File No: NA/625

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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Behenamidopropyl PG-Dimonium Chloride

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Behenamidopropyl PG-Dimonium Chloride

1. APPLICANT

Bronson and Jacobs Pty Ltd of Parkview Drive, Australia Centre HOMEBUSH BAY NSW 2140 has submitted a standard notification statement in support of its application for an assessment certificate for 'Behenamidopropyl PG-Dimonium Chloride'.

2. IDENTITY OF THE CHEMICAL

Chemical Name: 1-propanaminium, 2, 3-dihydroxy-N, N-dimethyl-N-[3-[(1-oxodocosyl) amino] propyl]-, chloride

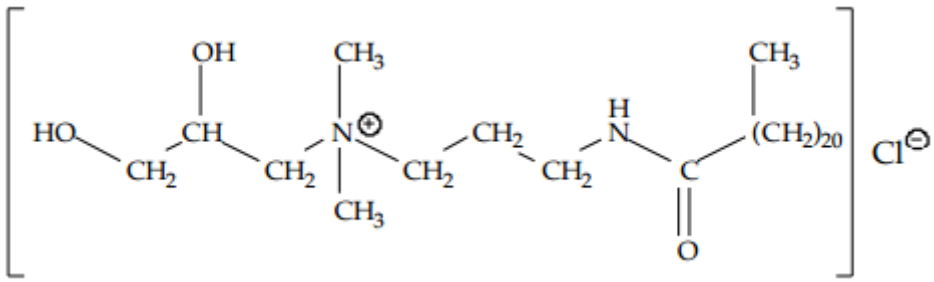
Chemical Abstracts Service (CAS) Registry No.: 136920-10-0

Other Names: Behenamidopropyl PG-dimonium chloride

Trade Name: Lexquat AMG-BEO

Molecular Formula: $C_{30}H_{63}N_2O_3$. Cl

Structural Formula:



Molecular Weight: 535

Method of Detection and Determination: IR, UV/Vis and NMR spectroscopy

Spectral Data: major peaks in IR spectrum were at 2 986, 2 879, broad bands 2 793-2 107 and 2 107-1 757, 1 586, 1 500, 1 400, 1 314, 1 179, 1 143 and 1 007 cm^{-1}

3. PHYSICAL AND CHEMICAL PROPERTIES

Physical and chemical data listed below were derived from the product, Lexquat AMG-BEO, which contains 23-27% notified chemical.

Appearance at 20°C and 101.3 kPa:	clear, colourless, slightly viscous liquid
Boiling Point:	101.0°C for the aqueous component, the residue did not boil but decomposed before reaching 280°C
Specific Gravity:	approximately 1
Vapour Pressure:	2.4 kPa at 25°C (water component)
Water Solubility:	> 2 000 mg notified chemical/L at 25°C
Partition Co-efficient (n-octanol/water):	not determined (see comments below)
Hydrolysis as a Function of pH:	not determined (see comments below)
Adsorption/Desorption:	not determined (see comments below)
Dissociation Constant:	not determined (see comments below)
Particle Size Distribution:	not applicable, as the notified chemical is within a solution
Flash Point:	boiled at approximately 103°C without flashing
Flammability Limits:	not determined
Autoignition Temperature:	not determined
Explosive Properties:	not explosive

Reactivity/Stability: not reactive

Surface Tension: 40.5 mN/m at 30% solids content

Comments on Physico-Chemical Properties

The water solubility of the chemical has not been determined to saturation point. However, in the ecotoxicity studies stock solutions of 2 000 mg/L were prepared without any undissolved material being observed.

The hydrolytic behaviour of the chemical has not been investigated. The chemical contains an amide functional group which could potentially undergo hydrolysis. However, it is unlikely that this will occur within the environmental pH range (4-9).

The notifier indicates that the chemical is a surfactant and a reliable partition coefficient cannot be determined. Based on its high solubility the chemical is likely to have a low octanol/water partition coefficient (log P_{OW}) but this may be offset by its surface activity, which would also affect the measurement of partition coefficient.

No data were provided for the adsorption/desorption behaviour of the notified chemical. Again based on the high water solubility and expected low partition coefficient the chemical should not bind strongly to the organic matter in the soil and may potentially be mobile. However, its surface activity would increase the binding potential of the chemical to soils and sediments.

The notified chemical contains no functional groups which would be protonated or deprotonated in the environmental pH range (4-9).

4. PURITY OF THE CHEMICAL

Degree of Purity: > 80%

Hazardous Impurities: unknown

Non-hazardous Impurities (> 1% by weight):

Chemical name: sodium chloride

Weight percentage: ≤ 5.0%

CAS No.: 7647-14-5

Weight Percentage of Ingredients in Lexquat AMG-BEO:

Chemical Name	*CAS No.*	*Weight %*
Behenamidopropyl PG-dimonium chloride	136920-10-0	23-27
sodium chloride	7647-14-5	4.5-5.5
water	7732-18-5	63-67
propylene glycol	57-55-6	4.5-5.5

5. USE, VOLUME AND FORMULATION

The notified chemical will not be manufactured in Australia. It will be imported into Australia in 182 kg steel drums as a component of the formulation Lexquat AMG-BEO, containing 23-27% of the notified chemical. Import volumes of Lexquat AMG-BEO are expected to be around 5 tonnes per annum over the first 5 years. This corresponds to an import volume of approximately 1.35 tonnes of the notified chemical per annum.

The notified chemical will be used as an ingredient in personal care products. It will be formulated into body wash products and marketed to the general public. The products will contain typically 0.5% notified chemical.

6.
7. OCCUPATIONAL EXPOSURE

Dermal contamination is expected to be the main route of occupational exposure, as the notified chemical is available only in aqueous solution and misting of solutions is unlikely to occur.

Transport and storage
The notified chemical will be imported in 182 kg steel drums and formulated in Australia. It will be transported from the dockside to the notifier's warehouse by road prior to distribution to customer reformulation sites. There will be 4-6 waterside and transport workers handling the notified chemical 1-2 hours per day and 2-4 days per year.

The warehouse workers will receive and store the steel drums containing the notified chemical. They will also store and load the formulated products for distribution. It is estimated that there will be 2-3 warehouse workers handling the notified chemical for 2 hours per day and 25 days per year.

It is anticipated that both transport and storage workers would only be exposed to the notified chemical in the event of an accident when the package is breached.

Formulation

Initially, there will be two formulation sites in Australia. The drums containing 23-27% of the notified chemical will be transferred from the storage and weighing areas to the mixing area on a trolley. The drum contents will be decanted through a hatch into an enclosed mixing tank using a hydraulic drum lifter. Lexquat AMG-BEO will then be blended with other ingredients in a batchwise process. Samples will be taken during the formulation for quality assurance. The final product containing 0.5% the notified chemical will be pumped via an automatic filling line to a multihead filling machine where 200 mL PET bottles are filled for marketing to the general public.

There will be 5-10 warehouse workers at the formulation sites handling the notified chemical for 2 hours/day and 20 days/year; 5-10 laboratory staff for 4 hours/day and 25 days/year; 10-20 formulators for 5 hours/day and 20 days/year; and 30-50 packaging operators for 8 hours/day and 40 days/year.

The sampling, dispensing and mixing operations will be carried out in a closed system or one designed not to create aerosols or spill hazards. Both the dispensary and the formulation areas are bunded and have a cross-flow ventilation system with 20 air changes per hour.

The warehouse workers at the formulation sites are not expected to be exposed to the notified chemical unless the package is broken. The formulators could be contaminated with the notified chemical when they open the drum lids, put drums on the hydraulic drum lifter, and connect and disconnect the pump lines. Workers at the formulation site will wear long sleeved overalls, a head covering, safety glasses, safety boots and impervious gloves while handling the notified chemical.

Laboratory staff will use a suitable sampling ladle to collect the samples. They only handle small amount of samples for analysis. Their exposure is expected to be infrequent. The laboratory staff will wear long sleeved laboratory coats or overalls, safety glasses and impervious gloves while handling the notified chemical.

The packaging operators pack the final product containing 0.5% the notified chemical in the 200 mL bottles in cartons ready for distribution to retail market outlets. Packing operators would only become contaminated with the product if they were required to fix a filling malfunction. The packaging operators will wear long sleeved overalls, a head covering, safety glasses, safety boots and impervious gloves while handling the final products containing the notified chemical.

Dermal exposure to the notified chemical may occur when cleaning process equipment and when carrying out any maintenance on the equipment.

Retail

There will be approximately 1 000 retail workers Australia wide in the supermarkets, pharmacies, and department/variety stores handling the products containing the notified chemical. These workers will unload the body wash products from the cartons and stack

them on the selves, a task estimated to take 1-2 hours per day and 100-150 days per year. Even if a 200 mL bottle were broken, they would only be exposed to the consumer products.

8. PUBLIC EXPOSURE

Since the notified chemical is used in personal care products (body washes), dermal contact, to a lesser extent ocular exposure, is the major route of exposure for consumers. Assuming that 10 g of body wash is used per application, with one application/day, and 1% remaining on the skin after rinsing, the maximum dermal dose of the notified chemical at the level of 0.5% in body washes for a 60 kg person would be 0.008 mg/kg/day.

In comparison with the dermal exposure from using body washes, public exposure from transport, storage and disposal is expected to be negligible.

The public may be exposed to the notified chemical from accidental spills. However, the exposure would be minimised by the emergency workers following the procedures described in the MSDS, i.e. the chemical would be contained and pumped into drums for recovery or disposal, or soaked up in inert materials for disposal.

9. ENVIRONMENTAL EXPOSURE

Release

The notifier estimates that 0.5 kg of the imported formulation may remain in the imported drums. This corresponds to approximately 3.8 kg of the notified chemical per annum which will find its way into the drum recycling process.

Rinsings from process equipment would account for a further 7 kg per annum of the notified chemical. These rinsings will be sent to onsite waste water treatment plants. The waste water treatment plants from both proposed formulation sites are discharged into the sewer.

The major release of the notified chemical will be through its use in body washes. It is anticipated that almost all the remaining imported chemical will be discharged to sewers throughout Australia as a result of this use.

Fate

The formulation Lexquat AMG-BEO, containing the notified chemical was examined for biodegradation potential using EEC Directive 92/69, Part C.4-C (Modified Sturm Test), and OECD Test Guideline 301B. Over the 28 day test, biodegradation was <38%, indicating that Lexquat AMG-BEO is not readily biodegradable under the conditions of the test. The results of the test would indicate that Lexquat AMG-BEO is inherently biodegradable.

Lexquat AMG-BEO will be used as a surfactant in a body washes and will be released to the environment via consumer use. It is anticipated that the notified chemical will be rinsed from

the body during bathing and into the sewerage system. In the sewer, some is expected to adsorb to sewage sludge due to the surface active nature of the chemical. The sludge will either be sent to landfill or incinerated. Incineration products will include chloride salts, water and oxides of carbon and nitrogen. The remainder will stay in solution, where it is expected that it will be further diluted.

The high water solubility and biodegradable nature of the notified chemical indicate that it is unlikely that the chemical will bioaccumulate (Connell, 1989).

10. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of Behenamidopropyl PG-Dimonium Chloride.

Test	*Concentration*	*Species*	*Outcome*	*Reference*
acute oral toxicity	44%	rat	$LD_{50} > 880$ mg/kg	(Glaza, 1996b)
	*23%	rat	$LD_{50} < 1\ 150$ mg/kg	(Shapiro, 1989c)
	*4-5%	rat	$LD_{50} > 100$-125 mg/kg	(Shapiro, 1989c)
acute dermal toxicity	44%	rat	$LD_{50} > 880$ mg/kg	(Glaza, 1996a)
	*23%	rabbit	$LD_{50} > 460$ mg/kg	(Shapiro, 1989b)
skin irritation	44%	rabbit	not irritating	(Glaza, 1996f)
	*23%	rabbit	slight to moderately irritating	(Shapiro, 1989e)
	*5%	rabbit	slight to moderately irritating	(Shapiro, 1989d)
eye irritation	44%	rabbit	risk of serious eye damage	(Glaza, 1996g)
	*23%	rabbit	risk of serious eye damage	(Shapiro, 1989f)
	*5%	rabbit	slightly irritating	(Shapiro, 1989g)
skin sensitisation	44%	guinea pig	sensitising	(Glaza, 1996e)
	25%	guinea pig	sensitising	(Glaza, 1996d)
	*23%	guinea pig	inconclusive	(Shapiro, 1990)
	5%	guinea pig	not sensitising	(Glaza, 1996c)

* study not acceptable to European regulatory authorities

9.1.1 Oral Toxicity (44% Notified Chemical) (Glaza, 1996b)

Species/strain:	rat/Cr1:CD(SD)BR
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	oral (gavage)
Clinical observations:	soft stool and/or dark, wet, or yellow-stained urogenital area for 7 days
Mortality:	nil
Morphological findings:	no visible lesions in any animals
Test method:	limit test, OECD TG 401 (Organisation for Economic Co-operation and Development, 1995-1996)
LD_{50}:	> 880 mg/kg
Result:	the test material (44% notified chemical) was of low acute oral toxicity in rats

9.1.2 Oral Toxicity (23% Notified Chemical) (Shapiro, 1989c)

Species/strain:	rat/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	oral (gavage)
Clinical observations:	diarrhea, facial and/or ano-genital staining, ocular and/or nasal discharge, bloated abdomen and lethargy
Mortality:	2 males and 3 females found dead on day 1 and another female died on day 4
Morphological findings:	discolouration of the lungs, intestines, pyloric region of stomach, adrenal glands, the walls of the

	abdominal and thoracic cavities, thymus and liver. Gaseous distention of the gastrointestinal tract was also noted.
Test method:	limit test, Product Safety Labs protocol
LD_{50}*:*	< 1 150 mg/kg
Result:	From the results of this study, the degree of acute oral toxicity of the undiluted notified chemical in rats could not be concluded.

9.1.3 Oral Toxicity (4-5% Notified Chemical) (Shapiro, 1989c)

Species/strain:	rat/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	oral (gavage)
Clinical observations:	nil
Mortality:	nil
Morphological findings:	no visible lesions in any animals
Test method:	limit test, Product Safety Labs protocol
LD_{50}*:*	> 100-125 mg/kg
Result:	the test material (4-5% notified chemical) was of low acute oral toxicity in rats

9.1.4 Dermal Toxicity (44% Notified Chemical) (Glaza, 1996a)

Species/strain:	rat/Cr1:CD(SD)BR
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	dermal application to the intact skin on each

	animal's back at a dose level of 1 760 mg/kg; covered with an occlusive dressing for 24 hours
Clinical observations:	1 male and 3 females had dark material around their eyes, red stained face and/or yellow stained urogenital area for 3 days
Mortality:	nil
Morphological findings:	mandibular lymph nodes in one male were enlarged and mottled dark red and tan; no treatment related lesions found in any animals
Test method:	limit test, OECD TG 402 (Organisation for Economic Co-operation and Development, 1995-1996)
LD_{50}:	> 880 mg/kg
Result:	the test material (44% notified chemical) was of low dermal toxicity in rats

9.1.5 Dermal Toxicity (23% Notified Chemical) (Shapiro, 1989b)

Species/strain:	rabbit/New Zealand Albino
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	dermal application to the intact skin at a dose level of 460 mg/kg; covered with an occlusive dressing for 24 hours
Clinical observations:	slight to moderate erythema was observed at all dose sites at patch removal. All but one animal gained or maintained weight.
Mortality:	nil
Morphological findings:	uneven surface of the spleen and kidney of 2 animals. Most animals also exhibited a red discolouration of the lungs.
Test method:	limit test, Product Safety Labs protocol

LD_{50}:	> 460 mg/kg
Result:	the test material (23% notified chemical) was of low dermal toxicity in rabbits.

9.1.6 Inhalation Toxicity

No studies were available.

9.1.7 Skin Irritation (44% Notified Chemical) (Glaza, 1996f)

Species/strain:	rabbit/Hra: (NZW)SPF
Number/sex of animals:	2 males and 1 female
Observation period:	72 hours
Method of administration:	dermal application (0.5 mL) to the intact skin on each animal's back; covered with a semiocclusive dressing for 4 hours
Test method:	similar to OECD TG 404 (Organisation for Economic Co-operation and Development, 1995-1996)
Draize scores:	Draize scores at 24, 48 and 72 hours after application were zero for all animals
Result:	the test material (44% notified chemical) was not irritating to the skin of rabbits

9.1.8 Skin Irritation (23% Notified Chemical) (Shapiro, 1989e)

Species/strain:	rabbit/New Zealand Albino
Number/sex of animals:	3/sex
Observation period:	not stated
Method of administration:	dermal application (0.5 mL) to both intact and abraded skin sites covered with an occlusive dressing for 24 hours

Primary dermal irritation (PDI) scores:*

Time after treatment (days)	***Animal #***					
	1	***2***	***3***	***4***	***5***	***6***
Intact Skin						
Erythema						
1	2	2	2	2	2	2
3	2	1	1	1	1	1
Oedema						
1	1	1	1	1	1	1
3	1	1	1	1	1	1
Abraded Skin						
Erythema						
1	2	2	2	2	2	2
3	2	1	1	1	1	1
Oedema						
1	1	1	1	1	1	1
3	1	1	1	1	1	1

* PDI score system was designed by FHSA (Federal Hazardous Substances Control Act), 16 CFR 1500.41, USA; it is similar to Draize score system.

Test method:	Product Safety Labs protocol
Comments:	The duration of skin contact was longer (24 h) than the standard 4 h in OECD test guideline 404
Result:	the 23% notified chemical was a slight to moderate irritant to the skin of rabbits

9.1.9 Skin Irritation (5% Notified Chemical) (Shapiro, 1989d)

Species/strain:	rabbit/New Zealand Albino
Number/sex of animals:	6 males
Observation period:	not stated
Method of administration:	dermal application (0.5 mL) to both intact and

abraded skin sites covered with an occlusive dressing for 24 hours

Primary dermal irritation (PDI) scores:*

Time after treatment (days)	***Animal #***					
	1	***2***	***3***	***4***	***5***	***6***
Intact Skin						
Erythema						
1	2	2	3	3	2	2
3	1	0	2	2	1	1
Oedema						
1	1	1	1	1	1	1
3	1	0	1	1	0	0
Abraded Skin						
Erythema						
1	2	2	3	3	2	2
3	1	0	3	2	1	1
Oedema						
1	1	1	1	1	0	1
3	1	0	1	1	0	0

* PDI score system was designed by FHSA (Federal Hazardous Substances Control Act), 16 CFR 1500.41, USA; it is similar to Draize score system.

Test method: Product Safety Labs protocol

Comments: The duration of skin contact was longer (24 h) than the standard 4 h in OECD test guideline 404

Result: the test material (5% notified chemical) was a slight to moderate irritant to the skin of rabbits

9.1.10 Eye Irritation (44% Notified Chemical) (Glaza, 1996g)

Species/strain: rabbit/Hra: (NZW)SPF

Number/sex of animals: 3 males

Observation period: 21 days

Method of administration: each rabbit received 0.1 mL undiluted material placed into the everted lower lid of the right eye, with the left eye serving as the untreated control

Draize scores (Draize, 1959) of eyes:

	Time after instillation																				
Animal	***1 day***			***2 days***			***3 days***			***4 days***			***7 days***			***14 days***			***21 days***		
Cornea	***o***	***a***		***o***	***a***		***o***	***a***		***o***	***a***		***o***	***a***		***o***	***a***		***o***	***a***	
1	1	4		1	4		1	4		2	2		1	2		1	1		0	0	
2	1	1		1	1		0	0		0	0		0	0		0	0		0	0	
3	1	3		1	3		1	3		1	2		1	1		1	1		1	1	
Iris																					
1		1			1			1			1			0			0			0	
2		1			0			0			0			0			0			0	
3		1			1			1			0			0			0			0	
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	2	4	3	2	4	2	2	4	2	2	3	2	2	2	1	1	1	1	1	0	1
2	2	2	0	2	1	0	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0
3	2	4	3	2	3	1	2	3	1	2	2	1	2	1	0	0	0	0	0	0	0

[1] see Attachment 1 for Draize scales
[o] opacity [a] area [r] redness [c] chemosis [d] discharge

Sodium fluorescein examination: sodium fluorescein examination results showed 1 rabbit became negative after 48 hours and other 2 became negative after day 7

Test method: OECD TG 405 (Organisation for Economic Co-operation and Development, 1995-1996)

Comments: The test material caused broad corneal opacity, lesions of the iris and moderate to severe irritation of the conjunctivae. Irritation was still present in two animals at the end of the observation period (21 days)

Result: the test material (44% notified chemical) caused severe damage to the eyes of rabbits

9.1.11 Eye Irritation (23% Notified Chemical) (Shapiro, 1989f)

Species/strain: rabbit/New Zealand Albino

Number/sex of animals: 2 males and 4 females

Observation period: not stated

Method of administration: each rabbit received 0.1 mL undiluted material placed into the right eye, with the left eye serving as the untreated control

Draize scores (Draize, 1959) of eyes:

				Time after instillation					
Animal	***1 day***			***2 days***			***3 days***		
Cornea	***o***		***a***	***o***		***a***	***o***		***a***
1	[1]3		4	2		4	2		4
2	3		4	2		4	2		4
3	3		4	3		4	3		4
4	3		4	2		4	3		4
5	3		3	3/2		1/ 2	3		3
6	3		3	2/1		1/ 3	2/1		2/2
Iris									
1		1			1			1	
2		1			0			1	
3		1			1			1	
4		1			1			1	
5		1			0			1	
6		1			0			1	
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	3	4	3	2	3	3	2	3	3
2	3	3	3	2	2	2	2	2	3
3	3	4	3	2	4	3	2	4	3
4	3	4	3	2	3	2	2	3	3
5	3	3	3	1	2	2	2	2	3
6	3	3	3	2	2	2	2	2	3

[1] see Attachment 1 for Draize scales

[O] opacity [a] area [r] redness [c] chemosis [d] discharge

Test method:	Product Safety Labs protocol
Result:	the 23% notified chemical caused severe damage to the eyes of rabbits

9.1.12 Eye Irritation (5% Notified Chemical) (Shapiro, 1989g)

Species/strain:	rabbit/New Zealand Albino
Number/sex of animals:	6
Observation period:	not stated
Method of administration:	each rabbit received 0.1 mL of 5% notified chemical in water into conjunctival sac of the right eye, with the left eye serving as the untreated control

Draize scores (Draize, 1959):

Animal	***Time after instillation***					
	1 day		***2 days***		***3 days***	
Cornea	***o***	***a***	***o***	***a***	***o***	***a***
1	[1]1	1	0	4	0	4
2	0	4	0	4	0	4
3	0	4	0	4	0	4
4	0	4	0	4	0	4
5	0	4	0	4	0	4
6	0	4	0	4	0	4
Iris						
1	1		0		0	
2	0		0		0	
3	0		0		0	
4	0		0		0	
5	0		0		0	
6	0		0		0	

Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	2	2	3	1	1	0	0	0	0
2	2	1	3	1	1	0	0	0	0
3	2	1	1	1	1	0	1	0	0
4	1	1	3	1	0	0	0	0	0
5	2	1	2	1	1	0	0	0	0
6	2	1	3	2	1	3	1	0	0

[1] see Attachment 1 for Draize scales
[o] opacity [a] area [r] redness [c] chemosis [d] discharge

Test method: Product Safety Labs protocol

Result: the test material (5% notified chemical) was a slight irritant to the eyes of rabbits

9.1.13 Skin Sensitisation Study (44% Notified Chemical) (Glaza, 1996e)

Species/strain: guinea pig/Cr1: (HA)BR

Number of animals: 20 (main test), 10 (control)

Induction procedure: day 1-intradermal induction: 3 pairs of injections

(0.1 mL) were made on the shoulder region of each animal

- Freund's Complete Adjuvant (FCA) (1:1) in water
- 5% (w/v) aqueous suspension of the test material
- 5% (w/v) aqueous suspension of the test material in FCA

day 8-topical induction: application of 0.5 mL of a 75% aqueous suspension of the test material and covered with an occlusive dressing for 48 hours

Challenge procedure:

day 22-initial challenge: application of 0.3 mL of undiluted or a 50% aqueous suspension of the test material and covered with an occlusive dressing for 24 hours

day 37-second challenge: same as the initial challenge on day 22, but for 50% aqueous suspension only

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
Initial challenge				
50% test material	14/20	13/20	0/10	0/10
100% test material	1/20	1/20	0/10	0/10
Second challenge				
50% test material	15/20	10/20	0/5	0/5

* time after patch removal
** number of animals exhibiting positive response

Test method:

Magnusson and Kligman maximisation test, OECD TG 406 (Organisation for Economic Co-operation and Development, 1995-1996)

Result:

the test material (44% notified chemical) was a sensitiser to the skin of guinea pigs

9.1.14 Skin Sensitisation Study (25% Notified Chemical) (Glaza, 1996d)

Species/strain: guinea pig/Cr1: (HA)BR

Number of animals: 20 (main test), 10 (control)

Induction procedure: day 1-intradermal induction: 3 pairs of injections (0.1 mL) were made on the shoulder region of each animal

- Freund's Complete Adjuvant (FCA) (1:1) in water
- 5% (w/v) aqueous suspension of the test material
- 5% (w/v) aqueous suspension of the test material in FCA

day 8-topical induction: application of 0.4 mL test material and covered by an occlusive dressing for 48 hours

Challenge procedure: day 22- challenge: application of 0.2 mL test material and covered by an occlusive dressing for 24 hours

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
100% test material	10/20	8/20	0/10	0/10

* time after patch removal
** number of animals exhibiting positive response

Test method: Magnusson and Kligman maximisation test, OECD TG 406 (Organisation for Economic Co-operation and Development, 1995-1996)

Result: the test material (25% notified chemical) was a sensitiser to the skin of guinea pigs

9.1.15 Skin Sensitisation Study (23% Notified Chemical) (Shapiro, 1990)

Species/strain: male guinea pig/Hartley strain

Number of animals: 10 (main test), 10 (positive control) and 5 (negative control)

Induction procedure: day 0 - 0.4 mL test material in a Hilltop dosing chamber was placed on the animal back with hypoallergenic tape for 6 hours.

days 7 and 14 – same procedure as day 0.

Challenge procedure: day 28 – a challenge dose was applied to a naïve site on the left side.

Challenge outcome:

	Test animals		***Positive controls***		***Naïve controls***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***	***24 hours***	***48 hours***
unspecified	4/10	2/10	10/10	10/10	3/5	3/5

* time after patch removal
** number of animals exhibiting positive response

Test method: Buehler method, Product Safety Labs protocol

Result: more than 15% of animals in test group had positive responses to the undiluted notified chemical, however, the naive animals had 60% positive response. Therefore the findings of this study are inconclusive.

9.1.16 Skin Sensitisation Study (5% Notified Chemical) (Glaza, 1996c)

Species/strain: guinea pig/Cr1: (HA)BR

Number of animals: 20 (main test), 10 (control)

Induction procedure: day 1-intradermal induction: 3 pairs of injections (0.1 mL) were made on the should region of each animal

- Freund's Complete Adjuvant (FCA) (1:1) in water
- 5% (w/v) aqueous suspension of the test material
- 5% (w/v) aqueous suspension of the test material in FCA

day 8-topical induction: application of 0.4 mL test material and covered by an occlusive dressing for 48 hours

Challenge procedure: day 22- challenge: application of 0.2 mL test material and covered by an occlusive dressing for 24 hours

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
100% test material	0/20	0/20	0/10	0/10

* time after patch removal
** number of animals exhibiting positive response

Test method: Magnusson and Kligman maximisation test, OECD TG 406 (Organisation for Economic Co-operation and Development, 1995-1996)

Result: the test material (5% notified chemical) was not a sensitiser to the skin of guinea pigs

9.2 Repeated Dose Toxicity on Material Containing 23% Notified Chemical (Thomford, 1996)

Species/strain:	rat/Cr1: CD(SD)BR
Number/sex of animals:	5/sex/group
Method of administration:	oral (gavage)
Dose/Study duration::	0, 6.9, 69 or 460 mg/kg/day for 4 weeks (vehicle: water)
Clinical observations:	all animals survived, excessive salivation was noted immediately after dosing for all high dose animals, from day 13 and continuing throughout treatment
Clinical chemistry/Haematology	slight to moderate increase in AST and ALT in high dose rats, slight increase in absolute neutrophil count in high dose males, and slight decrease in glucose and total protein and moderate increase in inorganic phosphorus in high dose females; these changes could not be correlated with histopathology
Histopathology:	no histopathological changes were associated with the test substance; an increase of adrenal gland weight in high dose males could not be related to pathological changes
Test method:	similar to OECD TG 407 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	Based on the slight increase in adrenal weights and slight changes in clinical chemistry parameters at the high dose, the no observable effect level (NOEL) for the test material (23% notified chemical) is 69 mg/kg/day

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (23% Notified Chemical) (Shapiro, 1989a)

Strains:	*S. typhimurium* TA98 and TA1535
Concentration range:	0.05 – 1.0 µg/plate with and without S-9
Test method:	similar to OECD TG 471 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	the test material (23% notified chemical) did not induce mutation in *S. typhimurium* strains TA98 and TA1535 in the absence or presence of metabolic activation

9.3.2 *Salmonella typhimurium* Reverse Mutation Assay (23% Notified Chemical) (Ballantyne, 1996)

Strains:	*S. typhimurium* TA98, TA100, TA1535 and TA1537
Concentration range:	experiment 1: 0.16, 0.8, 4, 20 and 100 µg/plate without S-9, and 0.8, 4, 20, 100 and 500 µg/plate with S-9; experiment 2: 3.125, 6.25, 12.5, 25 and 50 µg/plate without S-9, and 12.5, 25, 50, 100 and 200 µg/plate with S-9
Test method:	similar to OECD TG 471 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	the test material (23% notified chemical) did not induce mutation in four strains of *S. typhimurium* in the absence or presence of metabolic activation

9.3.3 Induction of Chromosome Aberrations in Cultured Chinese Hamster ovary (CHO) Cells (23% Notified Chemical) (Riley, 1997)

Species/strain:	cultured Chinese hamster ovary (CHO) cells
Doses:	experiment 1 trial 1: 98.95, 141.4, 201.9, 288.5, 412.1, 588.7, 841.0, 1201, 1716, 2452, 3503, and 5004 µg/mL in the absence or presence of S-9 trial 2: 12.89, 16.11, 20.13, 25.17, 31.46, 39.33, 49.16, 61.45, 76.81, 96.01, 120 and 150 µg/mL without S-9 and 156.9, 174.3, 193.7, 215.2, 239.1, 265.7, 295.2, 328, 364.5, 405, 450 and 500 µg/mL with S-9. experiment 2: 27.79, 32.7, 38.47, 45.26, 53.24, 62.64, 73.69, 86.7, 102 and 120 µg/mL without S-9 and 264.7, 278.6, 293.3, 308.7, 325, 342.1, 360.1, 379, 399 and 420 µg/mL with S-9
Test method:	similar to OECD TG 473 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	the test material (23% notified chemical) did not induce structural chromosomal aberrations in cultured CHO cells in the absence and presence of S-9; however, an increase in numerical aberrations was observed in both experiments following treatment in the presence of S-9. This increase was mainly attributable to endoreduplication and polyploidy; the biological significance of this in cell culture is poorly understood.

9.4 Overall Assessment of Toxicological Data

The toxicological studies were performed on test materials containing 5 to 44% of the notified chemical. Some studies have not been acceptable to European regulatory authorities.

The notified chemical was of low acute oral toxicity (LD_{50} > 880 mg/kg) and low acute dermal toxicity (LD_{50} > 880 mg/kg) in rats.

Several skin irritation studies were submitted for assessment. The notified chemical at 44% was not irritating to the skin of rabbits. In two other skin irritation studies, the notified chemical at 23% and 5% was slight to moderately irritating to the skin of rabbits. In the latter

studies, the skin contact time was 24 hours rather than the standard 4 hours stipulated in the OECD guidelines so, on this evidence, the notified chemical need not be classified as a skin irritant.

Several eye irritation studies were submitted for assessment. The notified chemical at 44% caused severe eye damage. In two other eye irritation studies, the notified chemical at 23% and 5% produced similar results that the notified chemical was slightly irritating to the eyes of rabbits. On this evidence, the risk phrase R41 – Causes serious eye damage is warranted for the notified chemical.

Several skin sensitisation studies were submitted for assessment. In a series of well-conducted maximisation studies in guinea-pigs, the notified chemical was a sensitiser at 25% and 23% but not at 5%. A Buehler study with undiluted chemical was inconclusive. On this evidence, the notified chemical should be classified as a skin sensitiser.

The 28-day repeat dose study was performed with a material containing 23% of the notified chemical. The NOEL was 69 mg/kg/day based on the increase of adrenal gland weight in both males and females, increased AST, ALT and neutrophil count in males and a decrease in glucose, total protein and inorganic phosphorus in females, all at the highest dose of 460 mg/kg/day.

Three genotoxicity studies were performed, all of them using the product containing 23% notified chemical. The notified chemical was not found to be mutagenic in several strains of *S. typhimurium* or clastogenic to CHO cells. However, in CHO cells, an increase in numerical aberrations was observed following treatment in the presence of S-9. This was attributable to endoreduplication and polyploidy. The biological significance of this effect in cell culture is poorly understood.

On the basis of the toxicological data provided, the notified chemical is a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1994a). The risk phrases R41 and R43 are appropriate.

11. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies have been supplied by the notifier for the formulation Lexquat AMG-BEO containing 23-27% of the notified chemical. The tests were carried out according to OECD/EEC Test Methods.

Species	*Test*	*Concentrations[a] (mg/L)*	*Result (mg/L)*	*Reference*
Rainbow trout *(Oncorhynchus mykiss)*	96 h acute	1.0, 0.5, 0.25, 0.125, 0.063, 0	$0.25 \leq LC_{50} \leq 0.5$ NOEC =0.063	Mattock 1997a
Water Flea *(Daphnia magna)*	48 h acute	1.0, 0.50, 0.25, 0.12, 0.06, 0	$0.25 \leq EC_{50} \leq 1.0$ NOEC =0.25	Mattock 1997b
Algae *(Selenastrum capricornutum)*	96 h growth	0.1, 0.05, 0.025, 0.013, 0.0063, 0	E_rC_{50} = 0.090 (CI 0.077-0.110) E_bC_{50} = 0.035 (CI 0.032-0.039) NOE_rC = 0.025 NOE_bC = 0.013	Mattock 1997c
Sewage micro-organisms	3 h respiration inhibition	200, 150, 100, 75, 50, 0	EC_{50} = 132 (CI 122-144)	Bealing 1996

[a]Nominal concentrations of Lexquat AMG-BEO containing 23-27% of the notified chemical.

By 24 h in the fish study, 100% mortality was observed at the highest test concentration. All fish in the 0.5 and 0.25 mg/L test concentrations and three out of seven of the fish at 0.125 mg/L were showing mild toxic effects (including increased cough frequency and different swimming positions in the test vessel compared to the control) by 24 h. After 72 h at 0.5 mg/L, 100% mortality was observed. At 96 h all fish in the 0.125 mg/L test concentration were exhibiting mild toxic effects, at 0.25 mg/L two out of the seven test animals were showing mild toxic effects and the remaining five were showing severe toxic effects (including abnormal swimming and lying on the bottom of the tank). As there were no partial mortalities recorded at 96 h it is not possible to determine the LC_{50} using probit analysis and the true LC_{50} lies between 0.25 and 0.5 mg/L.

In the daphnia study, 40% immobilisation was observed at the highest test concentration after 24 h with no immobilisation observed at lower concentrations. By 48 h, the percentage of immobile daphnids had increased to 100% at the highest concentration and 95% immobilisation was observed at 0.50 mg/L. No immobilisation was observed at lower concentrations. As there was only one partial response it is not possible to determine the EC_{50} using probit analysis and the true EC_{50} lies between 0.25 and 1.0 mg/L.

The algal toxicity study was conducted accordance with Annex 5 (92/69/EEC) to Commission Directive 92/32/EEC: C.3 Algal Inhibition Test following codes of Good Laboratory Practice. Algal cell numbers were counted electronically at 24 h intervals using a Z1 Coulter Counter. The E_rC50 and E_bC50 values were determined from the average specific growth rate and the area under the growth curves, respectively.

The ecotoxicity data for the notified chemical indicate that the formulation, Lexquat AMG-BEO, containing the notified chemical (23-27%) is highly toxic to fish and water fleas, very highly toxic to algae and practically non-toxic to sewage micro-organisms. Hence, if the toxicity of the formulation is entirely due to the notified chemical then the ecotoxicity

endpoints presented in the table above need to be divided by a factor of 4 to give the endpoints for the notified chemical.

12. ASSESSMENT OF ENVIRONMENTAL HAZARD

The vast majority of notified chemical will be discharged to sewer through product use. The notifier has provided predicted environmental concentrations (PECs) of 1.5 ppb and 37.5 ppb for the discharge of a single use of the notified chemical into a metropolitan and country sewer, respectively. Based on the aquatic toxicity data, these would be of environmental concern especially the latter which is greater than the algal E_bC50 value for the formulation. However, these concentrations represent an overestimate and are based on incorrect assumptions such as dilution rates which do not take into account the true volume of water used each day [approximately 150 L per person per day is a conservative estimate (EC, 1994)].

As the product will be available nationwide, and sent to sewage treatment plants in both city and country locations, a PEC based on continental use has been calculated for the use of the imported formulation, Lexquat AMG-BEO [Note: formulation concentrations have been used to allow direct comparison with the provided ecotoxicity data]:

Import Volume per annum of Lexquat AMG-BEO	5 000 kg
Amount discharged to sewer	100%
Volume discharged per day	13.7 kg
Sewer output per day*	2 700 ML
Concentration in Sewage Treatment Plant	5.07 µg/L (ppb)

*Sewer output based on an Australian population of 18 million, each using 150 L water per day.

The concentration within the sewerage plant is further diluted. The US EPA assumes that between 50 and 90% of cationic chemicals with molecular weights between 500 and 1,000, are removed through adsorption during the passage through a waste water treatment plant before the effluent is discharged (Boethling and Nabholz, 1997). Additionally, the treated effluent will be diluted on entering the receiving waters. Dilution factors vary with receiving waters. A 10:1 dilution for ocean outfall (corresponding to most Australian cities) is assumed and 2:1 for discharge into a river or creek (country cities and towns).

Taking the above into account and assuming 50% adsorption the worst case, the PECs for ocean and river discharge, are 0.25 and 1.3 ppb, respectively.

Despite the low level of notified chemical in the imported product, its widespread use, and the resultant low concentration of the chemical in surface waters, the predicted level in surface waters is well below (>150×) the toxicity to fish and daphnia but close (<30×) to the toxic levels for algae. The narrow safety margin is of concern, particularly if use in country areas becomes widespread. The overall environmental hazard of the notified chemical at the

proposed rate of import is acceptable, however, if importation is expected to exceed 4 tonnes a secondary notification would be required to allow a refinement of the hazard.

13. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Toxicity studies were conducted with Lexquat AMG-BEO containing 5-44% of the notified chemical in water with < 5.5% propylene glycol and < 5.5% sodium chloride. The notified chemical is of low acute oral and dermal toxicity in animals. It is not a skin irritant but a severe eye irritant and skin sensitiser. In a 28-day repeat oral study in rats, the NOEL was observed at 69 mg/kg/day based on increased adrenal weights and changes in clinical chemistry parameters at the higher dose. Lexquat AMG-BEO did not induce reverse mutation in the *S.typhimurium* in the absence or presence of metabolic activation. The notified chemical is classified as a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1994a) with the risk phrases, R41 (Risk of serious damage to eyes) and R43 (May cause sensitisation by skin contact).

Therefore, skin sensitisation and eye damage are the critial effects for the notified chemical. Appropriate personal protective equipment is needed for workers handling the notified chemical to minimise the occupational exposure. Any workers who become sensitised to the notified chemical should not continue to handle it in the work place.

Transport and storage
It is anticipated that waterside, transport and storage workers would have negligible health risk when handling the notified chemical except in the event of an accident when the package is breached.

Formulation
The formulating and packaging processes will be carried out in a closed system. Both the dispensary and the formulation areas are bunded and have a cross-flow ventilation system. Formulation workers could be contaminated with the notified chemical when they handle the drums, connect and disconnect the pump lines and when cleaning and maintaining process equipment. Workers at the formulation sites should wear overalls, goggle, safety skin boots and impervious gloves to minimise the risk of skin sensitisation and eye damage.

Laboratory staff could be exposed to small amount of the notified chemical when analysing the samples. The laboratory staff should wear laboratory coats or overalls, safety glasses and gloves while handling the samples containing the notified chemical.

The packaging operators will handle the products containing 0.5% the notified chemical. Unless the bottles are breached, their exposure is expected to be negligible. Under current conditions, packers may pack the product for 40 days per year. The packaging operators should wear overalls, safety glasses and gloves while packing the final products containing the notified chemical to minimise any risk of adverse health effects.

Retail
The occupational health risk for retail workers is considered to be negligible, as exposure would occur only if the packaging were breached.

Public Health
Since the notified chemical will be used in body washes, widespread public exposure will occur by the dermal route, and possibly into the eyes. The notified chemical at 23% or 44% is a severe eye irritant and a skin sensitiser; however, a solution containing 5% of the notified chemical is slightly to moderately irritating to the eyes and non-sensitising to the skin. At the use level of 0.5 % in body washes, behenamidopropyl PG-dimonium chloride is unlikely to be a skin irritant or sensitiser, but may cause slight eye irritation.

Assuming a daily dose of 0.008 mg/kg/day, this gives a safety margin of greater than 8 600, based on the oral NOEL of 69 mg/kg/day established in a 28 day rat study. In practice, the safety factor would be higher, given that absorption through the skin is likely to be less extensive than via the oral route. Based on the provided information and proposed use pattern, the notified chemical does not appear to pose a significant hazard to public health.

14. RECOMMENDATIONS

To minimise occupational exposure to Behenamidopropyl PG-Dimonium Chloride the following guidelines and precautions should be observed:

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992);
- Industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987) and AS 3765.1 (Standards Australia, 1990);
- Impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia/Standards New Zealand, 1998);
- All occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994);
- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;
- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the MSDS should be easily accessible to employees.

- Workers who become sensitised to the notified chemical should not continue to handle it in the work place.

15. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (National Occupational Health and Safety Commission, 1994b).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

16. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. Secondary notification shall be required if the import volume of the notified chemical exceeds or is expected to exceed 4 tonnes per year. No other specific conditions are prescribed.

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Attachment 1

The Draize Scale for evaluation of skin reactions is as follows:

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
No erythema	0	No oedema	0
Very slight erythema (barely perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale for evaluation of eye reactions is as follows:

CORNEA

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

CONJUNCTIVAE

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
Diffuse beefy red	3 severe	Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
		Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe