File No: EX/160 (STD/1289)

May 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Y-17112

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

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

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

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

TABLE OF CONTENTS

FULL PUBLIC REPORT

This assessment report is for an extension of original assessment certificate for Y-17112. Based on the submission of new information by the extension notifier, some sections of the original assessment report for Y-17112 have been modified. These modifications have been made under the heading 'Extension Application' in the respective sections.

Y-17112

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Momentive Performance Materials Australia Pty Ltd (ABN 47 105 651 063)
Level 2, 600 Victoria Street
RICHMOND VIC 3121

Applicant for an Extension of the Original Assessment Certificate:
Connell Bros Company Australasia Pty Ltd (ABN 53 079 159 327)
Unit 3, 32 Windorah Street
STAFFORD QLD 4053

NOTIFICATION CATEGORY
Standard: Synthetic Polymer with Mn < 1000 Da (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Chemical name, Molecular formula, Structural formula, Molecular weight, Spectral data, Methods of detection and determination, Residual Monomers, Purity, Import volume, Use concentrations, Details of analogue and Physical and chemical properties.

Extension Application:
Concentration in imported product.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
Melting point, Boiling point, Vapour pressure, Hydrolysis as a function of pH, Adsorption/Desorption, Flammability, Autoignition temperature, Explosive properties.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
No

NOTIFICATION IN OTHER COUNTRIES
USA

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Y-17112

Extension Application:
Silwet Hydrostable 212 (contains < 50% notified polymer)

OTHER NAME(S)
Silicone polyether copolymer

MOLECULAR WEIGHT
< 1000 Da

ANALYTICAL DATA

Reference NMR, IR and HPLC spectra were provided.

3. COMPOSITION

DEGREE OF PURITY > 70%

ADDITIVES/ADJUVANTS None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Light yellow liquid

Property	Value	Data Source/Justification
Melting Point/Freezing Point	-1°C	MSDS
Boiling Point	449°C	Estimated (EPIWIN v3.20))
Density	1000 kg/m^3 at 25°C	MSDS (estimated)
Vapour Pressure	2.3x10^{-9} kPa	Estimated (EPIWIN v3.20)
Water Solubility	0.087 g/L	Measured
Hydrolysis as a Function of pH	Not determined	The rate of hydrolysis is expected to be slow (half-life more than a year) based on the structure and intended use.
Partition Coefficient (n-octanol/water)	log Pow = 4.9	Measured (HPLC method)
Adsorption/Desorption	Not determined	The notified polymer is a wetting agent classed as a superspreader, and can therefore be expected to sorb to soils.
Dissociation Constant	Not determined	No dissociable groups.
Flash Point	127°C at 103 kPa (closed cup)	Measured
Flammability	Not expected to be highly flammable	Estimated from measured flash point.
Autoignition Temperature	Not determined	Not expected to autoignite under normal conditions of use.
Explosive Properties	Not expected to be explosive	The structural formula contains no explosophores

Extension Application:
The Extension Applicant has provided further tests on the physical and chemical properties for the notified polymer summarised in the table below. Details of these tests have been included in Appendix A under 'Extension Application'.

Property	Value	Data Source/Justification
Freezing Point	1.43°C	Measured
Boiling Point	> 150°C	Measured
Relative Density	998.6 kg/m^3 at 24.2°C	Measured
Vapour Pressure	0.213 kPa at 20°C	Measured
Adsorption/Desorption	Test 1: log K_{oc} < 1.25 and 3.4 at 25°C Test 2: log K_{oc} = 2.69 – 4.90 at (20 ± 2)°C	Measured
Flash Point	125°C at 103 kPa (closed cup)	Measured
Autoignition Temperature	280°C	Measured
Explosive Properties	Not explosive	Measured
pH	5.59	Measured

Apart from vapour pressure which is several orders of magnitude higher than estimated the test results for the notified polymer supplied by the Extension Applicant are in good agreement with the estimated values supplied by the original applicant.

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties, please refer to Appendix A.
The notified polymer is classed as a "superspreader", a chemical adjuvant that enhances spreading of aqueous formulations on solid surfaces to far greater values than conventional surfactants.

Based on the measured flash point, the notified polymer is not classified as flammable but would be considered to be a C1 combustible liquid [NOHSC:1015(2001)].

Reactivity
The notified polymer is predicted to be stable under normal conditions of use.

Dangerous Goods classification
Based on the submitted physical-chemical data in the above table the notified polymer is not classified according to the Australian Dangerous Goods Code (NTC, 2007). However the data above do not address all Dangerous Goods endpoints. Therefore consideration of all endpoints should be undertaken before a final decision on the Dangerous Goods classification is made by the introducer of the polymer.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED POLYMER (100%) OVER NEXT 5 YEARS
The notified polymer will be introduced in the neat form (at > 70% purity) or as a component of household care products (at < 0.5%) including dishwashing detergents, hard-surface cleaners and carpet cleaners, and surface coatings (at < 3%).

Extension Application
The notified polymer will be introduced as a solution at < 50%. No end use products containing the notified polymer will be introduced.

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

Original Application

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 5	< 5	< 5	< 7	< 10

Extension Application

Year	*1*	*2*	*3*	*4*	*5*
*Tonnes**	< 5	< 5	< 5	< 7	< 10

*Combined total for original and extension applicants.

PORT OF ENTRY
Melbourne and Sydney

TRANSPORTATION AND PACKAGING
The notified polymer will be imported by sea and transported from the wharf by road to the notifier's warehouse as the neat form in 20 L and 200 L drums, and in household care products and surface cleaners in ready-to-use packaging (0.5-5 L).

USE
The notified polymer will be used as a wetting agent in household care products at concentrations of < 0.5% (50% of the import volume) including dishwashing detergents, hard-surface cleaners and carpet cleaners, and as a wetting and levelling agent in water-based surface coatings at concentrations of < 3% (50% of the import volume) for application onto metal, glass, wood and plastic substrates.

Extension Application:
The notified polymer will be used as a wetting agent in household care products at concentrations of < 0.5% including in dishwashing detergents, hard-surface cleaners and carpet cleaners.

OPERATION DESCRIPTION

Re-packing

On rare occasions, the neat form of the notified polymer (at > 70%) will be re-packed from the 200 L drums into 2 L containers for customer evaluation. The re-packing operation will use a closed dispensing process with general air extraction in the immediate area, backed by localised extraction where the operator is loading and unloading the small containers at the dispensing point.

Formulation

The notified polymer (at > 70%) will be meter fed from the import drums via lance and pump to enclosed blending vessels, where it will be mixed with water and other ingredients to form the desired end-use household care products containing < 0.5% of the notified polymer. These products will then be directly pumped from the blending vessels to 0.5 L and 1 L containers by an automated filling process.

End use

Hard-surface cleaners and carpet cleaners containing the notified polymer (at < 0.5%) will likely be applied by spray application and wiped off using a cloth. Dishwashing products containing the notified polymer (at < 0.5%) will be used in automatic dishwashers and for manual dishwashing.

There will be no reformulation of the imported surface coating products containing the notified polymer at < 3%. These products will be applied to surfaces by spray, brush or roller by professional contractors and tradespeople. Spray applications are expected to be applied in a spray booth with local exhaust ventilation.

Extension Application:

No re-packaging of the imported product containing the notified polymer at < 50% will be conducted by the extension applicant. The operation descripton for formulation and end-use will be similar to the original notification.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storage	1	0.3	10
Formulation	2	1	20
QC technicians	1	0.6	20
Repackers	1	0.5	20

EXPOSURE DETAILS

Dermal exposure to the notified polymer (at > 70%) may occur when connecting and disconnecting transfer lines to the blending vessels and through contact with drips from the lance when it is transferred from one drum to another. Dermal exposure to the notified polymer (at < 0.5%) may occur during routine clean-up operations, when taking samples of blended products by technicians for quality control testing and when connecting and disconnecting transfer lines for package filling. Inhalation exposure is not likely as the notified polymer has low volatility and blending occurs in enclosed vessels. Local exhaust ventilation will also be used.

Where dermal exposure to the notified polymer is likely, PPE including gloves and safety glasses are expected to be worn by workers to minimise exposure.

Once the household products (containing the notified polymer at < 0.5%) are packaged for distribution, no further worker exposure is expected from contact with the sealed packages. However, use of the products by commercial users is possible, and would be similar to the pattern of public exposure. The level of PPE used is likely to vary and would include gloves in many cases.

Dermal and ocular exposure may occur when applying the surface coating products (containing the notified polymer at < 3%) by brush or roller and when cleaning the application equipment with water. However, exposure will be minimised by workers wearing personal protective equipment (PPE) such as coveralls, goggles, and impervious gloves.

Inhalation exposure may occur during spray application. However inhalation exposure should be minimised if spray painting is conducted as expected in spray booths with local exhaust ventilation.

Extension Application:
Under the extension application there is no proposed increase in introduction volume or proposed changes in use, hence the circumstances in the extension application will not alter occupational exposure.

6.1.2. Public exposure

Household care products including dishwashing liquids, hard-surface cleaners and carpet cleaners, containing up to 0.5% of the notified polymer will be used widely by consumers. The main exposure to the notified polymer is likely to be dermal, when hand washing dishes in water containing the product or washing hands with the neat dishwashing liquid containing the notified polymer (at < 0.5%). In addition dermal exposure may also occur to the notified polymer (at < 0.5%) when applying the surface cleaners through drips and spills, and when cleaning the applied surfaces with a cloth.

Inhalation exposure may occur due to the formation of aerosols when applying the hard-surface cleaners or carpet cleaners by spray application. Inhalation exposure is unlikely from the dishwashing liquid or from water containing it, as the chemical has low volatility and aerosols are unlikely to be formed.

Systemic exposure to the notified chemical through inhalation of aerosols and mists is estimated to be 1.6×10^{-5} mg/L bw/day. This is based on the following assumptions (SDA, 2005) and a bodyweight of 65.4 kg:

Use frequency of trigger spray cleaners 1 use/day
Respirable product conc. in breathing zone 0.72 mg/m^3
Inhalation rate 1.0 m^3/hr
Exposure duration 0.25 hr
Bioavailable fraction 100%

Oral exposure could occur from ingestion of residues of the dishwashing liquid remaining on plates and utensils.

The worst case systemic exposure to the notified chemical via the oral route through ingestion of residual chemical remaining on non-rinsed dinnerware is estimated to be 2.5×10^{-4} mg/kg bw/day. This is based on the following assumptions (HERA, 2005) and a bodyweight of 65.4 kg:

Area of dishes/eating utensils in daily contact with food 5400 cm^2
Amount of dishwashing water retained on non-rinsed dinnerware 5.5×10^{-4} ml/cm^2
Concentration of dishwashing liquid 0.001 g/cm^3
Concentration of notified chemical in liquid detergent 0.5%
Fraction ingested100%
It is expected that some consumers would wear gloves while using the household care products, and others would not.

Extension Application:
Under the extension application there is no proposed increase in introduction volume or proposed changes in use, hence the circumstances in the extension application will not alter public exposure.

6.2. Human health effects assessment

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

Endpoint	*Result and Assessment Conclusion*

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 = 500 mg/kg bw; harmful
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute inhalation toxicity	LC50 = 2 mg/L/4 hour; harmful (*analogue*)
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Rat, repeat dose oral toxicity – 14 days	NOAEL < 97 mg/kg bw/day (*analogue*)
Rat, repeat dose dermal toxicity – 11 days	NOAEL > 1551 mg/kg bw/day (*analogue*)
Rat, repeat dose inhalation toxicity – 9 days	NOEL < 0.025 mg/L bw/day (*analogue*)
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro Mammalian Chromosome Aberration Test (Chinese Hamster ovary cells)	non genotoxic (*analogue*)
Genotoxicity – in vitro Mammalian Cell Gene Mutation Test (Chinese Hamster ovary cells)	non-genotoxic (*analogue*)
Genotoxicity – in vivo Mouse Micronucleus Test	non genotoxic (*analogue*)

Extension Application:
The Extension Applicant has provided further toxicological studies for the notified polymer. The results of these studies are summarised in the table below. Details of these studies have been included in Appendix B under 'Extension Application'.

Endpoint	*Result and Assessment Conclusion*
Rat, acute inhalation toxicity	1.6 < LC50 < 2.1 mg/L/4 hour; harmful
Rat, repeat dose oral toxicity – 28 days	NOAEL 400 mg/kg bw/day NOEL 40 mg/kg bw/day
Genotoxicity – in vitro Mammalian Chromosome Aberration Test (Human lymphocytes)	non genotoxic

Toxicokinetics, metabolism and distribution
Given its high lipophilicity and low water solubility, the notified polymer is expected to penetrate the stratum corneum but transfer into the hydrophilic epidermis layer is not expected, hence systemic toxicity is unlikely via the dermal route.

Although the notified polymer has a low water solubility, it is a surfactant with superspreading capabilities and as such is expected to be attracted to and disperse along the walls of the GI tract, a property that should assist in the passive uptake of the notified polymer, hence systemic toxicity via the oral route is a possibility.

However, given the low vapour pressure of the notified polymer toxicity by inhalation is unlikely except where mists or aerosols are formed.

Acute toxicity
The notified polymer has a low acute dermal toxicity but is considered harmful if swallowed based on acute oral toxicity studies in rats (LD50 = 500 mg/kg bw). Both animals dosed at 2000 mg/kg bw died within 5 hours post-dose. However no treatment related signs of toxicity were observed in six animals dosed at 300 mg/kg bw.

Based on the results of the acute oral toxicity study the notified polymer is classified as 'Harmful if swallowed (R22)' according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

Acute inhalation
The notified polymer is considered to be toxic (LC50 2 mg/L 4h) by inhalation based on a 4-hour whole body aerosol exposure on rats in a study conducted on an acceptable analogue of the notified polymer at exposure concentrations of 0.26, 1.1 and 2.0 mg/L. Five animals out of 10 tested died or were euthanized when exposed to 2.0 mg/L and 2 out of 10 died or were euthanized when exposed to 1.1 mg/L.

Based on the results of the acute inhalation toxicity study the acceptable analogue of the notified polymer is classified as 'Harmful by inhalation (R20)' according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

Extension Application:
The extension applicant has provided an acute inhalation toxicity study for the notified polymer. Rats were exposed nose only to an aerosol of the notified polymer for 4 hours at exposure concentrations of 1.0, 1.6 and 2.1 mg/L. Six animals out of 10 tested were euthanized when exposed to 2.1 mg/L and 1 out of 10 were euthanized when exposed to 1.6 mg/L. Based on these results, the LC50 was established as < 2.1 and > 1.6 mg/L 4h which is consistent with that observed with the analogue polymer thereby confirming the notified polymer is classified as 'Harmful by inhalation (R20)' according the to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

Irritation and Sensitisation

Based on a test conducted in rabbits the notified polymer is not considered a skin irritant. However, the notified polymer did cause some irritation when tested on the eyes of rabbits but was not severe enough to be classified for eye irritation according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)]. Irritation effects observed included conjunctiva redness and swelling that persisted for up to 6 days. All symptoms were resolved after 7 days.

The notified polymer is not considered to be a skin sensitiser based on the results of a guinea pig maximisation test study.

Repeated Dose Toxicity

- *Oral:* In a 14-day repeat dose study conducted on rats fed with an acceptable analogue of the notified polymer in their diets, treatment related effects were observed at all dose levels tested. Hence the no observed adverse effect level NO(A)EL can not be established but can be considered as < 97 mg/kg bw/day based on the lowest dose tested. However at this lowest dose, biological significant effects were minimal in nature, and were observed only in the thyroid gland, testes and ovaries. At higher dose levels effects upon body weight, food and water consumption, hematologic and clinical chemistry parameters and microscopic changes in testes, ovaries and thyroid glands were observed.

Extension Application:
The extension applicant has provided a 28-day repeat dose oral toxicity study where rats were administered the notified polymer by gavage. Test item-related findings were generally restricted to reductions in the mean daily food consumption at 400 mg/kg/day and 100 mg/kg/day and reduced body weight in males and females treated with 400 mg/kg/day. Based on the results of this study, the study authors established for the notified polymer a NO(A)EL of 400 mg/kg bw/day and a no-observed-effect-level (NOEL) of 40 mg/kg bw/day.

- *Dermal:* No treatment related systemic effects were observed in a repeated dose dermal toxicity study (6 hours/day for 9 out of 11 days) on an acceptable analogue of the notified polymer at all dose levels studied. As such the (NO(A)EL) was established as > 1551 mg/kg bw/day.

- *Inhalation:* In a 9-day whole of body repeat dose inhalation study conducted in rats exposed to an aerosol of the notified polymer at 0.025, 0.08 (mid) and 0.25 (high) mg/L for 6 hours/day, treatment related effects were observed at all dose levels. Hence the NO(A)EL can not be established but can be considered as < 0.025mg/L bw/day based on the lowest exposure concentration tested. However, at this exposure concentration there was a low incidence of ocular opacity (1 animal) and rales (2 males and 2 females one hour following exposure on study days 0, 1 or 2), and a single occurrence of mild necrosis in the nasal respiratory epithelium. Two mortalities out of 20 animals tested were observed in the high dose group (high dose). The notified polymer also caused clinical signs of toxicity (particularly rales, but also ocular opacities) (mid and high dose), inhibition of body weight gain and food consumption (mid and high dose), changes in clinical pathology (high dose), decreased thymus gland weights (high dose) and microscopic lesions in the nasal cavity (mid and high dose).

Mutagenicity

The notified polymer was found to be not mutagenic in bacteria under the conditions of the Ames test used. In addition, an acceptable analogue of the notified polymer did not induce chromosomal aberrations or mutations in mammalian cells. On the basis of weight of evidence the notified polymer is not expected to be genotoxic.

Extension Application:
In an *in vitro* study provided by the extension applicant, the notified polymer was not clastogenic to human lymphocytes providing further evidence that the notified polymer is not genotoxic.

Health hazard classification
Based on the result of the acute oral toxicity study, the notified polymer is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrases:

- R22 Harmful if swallowed

In addition based on the result of the acute inhalation toxicity study conducted on an acceptable analogue of the notified polymer, the notified polymer should be considered as if it is classified as:

- R20 Harmful by inhalation

Extension Application:
Based on the additional toxicological information provided by the extension applicant, the classification provided previously for the notified polymer (R20/22) is confirmed.

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
Based on the available data, the notified polymer is considered harmful by the oral and inhalation routes. The notified polymer also has some potential for eye irritation. Hazards from dermal exposure to the notified polymer are not expected.

Given the low vapour pressure of the notified polymer toxicity by inhalation is unlikely except where mists or aerosols are formed. Exposure to aerosols containing the notified polymer at < 0.5% may occur during blending and when commercial cleaners apply the hard-surface cleaners and carpet cleaners using trigger-based spray applicators. In addition inhalation exposure may occur when applying surface coatings containing the notified polymer at < 3% by spray application.

During blending inhalation exposure should be minimised through the expected use of enclosed reaction vessels and local exhaust ventilation (LEV). Similarly, inhalation exposure during spray application of surface coatings should be minimised as they are expected to occur in a spray booth with LEV. The use of respiratory protection would further reduce exposure.

The risk to commercial cleaners from inhalation exposure to the notified polymer is expected to be similar to the risk posed to the public from use of trigger based household cleaners (see Public Health). Based on the known systemic toxicity of the notified polymer and estimated margin of exposure (MOE), the risk to workers health after use of the cleaning products containing the notified polymer at < 0.5% is not considered unacceptable.

Eye irritation may occur when handling the neat form of the notified polymer (at > 70%). The expected use of safety goggles should minimise this risk.

Overall, given the expected engineering controls in place and use of PPE, the risk to the health of workers to the notified polymer introduced and used as described is not considered unacceptable.

Extension Applicant:
The measured vapour pressure (0.213 kPa at 20°C) of the notified polymer supplied by the extension applicant is several orders of magnitude greater than the estimated value ($2.3x10^{-9}$ kPa). However, given substances having a vapour pressure of less than 0.5 kPa are considered to have low volatility (EC, 2003), this additional information does not impact the original risk assessment for inhalation exposure.

Overall, the circumstances in the extension application do not alter the risk to the health of workers to the notified polymer.

6.3.2. Public health
Inhalation exposure may occur when the public apply household care products such as surface cleaners and carpet cleaners by trigger-based spray applicators.

Considering the systemic exposure to the notified polymer through inhalation of aerosols and mists from use of trigger-based household cleaning products (surface cleaners and carpet cleaners) containing the notified

polymer at 0.5% is estimated to be 1.6 x 10^{-5} mg/L bw/day (see Sec. 6.1.2). Using the NOEL of 0.025 mg/L bw/day from a 9-day inhalation toxicity study for an analogue of the notified polymer, a MOE of >1000 is calculated.

Exposure by the oral route may be possible from ingestion of any residual notified polymer remaining on dinnerware after washing. Considering the systemic exposure to the notified polymer via the oral route from ingestion of residual notified polymer on non-rinsed dinnerware is estimated to be 2.5 x 10^{-4} mg/kg bw/day (see Sec. 6.1.2), using the NOEL of 97 mg/kg bw/day from a 14-day oral toxicity study conducted on an analogue of the notified polymer, a MOE of >> 1000 is calculated.

MOE greater than or equal to 100 are considered acceptable to account for intra- and inter-species differences. The MOE is based on conservative assumptions (e.g. 100% bioavailability) and therefore likely to overestimate the risk.

Overall, the risk to the public from the use of household products containing the notified polymer at up to 0.5% is not considered to be unacceptable based on the toxicity data provided and the estimated MOE.

Given the public will only be exposed to products containing low concentrations of the notified polymer (< 0.5%) the risk of eye irritation is not expected.

Overall, the risk to public health from use of products containing the notified polymer at up to 0.5% is not considered unacceptable.

Extension Application:
The circumstances in the extension application do not alter the risk to public health to the notified polymer.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE
No significant releases are expected from local formulation as production areas will be contained and liquid from equipment and drum cleaning will be used in the next batch of product. Waste from spillage will be salvaged for reuse or adsorbed and collected for landfill disposal via a licensed contractor. It is expected that less than 1% will be wasted in this way.

RELEASE OF CHEMICAL FROM USE
In general, cleaning agents containing the notified polymer will be wiped off on cloths that are either rinsed to sewer or disposed of with household rubbish. When used for dishwashing, the notified polymer will be washed to sewer. When used as an additive in coatings, the notified polymer will be incorporated into the coating. It is non-reactive and will not be covalently bound to the cured polymer matrix, but will not be bioavailable because of its containment in the coating. Small amounts of the cured paint will be collected as overspray when application occurs in spray booths, and will be sent to landfill. Similarly, coated articles are likely to be sent to landfill at the end of their useful life. Minor amounts may be washed to sewer during cleaning of application equipment.
RELEASE OF CHEMICAL FROM DISPOSAL
Small amounts of the notified polymer are likely to be disposed of to landfill as drum residues and waste material from spills. Cured coatings containing the notified polymer will also be sent to landfill, either as overspray or on discarded articles.

7.1.2 Environmental fate

Substantial removal with sludge during sewage treatment can be assumed because of its superspreading properties. The notified polymer is hydrolytically stable and not readily biodegradable, but should undergo slow degradation in landfills and the environment. It is not expected to bioaccumulate because of its molecular weight and surface activity. For the details of the environmental fate studies, please refer to Appendix C.

Extension Application

The test results for adsorption/desorption support the assumption that substantial removal of notified polymer in STPs will occur due to sorption to sludge.

7.1.3 Predicted Environmental Concentration (PEC)

The PEC has been estimated as tabulated below based on an annual import volume of 10,000 kg and worst case assumptions, namely 50% use in applications such as dishwashing formulations that entail washing to sewer, and transfer of 100% through sewage treatment works into receiving waters. Note that this scenario is used as a conservative basis for risk assessment, and will overestimate the environmental exposure since only small amounts will be washed to sewer when the notified polymer is used in surface coatings. The assumption of complete passage through sewage treatment works is an overestimate as the notified polymer is surface active and can be expected to undergo significant removal during sewage treatment by sorption to sludge.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	10,000	kg/year
Proportion expected to be released to sewer	0.5	
Annual quantity of chemical released to sewer	5000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	13.7	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	21.374	million
Removal within STP	0%	
Daily effluent production:	4,275	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	3.2	µg/L
PEC - Ocean:	0.32	µg/L

Extension Application

The Extension Applicant proposes that the notified polymer is only used in household care products. In a worst case scenario, 100% of the notified polymer will be disposed of to sewer. The PECs for river and ocean are updated to 6.4 µg/L and 0.64 µg/L respectively.

Assuming 100% release of notified polymer to sewer the following estimate of notified polymer released to soils is included:

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1000 L/m^2/year (10 ML/ha/year). The notified polymer in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 6.474 µg/L may potentially result in a soil concentration of approximately 43.16 µg/kg. Assuming accumulation of the notified polymer in soil for 5 and 10 years under repeated irrigation, the concentration of notified polymer in the applied soil in 5 and 10 years may be approximately 215.8 µg/kg and 431.6 µg/kg, respectively.

7.2. Environmental effects assessment

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

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	LC50 = 2.94 mg/L	Toxic
Daphnia Toxicity	EC50 = 4.8 mg/L	Toxic
Algal Toxicity	EC50 = 6.79 mg/L	Toxic

Extension Application:
The Extension Applicant has provided two further ecotoxicity studies for the notifier polymer. The results of these studies are summarised below. Details of the studies have been included in Appendix C under 'Extension Application'.

Endpoint	*Result*	*Assessment Conclusion*
Inhibition of microbial respiration	3 h IC50 >1000 mg/L	Not inhibitory to microbial respiration
Earthworm toxicity	14 d LC50 > 1272 mg/kg dry soil 14 d NOEC = 636 mg/kg dry soil	Very slightly toxic (Mensink 1995)

The results from aquatic toxicity testing indicate that the notified polymer is toxic to aquatic life. All results are expressed as nominal concentrations, which were confirmed by DOC analysis to have been maintained throughout the test.

7.2.1 Predicted No-Effect Concentration

The PNEC can be determined by application of an assessment factor of 100 to the endpoints obtained in the most sensitive aquatic species from three trophic levels.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
Median acute lethal concentration in fish	2.9	mg/L
Assessment Factor	100	
PNEC:	29	µg/L

7.3. Environmental risk assessment

Risk Quotients can be calculated as tabulated below.

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	3.2	29	0.11
Q - Ocean	0.32	29	0.01

The notified polymer is not expected to pose a risk to the environment, as the estimated freshwater and marine risk quotients are well below unity.

Extrapolating from the above calculations, and using the same assumptions and scenario, the maximum import volume limit for cleaning applications that maintains a Q value ≤ 1 is shown in the following table:

Secondary Notification Limit Volume	***Limit (Max)***	***Limit (Practical)***
Q - River:	46138 kg/yr	46,000 kg/yr
Q - Ocean:	461,380 kg/yr	460,000 kg/yr

Extension Application:
Assuming accumulation of the notified polymer in soil for 5 and 10 years under repeated irrigation, the concentration of notified polymer in the applied soil may be approximately 215.8 µg/kg and 431.6 µg/kg, respectively. However, acute toxicity study to earthworm showed a NOEC of 636 mg/kg, indicating no concern to the terrestrial environment.

Under the extension application there is no proposed increase in introduction volume of the notified polymer. However, there may be a variation to the environmental exposure of the notified polymer due to the extension application use pattern which will modify the freshwater and marine worst-case PECs to 6.4 µg/L and 0.64 µg/L, respectively. The risk quotients for river and ocean will therefore increase to 0.22 and 0.02, respectively. This will not affect the environmental risk assessment as the estimated freshwater and marine risk quotients are still well below unity.

Since the original secondary notification limit volume was based on release of 100% of the imported notified polymer to sewer, the limit remains unchanged.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available data the notified polymer is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] with the following risk phrases:

– R22 Harmful if swallowed

In addition based on the result of the acute inhalation toxicity study conducted on an acceptable analogue of the notified polymer, the notified polymer should be considered as though classified as:

– R20 Harmful by inhalation

Extension Application:
Based on the additional toxicological information provided by the extension applicant, the classification provided previously for the notified polymer (R20/22) is confirmed.

and

As a comparison only, the classification of the notified polymer using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2009) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	***Hazard statement***
Health		
Acute (oral)	4	Harmful if swallowed
Acute (inhalation)	2	Fatal if inhaled
Environment		
Acute	2	Toxic to aquatic life
Chronic	2	Toxic to aquatic life with long lasting effects

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

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

Environmental risk assessment
On the basis of the PEC/PNEC ratio and the reported use pattern, the notified polymer is not considered to pose a risk to the environment.

Risk assessment and recommendations relating to the extension application
The proposed use, introduction volume and fate of the notified polymer will not change significantly under the proposed extension. The circumstances in the extension application are not expected to impact on the original human health and environmental risk assessment and recommendations.
Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia should consider the following health hazard classification for the notified polymer:
  - R20/22 Harmful by inhalation and if swallowed

- Use the following risk phrases for products/mixtures containing the notified polymer:
  - Conc ≥ 25%: R20/22

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following isolation and engineering controls to minimise occupational exposure to the notified polymer during formulation:
  - Local exhaust ventilation
  - Enclosed blending vessels

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified polymer:
  - Avoid aerosol formation
  - Avoid contact with eyes when introduced in neat form

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified polymer as introduced in the neat form:
  - Safety goggles
  - Respiratory protection

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

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

- If products and mixtures containing the notified polymer are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified polymer should be incinerated in an appropriate incinerator equipped with exhaust gas cleaning if available or be disposed of by landfill.

Emergency procedures

- Spills or accidental release of the notified polymer should be handled by 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 polymer, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified polymer is listed on the Australian Inventory of Chemical Substances (AICS).

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

(1) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a wetting agent for household care cleaning products at concentrations of < 0.5% and surface coatings at concentrations of < 3%, or is likely to change significantly;
- the amount of chemical being introduced has increased from 10 tonnes per annum, or is likely to increase, significantly;
- if the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

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

No additional secondary notification conditions are stipulated.

Material Safety Data Sheet
The MSDS of the notified polymer provided by the notifier was reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

Extension Application:
The MSDS of the imported product containing the notified polymer provided by the notifier was reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility 0.087 g/L

Method OECD TG 105 Water Solubility.
Remarks Flask Method. Study not conducted to GLP.
The notified polymer (0.75 g) was vigorously shaken for 10 minutes in 200 mL water, forming a slightly hazy dispersion, and analysed by reverse-phase HPLC after settling and triple filtration through 0.2 micron syringe filters. Note that the test material contained unreacted polyether.
Test Facility Momentive Performance (2008a)

Hydrolysis as a Function of pH

Method OECD TG 111 Hydrolysis as a Function of pH.

pH	*T (°C)*	$t_{½}$
4	50	> 1 year
7	50	> 1 year
9	50	> 1 year

Remarks Preliminary test only, on the analogue substance Silwet L-77. Details are unclear as the test report was written in Portuguese and no English translation was provided. It is assumed that the notified polymer is hydrolytically stable, as might be expected from its chemical structure and intended use pattern.
Test Facility TASQA (1994).

Partition Coefficient (n-octanol/water) log Pow = 4.9

Method OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks HPLC Method. Study not conducted to GLP.
The notified polymer was determined to have a log Pow ranging from 4.1 to 5.7 due to the wide elution range. The majority of the notified polymer had a log Pow of 4.9. Note that the test material contained unreacted polyether.
Test Facility Momentive Performance (2008b)

Extension Application:

Freezing Point 1.43°C

Method OECD TG 102 Melting Point/Melting Range.
Test Facility Toxikon Corporation (2010a)

Boiling Point > 150°C at 101.3 kPa

Method OECD TG 103 Boiling Point.
Test Facility Toxikon Corporation (2010b)

Relative Density 998.6 kg/m^3 at 24.2°C

Method OECD TG 109 Density of Liquids and Solids.
Remarks Density measured using a pycnometer.
Test Facility Toxikon Corporation (2010c)

Vapour Pressure 0.213 kPa at 20ºC

Method OECD TG 104 Vapour Pressure.
Remarks Determined by static method.
Test Facility Springborn Smithers Laboratories (2010a)

Adsorption/Desorption (Test 1) log K_{oc} < 1.25 and 3.4 at 25)°C
– screening test

Method OECD TG 121 Estimation of the Adsorption Coefficient (K_{OC}) on Soil and on Sewage Sludge Using High Performance Liquid Chromatography (HPLC)
Remarks HPLC Method. The adsorption coefficient was determined by interpolation from a regression curve constructed from known standards (log Koc range 1.25 - 5.63) in accordance with the guidelines above. Two peaks were observed in the chromatograms and hence two log Koc values were determined. The notified polymer has components that are both slightly mobile and very mobile in soil (McCall et al, 1980).
Test Facility Harlan Laboratories (2010a)

Adsorption/Desorption (Test 2) log K_{oc} = 2.69 – 4.90 at (20 ± 2)°C
– preliminary/screening

Method OECD TG 106 Adsorption - Desorption Using a Batch Equilibrium Method

Soil Type	*Organic Carbon Content (g/100 g soil)%*	*pH*	*Koc (mL/g)**	*log Koc**	*K_d**
silt loam	2.51	7.3	11174, 17880, 40939	4.05,4.25, 4.61	280, 449, 1028
sandy clay loam**	0.8	8.1	nd, nd, nd	nd, nd, nd	nd, nd, nd
sandy loam	0.89	5.85	25952, 40211, 79485	4.41, 4.60, 4.90	231, 358, 707
sewage sludge	35.10	6.18	17060, 908, 487	4.23, 2.96, 2.69	599, 319, 171

nd Not defined
*Results for 3 representative compounds of the test substance are reported
**Koc could not be calculated as no analytes could be desorbed from this soil

Remarks A preliminary test and screening test were conducted on three soils and one sludge according to test guidelines with no significant deviations to protocol reported. The test material was a mixture of four polymeric components, one of which was the notified polymer. An advanced test was not considered feasible because of the very strong sorption of the test substance in most soils/sludges and non-attainment of sorption equilibrium. The silt loam, sandy clay loam and sandy loam were obtained from Alsace (France), Murcia (Spain) and Brandenburg (Germany), respectively. The sewage sludge was obtained from a municipal sewage treatment plant ARA Füllinsdorf, Switzerland. Chemical analysis was conducted using LC/MS-MS on three representative homologues of the notified polymer. The mass balance was performed at a soil/sludge-to-solution ratio of 1/25 after 48 h of incubation. The recoveries of the 3 components of the test substance analysed in the various soil/sludge batches ranged between 92% and 114% for the various substrates, which is deemed acceptable. Since the LC/MS-MS technique is analyte-specific, stability of the test item in the test systems was, thus, demonstrated. Based on soil/sludge-to-solution ratio of 1/25 after 48 h, K_d was calculated to be 171 - 1028. An equilibrium distribution was not reached within 48 h of equilibration, hence the reported adsorption coefficients represent a lower limit and should be treated with caution. The test substance has components with mobility in soil and sludge ranging from medium to immobile (McCall et al, 1980).
Test Facility Harlan Laboratories (2010b)

Flash Point 125ºC at 103 kPa

Method	EC Directive 92/69/EEC A.9 Flash Point.
Test Facility	Springborn Smithers Laboratories (2010b)

Autoignition Temperature 280°C

Method	EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Test Facility	Springborn Smithers Laboratories (2010c)

Explosive Properties Not explosive

Method	EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks	*Mechanical explosivity*: No reaction was observed during all six trials of the mechanical sensitivity test. *Thermal explosivity*: No reaction was observed during the thermal sensitivity test with 6.0- or 2.0-mm diameter orifice plates.
Test Facility	Springborn Smithers Laboratories (2010d)

pH 5.59

Method	ASTM E70-07 Standard Test Method for pH of aqueous solutions with the glass electrode
Test Facility	Toxikon Corporation (2010d)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute oral toxicity

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/HsdRccHan:WIST (Full-Barrier)
Vehicle	Cotton seed oil
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	2F	2000	2/2
2	3F	300	0/3
3	3F	300	0/3

LD50	LD50 = 500 mg/kg bw
Signs of Toxicity	In the animals dosed at 2000 mg/kg bw, both animals died within 5 hours post-dose. No treatment related signs of toxicity were observed in the animals dosed at 300 mg/kg bw.
Effects in Organs	No treatment related effects were observed in any of the animals dosed at 300 mg/kg bw. Residual liquid of the test substance was found in the stomach of the animals dosed at 2000 mg/kg bw.
Remarks - Results	
CONCLUSION	The notified polymer is harmful via the oral route.
TEST FACILITY	BSL Bioservice (2006a)

B.2. Acute dermal toxicity

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test.
Species/Strain	Rat/HsdRccHan:WIST (Full-Barrier)
Vehicle	None
Type of dressing	Occlusive
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5M	2000	0
2	5F	2000	0

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	No treatment related effects observed
Signs of Toxicity - Systemic	No treatment related effects observed
Effects in Organs	No treatment related effects observed
Remarks - Results	No deaths occurred
CONCLUSION	The notified polymer is of low toxicity via the dermal route.
TEST FACILITY	BSL Bioservice (2006b)

B.3. Acute inhalation toxicity (analogue)

TEST SUBSTANCE	Acceptable analogue of notified polymer
METHOD	OECD TG 403 Acute Inhalation Toxicity.
Species/Strain	Albino Rat/Crl:CD®BR
Vehicle	None
Method of Exposure	Whole body (aerosol) Post exposure observation period: 14 days
Exposure Period	4 hours
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Concentration mg/L*	*Mortality*
1	5M/5F	0.26	0
2	5M/5F	1.1	1M/1F
3	5M/5F	2.0	2M/3F

LC50	2 mg/L/ 4 hours
Signs of Toxicity	Seven animals out of thirty animals exposed either died or were euthanized for humane reasons during the study. On Day 3, one female was found dead and one male was euthanized in the 1.1 mg/L group. In the 2.0 mg/L group, two females were found dead on Day 3 and one was euthanized on Day 5. Two males were euthanized on Day 4 in the 2.0 mg/L group. All animals at each dose tested showed clinical signs of toxicity to varying degrees during the observation period including matting of various areas of the body and rales, the number of incidence of which increased with increasing dose. Corneal opacity occurred in 9 animals in the 1.1 and 2.0 mg/L group. All the animals in the 1.1 and 2.0 mg/L groups lost 10 to 70 grams from the first day of exposure to Day 3. All animals that survived recovered to or surpassed their initial body weights by Day 14.
Effects in Organs	No abnormal findings were noted in any animals in the 0.26 mg/L group. All animals that were found dead or were euthanized had darkened intestines, distension of the intestines, bilateral ocular opacity, white areas in the liver, mottled lungs, and various stomach abnormalities. Findings for animals that survived to the scheduled necropsy included four animals with hair loss on various locations (one 1.1 mg/L female; one male and two females in the 2.0 mg/L group), ocular opacity (one male and one female in the 2.0 mg/L group), and one rat with dark red areas in the lungs (1.1 mg/L).
Remarks - Results	The LC50 of the analogue polymer was determined to be 2.0 mg/L when male and female albino rats were exposed for a single, four-hour period under the conditions of the study.
CONCLUSION	Based on the results of the acceptable analogue of the notified polymer, the notified polymer is expected to be harmful via inhalation.
TEST FACILITY	WIL Research Laboratories (1995a)

B.4. Skin irritation

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations

RESULTS

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

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

Remarks - Results	No irritation effects were observed
CONCLUSION	The notified polymer is non-irritating to the skin.
TEST FACILITY	BSL Bioservice (2006c)

B.5. Eye irritation

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Observation Period	7 days
Remarks - Method	No significant protocol deviations

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	2.0	2.0	2.0	2	6 days	0
Conjunctiva: chemosis	1.0	1.3	1.0	2	5 days	0
Conjunctiva: discharge	0	0	0.3	3 (1 hr)	24 hr	0
Corneal opacity	0.7	0.3	0.3	1	5 days	0
Iridial inflammation	1.0	0	0.3	1	5 days	0

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

Remarks - Results

Redness of the conjunctiva (Grade 2) was observed in all animals at 24-hours, 48-hours and 72-hours after treatment. This reaction had completely resolved in all animals by Day 7.

Some swelling of the conjunctiva was observed in all animals at 24-hours, 48-hours and 72-hours after treatment with one animal experiencing obvious swelling at the 24-hour observation period. The swelling had completely resolved in all animals by Day 6.

	Conjunctival discharge was observed in all animals after 1-hour and was completely resolved by Day 2. Slight corneal opacity and iridial inflammation was observed in all animals. These reactions had completely resolved by Day 6.
CONCLUSION	The notified polymer is slightly irritating to the eye.
TEST FACILITY	BSL Bioservice (2006d)

B.6. Skin sensitisation

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 406 Skin Sensitisation - GPMT
Species/Strain	Guinea pig/Hsd Poc : DH (Full-Barrier)
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: 0.1% v/v isotonic saline NaCl (0.9%) topical: 50% v/v isotonic saline NaCl (0.9%)
MAIN STUDY	
Number of Animals	Test Group: 10 Control Group: 5
INDUCTION PHASE	Induction Concentration: intradermal: 0.25% v/v isotonic saline NaCl (0.9%) topical: 100%
Signs of Irritation	intradermal: slight erythema was observed in most test animals at sites receiving the notified polymer (0.25% v/v). Slight erythema was also observed in some control animals receiving the saline solution for washing only. topical: slight erythema was observed after topical application (50% v/v) in 4 of 10 test animals immediately after patch removal. No signs of irritation were observed in any of the remaining test and control animals.
CHALLENGE PHASE	
1st challenge	topical: 50% v/v isotonic saline NaCl (0.9%)
RESULTS	
Remarks - Results	There were no dermal reactions observed in any of the test or control animals following challenge.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified polymer under the conditions of the test.
TEST FACILITY	BSL Bioservice (2007)

B.7. Repeat dose oral toxicity (analogue)

TEST SUBSTANCE	Acceptable analogue of notified polymer
METHOD	14-day Oral Toxicity Study in Rodents.
Species/Strain	Rat/Fischer 344
Route of Administration	Oral – diet
Exposure Information	Total exposure days: 14 days Dose regimen: 7 days per week Post-exposure observation period: 28 days
Vehicle	None
Remarks - Method	The protocol is similar to the OECD TG407 except for total exposure days (OECD TG 407 has 28 days).

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	15M/15F	0	0
low dose	10M/10F	96.5(M);98.8(F)	0
mid 1 dose	10M/10F	706.3(M);751.6(F)	0
mid 2 dose	10M/10F	1262.3(M);1384.9(F)	0
high dose	10M/10F	1577.0(M);1791.2(F)	0
control recovery	5M/5F	0	0
high dose recovery	5M/5F	1577.0(M);1791.2(F)	0

Mortality and Time to Death

No mortalities were observed at any dose group.

Clinical Observations

Body weights: During the dosing period in the mid and high dose group for both males and females, there was an apparent dose-related decrease in absolute body weight and body weight gain. This trend persisted during the recovery period. The smallest body weight gain was observed in the high dose group. However, no effects on body weight were observed in the low dose group.

Food and water consumption:

Moderate decreases in food consumption was noted in both males and females in the mid and high dose groups throughout the study. Slight reduction in water consumption was noted in both males and females in the mid and high dose groups during the first two weeks of dosing.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Haematology

Moderate dose-related decreases in reticulocytes and small dose-related decreases in platelets were noted in males and females in the mid and high dose groups at week 2. Some changes in hematologic parameters in both sexes tended to persist at the end of the study period suggesting an effect upon the erythron which may include changes in the production of platelets and erythrocytes.

Clinical chemistry

In males, urea nitrogen (mid 2 and high) was increased while phosphorus (mid 2 and high) and potassium (mid and high) was decreased at week 2. In females, urea nitrogen was increased in the high dose group and phosphorus was decreased in all dose groups at week 2 suggesting effects upon the kidney. Moderate decreases in serum enzyme activity and protein fraction changes in both males and females associated with increased protein clearance may also indicate effects upon the kidney, such as functional changes in this organ. At week 2 in the mid and high dose groups (male and female), aspartate aminotransferase was decreased. Alanine aminotransferase and alkaline phosphatase (ALK) were moderately decreased in males in the mid and high dose groups. Lactate dehydrogenase (LDH) was reduced in males in all dose groups. LDH was reduced in females (mid 2 and high) at week 2, while ALK was decreased in the mid and high dose groups at week 2.

Urinalysis

Evidence for functional changes in the kidney were also noted in the urinalysis data. In males, urine volume increased at week 2 in the low, mid 1 and high dose groups with no increase in water consumption suggesting a loss of urine concentrating ability. Small decreases in urine creatine and calculated creatine clearance were noted in males from the mid and high dose groups. Urine N-acetyl-β-D-glucosaminidase was increased in males in the mid and high dose groups at week 2.

Effects in Organs

Moderate organ weight increases in the liver and thyroid glands were observed in males and females in the mid and high dose groups. Minimal increases were observed in the low dose group. The liver and thyroid gland increases were resolved by week 6. The study authors suggest that these weight changes may indicate an adaptive change in the organ resulting in up-regulation of xenobiotic metabolising enzymes, which dissipated upon removal of the test substance during the recovery period.

Absolute testes weights were markedly reduced in all dose groups at week 2 that persisted until week 6. In

females in the mid and high dose groups, spleen and ovary weights were decreased at week 2. At week 6, no differences in ovary weight were noted while spleen weights continued to be lower than controls. These results suggest recovery from the effects of the test substance in thyroid gland, liver and ovaries, while the testes continued to be effected at the end of the study period, although some recovery was evident in the testes as well.

Microscopic evaluation revealed dose-related changes of the thyroid glands and genital systems of males and females. At week 2, follicular hyperplasia/hypertrophy of the thyroid gland with increased epithelial cell height, mitotic figures, and vesiculation of some follicular cells was noted for males and females at all dose levels, with hypertrophy being the predominant lesion and the hyperplasia being minimal. Dose-related changes in the genital system of males included decreased epididymis size, undeveloped seminal vesicles and inhibition of the process of spermatogenesis. Incomplete maturation of spermatids was observed, with the nurturing influence of the Sertoli cells no longer supporting maturation. This finding persisted in males in the high dose group at week 6, although some recovery was observed. In females at week 2, dose related vacuolation of the corpora lutea was observed. The estrous cycle of all dosed females appeared to be halted in metestrus phase, as if the normal internal cycling influences in these females were overridden. This finding was not evident at the end of the study period.

Remarks – Results

The report concluded that the dietary dosing of the analogue of the notified polymer in the feed for 14 days produced effects upon body weight, food and water consumption, hematologic and clinical chemistry parameters and microscopic changes in testes, ovaries and thyroid glands of males and females in the mid and high dose groups. At the lowest dose level, biologically significant effects were minimal in nature, and were observed only in the thyroid gland, testes and ovaries.

CONCLUSION

The No Observed (Adverse) Effect Level (NO(A)EL) for an acceptable analogue of the notified polymer was established as < 97 mg/kg bw/day in this study, based on observation of treatment-related effects at all dose levels, albeit only minimal effects were observed in the thyroid gland, testes and ovaries for the low dose level.

TEST FACILITY BRRC (1992a)

B.8. Repeat dose dermal toxicity (analogue)

TEST SUBSTANCE	Acceptable analogue of notified polymer
METHOD	Repeated Dose Dermal Toxicity: 11-day Study.
Species/Strain	
Route of Administration	Dermal – occluded
Exposure Information	Total exposure days: 9 days Duration of exposure: 6 hours/day Post-exposure observation period: 28 days for 10M/10F of control and high-dose group. All other animals sacrificed at Day 12.
Vehicle	Carbowax polyethylene glycol (PEG) 200
Remarks - Method	The protocol is similar to OECD TG410 except for total exposure days (OECD TG410 has 21 days).

RESULTS

Group	*Number and Sex of Animals*	*Dose* mg/kg bw/day*	*Mortality*
control	20M/20F	0	0
low dose	10M/10F	547	0
mid dose	10M/10F	1064	0
high dose	20M/20F	1551	0

Concentrations were not adjusted for percent active ingredient of analogue chemical

Mortality and Time to Death

No mortalities were observed in any dose group throughout the study.

Clinical Observations
No treatment related clinical signs of toxicity were observed other than slight to moderate irritation of the skin that was observed in all treated animals. The irritation had completely resolved by Day 22.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
For males in the high dose group, there were increases in eosinophils, alpha 1 and 2 globulin and gamma globulin. Alpha 1 globulin was also increased in males of the mid dose group. These changes were attributed as a response to the skin irritation

Effects in Organs
No treatment related effects were observed.

Remarks – Results
No treatment related effects were observed at all dose groups other than slight to moderate skin irritation which was resolved by Day 22.

CONCLUSION
The No Observed (Adverse) Effect Level (NO(A)EL) for an acceptable analogue of the notified polymer was established as > 1551 mg/kg bw/day in this study, based on no treatment related systemic effects at all dose levels studied.

TEST FACILITY BRRC (1992b)

B.9. Repeat dose inhalation toxicity (analogue)

TEST SUBSTANCE	Acceptable analogue of notified polymer
METHOD	Repeated Dose Inhalation Toxicity: 9-day Study.
Species/Strain	Rats/Fischer-344
Route of Administration	Inhalation – whole body (aerosol)
Exposure Information	Total exposure days: 9 days Duration of exposure: 6 hours/day Post-exposure observation period: None. All animals were sacrificed at Day 9.
Vehicle	None
Remarks - Method	The protocol is similar to the OECD TG412 except for total exposure days (OECD TG412 has 14 or 28 days).

RESULTS

Group	*Number and Sex of Animals*	*Dose/Concentration mg/L*	*Mortality*
control	10M/10F	0	0
low dose	10M/10F	0.025	0
mid dose	10M/10F	0.08	0
high dose	10M/10F	0.25	1M/1F

Mortality and Time to Death
In the high dose group, one male animal died (Day 4) and one female animal was euthanised (Day 5).

Clinical Observations
Clinical signs of toxicity included rales and ocular opacities in all dose groups, yellow matting on various body surfaces and red material around the nose and mouth in the mid to high dose group and clear matting in the facial area of the low dose group.

Statistically significant mean body weight losses or reduced mean body weight gains were observed in the high dose group males during days 1 to 2 and 2 to 5. In the mid dose group, a statistically significant reduced mean body weight gain occurred in the males during days 1 to 2. Food consumption was inhibited in the mid and high dose groups males throughout the study and in the high dose group for females from days 0 to 1

through 4 to 5.

Upon microscopic examination, lesions were observed in the nasal cavities of animals in the mid and high dose groups. Exudate was present in the ventral meatus (mid dose: 2 animals and high dose: 13 animals) and necrosis was observed in the squamous epithelium (mid dose: 1 animal and high dose: 3 animals). Necrosis of the respiratory epithelium was observed in one male each in the low and mid dose groups, and 3 females in the high dose group. Lymphocytic infiltration occurred at an increased incidence in the high dose group when compared to the control and low and mid dose groups. The remaining treatment related findings in the nasal cavities were observed only in the high dose group and consisted of mucosal atrophy, erosion, suppurative inflammation, ulceration and exudate in the dorsal meatus of one to five animals.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Clinical Chemistry: Albumin levels (and corresponding A/G ratios) were significantly decreased in the high dose group for both males and females.

Haematology: In high dose group, increased mean white blood cell count in males and increased absolute numbers and percentages of segmented neutrophils for both males and females were observed.

Urinalysis: Significant increase in specific gravity and possibly reduced urine volume in high dose group were observed.

Effects in Organs

Two females in the high dose group had small thymus glands. In addition, mean absolute and relative thymus gland weights in the same group for both males and females were significantly lower than the control group values. No other treatment related effects were observed.

Remarks – Results

The notified polymer caused mortalities (high dose), clinical signs of toxicity (particularly rales, but also ocular opacities) (mid and high dose), inhibition of body weight gain and food consumption (mid and high dose), changes in clinical pathology (high dose), decreased thymus gland weights (high dose) and microscopic lesions in the nasal cavity (mid and high dose).

In the low exposure group (0.025 mg/L) there was a low incidence of ocular opacity (1 animal) and rales (2 males and 2 females one hour following exposure on study days 0, 1 or 2), and a single occurrence of mild necrosis in the nasal respiratory epithelium.

CONCLUSION

The No Observed Effect Level (NOEL) was established as < 0.025 mg/L in this study, based on a low incidence of ocular opacity and rales in the low dose group.

TEST FACILITY WIL Research Laboratories (1995b)

B.10. Genotoxicity – bacteria (notified polymer)

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 471 Bacterial Reverse Mutation Test.
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 liver microsomal fraction of Phenobarbital and β-naphthoquinone
Concentration Range in Main Test	a) With metabolic activation: 31.6-5000 µg/plate b) Without metabolic activation: 31.6-5000 µg/plate
Vehicle	DMSO
Remarks - Method	No significant protocol deviations. The plate incorporation method (Test 1) and pre-incubation method (Test 2) were used. The TA1535 strain was not tested in the pre-incubation method.

RESULTS

Metabolic	*Test Substance Concentration (µg/plate) Resulting in:*

Activation	*Cytotoxicity in Preliminary Test*	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	> 5000			
Test 1		≥ 316	> 5000	Negative
Test 2		≥ 316	> 5000	Negative
Present	> 5000			
Test 1		≥ 1000	> 5000	Negative
Test 2		≥ 2500	> 5000	Negative

Remarks - Results

In the preliminary dose range finding study conducted on TA98 and TA100 strains only no toxicity was observed with dose levels of up to 5000 µg/plate.

Test 1: Cytotoxic effects were observed in tester strains TA1535 at doses of 2500 µg/plate and higher (without metabolic activation). In tester strain TA1537 cytotoxic effects were noted at doses of 316 µg/plate and higher (without metabolic activation) and at doses of 1000 µg/plate (with metabolic activation).

Test 2: Cytotoxic effects were observed in tester strains TA98 at doses of 1000 µg/plate and higher (without metabolic activation) and at a dose of 5000 µg/plate (with metabolic activation). In tester strain TA100 cytotoxic effects were noted at doses of 316 µg/plate and higher (without metabolic activation). In tester strain TA1535 cytotoxic effects were observed at doses of 1000 µg/plate and higher (without metabolic activation). In tester strain TA1537 cytotoxic effects were observed at doses of 316 µg/plate and higher (without metabolic activation) and at doses of 2500 µg/plate and higher (with metabolic activation).

No substantial increase in revertant colony numbers of any of the tester strains were observed following treatment with the notified polymer at any dose level, with and without metabolic activation, in either mutation test.

The concurrent positive control compounds demonstrated the sensitivity of the assay and the metabolising activity of the liver preparations.

CONCLUSION

The notified polymer was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY

BSL Services (2006e)

B.11. Genotoxicity – in vitro chromosome aberration (analogue)

TEST SUBSTANCE

Acceptable analogue of notified polymer

METHOD

In vitro Mammalian Chromosome Aberration Test.

Species/Strain: Chinese hamster

Cell Type/Cell Line: Chinese hamster ovary (CHO) cells

Metabolic Activation System: S9 fraction from Aroclor 1254 induced rat liver.

Vehicle: DMSO

Remarks - Method: No significant protocol deviations from OECD TG 473

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0.9, 1.79, 3.57, 7.14, 11.9, 14.28	4 hr	20 hr
Test 2	0.23, 0.45, 0.90, 1.79, 3.57, 7.14	4 hr	44 hr
Present			
Test 1	8.5, 17.5, 35, 70, 75, 85	4 hr	20 hr

Test 2	9, 17.9, 35.7, 71.4, 142.8*	4 hr	44 hr

*Culture not 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	≥ 3.57		1190	
Test 1		≥ 7.14	> 14.28	Negative
Test 2		≥ 1.79	> 7.14	Negative
Present	≥ 119			
Test 1		≥ 75	> 85	Negative
Test 2		≥ 71.4	> 142.8	Negative

Remarks - Results

Preliminary test
Precipitation was only observed in the preliminary test at a concentration of 1190 µg/mL. Results from the preliminary test determined the concentrations to be tested in the main test.

Main test
No precipitation was observed in the main test at any concentration studied. Excessive toxicity (i.e. complete mitotic inhibition) precluded the analysis of the 142.8 µg/mL test concentration in the S9 activated 44-hour harvest. Cytotoxicity was determined as a reduction in the mitotic index of > 50%.

The notified polymer did not induce chromosomal aberrations with and without metabolic activation at any dose level studied.

The concurrent positive control compounds demonstrated the sensitivity of the assay and the metabolising activity of the liver preparations.

CONCLUSION

The acceptable analogue of the notified polymer was not clastogenic to Chinese hamster ovary cells treated in vitro under the conditions of the test.

TEST FACILITY

Microbiological Associates (1994)

B.12. Genotoxicity – in vitro gene mutation test (analogue)

TEST SUBSTANCE

Acceptable analogue of notified polymer

METHOD

In vitro Mammalian Cell Gene Mutation Test.
Species/Strain: Chinese hamster
Cell Type/Cell Line: Ovary cells/CHO-K_1-BH_4
Metabolic Activation System: S9 fraction from Aroclor 1254 induced rat liver.
Vehicle: DMSO
Remarks - Method: The protocol is similar to OECD TG476

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	2.5, 5, 10, 20, 40	5 hr	18-24 hr	7-9 days
Test 2	5, 10, 20, 30, 40	5 hr	18-24 hr	7-9 days
Present				
Test 1	12.5, 25, 50, 75, 125	5 hr	18-24 hr	7-9 days
Test 2	50, 60, 70, 85, 100	5 hr	18-24 hr	7-9 days

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent	≥ 50			
Test 1		40	> 5000	Negative
Test 2		40	> 5000	Negative
Present	≥ 150			
Test 1		125	> 5000	Negative
Test 2		100	> 5000	Negative

Remarks - Results

CONCLUSION The acceptable analogue of the notified polymer not clastogenic to Chinese hamster cells treated in vitro under the conditions of the test.

TEST FACILITY Microbiological associates (1994)

B.13. Genotoxicity – in vivo micronucleus test (analogue)

TEST SUBSTANCE Acceptable analogue of notified polymer

METHOD Mammalian Erythrocyte Micronucleus Test.
Species/Strain Mice/Sprague Dawley
Route of Administration Intraperitoneal injection
Vehicle Distilled water
Remarks - Method Method similar to OECD TG 474 Mammalian Erythrocyte Micronucleus Test. Bone marrow cells collected and analysed for micronucleated polychromatic chromosomes at 24, 48 and 72 hours

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5M/5F	0	24, 48 and 72 hrs
II (low dose)	5M/5F	40	24, 48 and 72 hrs
III (mid dose)	5M/5F	80	24, 48 and 72 hrs
IV (high dose)	5M/5F	160	24, 48 and 72 hrs
V (positive control, cyclophosphamide)	5M/5F	40	24 hrs

RESULTS
Doses Producing Toxicity Mortality occurred within one hour of dose administration as follows: 3/5 males and 5/5 females treated with 250 mg/kg and 5/5 males and 5/5 females treated with 500, 1000 and 2000 mg/kg.
Genotoxic Effects No significant increase in the number of micronucleated polychromatic erythrocytes was observed.
Remarks - Results Positive control group showed a marked increase in the incidence of micronucleated polychromatic erythrocytes, demonstrating the sensitivity of the test.

CONCLUSION The acceptable analogue of the notified polymer was not clastogenic under the conditions of this in vivo mouse micronucleus test.

TEST FACILITY Microbiological associates (1994)

Extension Application:

B.14. Acute inhalation toxicity (notified polymer)

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 403 Acute Inhalation Toxicity.
Species/Strain	Albino Rat/RccHan:WIST(SPF)
Vehicle	None
Method of Exposure	Nose-only (aerosol). Post exposure observation period: 14 days (Group 3) and 28 days (Group 1 and 2)
Exposure Period	4 hours
Particle size	MMAD 1.34-2.07 µm
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Concentration <mg/L>*		*Mortality*
		Nominal	*Actual*	
1	5M/5F	1.1	1.0	0
2	5M/5F	1.89	1.6	1M
3	5M/5F	2.31	2.1	3M/3F

LC50	< 2.1 and > 1.6 mg/L/4 hours
Signs of Toxicity	Three male and female animals of group 3 (2.1 mg/L) were killed due to ethical reasons on day 8 or 10 of the scheduled observation period. All animals of group 1 (1.0 mg/L) survived the scheduled observation period. All animals of group 2 (1.6 mg/L) survived the scheduled observation period except for one male that was killed due to ethical reasons on day 5. Treatment-related body weight loss was noted for most of the animals of all groups between test days 1 and 4. In the following days single animals of groups 2 and 3 were humanely killed due to excessive body weight loss of more than 20%. A normal development in body weight was recorded in the majority of the remaining animals until the end of the scheduled observation period. Slight or marked salivation and a slightly decreased spontaneous activity were noted on test day1 at and/or after the end of the exposure in group 1 (1.0 mg/L). Slight to moderate ruffled fur was recorded for all animals from the end of exposure generally up to test day 3 of the study. In all animals slight to moderate breathing noises persisted with a decreasing incidence and severity from the end of exposure up to the end of the observation period. Bradypnea was recorded in all animals on test day 2 and in single animals up to test day 4. Furthermore, tachypnea was observed in one female animal approximately 2 weeks after exposure. Salivation, breathing noise, decreased spontaneous activity and ruffled fur were recorded in all animals with a slight or moderate severity during and/or at the end of exposure to 1.6 mg/L (group 2). Most of these clinical signs were restricted to week 1 of the observation period, except for breathing noises that persisted with interruptions up to week 4. Furthermore, bradypnea was observed in one male animal one day after exposure. Slight to moderate breathing noises and ruffled fur were recorded for all animals of group 3 treated with 2.1 mg/L. Breathing noises were present from the end of exposure onwards and persisted in most of the animals until they were killed due to ethical reasons. Ruffled fur was mainly observed on days 1 and 2 but in some animals also in week 2 of the observation period. Furthermore bradypnea, slight to moderate labored

	respiration, a hunched posture and a slightly decreased spontaneous activity were observed in single animals shortly before they were killed due to ethical reasons in the second week of the observation period.
Effects in Organs	Incompletely collapsed lungs and/or an intestine distended with gas were recorded in four of the animals that were killed due to ethical reasons at 2.1 mg/L (group 3). There were no macroscopic findings in the animals of groups 1 and 2.
Remarks - Results	The LC50 of the notified polymer was determined to be < 2.1 and > 1.6 mg/L when male and female albino rats were exposed for a single, four-hour period under the conditions of the study.
CONCLUSION	The notified polymer is harmful via inhalation.
TEST FACILITY	Harlan Laboratories (2010c)

B.15. Repeat dose oral toxicity (notified polymer)

TEST SUBSTANCE	Notified polymer
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.
Species/Strain	Rat/ RccHan: WIST(SPF)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period: None
Vehicle	Bidistilled water
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	5M/5F	0	0
low dose	5M/5F	40	0
mid dose	5M/5F	100	0
high dose	5M/5F	400	1F

Mortality and Time to Death

One female in the high dose group was found dead on day 21 of treatment and the cause of death was considered to be dosing error. All other animals survived until scheduled necropsy.

Clinical Observations

No treatment related clinical signs of toxicological relevance were noted.

There was no treatment related effects during the functional observational battery including no changes in the mean fore- or hind-limb grip strength or locomotor activity.

Test item-related differences in the mean daily food consumption were noted in males and females treated with 100 mg/kg/day and 400 mg/kg/day. Males and females treated with 400 mg/kg/day had reduced food consumption throughout the treatment phase. Although males at 100 mg/kg/day had marginally reduced food consumption during the first three weeks of treatment, females at this dose level had reduced food consumption throughout treatment.

Test item-related effects on body weight were noted in males and females treated with 400 mg/kg/day.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

No test item-related changes of toxicological relevance were noted in the hematology or clinical biochemistry parameters when compared with the controls.

Effects in Organs

No test item-related findings of toxicological relevance were noted in organ weights when compared with the controls.

No macroscopic or microscopic findings considered to be related to the administration of the test item were diagnosed. All findings noted in this study were considered to be incidental findings commonly noted in rats of this strain and age.

Remarks – Results

Test item-related findings were generally restricted to reductions in the mean daily food consumption at 400 mg/kg/day and 100 mg/kg/day and reduced body weight in males and females treated with 400 mg/kg/day.

Based on the results of this study, the study authors established 40 mg/kg body weight/day of Y-17112 as the no-observed-effect-level (NOEL) and 400 mg/kg body weight/day of Y-17112 as the no-observed-adverse-effect-level (NOAEL).

CONCLUSION

The No Observed (Adverse) Effect Level (NO(A)EL) was established as 400 mg/kg bw/day in this study, based on no affects considered as adverse were observed at the highest dose tested.

TEST FACILITY Harlan Laboratories (2010d)

B.16. Genotoxicity – in vitro chromosome aberration (notified polymer)

TEST SUBSTANCE Notified polymer

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.

Species/Strain	Human
Cell Type/Cell Line	Lymphocytes
Metabolic Activation System	S9 fraction from phenobarbital/β-naphthoflavone induced rat liver
Vehicle	Deionised water
Remarks - Method	No significant protocol deviations.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	1.6, 2.8, 5.0*, 8.7*, 15.2*, 26.7*, 46.6, 81.6, 142.9, 250.0	4 hr	22 hr
Test 2	1.6*, 2.8*, 5.0*, 8.7, 15.2, 26.7, 46.6, 81.6, 142.9, 250.0	22 hr	22 hr
Present			
Test 1	1.6, 2.8, 5.0, 8.7, 15.2, 26.7, 46.6*, 81.6*, 142.9*, 250.0	4 hr	22 hr
Test 2	25.0, 50.0, 75.0*, 100.0*, 125.0*, 150.0, 175.0, 200.0, 225.0, 250.0	4 hr	22 hr

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*		
	Cytotoxicity in Main Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	≥ 26.7	> 250	Negative
Test 2	≥ 5.0	> 250	Negative
Present			
Test 1	250.0	> 250	Negative
Test 2	≥ 125	> 250	Negative

Remarks - Results In both experiments, in the absence and presence of S9 mix, no biologically relevant increase in the number of cells carrying structural chromosome aberrations was observed. No evidence of an increase in

	polyploid metaphases was noticed after treatment with the test item as compared to the control cultures. The validity of the study was demonstrated by a positive genotoxic effect with the positive controls cyclophosphamide (with metabolic activation) and ethylmethane sulfonate (without metabolic activation).
CONCLUSION	The notified polymer was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.
TEST FACILITY	Harlan Laboratories (2009)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified polymer (> 70%)
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge from domestic sewage treatment plant, Rossdorf, Germany
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	Manometry (change of pressure in test flasks due to oxygen consumption).
Remarks - Method	Oxygen demand of inoculum control and pH values of test flasks met validity criteria.

RESULTS

Test substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
4	0	4	64
28	2	16	100

Remarks - Results	The ready biodegradability of the reference substance sodium benzoate was confirmed under the culture conditions used for the test. There was no microbial inhibition in the toxicity control (test and reference substances combined).
CONCLUSION	The notified polymer is not readily biodegradable.
TEST FACILITY	IBACON (2006)

C.1.2. Bioaccumulation

No bioaccumulation test was provided. The notified polymer is poorly degradable and has a log Pow of 4.9, but is not expected to bioaccumulate because of its molecular weight and surface activity.

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified polymer (> 70%)
METHOD	OECD TG 203 Fish, Acute Toxicity Test - static.
Species	Rainbow trout (*Oncorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	DOC measurement after filtration (0.2 micron).
Remarks – Method	Test media were slightly aerated during the test. Measured concentrations were 91% of nominal at the start of the test and 100% in the aged test media.

RESULTS

Nominal Concentration mg/L	*Number of Fish*	*Mortality*				
		1 h	*24 h*	*48 h*	*72 h*	*96 h*
0	7	0	0	0	0	0
0.43	7	0	0	0	2	2
0.94	7	0	0	0	0	0
2.1	7	0	0	0	0	0
4.6	7	0	7			
10	7	0	7			

LC50	2.94 mg/L at 96 hours.
NOEC	0.43 mg/L at 96 hours.
Remarks – Results	Test media remained clear throughout the exposure period. All fish were killed within 2 hours at 10 mg/L, after showing signs of intoxication (strong ventilation and strongly extended gills). The mortalities observed at the lowest test concentration reflect territorial aggression by one fish, rather than intoxication by the test substance.

CONCLUSION The notified polymer is toxic to fish.

TEST FACILITY IBACON (2007a)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified polymer (> 70%)

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	250 mg $CaCO_3$/L
Analytical Monitoring	DOC measurement after filtration (0.2 micron).
Remarks - Method	Test media were prepared immediately before testing. Measured concentrations were 93% of nominal at the start of the test and 115% in the aged test media.

RESULTS

Nominal Concentration mg/L	*Number of D. magna*	*Number Immobilised*	
		24 h	*48 h*
0	20	0	0
0.43	20	0	0
0.94	20	0	0
2.1	20	0	0
4.6	20	0	7
10	20	18	20

EC50	7.1 mg/L at 24 hours 4.8 mg/L at 48 hours
NOEC	4.5 mg/L at 24 hours 2.1 mg/L at 48 hours
Remarks – Results	Test media remained clear throughout the exposure period.

CONCLUSION The notified polymer is toxic to daphnids.

TEST FACILITY IBACON (2007b)

C.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified polymer (> 70%)
METHOD	OECD TG 201 Alga Growth Inhibition Test.
Species	*Desmodesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 0.0093-10 mg/L (confirmed by analysis)
Auxiliary Solvent	None
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	DOC measurement after filtration (0.2 micron).
Remarks - Method	Test media were prepared immediately before introduction of the algae
RESULTS	The 72 hour EC50s were 6.79 mg/L based on growth rate, 1.87 mg/L based on biomass, and 1.31 mg/L based on yield.
Remarks – Results	Test media remained clear throughout the exposure period. The cell density in controls increased 164 fold within 72 hours, satisfying the validity criterion. Microscopic examination of the algae after 72 hours at the highest exposure found no difference in shape compared with controls.
CONCLUSION	The notified polymer is toxic to green algae.
TEST FACILITY	IBACON (2007c)

Extension Application:

C.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified polymer (> 70%)
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test.
Inoculum	Sewage sludge from domestic sewage treatment plant
Exposure Period	3 hours
Concentration Range	1000 mg/L
Remarks – Method	No significant test protocol deviations.
RESULTS	
IC50	> 1,000 mg/L
NOEC	> 1,000 mg/L
Remarks – Results	All acceptability criteria were met, thereby validating this test. The test substance showed no inhibitory effect on the respiration rate of activated sludge at the test concentration of 1,000 mg/L. Based on this result, under the conditions of the study the NOEC and IC50 for the test substance was determined to be >1,000 mg /L.
CONCLUSION	The notified polymer is not inhibitory to microbial respiration.
TEST FACILITY	Harlan Laboratories (2010e)

C.2.5. Acute toxicity to earthworms

TEST SUBSTANCE	Notified polymer (> 70%)
METHOD	OECD TG 207 Earthworm Acute Toxicity Test
Species	*Eisenia foetida*
Exposure Period	14 days
Remarks – Method	The test substance was mixed with artificial soil. The mean body wet weights of the test organisms were determined at the start and end of the test. The test was conducted according to guidelines with no significant deviations from protocol reported.

RESULTS

Concentration mg/kg dry soil		*Number of Earthworms*	*Number missing or dead*	
Nominal	*Actual*		*7 days*	*14 days*
0	nd	40	0	0
79.5	nd	40	0	0
159	nd	40	0	0
318	nd	40	0	0
636	nd	40	0	0
1272	nd	40	2	3

nd Not determined

LC50	> 1272 mg/kg dry soil at 14 days
NOEC	636 mg/kg dry soil at 14 days (for both mortality and body weight loss)
Remarks – Results	A positive control was run with 2-chloroacetamide was run once a year. The most recent test gave a 14 day LC50 of 42 mg/kg dry soil which was within the internal historical range (19 – 55 mg/kg dry soil). Hence the suitability of the test species and experimental conditions was confirmed. There were no mortalities in the control group and hence the validity criterion for the test was satisfied. According to the results of a Welch t-test for inhomogeneous variances (one-sided greater, $\alpha = 0.05$), the loss of the mean body wet weight of the living worms was not statistically significantly greater than in control up to and including the test concentration of 636 mg/kg dry soil. At the highest test concentration of 1272 mg/kg dry soil, the mean loss in body wet weight of the surviving worms was statistically significantly higher compared to the control.
CONCLUSION	The notified polymer is very slightly toxic to earthworms (Mensink 1995)
TEST FACILITY	Harlan Laboratories Ltd (2011)

BIBLIOGRAPHY

BRRC (1992a) *Analogue chemical:* Fourteen-day dietary study in Fischer 344 rats (Project ID 93U1237, 29 June 1994). Bushy run research center, Union Carbide Chemicals and Plastics Company Inc., Export, Pennsylvania, USA. (Unpublished report provided by notifier).

BRRC (1992b) *Analogue chemical*: Nine-day repeated dose toxicity cutaneous dose toxicity study in Fischer 344 rats (Project ID 91O0011, 5 November 1992). Bushy run research center, Union Carbide Chemicals and Plastics Company Inc., Export, Pennsylvania, USA. (Unpublished report provided by notifier).

BSL Bioservice (2006a) Acute oral toxicity – Acute toxic class method with Y-17112 (Project No. 061786, 18 September 2006). BSL Bioservice Scientific Laboratories GmbH, Planegg, Germany. (Unpublished report provided by notifier).

BSL Bioservice (2006b) Acute dermal toxicity (Limit test) with Y-17112 (Project No. 061787, 31 August 2006). BSL Bioservice Scientific Laboratories GmbH, Planegg, Germany. (Unpublished report provided by notifier).

BSL Bioservice (2006c) Acute dermal irritation/corrosion with Y-17112 (Project No. 061788, 31 August 2006). BSL Bioservice Scientific Laboratories GmbH, Planegg, Germany. (Unpublished report provided by notifier).

BSL Bioservice (2006d) Acute eye irritation/corrosion with Y-17112 (Project No. 061789, 28 September 2006). BSL Bioservice Scientific Laboratories GmbH, Planegg, Germany. (Unpublished report provided by notifier).

BSL Bioservice (2007) Test for sensitization (Guinea pig maximization test) with Y-17112 (Project No. 061790, 18 January 2007). BSL Bioservice Scientific Laboratories GmbH, Planegg, Germany. (Unpublished report provided by notifier).

BSL Bioservice (2006e) Reverse mutation assay using bacteria (Salmonella *typhimurium* and Escherichia *coli*) with Y-17112 (Project No. 061791, 18 August 2006). BSL Bioservice Scientific Laboratories GmbH, Planegg, Germany. (Unpublished report provided by notifier).

EC (2003) Technical guidance document on risk assessment Part I. European Commission – p258.

Harlan Laboratories (2009) Chromosome aberration test in human lymphocytes *in vitro* with Y-17112 (Study No. 1288000, 4th May 2009). Harlan Laboratories Ltd, 4452 Itingen, Switzerland. (Unpublished report provided by notifier).

Harlan Laboratories Ltd (2010a) Y-17112: Estimation of the Adsorption Coefficient on Soil using High Performance Liquid Chromatography (HPLC) (Study No. D10491, 20 December 2010). Harlan Laboratories Ltd, 4452 Itingen, Switzerland. (Unpublished report provided by notifier).

Harlan Laboratories Ltd (2010b) Adsorption/Desorption of Y-17122 on Soil/Sludge (Study No. C55984, 6 August 2010). Harlan Laboratories Ltd, 4452 Itingen, Switzerland. (Unpublished report provided by notifier).

Harlan Laboratories (2010c) Y-17112: 4-Hour Acute Inhalation Toxicity Study in the Rat (Study No. C55938, 19th May 2010). Harlan Laboratories Ltd, 44414 Füllinsdorf, Switzerland. (Unpublished report provided by notifier).

Harlan Laboratories (2010d) Y-17112: 4-Week Oral Toxicity (Gavage) Study in the Wistar Rat (Study No. C55951, 26th March 2010. Harlan Laboratories Ltd, 4452 Itingen, Switzerland. (Unpublished report provided by notifier).

Harlan Laboratories Ltd (2010e) Toxicity of Y-17112 to activated sludge in a respiration inhibition test (Study No. C55973, 1 April 2010). Harlan Laboratories Ltd, 4452 Itingen, Switzerland. (Unpublished report provided by notifier).

Harlan Laboratories Ltd (2011) Y-17112: Acute Toxicity to the earthworm *Eisenia fetida* in a 14-day test (Study No. D10480, 10 January 2010). Harlan Laboratories Ltd, 4452 Itingen, Switzerland. (Unpublished report provided by notifier).

HERA (2005) Guidance Document: Methodology. Human & Environmental Risk Assessment on Ingredients of Household Cleaning Products; February 2005

IBACON (2006) Ready biodegradability of Y-17112 in a manometric respirometry test (IBACON study 31124163, 7 September 2006). Rossdorf, Germany (Unpublished report provided by notifier).

IBACON (2007a) Acute toxicity of Y-17112 to rainbow trout (*Oncorhynchus mykiss*) in a 96-hour static test (IBACON study 31123230, 28 March 2007). Rossdorf, Germany (Unpublished report provided by notifier).

IBACON (2007b) Acute toxicity of Y-17112 to *Daphnia magna* in a static 48-hour immobilisation test (IBACON study 31122220, 23 March 2007). Rossdorf, Germany (Unpublished report provided by notifier).

IBACON (2007c) Toxicity of Y-17112 to *Desmodesmus subspicatus* in an algal growth inhibition test (IBACON study 31121210, 26 February 2007). Rossdorf, Germany (Unpublished report provided by notifier).

McCall PJ, Swann RL, Laskowski DA, Unger SM, Vrona SA & Dishburger HJ (1980) Estimation of Chemical Mobility in Soil from Liquid Chromatographic Retention Times. Bull. Environm. Contam. Toxicol. **24**, pp190-195.

Mensink (1995) B.J.W.G. Mensink, M.Monforts, L. Wijkhuizen-Maslankiewicz, H.Tibosch, J.B.H.J.Linders (National Institute of Public Health and Environmental Protection Bilthoven, The Netherlands. 15 - 40) Manual for Summarising and Evaluating the Environmental Aspects of Pesticides.

Microbiological Associates (1994) [Analogue]: In vitro mammalian cytogenetic test (Study No. G94AT04.332, 12 December 1994). Microbiological associates, Inc., Rockville, Maryland, USA. (Unpublished report provided by notifier).

Microbiological Associates (1994) [Analogue]: Micronucleus cytogenic assay in mice (Study No. G94AT04.122, 11 November 1994). Microbiological associates, Inc., Rockville, Maryland, USA. (Unpublished report provided by notifier).

Microbiological Associates (1994) [Analogue]: CHO/HGPRT mutation assay with confirmation (Study No. G94AT04.782001, 14 December 1994). Microbiological associates, Inc., Rockville, Maryland, USA. (Unpublished report provided by notifier).

Momentive Performance (2008a) Analysis of water extractability of Y-17112 Lot K36A061207 by HPLC. Momentive Performance Materials, Research and Development, Silicones Building, Tarrytown, USA. (Unpublished report provided by notifier). (Unpublished report provided by notifier).

Momentive Performance (2008b) Analysis of octanol/water partition coefficient of Y-17112 Lot K36A061207 by HPLC. Momentive Performance Materials, Research and Development, Silicones Building, Tarrytown, USA. (Unpublished report provided by notifier).

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

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

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

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

SDA (2005) Exposure and Risk Screening Methods for Consumer Products Ingredients. Washington, The Soap and Detergent Association

Springborn Smithers Laboratories (2010a) Y-17112 - Determination of the vapor pressure by the static procedure following OECD Guideline 104 (Study No. 13935.6106, 20th July 2010). Springborn Smithers Laboratories, Wareham, Massachusetts, USA. (Unpublished report provided by notifier).

Springborn Smithers Laboratories (2010b) Y-17112 - Determining the flash point of a test substance following the official Journal of the European Communities L383A, Method A.9 (Study No. 13935.6108. 20th July 2010). Springborn Smithers Laboratories, Wareham, Massachusetts, USA. (Unpublished report provided by notifier).

Springborn Smithers Laboratories (2010c) Y-17112 - Determining the auto-flammability (Temperature of Self Ignition of Liquids or Gases) following the Official Journal of the European Communities L383A, Method A.15 (Study No. 13935.6107, 2nd July 2010). Springborn Smithers Laboratories, Wareham, Massachusetts, USA. (Unpublished report provided by notifier).

Springborn Smithers Laboratories (2010d) Determination of the explosive properties of a test substance following the Official Journal of the European Communities L383A, Method A.14, Springborn Smithers Laboratories Protocol No.: 082010/EU/Explosive Properties (Study No. 13935.6111, 16/17th September 2010). Springborn Smithers Laboratories, Wareham, Massachusetts, USA. (Unpublished report provided by notifier).

TASQA (1994) [Analogue]: Determinacao da taxa de hidrolise em funcao do pH. TASQA study TSQ-P399/93 dated 29th March 1994, Paulinia, Brazil. (Unpublished report provided by notifier).

Toxikon Corporation (2010a) Analysis of melting/freezing point (Report No. 10-2995-G1, 28th July 2010). Toxikon Corporation, Bedford, Massachusetts, USA. (Unpublished report provided by notifier).

Toxikon Corporation (2010b) Determination of boiling point (Report No. 10-2995-G2, 27th July 2010). Toxikon Corporation, Bedford, Massachusetts, USA. (Unpublished report provided by notifier).

Toxikon Corporation (2010c) Analysis of relative density (Report No. 10-2995-G3, 27th July 2010). Toxikon Corporation, Bedford, Massachusetts, USA. (Unpublished report provided by notifier).

Toxikon Corporation (2010d) Analysis of pH (Report No. 10-2995-G4, 27th July 2010). Toxikon Corporation, Bedford, Massachusetts, USA. (Unpublished report provided by notifier).

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

WIL Research Laboratories (1995a) An acute inhalation toxicity study of *analogue chemical* in Albino Rats (Project No. WIL-242003, September 1995). WIL Research Laboratories, Ashland, Ohio, USA. (Unpublished report provided by notifier).

WIL Research Laboratories (1995b) A 9-day inhalation toxicity study of *analogue chemical* in rats (Project No. WIL-242004, 3rd October 1995). WIL Research Laboratories, Ashland, Ohio, USA. (Unpublished report provided by notifier).