File No: STD/1382

October 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Polyurethane Prepolymer in Liofol UR 7729

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 Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This 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

SUMMARY

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

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS SUBSTANCE	INTRODUCTION VOLUME	USE
STD/1382	HENKEL AUSTRALIA PTY LTD	Polyurethane Prepolymer in Liofol UR 7729	Yes	<50 tonnes per annum	Adhesive

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the data provided for Analogue chemicals, the notified polymer should be considered as though it is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008 (2004)] with the following risk phrases:

R23 or R26 Toxic or Very Toxic by inhalation
R36/37/38 Irritating to eyes, respiratory system and skin
R40 Limited evidence of a carcinogenic effect
R42/43 May cause sensitisation by inhalation and skin contact
R39/23 Toxic: danger of very serious irreversible effects through inhalation; or
R39/26 Very toxic: danger of very serious irreversible effects through inhalation.

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 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	*Hazard statement*
Acute inhalation	1	Fatal if inhaled
Skin irritation	2	Causes skin irritation
Eye irritation	2B	Causes eye irritation
Respiratory sensitisation	1	May cause allergy or asthma symptoms or breathing difficulties if inhaled
Skin sensitisation	1	May cause an allergic skin reaction
Repeated exposure	1	Causes damage to organs (respiratory system) through prolonged or repeated inhalation exposure
Carcinogenicity	2	Suspected of causing cancer

Human health risk assessment
This risk to occupational health and safety is considered acceptable provided that the notified polymer is only used under controlled conditions by trained workers wearing PPE.

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 low hazard and the assessed use pattern, the notified polymer is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS
Hazard Classification and Labelling

- Based on the data provided for analogue chemicals, use the following risk phrases for products/mixtures containing the notified polymer:

  - Conc ≥ 25%: R36/37/38, R40, R42/43
  - ≥ 10% Conc < 25%: R36/37/38, R40, R42/43;
  - Conc ≥ 10%: R39/R26
  - Conc ≥ 7%: R26
  - ≥ 5% Conc < 10%: R36/37/38, R40, R42/43,
  - 3% ≤ Conc <25%: R20; Conc ≥ 25%: R23
  - 1% ≤ Conc < 10%: R39/23
  - 1% ≤ Conc < 7%: R23;
  - 1% ≤ Conc < 5%: R40, R42/43
  - ≥ 0.1% Conc < 1%: R42, *R20, R68/20*

Health Surveillance

- As the notified polymer contains functional groups of concern, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a history of sensitivity, asthma or other pulmonary condition and who may be adversely affected by isocyanate exposure.

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified polymer as introduced at <70% concentration in Liofol UR 7729 Polyurethane Adhesive:
  - Do not breathe vapours/spray
  - Avoid contact with skin and eyes
  - The Safe Work Australia exposure standard for isocyanates of 0.02 mg/m^3 (TWA) and 0.07 mg/m^3 (STEL) should be observed ([NOHSC:3008 (1995)] and [NOHSC:1003 (1995)]

- Employers should implement the following safe engineering controls to minimise occupational exposure during handling of the notified polymer as introduced at <70% concentration in Liofol UR 7729 Polyurethane Adhesive:
  - Ventilation system, including local exhaust ventilation

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified polymer as introduced at <70% concentration in Liofol UR 7729 Polyurethane Adhesive:
  - Safety glasses
  - Coveralls
  - Gloves
  - Respirator

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

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

- If products and mixtures containing the notified 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.

Public Health

- The following measures should be taken by manufacturers of food packaging to minimise public exposure to adhesives containing the notified polymer:
  - the adhesive containing the notified polymer should be fully cured.

Disposal

- The notified polymer should be disposed of to landfill.

Storage

- The following precautions should be taken by the notifier regarding storage of the notified polymer:
  - Check all containers against leakage and ensure lids and caps are tightly sealed.
  - Store in a ventilated and bunded area.
  - Store in a cool dry place away from direct sunlight.
  - Store away from acids, alkalis or amines.

Emergency procedures

- Spills or accidental release of the notified polymer should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified 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 polymer has changed from a component of a polyurethane adhesive system for use in food packaging, or is likely to change significantly;
  - the amount of polymer being introduced has increased, or is likely to increase, significantly;
  - the polymer has begun to be manufactured in Australia;
  - additional information has become available to the person as to an adverse effect of the polymer on occupational health and safety, public health, or the environment.

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

Material Safety Data Sheet
The MSDS of a 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.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Henkel Australia Pty Ltd (ABN 82 001 302 996)
7 Stanton Road
SEVEN HILLS NSW 2147

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, CAS number, molecular and structural formulae, molecular weight, analytical data, polymer constituents, residual monomers, additives/adjuvants, use details, import volume and identity of manufacturer.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for all the data required under the schedule of data requirements.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
None

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Liofol UR 7729 (contains the notified polymer at <70%)

MOLECULAR WEIGHT
Mn >500 Da.

ANALYTICAL DATA
Reference IR and GPC spectra were provided.

3. COMPOSITION

DEGREE OF PURITY >99%

4. PHYSICAL AND CHEMICAL PROPERTIES

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

Property	Value	Data Source/Justification
Melting Point#	5-38 °C	Analogue data
Boiling Point#	>300 °C at 101.3 kPa	Analogue data
Density*	1140-1160 kg/m^3 at 20 °C	MSDS
Vapour Pressure#	<1.4x10^{-6} kPa	Analogue data
Water Solubility	Not determined	Not tested due to the presence of end-groups that readily react with water to form carbon dioxide and insoluble polymeric masses
Hydrolysis as a Function of pH	Not determined	Not tested due to the presence of end-groups that readily react with water to form carbon dioxide and insoluble polymeric masses
Partition Coefficient	Not determined	Expected to react with water and

(n-octanol/water)		octanol to form carbon dioxide and insoluble polymeric masses
Adsorption/Desorption	Not determined	Not tested due to the presence of end-groups that readily react with water to form carbon dioxide and insoluble polymeric masses
Dissociation Constant	Not determined	The notified polymer has no dissociable functional groups
Flash Point	>150ºC	MSDS
Autoignition Temperature[#]	>600ºC	Analogue data
Explosive Properties	Not predicted to be explosive	Estimated based on structure

***** For the imported product Liofol UR 7729 containing the notified polymer at <70% concentration.
[#] Data based on Analogue 1 and Analogue 2. See section 6.2 Human Health Effects Assessment for the suitability of these analogues.

DISCUSSION OF PROPERTIES
Reactivity
The notified polymer is expected to be stable while stored in sealed vessels with no exposure to the atmosphere. Analogue 1 is known to react with water to form carbon dioxide, heat and insoluble urea. The notified polymer will also react with alcohols, acids, alkalis and amines.

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 CHEMICAL (100%) OVER NEXT 5 YEARS
The notified polymer will be imported at <70% concentration as a component of a polyurethane adhesive.

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

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

PORT OF ENTRY
Melbourne

IDENTITY OF RECIPIENTS
Henkel Australia Pty Ltd, Victoria

TRANSPORTATION AND PACKAGING
The notified polymer will be imported by air or sea in 230 kg hermetically sealed steel drums and then transported by road directly to the customer's site for end use.

USE
The notified polymer will be imported at <70% as a component of a polyurethane adhesive for use in film lamination for food packaging.

OPERATION DESCRIPTION
The notified polymer at <70% will be transferred from import drums to laminating equipment using an automated volumetric dispensing system. The notified polymer will be automatically blended with the other part of the two part adhesive and applied to food packaging film using a roll to roll laminator. The automated dispensing system and laminating equipment will be cleaned following use.

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	1-5	1	200
Application	2	6	100
Cleaning and Maintenance	1	0.5	100

EXPOSURE DETAILS
Transport workers are not likely to be exposed to the notified polymer except in the case of an accident involving damage to the import containers.

Workers involved in the application of the polyurethane adhesive system containing the notified polymer to food packaging may experience dermal, ocular and inhalation exposure to the notified polymer at <70% concentration when opening import containers and attaching them to the automated dosing machine and during operation of the roll-to-roll laminating equipment. However, exposure should be minimised by the use of personal protective equipment (PPE) such as gloves, safety glasses and coveralls. Ventilation will also be used to minimise inhalation exposure.

Workers may be exposed to residues of the notified polymer during periodical cleaning of the laminating equipment. However, exposure should be minimised by the use of PPE including safety glasses, gloves, coveralls and if necessary, respiratory protection.

6.1.2. Public Exposure
The notified polymer will not be available to the public. Food packaging containing adhesive containing the notified polymer may be handled by the public. However, the notified polymer will react with other components of the adhesive to form a high molecular weight polymer matrix and therefore, exposure is not anticipated.

6.2. Human Health Effects Assessment

No toxicity data were submitted on the notified polymer itself. However, toxicological data on 2 analogues are presented below. These analogues have molecular weight <500 Da., whereas the notified polymer has a molecular weight >500 Da. The notified polymer shares the same reactive functional group as the analogues and is expected to undergo similar reactions, however the difference in molecular weight is expected to result in a significantly slower rate of absorption of the notified polymer compared to the analogues,. Therefore, the analogue chemicals are expected to provide a worst-case estimate of the toxicity of the notified polymer.

Endpoint	*Analogue 1*	*Analogue 2*
Rat, acute oral toxicity (mg/kg bw)	31,600 at 25% in corn oil	>10,000
Rabbit, acute dermal toxicity (mg/kg bw)	Not Available	>9,400
Rat, acute inhalation toxicity (mg/m^3)	172-187 (1-hr exposure)	490 (4-hrs exposure)
Rabbit, skin irritation	irritating	irritating
Rabbit, eye irritation	irritating	irritating
Guinea pig, skin sensitisation – Maximisation test	evidence of sensitisation	evidence of sensitisation
Mouse, skin sensitisation – Ear swelling test	evidence of sensitisation	Not Available
Human, patch test	evidence of sensitisation	Not Available
Guinea pig, respiratory sensitisation	evidence of sensitisation	evidence of sensitisation
Human, IgG and IgE	Not Available	evidence of sensitisation
Rat, repeat dose inhalation toxicity – 14 days. (mg/m^3)	Not Available	LOAEL = 1
Rat, repeat dose inhalation toxicity – 2 years. (mg/m^3)	Not Available	NOAEL = 0.2

Toxicokinetics, metabolism and distribution

A generic form of the analogue chemicals has a molecular weight < 500 Da., a water solubility of approximately 1.39 mg/L and a partition coefficient (log Pow) of 4.5 and would therefore be expected to be absorbed via the oral, dermal and inhalation route.

Analogue 1: Absorption (oral) of Analogue 1 in humans is evidenced by the presence of associated haemoglobin adducts and urinary metabolites. The half-life in urine was determined by acid hydrolysis to be 70-80 hours while the half-life in serum was estimated to be 21 days.

Toxicokinetic information on Analogue 1 following inhalation exposure to animals, indicated that it was absorbed through the lungs and distributed throughout the organism with a predominance for the lungs, muscle, kidneys and digestive tract. Approximately 79% of Analogue 1 was excreted in faeces and 5% excreted in urine. The transplacental distribution of Analogue 1 and its metabolites following absorption via inhalation has been confirmed. The highest metabolite levels were found in the maternal blood, followed by the placenta, foetus and amniotic fluid.

Based on results of toxicokinetic studies on analogue chemicals as described above, the notified polymer is expected to be readily absorbed following inhalation exposure.

The extent of dermal absorption of the analogue chemicals is uncertain. However, absorption of 1% has been used as an estimate to calculate body burden in a risk assessment indicating it is likely to be low.

Acute toxicity
Based on the oral LD50 values obtained for analogues as shown above, the notified polymer is considered to be of low acute oral toxicity.

Based on the dermal LD50 value obtained for Analogue 2 as shown above, the notified polymer is likely to be of low acute dermal toxicity.

Analogue 1: In an acute inhalation toxicity study in rats using Analogue 1, no deaths or gross lesions were reported in any of the groups of 6 rats exposed to the chemical for 1 hour at concentrations of 0.6, 81, 162 or 172 mg/m^3. However, 4 deaths were reported in the group treated at 187 mg/m^3 and therefore the LC50 was considered to be 172-187 mg/m^3. It should be noted that this study was not conducted according to accepted international test guidelines

Analogue 2: An acute inhalation study on Analogue 2 was conducted on rats at concentrations of 384, 418, 500 and 523 mg/m^3 according to the EU Directive 84/449/EEC.B.2. However, the analytical method for determining the mean concentration of the test substance has since been shown to be questionable. Haemorrhages and oedema of the lungs was observed in animals sacrificed at the end of 4 hours exposure at concentrations of 384, 418 and 523 mg/m^3. Most animals exposed at 523 mg/m^3 had greyish, wet lungs. Haemorrhages of the lung were reported in some animals that died during the observation period or were terminated at the end of the study. This was particularly prevalent in animals exposed at 418 mg/m^3. The LC50 was calculated as 490 mg/m^3 by the authors of the study.

Analogues 1 and 2 are classified as R20: Harmful by inhalation, according to the Safe Work Australia Hazardous Substances Information System adopted from the EU classification of these analogues. However, based on the results of acute inhalation studies on Analogues 1 and 2, the notified polymer is likely to have an inhalation LC50 of 172 (1 hr) - 490 (4hr) mg/m^3 or 0.17-0.49 mg/L, indicating it has the potential to be very toxic or toxic by inhalation.

Irritation
The notified polymer is expected to be irritating to the skin, eyes and respiratory tract based on the results of reports on analogue chemicals as summarised below.

A generic form of the analogue chemicals has been reported to be severely irritating to the skin in rabbits according to the draize test. Other tests in rabbits on Analogues 1 and 2 that were not conducted according to accepted test guidelines reported that the analogues were either irritating or slightly irritating to the skin in rabbits. Reports of persistent skin irritation resulting from occupational exposure to Analogue 1 in humans have not been conclusive. The effects observed may have been a primary irritant inflammatory response but could also be attributable to local cytotoxicity and/or sensitisation.

A generic form of the analogue chemicals has been reported not to produce irritation to the eye of rabbits. However, other tests on Analogue 1 and 2 that were not conducted according to accepted test guidelines have shown the analogues to be either slightly irritating or irritating. There have been several reports of eye irritation following exposure to unintentional contact with the solid form of Analogue 1 or its vapours.

Respiratory irritation studies conducted on Analogues 1 and 2 have shown them both to be pulmonary irritants.

Sensitisation
The notified polymer is considered to be a skin and respiratory sensitiser based on the results of numerous sensitisation studies conducted on analogue chemicals in various species.

Repeated dose toxicity
No repeat dose toxicity data were available on the analogue chemicals for exposure via the oral or dermal routes.

A subacute inhalation study conducted on Analogue 2 in rats reported a lowest observed adverse effect level (LOAEL) of 1 mg/m^3 for effects on the surfactant homeostasis. A LOAEL for chronic inhalation toxicity in rats exposed to Analogue 2 was determined to be 1 mg/m^3 and a no observed adverse effect level (NOAEL) established at 0.2 mg/m^3. Adverse effects observed at higher concentrations in this study included bronciolo-alveolar adenoma, bronchiolo-alveolar hyperplasia, interstitial fibrosis and mineralised deposits. Pulmonary adenomas and pre-neoplastic lesions were found in animals exposed to the highest dose.

Based on the results of studies on analogue chemicals, the notified polymer is considered likely to cause damage to the respiratory tract and the NOAEL for chronic inhalation to the notified polymer is expected to be approximately 0.2 mg/m^3.

Mutagenicity
Numerous mutagenicity (AMES) tests have been carried out using Analogues 1 and 2 both with and without metabolic activation. However, most of the tests have not been conducted according to accepted test guidelines. Some of the tests have reported positive results, although the use of dimethyl sulfoxide (DMSO) as a solvent, which has been shown to convert the analogues into a known mutagen, appears to provide sufficient justification for the analogues not to be considered mutagens.

A study to assess the potential of Analogue 1 to induce chromosome aberrations and sister-chromatid exchanges was tested in human whole blood lymphocyte cultures in the absence and presence of metabolic activation. Analogue 1 induced chromosome aberrations at all doses tested (0.54-4.30 µL/mL) in the absence of metabolic activation and at the highest dose (4.30 µL/mL) in the presence of metabolic activation. Toxicity was not able to be determined due to Analogue 1 forming chemical-like fibres after addition to the culture medium. The chromosome aberrations observed were considered to have been caused by the by-products of the reaction of Analogue 1 with water in the culture medium and not necessarily Analogue 1 itself. This was partially supported by the lack of a dose-response.

Several *in vivo* genotoxicity studies have also been carried out on Analogues 1 and 2. Positive results obtained in micronucleus tests were not necessarily considered to indicate genotoxicity of the notified polymer due to problems with the way the tests were conducted. In one test, the number of micronucleated erythrocytes observed in the treated animals was high but not significantly different to the number observed in control animals. In another study, the method was not in accordance with accepted test guidelines and therefore, the positive results were not considered reliable. In a micronucleus study conducted in rats on Analogue 1, no cytogenetic damage was observed following inhalation exposure to concentrations sufficient to cause respiratory toxicity.

In a micronucleus assay conducted in the bone marrow of Brown-Norway rats, no significant increases in the number of micronucleated polychromatic erythrocytes were reported in rats exposed at 118 mg/m^3 (whole-body) or at 110 mg/m^3 (nose-only) to Analogue 1 for 1 hour per day, 1 exposure per week for 3 weeks.

Other studies have shown that Analogues 1 and 2 do not have significant DNA-binding potential in animals following topical or inhalation exposure.

Therefore, on the basis of various mutagenicity/genotoxicity studies conducted on Analogues 1 and 2 as described above, the notified polymer is not considered likely to have the potential to be mutagenic or genotoxic.

Carcinogenicity
The carcinogenic potential of Analogues 1 and 2 was investigated during chronic inhalation exposure studies in rats. A study using Analogue 1 found bronchio-alveolar adenoma in animals exposed at 2.05 mg/m^3. The study using Analogue 2 found no increased incidence in tumours apart from the tumours in the lungs which were believed to have developed as a result of the local irritation caused by the chemical. The LOAEL for Analogue 2 was considered to be 6 mg/m^3. A NOAEL of 0.2 mg/m^3 (exposure = 6 hours/day, 5 days/week for 24 months) was considered appropriate for Analogues 1 and 2.

Several epidemiological studies on Analogues 1 and 2 and similar chemicals have failed to establish a causal relation between lung cancers observed in workers and their exposure to chemicals similar to the notified polymer.

There was an increased rate of pulmonary tumours observed in animals treated with analogue chemicals. However, the mechanism of tumour development was not definitively identified. One possible explanation for the tumour development was a secondary reaction to the irritation caused by the aerosols of the analogue chemicals. In this case, the tumours would be produced via epigenetic mechanisms rather than genotoxic. Therefore, due to the uncertainty of the role of the analogue chemicals in causing an increased rate of tumours in animals, the International Agency for Research on Cancer has determined that there was inadequate evidence of carcinogenicity caused by analogue chemicals in humans and limited evidence in experimental animals.

Based on the structural similarities between the analogues and the notified polymer, the potential carcinogenicity of the notified polymer is considered to be similar to the analogue chemicals (Group 3: Not classifiable as to its carcinogenicity to humans - IARC, 1999).

Reproductive toxicity
No multigenerational or fertility studies were conducted on either of the analogues. In a 2 year chronic inhalation study on Analogue 2, statistically significant increased weight of the testes was reported in males exposed to 0.2 mg/m^3. Increased testes weights were also observed in male rats treated at 1.0 and 6.0 mg/m^3, however, the increases were not statistically significant. In the absence of any histopathological changes, the increased weight of the testes was not considered related to treatment with the chemical. In females, tumours and secretory activity in the mammary glands as well as ovarian cysts and uterine polyps were reported in rats from all groups including females from the control groups. The authors stated the incidence of these findings was comparable with that expected of ageing Wistar rats. However, historical data on these parameters was not provided in the study report. Furthermore, no histological examination was undertaken on the reproductive organs. No data was presented on the ovaries.

The available data on analogue chemicals are not considered sufficient to predict the likely toxicity of the notified polymer to the reproductive system.

Developmental toxicity
No multigenerational studies were available on either of the analogue chemicals. However, results of developmental range-finding studies in rats were available.

A NOAEL (developmental) for Analogue 1 was considered to be 3 mg/m^3, based on the significant increase in litters with foetuses displaying asymmetric sternebrae from the dams treated with 9 mg/m^3 in a subchronic toxicity study in rats.

An examination of the results of two developmental range-finding studies in rats determined the NOAEL for Analogue 2 to be 4 mg/m^3. This was based on effects such as statistically significant decreases in food intake and decreased (but not statistically significant) bodyweight gain at 8 mg/m^3.

From the limited data available on analogue chemicals, the NOAEL for developmental toxicity could not be estimated with any certainty. However, chronic inhalation exposure to concentrations $\geq$ 3 mg/m^3 may be considered likely to cause adverse effects.

Health hazard classification
Based on the data provided for Analogue chemicals, the notified polymer should be considered as though it is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008 (2004)] with the following risk phrases:

R23 or R26 Toxic or Very Toxic by inhalation
R36/37/38 Irritating to eyes, respiratory system and skin
R40 Limited evidence of a carcinogenic effect
R42/43 May cause sensitisation by inhalation and skin contact
R39/23 Toxic: danger of very serious irreversible effects through inhalation; or
R39/26 Very toxic: danger of very serious irreversible effects through inhalation.

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The notified polymer will be handled by workers at <70% concentration. At such concentrations, the notified polymer is classified as a respiratory sensitiser and is considered to be a potential eye and skin irritant as well as a skin sensitiser. Dermal and ocular exposure to the notified polymer during transfer and application of the adhesive is expected to be limited by the use of PPE. Due to the expected low volatility of the notified polymer and given the expected use of exhaust ventilation, inhalation exposure is not anticipated. Therefore, provided control measures are in place to reduce exposure, the risk to the health of workers from use of the notified polymer is not considered to be unreasonable.

6.3.2. Public Health
The notified polymer is intended for use in industrial applications only. The public may be exposed to food packaging manufactured using the notified polymer. The notifier has advised that exposure is not likely as the notified polymer is not expected to migrate from the adhesive as it will be fully reacted into an inert matrix. The manufacturer of the food packaging is responsible for ensuring the adhesive containing the notified polymer has fully cured so that the levels of reactive, low molecular weight species are below the limits of detection. Therefore provided end-users i.e. food packaging manufacturers employ good manufacturing processes to ensure complete curing of the adhesive the risk to public health is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE
The notified polymer is not manufactured or reformulated in Australia; therefore, there is no release from these activities. Accidental spills during transport are expected to be absorbed onto suitable material and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE
Most of the notified polymer will be applied as adhesive to food packaging films. The notified polymer will be reacted with other part of the two part adhesive and cured to form an inert matrix. The roll to roll laminator is cleaned periodically and equipment washings are estimated to contain 1% of the annual import volume of notified polymer. A further 1% of the notified polymer is estimated to remain as residues in import containers. The residues in equipment washings and import containers are expected to be collected by a licensed waste disposal contactor and disposed of in accordance with local regulations.

RELEASE OF CHEMICAL FROM DISPOSAL
The majority of notified polymer is expected to share the fate of the films to which it has been applied and be disposed of to landfill.

7.1.2. Environmental Fate

No environmental fate data for the notified polymer were provided. Summaries of literature and unpublished studies were provided for two analogues, with the same reactive functional group as the notified polymer, in

reliable internationally peer-reviewed publications.

Analogue 1 is known to rapidly react in water with a half life of up to one minute. Due to this high reactivity, Analogue 1 only exists transiently in water and is essentially unavailable for uptake, bioaccumulation and biodegradation. This has been shown in a literature study, where Analogue 1 was added to an artificial pond up to a concentration of 10 g/L and could not be detected (LOD = 0.006 mg/L) over the course of 112 days of the study. When Analogue 1 is added to water, its end groups readily react with water to form products, which in turn readily react with the parent compound to produce intractable solid polymers. The polymer crust that is formed under environmental conditions (that is, poor dispersion) can slow the rate of hydrolysis of Analogue 1. Another study showed that the degradation rate (half life) of Analogue 1 spilled in a natural aquatic environment (where hydrological conditions correspond to moderate mixing of the spill and temperatures as low as 12ºC) would be approximately 143 hours.

An Activated Sludge, Respiration Inhibition test was carried out on a mixture of Analogue 1 and Analogue 2 according to OECD TG 209. No inhibition of activated sludge respiration was observed at 100 mg (Analogue 1 equivalents)/L of test medium.

Two Inherent Biodegradability tests were performed on analogues of the notified polymer according to OECD TG 302C (Modified MITI (II)). The first study was conducted on a mixture of Analogue 1 and 2 and did not detect any biodegradation with a concentration of 30 mg Analogue 1/L after 28 days. The second study did not detect any biodegradation of Analogue 1 oligomers.

The analogues tested in environmental fate studies most likely formed intractable solid polymers and hence the results pertain to the reaction products with water rather than the analogues themselves. However, the notified polymer is expected to form similar reaction products on contact with water and the results are therefore relevant to the notified polymer. It can be concluded that the analogues and their reaction products with water, and by inference the notified polymer, are not inherently biodegradable or readily biodegradable. The analogues, and by inference the notified polymer, do not inhibit waste water microbial respiration.

The majority of the notified polymer is expected to be cured to form an inert matrix and is not therefore expected to be bioavailable or biodegradable. When disposed of to landfill the notified polymer will be immobile and will slowly degrade to form water and oxides of carbon and nitrogen.

7.1.3. Predicted Environmental Concentration (PEC)

A predicted environmental concentration was not determined because the notified polymer is not expected to persist in water due to its hydrolytic instability. Further, aquatic exposure of the notified polymer and its hydrolysis products is not expected based on the reported use pattern.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted for the notified polymer. Summaries of study results were provided for acceptable analogues, with the same reactive functional groups to the notified polymer, from reliable internationally peer-reviewed publications. The lowest relevant ecotoxicity endpoints from the submitted studies are outlined below. A discussion of the submitted results follows in the table below.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity (24 hour)*	NOEL = 500 mg/L	Not harmful to fish
Daphnia Toxicity (24 hours)*	EL50 = 129.7 mg/L	Not harmful to aquatic invertebrates
Algal Toxicity (72 hours) OECD TG 201	NOEL = 1640 mg/L	Not harmful to algae
Inhibition of Bacterial Respiration (3 hours) OECD TG 209	IL50 >100 mg/L	Does not inhibit respiration of waste water microorganisms

*Non OECD guidelines

The reliability indexes for the tests indicated that they all fell into one of two categories. Either they were not done to test guidelines, or done in accordance with test guidelines but without monitoring of the test substance, or fell short of highest standards of protocol or reporting. The tests are considered reliable for regulatory purposes as monitoring of the test substances would have been impossible due to their hydrolytic instability. Moreover, the endpoints are well above expected environmentally relevant concentrations. Therefore, the

analogues, and by interference the notified polymer, are considered not harmful to aquatic biota.

Fish Studies
Concise test details and toxicity endpoints for acute fish studies on Analogue 1 (1 study) and Analogue 2 (5 studies) were submitted by the notifier. The tests had nominal test substance concentrations of 500 – 3,000 mg/L and no lethal effects were observed in any of the studies. The lowest concentration tested was 500 mg/L so this was equated to the NOEL. The notified polymer is therefore considered to be not harmful to fish.

Two long term fish studies were submitted. No direct toxic effects have been observed in studies with nominal concentrations in the range 0.1 – 10,000 mg/L. An indirect impact was observed on fish through decrease of their natural food (cladocerans) in an artificial pond to which was added 10,000 mg/L of Analogue 2. This result is not considered relevant as the loading rate is much greater than the expected environmental release.

Daphnia Studies
Concise test details and toxicity endpoints for acute daphnia studies on Analogue 1 (2 studies) and Analogue 2 (3 studies) were submitted by the notifier. The tests had nominal test substance concentrations of 0.5 – 3,000 mg/L and no lethal effects were observed except in one study. In this study Analogue 2 was dispersed into the medium by high speed shearing rather than the usual stirring method. This was thought to have led to an increased production of a product to which invertebrates are known to be sensitive (EC50 for *Moina macropa* = 2.3 mg/L). The authors considered these data as irrelevant because the dispersing method does not reflect a plausible exposure mechanism in the environment. In the same study the endpoint obtained when the test substance was magnetically stirred was an EC50 >1000 mg/L.

Two long-term studies showed that Analogue 2 had indirect effects on aquatic invertebrates. In the study there was a physical effect noted on benthic organisms. On a local scale an accidental spill would have a dramatic effect on those organisms. However, the authors thought that if the crust was removed from the sediment as a restoration measure, a re-colonisation by animals from the surroundings would rapidly occur.

Algae Studies
Concise test details and toxicity endpoints for algal studies on Analogue 2 (3 studies) were submitted by the notifier. The tests had nominal test substance concentrations of 3 – 10,000 mg/L and no significant effects were observed except the physical hindrance of macrophyte emergence due to the polymeric solid crust formation.

Microorganism Studies
Concise test details and toxicity endpoints for two microorganism studies on Analogue 2 were submitted by the notifier. No toxic effect was observed on microorganisms, but as in all the other tests, the analogue would have reacted with water producing insoluble polymeric masses.

7.2.1. Predicted No-Effect Concentration

A predicted no-effect concentration (PNEC) has not been calculated for the notified polymer as no aquatic exposure is expected based on its reported use pattern.

7.3. Environmental Risk Assessment
The risk quotient (Q = PEC/PNEC) for the notified polymer has not been calculated as release to the aquatic environment is not expected based on its reported use pattern.

The majority of the notified polymer will ultimately be disposed of to landfill as cured polymer. Once cured, the notified polymer is irreversibly bound within an inert matrix, and is not expected to be bioavailable or mobile. If the notified polymer is released to environmental waters, it is expected to hydrolyse on contact with water to form intractable polymeric masses which are expected to be neither bioavailable or bioaccumulative. On the basis of analogue data, the notified polymer and its hydrolysis products are considered not harmful to aquatic organisms although some localised physical effects may be expected in the event of an accidental spill. However, no aquatic exposure is expected and the notified polymer is not considered to pose an unreasonable risk to the environment based on the low hazard and assessed use pattern.

BIBLIOGRAPHY

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

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), <http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html >.