Genotoxicity – bacteria

TEST SUBSTANCE Analogue 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
Metabolic Activation System	S9-Mix from Aroclor 1254 induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 8 – 5000 µg/plate b) Without metabolic activation: 8 – 5000 µg/plate
Vehicle	Ethanol
Remarks - Method	GLP Certificate 2-Aminoanthracene was used as the sole indicator of the efficacy of the S9-mix. The following positive controls were used in the absence of S9-mix: - Nitrofurantoin (TA100) - 4-nitro-1, 2-phenylene diamine (TA1537 and TA98) Deviations from protocol: - Neither *S. typhimurium* strain T102 or *E.coli* WP2 strains, which may detect cross-linking mutagens, were included in the assay.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	≥ 1,000 (TA1537) ≥ 8 (TA 98)	≥ 5,000 (All strains)	negative
Test 2	≥ 1,000 (TA1537)	≥ 5,000 (All strains)	negative
Present			
Test 1	> 5000 (All strains)	≥ 5,000 (All strains)	negative

Test 2	> 5000 (All strains)	≥ 5,000 (All strains)	negative

Remarks - Results
The reported cytotoxicity was based on a reduction in background lawn. It was stated by the study authors that there was an indication of a bacteriotoxic effect at all test doses.

The test substance did not cause a marked increase in the number of revertants per plate of any of the tester strains either in the presence or absence of activation.

Negative controls were within historical limits. Positive controls confirmed the sensitivity of the test system.

CONCLUSION
The analogue was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY
[Test Facility A] (1991b)

B.9. Genotoxicity – *in vivo*

TEST SUBSTANCE
Analogue chemical

METHOD
OECD TG 474 Mammalian Erythrocyte Micronucleus Test
EC Directive 2000/32/EC B.12 Mutagenicity - Mammalian Erythrocyte Micronucleus Test

Species/Strain
Mouse/Bor: NMRI

Route of Administration
Intraperitoneal injection

Vehicle
None. The analogue chemical was directly applied.

Remarks - Method
No significant protocol deviations were noted.

With one exception the study conformed to the OECD principles of GLP. The deviation was that no data were available on complete analytical characterisation of the test substance.

Limit test was performed. Animals were treated with the test substance once. Dose was selected based on a preliminary test.

Group	*Number and Sex of Animals*	*Dose*	*Sacrifice Time (hours)*
I (vehicle control, PS)	5M, 5F	0	24
II	5M, 5F	5 (mL/kg bw)	16
III	5M, 5F	5 (mL/kg bw)	24
IV	5M, 5F	5 (mL/kg bw)	48
V (positive control, CP)	5M, 5F	20 (mg/kg bw)	24

PS = physiological saline. CP = cyclophosphamide.

RESULTS

Doses Producing Toxicity
Treated animals (group II, III, IV) showed the following signs of toxicity: apathy, roughened fur, distended abdomen, staggering gait, spasm, twitching, difficulty in breathing, eyelids stuck together and reduced discharge of faeces. There were no mortalities in these groups.

Genotoxic Effects
The test substance did not lead to any increase in the rate of micronuclei. The number of normochromatic (NCE) or polychromatic (PCE) erythrocytes containing small nuclei did not deviate from the vehicle control. The decrease in ratio of PCE/NCE in the treated groups (group II, III, IV) was considered to be biologically relevant (44-70%) indicating that the test substance was toxic to the bone marrow.

Results from the vehicle and positive control demonstrated that the test method was operating satisfactorily.

Remarks - Results
The decrease in the PCE/NCE ratio confirmed that the test substance

reached the bone marrow.

CONCLUSION The analogue was not clastogenic under the conditions of this *in vivo* erythrocyte micronucleus test.

TEST FACILITY [Test Facility A] (1992d)

B.10. Developmental toxicity

TEST SUBSTANCE Analogue chemical

METHOD OECD TG 414 Prenatal Developmental Toxicity Study
Species/Strain Rat/Wistar (Hsd Cpb: WU)
Route of Administration Oral – gavage
Exposure Information Exposure days: Day 6–20 post-coitum, inclusive
Post-exposure observation period: 1 day
Vehicle Polyethylene glycol 400
Remarks - Method GLP Certificate
No significant protocol variation

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
1	25F	0	0/25
2	25F	100	0/25
3	25F	300	0/25
4	25F	1,000	0/25

Mortality and Time to Death
There were no unscheduled deaths in the study.

Effects on Dams
No clinical signs or necropsy findings noted were considered to be related to treatment with the test substance at all dose levels up to 1,000 mg/kg bw/day. Appearance, behaviour, mean body weights, body weight gains, food consumption and faecal/urinary excretions for treated animals were similar to control animals.

Effects on Foetus
Foetal weight and sex distribution were unaffected by treatment at all dose levels up to 1,000 mg/kg bw/day.

Treatment related effects on foetal malformations and external/visceral deviations were not evident at all dose levels up to 1,000 mg/kg bw/day.

Remarks – Results
A small amount of foetal malformations were observed in this study, but the number of malformation was within the range of historical control data with no statistical significance.

A small amount of foetuses with external and visceral deviations were observed in this study, but these were all of common types and comparable to spontaneous findings within the current and historical control groups, and represented the normal range of scattering in the strain used.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) for systemic toxicity was established as 1,000 mg/kg bw/day in this study, based on the fact that minor clinical signs observed at this level were not considered to be adverse.

The No Observed Effect Level (NOEL) for reproductive toxicity was established as 1,000 mg/kg bw/day under the conditions in this study, based on the fact that no treatment-related effects were observed.

TEST FACILITY [Test Facility A] (2013)

B.11. Toxicity to reproduction – two generation study

TEST SUBSTANCE	Analogue chemical
METHOD	OECD TG 416 Prenatal Developmental Toxicity Study
Species/Strain	Rat/Wistar (Crl: (Wi) WU BR)
Route of Administration	Oral – gavage
Exposure Information	Exposure period - female: 10 weeks Exposure period - male: 10 weeks
Vehicle	Polyethylene glycol 400
Remarks - Method	GLP Certificate No significant protocol variation Doses corrected for purity

Generation	*Parental (F0)*	*Offspring (F1)*	*Offspring (F2)*
Total exposure period (weeks)	> 10 (till necropsy)	> 10 (till necropsy)	0

Generation	*Group*	*Number and Sex of Animals*	*Dose (mg/kg bw/day)*	*Mortality*
F0	1	25M	0	0/25
F0	2	25M	40	0/25
F0	3	25M	200	1/25
F0	4	25M	1,000	2/25
F0	5	25F	0	1/25
F0	6	25F	40	0/25
F0	7	25F	200	1/25
F0	8	25F	1,000	2/25
F1	9	25M	0	0/25
F1	10	25M	40	0/25
F1	11	25M	200	0/25
F1	12	25M	1,000	1/25
F1	13	25F	0	0/25
F1	14	25F	40	1/25
F1	15	25F	200	0/25
F1	16	25F	1,000	0/25

RESULTS

Mortality and Time to Death

In both generations, unscheduled deaths occurred in each dose group. No test substance-specific deaths were observed and all recorded deaths were assumed to be caused by administration errors, hostile behaviour from other animals, or regurgitation of administration formulation.

Survival of the rats was concluded to be unaffected by the treatment with the analogue chemical at concentrations up to 1,000 mg/kg bw/day.

Effects on Parental (F0) animals:

There were no changes in survival and clinical appearance up to 1,000 mg/kg bw/day in parental rats.

Body weights were inconspicuous up to 200 mg/kg bw in F0 males and 1,000 mg/kg bw/day in F0 females. Body weight and body weight gains were decreased in F0 males during the premating phase.

Investigation of the oestrus cycling and sperm analyses revealed no test substance-related effects on all F0 rats. Other parameters for reproductive performance such as insemination, fertility, gestation and litter data were not influenced by the test substance. A reduction in rearing and lactation indices was observed in F0 females, but these deviations were very small and not interpreted by the study authors as a reproductive toxic effect.

An increase in severity of basophilic tubules and in frequency of focal tubular dilation/casts was observed in F0 males at 1,000 mg/kg bw/day, which was implied to be adverse. Non-adverse tubular changes were observed in F0 females at 1,000 mg/kg bw/day. Liver weights were increased in all F0 rats at 1,000 mg/kg bw/day. These deviations did not reflect liver damage but indicated some changes in liver function. There were signs of kidney

damage in F0 males treated at 1,000 mg/kg bw/day and indications of changes in kidney function in F0 females treated at same dose level. Adrenal weights increased slightly for all F0 animals treated at 1,000 mg/kg bw/day, but this was not assumed by the study authors to be a toxic effect. Histopathology of the remaining organs showed no test substance-related changes.

The rearing and lactation indices were reduced in F0 generation at 1,000 mg/kg bw/day treatment level. These changes were not seen in F1 females. A reproductive toxicity effect was not assumed by the study authors.

Effects on 1st Filial Generation (F1)
There were no changes in survival and clinical appearance up to 1,000 mg/kg bw in F1 pups.

Body weights were inconspicuous for all animals in the F1 generation.

Investigation of the oestrus cycling and sperm analyses revealed no test substance-related effects on all F1 rats. Other parameters for reproductive performance such as insemination, fertility, gestation and litter data were not influenced by the test substance.

Statistically significant elevated kidney weights were observed in all F1 rats and increased liver weights were observed in F1 males treated at 1,000 mg/kg bw/day. These deviations did not reflect liver damage but indicated some changes in liver function. However, indications of changes in kidney function were noted for the F1 rats in this group. Adrenal weights increased slightly for all F1 animals treated at 1,000 mg/kg bw/day, but this was not assumed by the study authors to be a toxic effect. Histopathology of the remaining organs showed no test substance-related changes.

Sexual maturation in F1 rats revealed no test substance-related changes up to 1,000 mg/kg bw/day.

Effects on 2nd Filial Generation (F2)
There were no clinical findings in F2 pups with F1 rats treated up to 1,000 mg/kg bw/day. However, body and litter weights had depressed at 1,000 mg/kg bw/day dose level. Concerning the marginal lower pup weights at 200 mg/kg bw/day dose level, a test substance-related effect was unlikely.

There were slightly decreased spleen weights in F2 males at 200 and 1,000 mg/kg, but these did not correlate with corresponding relative weights and were within the range of historical controls.

Remarks – Results
No indication of the effects of reproductive performance was observed. Test substance-related effects on offspring were limited to a decrease in F2 pup weight gain at 1,000 mg/kg bw/day level, with no other obvious effects observed.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) and No Observed Effect Level for reproductive toxicity was established as 200 mg/kg bw/day in this study, based on the treatment-related effects observed at 1,000 mg/kg bw/day does level.

TEST FACILITY [Test Facility A] (2009)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Analogue chemical
METHOD	OECD TG 302 C "Inherent Biodegradability: Modified MITI Test (II)"
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	No
Analytical Monitoring	The biological oxygen demand (BOD) was determined by measuring the quantity of oxygen electrolytically.
Remarks - Method	A solution of the test substance in a mineral medium was inoculated with sludge from two different municipal sewage treatment plants (STP) and sludge from an industrial STP. The mixture was incubated under aerobic conditions for 28 days. During this period, degradation was followed by BOD determinations.

RESULTS

Test substance		*Benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
7	3	7	78
14	9	14	80
21	13	21	78
28	6	28	78

Remarks - Results	The validity criteria of the test method were met. The percent degradation of reference compound sodium benzoate reached the level of ≥ 40 % after 7 days and ≥ 65 % after 14 days. The test substance did not show toxic effects to bacteria at the test concentration in the toxicity control.
CONCLUSION	The analogue and by inference, the notified chemical and polymer are considered to be not inherently biodegradable
TEST FACILITY	Currenta, Germany (2009a)

C.2. Ecotoxicological Investigations

C.2.1. Chronic toxicity to aquatic invertebrates

TEST SUBSTANCE	Analogue chemical
METHOD	OECD TG 202 "Daphnia sp. Reproduction Test" – semi-static
Species	*Daphnia magna*
Exposure Period	21 d
Auxiliary Solvent	None
Water Hardness	266-287 mg/L $CaCO_3$
Analytical Monitoring	HPLC
Remarks - Method	The living offspring were counted three times a week along with the renewal of the test medium every 48 hours. The test vessels were inspected daily for the occurrence of juveniles and marked accordingly. The test was conducted according to the test guideline above with no significant deviation from the protocol.

RESULTS
Nominal loading retested, daphnid survival and cumulative mean number of offspring released, mean total body length and dry weight of daphnids (*Daphnia magna*)

Test Day 21					
Nominal Loading rate (mg/L)	*Geometrically measured concentration (mg/L)*	*Mean Percent Survival (%)*	*Mean Number of Offspring Released per female*	*Mean Total Body Length in mm*	*Mean Dry Weight in mg*
Control	-	90	95		
0.032	0.005	100	99		
0.1	0.013	100	99	No data	No data
0.32	0.041	90	80		
1	0.12	100	63		

No Observed Effect Concentration (mg/L)
21 day NOEC $_{(reproduction)}$ = 0.013 (based on geometric mean measured concentrations)
21 days NOEC $_{(mortality)}$ ≥ 0.012 (based on geometric mean measured concentrations)

Remarks - Results
The test substance is unstable during the test period and the test results are expressed in terms of geometric mean measured concentrations. Recovery rates ranged from 23.5 – 78.1 % of the nominal values in the freshly prepared media and from 3.2 – 6.7 % in the media after 48 hours.

The validity criteria of the test are satisfied. The mortality rate in the controls did not exceed 20% by the end of the test. Living offspring produced per parent *Daphnia* surviving at the end of the test was ≥ 60 in the controls.

CONCLUSION
The analogue and by inference, the notified chemical and polymer are considered to be toxic to aquatic invertebrate with long lasting effects

TEST FACILITY
Currenta, Germany (2009b)

C.2.2. Algal growth inhibition test

TEST SUBSTANCE
Analogue chemical

METHOD
OECD TG 201 Alga, Growth Inhibition Test.
EC Council Regulation No 440/2008 C.3 Algal Inhibition Test.

Species *Desmodesmus subspicatus*
Exposure Period 48 hours
Concentration Range Nominal: Control and 5.9 mg/L
Actual: Control, 5.94, 0.688 and 0.561 mg/L at 0, 24 and 48 hours
Auxiliary Solvent No
Water Hardness 22.5 mg $CaCO_3$/L
Analytical Monitoring HPLC
Remarks - Method Algae was exposed to the test substance at a limited nominal concentration of 5.9 mg/L, the solubility limit of the test substance as stated by the test report. The study was terminated after 48 hours because the measured concentration of the test substance decreased markedly over time.

RESULTS

Biomass EyC50 mg/L at 48 h	*Growth ErC50 mg/L at 48 h*
> 1.319	> 1.319

Remarks - Results	The test concentration decreased markedly during 48 hours test period and the EC50 values were based on geometric mean test concentrations at 0 hour, 24 hours and 48 hours. Effective concentrations ranged from 100.7-111.5% of nominal values at 0 hours, from 11.7-11.8% of nominal values at 24 hours and correspond to 9.5% of nominal values at 48 hours, respectively. Whether the test substance has toxic effects up to water solubility is undetermined solely based on data from this algal study given the test substance has a solubility of 5.9 mg/L, higher than the measured endpoint EC50 > 1.319 mg/L.
CONCLUSION	The toxic effects of the analogue and by inference, the notified chemical and polymer against alga are considered to be inconclusive.
TEST FACILITY	Currenta, Germany (2010)

C.2.3. Acute toxicity in earthworm

TEST SUBSTANCE	Analogue
METHOD	OECD TG 207 "Earthworms, Acute Toxicity Tests"
Species	*Eisenia fetida*
Auxiliary solvent	Acetone
Exposure Period	14 days
Remarks – Method	The test substance was dissolved in acetone to prepare a stock solution. This stock solution was used to prepare the test solutions. The test earthworms were exposed to the test substance by dermal and alimentary uptake. The test was conducted according to test guideline without significant deviation from the protocol.

RESULTS

Concentration mg/kg		*Number of Earthworms*	*Mortality (%)*
Nominal(mg/L)	*Actual*		*14 days*
Control	-	40	2.5
Solvent control	-	40	0
100	Not determined	40	0
1,000	Not determined	40	0

NOEC	≥ 1000 mg/kg at 14 days
Remarks – Results	All validity criteria for the test are satisfied. No significant difference in biomass development between the control and the two test concentrations was determined. No effects on the morphology and the behaviour of the earthworms were observed.
CONCLUSION	The analogue and by inference, the notified chemical and polymer are considered to be of low toxicity to Earthworm.
TEST FACILITY	ECT, Germany (2009a)

C.2.4. Terrestrial Plant Seeding Emergence Test

TEST SUBSTANCE	Analogue
METHOD	OECD TG 208 Terrestrial plant test
Species	*Allium cepa* (Onion), *Avena sativa* (oat) and *Brassica napus* (oilseed rape)
Exposure Period	14 days
Auxiliary Solvent	Acetone
Analytical Monitoring	HPLC
Remarks – Method	Seeds of two monocotyledonous species (onion and oat) and one dicotyledonous species (oilseed) were planted in soil that was treated with

test substance. The soil was mixed with quartz sand that was sparked with test substance diluted in acetone.

At day 7 and 14, all seedlings were evaluated visually according to a six-point rating system. Final counting of seedlings, visual evaluation and harvest to determine shoot length and shoot fresh weight were conducted on day 14 of the test.

RESULTS

Test concentration (mg/kg soil)	*Plant species*					
	Onion		*Oat*		*Oilseed rape*	
	Shoot length	*Shoot weight*	*Shoot length*	*Shoot weight*	*Shoot length*	*Shoot weight*
Control	137	0.181	350	0.961	140	1.148
Solvent control	128	0.148	320	0.792	140	1.154
1.00	142	0.17	359	0.947	162	1.485
3.16	128	0.145	350	0.930	147	1.205
10.00	130	0.153	359	1.007	145	1.358
31.62	121	0.132	351	0.949	143	1.266
100	110	0.157	368	0.982	134	1.048

NOEC > 100 mg/kg soil dry mass at 14 days

Remarks – Results Seedling emergence was at least 85% in the untreated control and survival was 100% for all three test species. No phytotoxicity was observed in the controls.

No significant effects on seedling emergence and growth were observed at concentrations up to and including 100 mg/kg soil dry mass,

CONCLUSION The analogue and by inferences, the notified chemical and polymer have no negative effects on seedling emergence and growth of higher plants at concentrations up to 100 mg/kg soil dry mass.

TEST FACILITY ECT, Germany (2009b)

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