File No PLC/693

May 2007

**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)**

# FULL PUBLIC REPORT

## Pullulan

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

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

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


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


**Director**
**NICNAS**

# TABLE OF CONTENTS

# FULL PUBLIC REPORT

## Pullulan

### 1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Hayashibara International Australia Pty Ltd (ABN 61 120 127 488)
Level 31, ABN AMRO Tower
88 Phillip St
Sydney NSW 2000

NOTIFICATION CATEGORY
Polymer of Low Concern

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
No details are claimed exempt from publication.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
US FDA (2002)
US TSCA (2001)
Canada (1998)
EU (1990)
European Food Safety Authority (2006)
Korea (1997)

### 2. IDENTITY OF CHEMICAL

CHEMICAL NAME
Pullulan

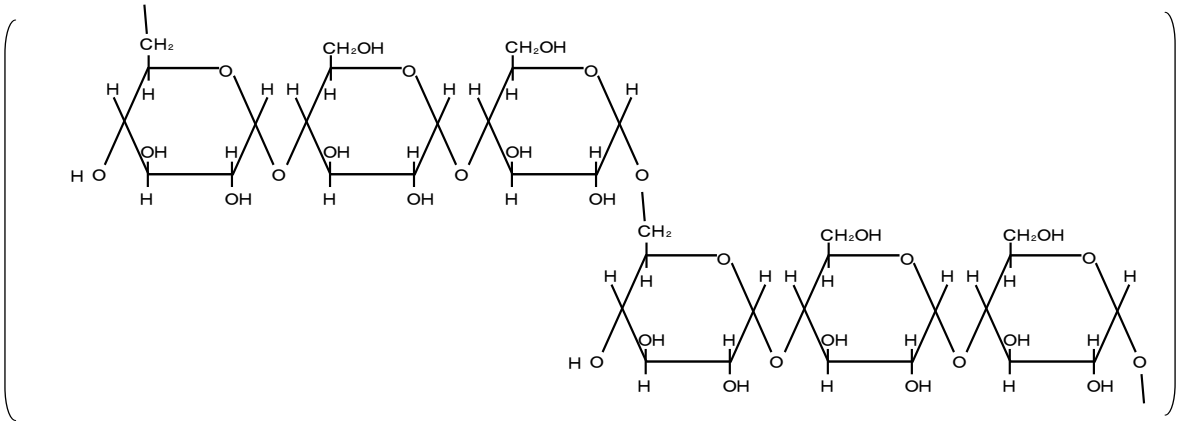
OTHER NAME(S)
1,4-2,6-alpha-D-glucan
1,6-alpha-linked maltotriose

MARKETING NAME(S)
Pullulan (INCI Name)
Pullulan PI-20

CAS NUMBER
9057-02-7

MOLECULAR FORMULA
Unspecified

STRUCTURAL FORMULA



where n = approximately 210

MOLECULAR WEIGHT

| | |
|---|---|
| Number Average Molecular Weight (Mn) | 97,000-101,000 |
| Weight Average Molecular Weight (Mw) | 433,000-479,000 |
| Polydispersity Index (Mw/Mn) | 4.3-4.9 |
| % of Low MW Species < 1000 | 1.2-2.4 (consists of oligosaccharides with 3-7 glucose subunits) |
| % of Low MW Species < 500 | 0 |

POLYMER CONSTITUENTS

Pullulan is a fungal polysaccharide. It is produced on an industrial scale by fermentation of food grade corn syrup under controlled conditions using a specific, not genetically modified strain of *Aureobasidium pullulans*, a ubiquitous, non-pathogenic and non-toxigenic yeast-like fungus. The raw material (corn syrup) consists of a number of saccharides including glucose, fructose and maltose. The amount of residual mono and di-saccharides is typically 1.5-3.4%. There was no evidence for the presence of *Aureobasidium pullulans* in ten examined batches of pullulan.

REACTIVE FUNCTIONAL GROUPS

The notified polymer contains only low concern functional groups.

## 3. PLC CRITERIA JUSTIFICATION

| *Criterion* | *Criterion met (yes/no/not applicable)* |
|---|---|
| Molecular Weight Requirements | Yes |
| Functional Group Equivalent Weight (FGEW) Requirements | Yes |
| Low Charge Density | Yes |
| Approved Elements Only | Yes |
| Stable Under Normal Conditions of Use | Yes |
| Not Water Absorbing | Yes |
| Not a Hazard Substance or Dangerous Good | Yes |

The notified polymer meets the PLC criteria.

## 4. PHYSICAL AND CHEMICAL PROPERTIES

| | |
|---|---|
| **Appearance at 20°C and 101.3 kPa** | White to off-white free flowing powder |
| **Melting Point/Glass Transition Temp** | Decomposes at 250°C |
| **Density** | 280 kg/m$^3$ at 25°C |
| **Water Solubility** | ≥ 170 g/L at 20±5°C<br>The test substance was vigorously shaken for 30 seconds at 5 minute intervals for 30 minutes. The viscosity of the resulting solution prevented testing of water solubility at higher concentrations. |
| **Particle Size** | Inhalable (< 100 μm): 7.1%<br>Determined by a sieving method. No values given for MMAD or respirable fraction (<10 μm). |
| **Reactivity** | Stable under normal conditions of use. |
| **Degradation Products** | None under normal conditions of use. Self ignites at 250°C to give carbon oxides. |

## 5. INTRODUCTION AND USE INFORMATION

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

| *Year* | *1* | *2* | *3* | *4* | *5* |
|---|---|---|---|---|---|
| *Tonnes* | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |

USE AND MODE OF INTRODUCTION AND DISPOSAL

**Mode of Introduction**

The notified polymer will be imported as a powder in 10 kg polyethylene bags with rubber seals inside cardboard boxes. The notified polymer will be transported by road to the notifier's warehouse, dedicated to the storage of chemical products, before being transported to customer sites (cosmetic formulators). The notified polymer may also be imported as part of preformed articles (up to 30% notified polymer).

**Reformulation/manufacture processes**

The notified polymer will not be manufactured in Australia.

*Cosmetics*

Reformulation is anticipated to occur at a number of cosmetics manufacturing sites. This will involve blending the notified polymer with other ingredients, and will not involve reaction of the notified polymer.

In a typical process, a compounder will weigh out the notified polymer manually. This will then be manually added to a mixing tank, along with other ingredients. During the blending a chemist may take samples of the product containing the notified polymer (concentration up to 20%) using a dip tube. After the blending is complete a packer will supervise the use of a line filler and capper to transfer the finished product into the retail bottles. The packaged cosmetic products will then be stored and handled by a store person.

*Biodegradable articles*

There are currently no plans to manufacture biodegradable articles containing the notified polymer in Australia.

**Use**

The notified polymer is used in biodegradable articles (concentration up to 30%), or in cosmetic products, such as:

- Shampoos (< 4%)
- Creams and lotions (< 1%)
- Styling products (as an impermeable, antistatic solid film) (< 10%)
- Toothpastes (< 20%)

## 6. HUMAN HEALTH IMPLICATIONS

### 6.1. Exposure Assessment

OCCUPATIONAL EXPOSURE

*Transport and storage*

Transport and warehousing workers are expected to have dermal and ocular contact with the notified polymer and products containing the notified polymer only in the event of accidental spillages. Inhalation exposure to the polymer powder may also occur if the packaging is breached.

*Reformulation*

Dermal, ocular and inhalation exposure to the notified polymer powder may occur during weighing out prior to reformulation. However, exposure to significant amounts of the notified polymer is typically reduced by the use of ventilation at the site of weighing, such as a dust extract hood, or by the use of a vacuum tube. The compounder is also expected to wear personal protective equipment such as glasses, gloves and coveralls.

Dermal and ocular exposure to the polymer solutions may also potentially occur during certain processes involving the notified polymer such as sampling, cleaning, maintenance, or by accidental spills during the packing process. However, exposure to significant amounts of the notified polymer is limited because of the largely automated processes, and the engineering controls and personal protective equipment worn by workers.

*Beauty Industry*

Intermittent, wide-dispersive use with direct handling is expected to occur among hairdressers, cosmeticians, and beauticians. According to EASE (1997) modelling of this work environment, dermal exposure in the range of 1-5 mg/cm$^2$/day of products containing up to 10% of the notified polymer (assuming maximum concentration from cosmetic/styling products) could result. Assuming 100% dermal absorption, a surface area of 420 cm$^2$ (half the area of the hands) and a bodyweight of 60 kg, this equates to a maximum systemic exposure of 3.5 mg/kg bw/day.

*Retail Industry*

Workers in the retail industry will only be exposed to the notified polymer (up to 20%) in the event of packaging breaches or accidental spillages.

PUBLIC EXPOSURE

*Biodegradable Articles*

The notified polymer will not be sold to the public except in the form of finished articles. There are no specific details on the types of articles, or their uses. However one possibility is trays comprised partly of the notified polymer. Although there is potential for extensive public exposure to these articles, blooming/leeching of the notified polymer from the articles is not expected and hence exposure to the notified polymer is considered to be low.

*Cosmetics*

Since the notified polymer will be in products sold to the general public, widespread public exposure is expected. Exposure to the notified chemical will vary depending on the type of cosmetic product and individual use patterns. Based on exposure estimates for a range of cosmetic products in Europe (SDA, 2005), public exposure (dermal and oral) to the notified polymer in Australia has been estimated using the following assumptions:

- Bodyweight of 60 kg;
- 100% dermal and oral absorption
- Product usage is similar in Australia to Europe.

| *Product used and exposure type* | *Amount of product used per day (g/day)* | *Product retained/ingested (%)* | *Concentration in product (%)* | *Exposure (mg/kg bw/day)* |
|---|---|---|---|---|
| Skin lotions (dermal) | 5.68 | 100 | < 1 | 0.95 |
| Shampoos (dermal) | 8 | 1 | < 4 | 0.05 |
| Styling products (dermal) | 10 | 5 | < 10 | 0.83 |
| Toothpastes (oral) | 2.4 | 35 | < 20 | 2.8 |
| Range of cosmetic products (dermal and oral) | | | | 4.63 |

The estimate of combined exposure to a range of cosmetic products (skin lotion, shampoo, styling product and toothpaste), 4.63 mg/kg bw/day, is expected to be an overestimate as it assumes all products used by one person contain the notified polymer and uses the maximum 'product amount used' from the range in the dataset.

Since products containing the notified chemical are stored and used in a domestic environment, there is the possibility of accidental ingestion by a child.

### 6.2. Toxicological Hazard Characterisation

The notified polymer meets the PLC criteria and can therefore be considered to be of low hazard. This is supported by toxicological endpoints observed in testing conducted on the notified polymer. Only studies for which reports were provided are summarised in the table below.

| *Endpoint* | *Result* | *Classified?* | *Effects Observed?* | *Test Guideline* |
|---|---|---|---|---|
| Skin irritation – human patch test | non-irritating at 25% | no | no | In-house method |
| Eye irritation, HET-CAM* test | no ocular irritation potential in vivo predicted at 100% | no | no | In-house method |
| Eye irritation, Bovine corneal opacity and permeability test | no negative effect at 20% compared to the control | no | no | In-house method |
| Skin sensitisation – human repeat insult patch test | no evidence of sensitisation or irritation at 25% | no | no | In-house method |
| Rat, oral repeat dose toxicity – 13 weeks (notified polymer in feed) | NOAEL:<br>7914 mg/kg bw/day (males);<br>and<br>9674 mg/kg bw/day (females) | no | yes | OECD TG 407 |
| Genotoxicity - bacterial reverse mutation | non mutagenic | no | no | In-house method |

* HET-CAM: Hen's egg test-chorio allantoic membrane.

Although the *in vitro* eye irritation tests and human patch tests are not validated for classification, the negative results in all tests indicate low hazard of the notified polymer.

In a 13 week repeat dose study in which the notified polymer was given to the rats in the feed, no adverse effects were observed. Test item-related macroscopic changes were restricted to a dose-dependently increased caecum weight and a distension of the caecum at necropsy in 1/10 males in the low dose group, 3/10 males in the mid dose group and 1/10 males in the high dose group. Since no microscopic changes were seen in the affected caeca these findings were not considered to be adverse. The NOAEL was therefore determined from the dose given to the high dose group (10% in feed).

No mutagenicity was observed in the strains *Salmonella typhimurium* TA1535, TA100, TA1537 or TA98 both with and without metabolic activation when tested with the notified polymer up to 10 mg/plate.

All results were indicative of low hazard. In addition, although no studies were cited the results for testing on the notified polymer are reported as:

- no adverse treatment related effects in a 62 week repeat dose study when treated at a maximum dose of 4500 mg/kg bw/day (males) / 5100 mg/kg bw/day (females);
- negative in a DNA repair test;
- negative in an in vitro chromosomal aberration assay;
- negative in an in vivo mouse micronucleus test.

The notified polymer is a soluble polymer with molecular weight > 13,000, and may therefore have the potential to cause lung overloading effects due to decreased clearance from the lung.

### 6.3. Human Health Risk Assessment

OCCUPATIONAL HEALTH AND SAFETY

Although limited exposure to the notified polymer could occur during reformulation processes and during use in the beauty industry, the risk to workers is considered to be low due to the intrinsic low hazard of the notified polymer. The maximum dermal exposure for workers involved in the beauty industry is estimated to be 3.5 mg/kg bw/day. A dermal NOAEL was not determined, however a lowest NOAEL of 7914 mg/kg bw/day was established in a 90-day feed study in the rat. The use of this NOAEL results in a margin of exposure (MOE) of 2261. MOE greater than or equal to 100 are considered acceptable to account for intra- and inter-species differences. In addition the MOE is based on conservative assumptions and may overestimate the risk.

Given the low percentage of inhalable/respirable particles and the typical engineering controls in place, the risk of lung overloading effects is considered to be low. However, the level of atmospheric nuisance dust should be maintained as low as possible. The NOHSC exposure standard for atmospheric dust is 10 mg/m$^3$.

PUBLIC HEALTH

Members of the public may make dermal contact with biodegradable products containing the notified polymer. However, the risk to public health will be negligible because the notified polymer is of low hazard, and is bound within a matrix.

The public will be exposed to the notified polymer during use of cosmetic and personal care products. The combined exposure to a range of cosmetic and personal care products is estimated to be 4.63 mg/kg bw/day. A dermal NOAEL was not determined, however a lowest NOAEL of 7914 mg/kg bw/day was established in a 90-day feed study in the rat. The use of this NOAEL results in a margin of exposure (MOE) of 1709. MOE greater than or equal to 100 are considered acceptable to account for intra- and inter-species differences. In addition the MOE is based on conservative assumptions and may overestimate the risk. In addition the risk of local effects after use of product containing the notified polymer is considered to be low due to the predicted low hazard of the notified polymer.

## 7. ENVIRONMENTAL IMPLICATIONS

### 7.1. Exposure Assessment

ENVIRONMENTAL RELEASE

The notified polymer is not manufactured in Australia but will be reformulated into cosmetic consumer products at customer sites. As the polymer is solid only a small quantity (<0.1%; < 0.5 kg per annum) is expected to remain in import packaging. Up to 3% (< 15 kg per annum) is expected to remain in blending tanks during reformulation. This will be flushed to sewer. It is expected that approximately 1% (< 5 kg per annum) of the formulated product will remain in the consumer product packaging. The remainder is expected to be used as intended, in consumer cosmetic products and will be eventually flushed to sewer.

ENVIRONMENTAL FATE

No biodegradation test was submitted, but two studies were provided which show that relatively rapid biodegradation is expected. The polysaccharide polymer is expected to degrade to simple sugars then to oxides of carbon and water vapour. The residue in packaging, and biodegradable articles containing the notified polymer, are expected to be sent to landfill where they will degrade. Similarly, the notified chemical is expected to degrade in the sewage treatment plant or in natural waterways after release.

### 7.2. Environmental Hazard Characterisation

No ecotoxicological data were submitted. PLCs without significant ionic functionality are of low concern to the aquatic environment.

### 7.3. Environmental Risk Assessment

The predicted environmental concentration (PEC) for a worst case scenario, where 99% of the polymer is flushed to sewer, throughout Australia without degradation or adsorption to sludge is calculated as 0.33 µg/L (495 kg per annum ÷ (200 L per person per day × 365 days × 20.5 million persons). A predicted no effect concentration (PNEC) cannot be calculated, but PLCs without significant ionic functionality are of low concern to the aquatic environment. Although a risk quotient (RQ) cannot be calculated from the PEC/PNEC ratio, there will be an adequate safety margin and the risk to the aquatic environment is expected to be acceptable. Furthermore the notified polymer is expected to degrade by biotic and abiotic processes, thus further reducing the risk to the environment.

## 8. CONCLUSIONS

### 8.1. Level of Concern for Occupational Health and Safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

### 8.2. Level of Concern for Public Health

There is No Significant Concern to public health when used in the proposed manner.

### 8.3. Level of Concern for the Environment

The polymer is not considered to pose a risk to the environment based on its reported use pattern.

## 9. MATERIAL SAFETY DATA SHEET

### 9.1. Material Safety Data Sheet

The notifier has provided MSDS as part of the notification statement. The accuracy of the information on the MSDS remains the responsibility of the applicant.

## 10. RECOMMENDATIONS

CONTROL MEASURES

Occupational Health and Safety

- No specific engineering controls, work practices or personal protective equipment are required for the safe use of the notified polymer itself, however, these should be selected on the basis of all ingredients in the formulation.

  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 NOHSC *Approved Criteria for Classifying Hazardous Substances*, 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 disposed of by authorised landfill.

Emergency procedures

- Spills and/or accidental release of the notified polymer should be handled by removing possible leaking containers and sweeping up spills for reuse to the extent practicable or disposal. Wash the area with water.

**10.1. Secondary Notification**

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under subsection 64(1) of the Act; if
  – the notified polymer is introduced in a chemical form that does not meet the PLC criteria.

or

(2) Under subsection 64(2) of the Act:
  - if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.