File No: NA/407

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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

1-(4-methoxy-5-benzofuranyl)-3-phenyl 1,3 propanedione

This Assessment has been compiled in accordance with the provisions of *the Industrial Chemicals (Notification and Assessment) Act* 1989 (the Act), and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by Worksafe Australia which also conducts the occupational health & safety assessment. The assessment of environmental hazard is conducted by the Department of the Environment, Sport, and Territories and the assessment of public health is conducted by the Department of Health and Family Services.

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Director
Chemicals Notification and Assessment

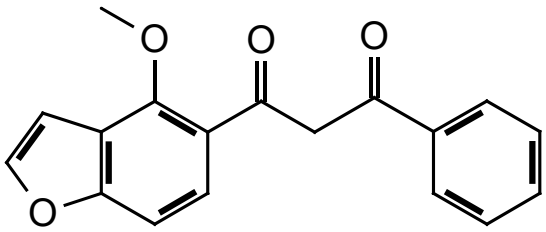
FULL PUBLIC REPORT

1-(4-methoxy-5-benzofuranyl)-3-phenyl 1,3 propanedione

1. APPLICANT

Quest International of 6 Britton Street SMITHFIELD NSW 2164, has submitted a limited notification statement for an assessment certificate for 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1,3 propanedione.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	1-(4-methoxy-5-benzofuranyl)-3-phenyl 1,3 propanedione
Chemical Abstracts Service (CAS) Registry No.:	484-33-3
Other Names:	Pongamol, Shade 1
Trade Name:	Pongamia extract
Molecular Formula:	$C_{18}H_{14}O_4$
Structural Formula:	
Molecular Weight:	294
Methods of Detection and Determination:	purity ascertained using Gas Liquid Chromatography (GLC); Infrared (IR) and Nuclear magnetic Resonance (NMR) used to confirm composition
Spectral Data:	IR, major characteristic peaks at: 3 436, 1 600, 1 554, 1 473, 1 434, 1 351, 1 330, 1 298, 1 262, 1 233, 1 219, 1 180, 1 160, 1 137, 1 062, 974, 803, 777, 749, 706 cm^{-1};

	Ultraviolet (UV) spectrum and GPC trace also supplied

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	off white cream or powder
Melting Point:	126 - 132°C (at 760 mm Hg)
Specific Gravity:	not available
Vapour Pressure:	101.3 kPa at 20°C
Water Solubility:	1 mg/L at 20°C (column elution method)
Partition Co-efficient (n-octanol/water):	log P_{ow} = 4.43 (flask shaking method)
Hydrolysis as a Function of pH:	not available
Adsorption/Desorption:	log K_{oc} = 3.04
Dissociation Constant:	not available
Flash Point:	not available
Flammability Limits:	not available
Autoignition Temperature:	not available
Explosive Properties:	not available
Reactivity/Stability:	not available

Comments on Physico-Chemical Properties

The notifier has provided a vapour pressure of 101.3 kPa which suggests high volatility. No test was submitted to substantiate this claim. ASTER gives a calculated vapour pressure of 2.11 x 10^{-8} mmHg (2.8 x 18^{-3} atm) and a Henrys Constant of 3.25 x 10^{-11} atm/m^3/mol (1). While these figures are calculated and a guide only, they do suggest the chemical is non-volatile.

The notified chemical is not expected to hydrolyse under environmental conditions due to its low solubility and lack of hydrolysable groups.

The low water solubility determined by the notifier, and high log P_{ow} value indicate a potential for bioaccumulation. This is dealt with in the Environmental Fate section of

this report.

The adsorption/desorption coefficient, log K_{oc} = 3.04, was obtained from the ASTER database (1).

There are no groups likely to dissociate within this chemical.

4. PURITY OF THE CHEMICAL

Degree of Purity: 100%

Toxic or Hazardous Impurities: none identified

Non-hazardous Impurities (> 1% by weight): none identified

Additives/Adjuvants: none added

5. USE, VOLUME AND FORMULATION

The notified chemical is imported into Australia as a raw material in sealed polyethylene lined steel kegs. The notified chemical is in a powdered form. Although the notified chemical is derived from botanical material it is not considered to be a naturally-occurring chemical and hence exempt from assessment due to the method employed to extract it. It is estimated that less than 1 tonne of the notified chemical with a 100% purity will be imported per annum. The chemical will be used as an ingredient in cosmetics at a concentration in the final products of approximately 1%.

6. OCCUPATIONAL EXPOSURE

The notified chemical is imported as a 100% pure material in sealed steel kegs. Occupational exposure during transport and warehousing is therefore unlikely and will only occur due to accidental spillage.

Occupational exposure is most likely to occur during the formulation of cosmetic preparations. Between 5 and 20 employees will be involved in cosmetic formulation and packaging. The notified chemical is weighed then added to mixing vessels. As the chemical is in a powdered form there is a possibility of inhalation of dusts during addition to mixing vessels and weighing operations. The notifier has indicated that employees wear dust respirators, gloves and eye protection during these operations. The blending occurs in either sealed or open vessels. The notifier states that where open vessels are used adequate ventilation is available to minimise particulate material.

The concentration of the notified chemical in the cosmetic formulations is < 1%, therefore occupational exposure to the notified chemical during packaging will be limited.

7. PUBLIC EXPOSURE

The pure pongamia extract is intended for use in cosmetics at concentrations of 1% or less to provide UV protection. The type and purpose of the cosmetics into which the notified substance is to be incorporated are not specified, as these will be formulated by companies purchasing the extract. However the nature of the compound suggests a wide range of hand face and body creams and lotions may eventually contain it. In these circumstances widespread and repeated exposure to the notified chemical would be expected, limited only by the commercial success of its marketing.

In the event of a transport accident the notified chemical would be wind dispersed. However recovery and containment prior to reprocessing, disposal in landfill or incineration would be readily achievable through simple sweeping or the use of spark proof vacuum equipment. As the notified chemical has a log P_{ow} of 4.4 any dispersed material would be expected not to contaminate surface waters but to bind to soils and sediments or settle into stream beds.

8. ENVIRONMENTAL EXPOSURE

Release

Pongamia will be blended with a number of other cosmetic ingredients to produce the final consumer cosmetic. This blending may be carried out in both sealed and open vessels. The final product is packaged in plastic or cardboard tubes or tubs containing 100 to 200 g of cream.

The notifier estimates losses through blending and packing operations to total less than 1%. For a tonne of imported product, annual release through reformulation and packaging should not exceed 10 kg. This waste would be spread over a number of sites in Australia, and over a number of days per site. The waste is likely to be either washed to sewer during cleaning operations, or collected with solid waste and landfilled or incinerated.

The double thickness polythene liners containing residues of the notified chemical from the importation containers will be landfilled where residues of the chemical would be expected to be immobile through association with soils.

Further release occurs from disposal of end use containers (tubes or tubs with 100 - 200 g of cream, or 1 to 2 g of the notified substance). It is unlikely that these containers will contain more than 5% of their contents when disposed of. This is a maximum of 50 kg per year of the notified chemical disposed of to landfill with household rubbish per year, spread over Australia.

The major release is expected to come from release of the chemical to the sewer as consumers wash the cosmetic residues from their skin. For this assessment, we will

assume all chemical not released with mechanisms dealt with above, will be released this way. Therefore, up to 940 kg could be expected to be released to sewer around Australia by this mechanism each year.

Fate

The majority of the notified chemical will be released via the sewer.

The level 1 Fugacity Model, as modelled by ASTER, indicates that, at equilibrium, 82.64% of the notified chemical will partition to the water compartment with the remainder partitioning to soil and sediment (1). These predictions are modelled on the chemical structure, from which water solubility, partition co-efficient and adsorption/desorption co-efficient are calculated. For these outcomes, a higher water solubility (252 ppm compared to 1 ppm determined as water solubility in laboratory tests), and a lower partition co-efficient (log P_{ow} 3.14 compared to log P_{ow} 4.43 as determined in laboratory tests) were used. Basing predictions on tested values, the EPA would expect a higher proportion of the released chemical to partition to soils and sediments and a lower proportion to partition to water at equilibrium.

Pongamia is not expected to readily hydrolyse under environmental conditions. Testing using the Modified Sturm Test showed the chemical to be not readily biodegradable (< 12% in 10 days).

Bioaccumulation

The lack of biodegradability and hydrolysis, combined with a low water solubility and high partition co-efficient suggests this chemical has the potential to bioaccumulate. General characteristics of organic chemicals which exhibit bioaccumulation, as given by Connell 1990 (2) include a high proportion of C-C (aromatic) bonds; molecular weight from 100 to a maximum capacity at about 350 (MW = 294 for the notified chemical); resistant to degradation; log P_{ow} > 2 (= 4.43 for the notified chemical) and low water solubility, giving a maximum capacity to bioaccumulate at 0.002 mol/m^3 (the notified chemicals solubility is 0.003 mol/m^3). All these characteristics are present in this chemical, and the potential for bioaccumulation is good.

ASTER (1) gives a calculated bioconcentration factor of 120 for Fathead minnow (*Pimephales promelas*). This figure suggests some potential for bioaccumulation, but not at significant levels.

9. EVALUATION OF TOXICOLOGICAL DATA

The Act does not require the provision of toxicology data for chemicals where the import volume is less than 1 tonne/annum. However, the following tests have been conducted and were submitted as part of the notification statement.

9.1 Acute Toxicity

Summary of the acute toxicity of 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1,3 propanedione

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	> 2 000 mg/kg	3
acute dermal toxicity	-	not available	-
skin irritation	rabbit	not an irritant	4
eye irritation	rabbit	*not an irritant	5
skin sensitisation	guinea pig	not a sensitiser	6

* not classified as hazardous according to the Worksafe Australia's *Approved Criteria for Classifying Hazardous Substances* (7), mild conjunctival reactions only.

9.1.1 Oral Toxicity (3)

Species/strain:	Sprague-Dawley rats
Number/sex of animals:	5/5
Observation period:	14 days
Method of administration:	gavage as 20% w/v in 1% aqueous methyl cellulose
Clinical observations:	piloerection in all rats within 5 minutes of dosing, abnormal body carriage in one rat; recovery was complete by day 3
Mortality:	none
Morphological findings:	one male rat had a slightly low bodyweight gain
Test method:	according to OECD Guidelines for Testing Chemicals (8)
LD_{50}*:*	> 2 000 mg/kg
Result:	low acute oral toxicity

9.1.2 Skin Irritation (4)

Species/strain:	New Zealand white rabbit
Number:	3
Observation period:	4 days
Method of administration:	0.5 g of test article under a gauze pad; the test area had been moistened using 0.5 ml distilled water
Draize scores (9):	0
Test method:	according to OECD Guidelines for Testing Chemicals (8)
Result:	not a dermal irritant

9.1.3 Eye Irritation (5)

Species/strain:	New Zealand white rabbit
Number/sex of animals(M/F):	2/1
Observation period:	7 days
Method of administration:	70 mg of test substance into lower everted lid of one eye

Draize scores (9) of unirrigated eyes:

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

[1] see Attachment 1 for Draize scales
[a] opacity [b] area [c] redness [d] chemosis

Test method: according to OECD Guidelines for Testing Chemicals (8)

Result: not a classifiable irritant (7), 1 hour after administration redness and chemosis in all rabbits, minor reaction (mild conjunctival reactions) still evident in 2/3 rabbits after 24 hours.

9.1.4 Skin Sensitisation (6)

Species/strain: Dunkin/Hartley guinea pig

Number of animals: 20 test, 10 control

Induction procedure: Intradermal injection, three pairs of injections of 0.1 ml: FCA in 0.01% dodecylbenzene sulphonate in 0.9% physiological saline; 0.1 ml of 0.5% test article in 6% acetone/20% polyethylene glycol 400/0.01% dodecylbenzene sulphonate in 0.9% physiological saline and same with FCA 50:50 so that test article was 0.5%; 7 days later filter patch attached saturated with 50% test article in 70% acetone/30% polyethylene glycol 400, held in place for 48 hours

Challenge procedure:	13 days after application of induction patch challenged by a saturated occluded patch of 10% test article in 70% acetone/30% polyethylene glycol 400 for 24 hours.
Challenge outcome:	no evidence of sensitisation in any test animals when challenged, controls also showed no response
Test method:	similar to OECD Guidelines for Testing Chemicals (8)
Result:	not a sensitiser under conditions of study

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (10)

Strains:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537
Concentration range:	50-5 000 μg/plate with or without rat liver S9 diluted in dimethyl sulphoxide
Test method:	in accordance with OECD Guidelines for Testing Chemicals (8)
Result:	not mutagenic in this bacterial system

9.3.2 Clastogenic Activity in Cultured Human Lymphocytes (11)

Doses:	13, 65 and 325 μg/ml of test article in dimethyl sulphoxide with and without rat liver S9; solvent and positive controls (chlorambucil, cyclophosphamide); doses were based on results of preliminary toxicity tests
Method of administration:	to 48 hour cultures established from whole human blood; cultures without S9 mix were exposed for 24 or 48 hours, those with for 3 hours
Test method:	in accordance with OECD Guidelines for Testing Chemicals (8)
Result:	under conditions of test the notified chemical showed no evidence of clastogenic activity

9.3.3 Other Toxicological Data

A study of photoirritation and photoallergy in guinea pigs (12) was also conducted. The notified chemical (in solvent) was applied to the clipped and shaved dorsal area of guinea pigs which were then exposed to near ultraviolet light and theyshowed no variation in degree of irritation with control animals.

A bacterial photomutagenicity study using *S. typhimurium* and *Escherichia coli* (13) using a protocol similar to that in 9.3.1 but with exposure to solar simulated irradiation gave no increase in revertant colonies to cultures exposed to the following concentrations of the notified chemical; 10.0, 3.16, 1.0, 0.316 and 0.1 mg/ml. This test was performed as the notified chemicals molecular configuration could potentially be changed by light absorption. This is relevant due to its use in cosmetic preparations.

9.4 Overall Assessment of Toxicological Data

The notified chemical has a low oral toxicity to rats (LD_{50} > 2 000 mg/kg). There are no results available for dermal toxicity or long term oral toxicity. It is not an eye and skin irritant in rabbits and was not a skin sensitiser in a study using guinea pigs. Further studies to determine the effect of near ultraviolet light on the skin irritation potential showed no enhancement in a study using guinea pigs. It gave negative results in two genotoxicity studies; a *S. typhimurium* reverse mutation assay (with and without rat liver S9 activation) with a maximum dose of 5 000 μg/plate and a cultured human lymphocyte study with a maximum dose of 325 μg/ml. A *S. typhimurium* reverse mutation assay where the cultures were exposed to simulated solar radiation also showed no enhancement of the mutagenic potential of the notified chemical at doses up to 10 mg/ml. On the basis of the these tests the notified chemical would not be classified as Hazardous according to Worksafe Australia's *Approved Criteria for Classifying Hazardous Substances* (14).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

While not required for substances imported in quantities of less than 1 tonne per annum the following ecotoxicity studies have been provided by the notifier. The tests were carried out following OECD guidelines.

Test	***Species***	***Results***
acute 72 h (nc)	Algae (*Scenedesmus subspicatus*)	EC_{50} > 0.43 mg/L
acute 96 h (s; nc)	Zebra fish (*Brachydanio rerio*)	LC_{50} > 0.45 mg/L
acute 48 h (s; nc)	*Daphnia magna*	EC_{50} > 0.59 mg/L

s = static; nc = nominal concentration.

For the algae test, at 72 hours, mean measured concentrations of Pongamia Extract were between 0 and 16% of nominal concentrations (0.32 - 5.6 mg/L). This concentration was measured by HPLC (at 24 hour intervals for the duration of the relative tests). Water solubility of the notified chemical is 1 ppm. One reason why the measured concentration is so low (0 ppm in one instance) could be that it was partitioning to the species being tested - no precipitates are recorded. The notifier should provide comments on this in any standard notification. The analytical method used had a detection limit around 0.02 mg/L and a quantitation limit of about 0.05 mg/L. Values lower than this are likely to be imprecise. This suggests that the results should be considered with extreme caution.

During testing on Zebra fish, analysis indicated that mean measured concentration were between 5 and 8.7% of the nominal concentration. Under the OECD Guideline 203, this test is considered invalid as the concentration should be at least 80% of the nominal concentration over the test period. Effect concentrations are based on mean measured values, and can only be considered as approximate, and again treated with caution.

Similarly for *Daphnia*, mean measured concentration were between 6 and 7% of the nominal concentration. Again, under OECD Guideline 202, this test is considered invalid because measured concentrations are not at least 80% of nominal concentrations. Again, sorption to test species or vessel walls may have occurred - no precipitates were recorded. Comments should be provided with any standard notification.

The company results indicate that Pongamia Extract is not toxic to aquatic species to the limit of solubility. Toxicity as calculated through ASTER (1) gives a toxicity range of LC_{50} = 8.7 ppm for Channel catfish (*Ictalurus punctatus*) to LC_{50} = 16.2 ppm for Bluegill sunfish (*Lepomis macrochirus*). These figures indicate that the notified chemical can be considered moderately to slightly toxic to aquatic species. These figures should only be considered as a guide as they are modelled, not measured.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

Under EU guidelines, Pongamia Extract is classified as R53 - may cause long term adverse effects in the aquatic environment. The projected volume of import of this chemical under the current submission is for less than 1 tonne per annum, and the notifier has stated that annual volumes would be unlikely to exceed 100 kg.

Due to the potential hazard of this chemical, a worst case scenario, based on 100 kg per annum imported, has been used to determine a predicted environment concentration (PEC), based on the following assumptions:

- All imported chemical is released to the sewer, and spread over 365 days per year. Therefore the daily release of the chemical will be 274 g.
- Sewer output is based on 18 million people in Australia, averaging 100 L of water per day. This gives a daily sewer output of 1 800 ML.
- No removal through adsorption to material in sewage treatment plants occurs.

Using these assumptions, a PEC of 0.15 ppb is obtained. This is three orders of

magnitude below the lowest EC_{50} > 0.43 mg/L for algae, and suggests a low hazard.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

In general the results of the submitted toxicity data indicate that the notified chemical has limited toxicological significance in mammals and is unlikely to cause concern from an occupational exposure perspective. The notified chemical was found to have a low acute oral toxicity in a study using rats. Systemic effects from prolonged exposure have not been assessed as no chronic repeat dose studies have been undertaken. Dermal toxicity is also unknown but the molecular weight would not preclude absorption through the skin. The chemical was not a skin or eye irritant in studies using rabbits nor was it a skin sensitiser in a study using guinea pigs. A further study to determine if UV light altered the irritation potential of the notified chemical was negative. In a number of genotoxicity studies the notified chemical was found not to be genotoxic. These tests included a *S. typhimurium* reverse mutation assay (with and without S9 activation), a further test using simulated solar radiation was also negative for mutagenicity. Another test used cultured human lymphocytes and again a negative result was recorded.

Occupational exposure will normally only occur during the formulation and packaging of cosmetics containing the notified chemical. Occupational exposure during transport and warehousing will only occur in the event of accidental spillage. There will be 5-20 employees who will be potentially exposed during the formulation of cosmetics. Exposure will be greatest during weighing and blending of the notified chemical. As the chemical is a powder the main routes of exposure will be dermal, ocular and via inhalation. The results of the toxicity tests described above indicate that if exposure via these routes were to occur there would be limited effects. The emphasis in the notifier's workplace is to reduce particulate material in the atmosphere by ensuring adequate ventilation. Additionally some of the blending operations are undertaken using sealed systems. The appropriate exposure standard for the notified chemical will be that for nuisance dusts of 10 mg/m^3 as specified in Worksafe Australia's *Exposure Standards for Atmospheric Contaminants in the Occupational Environment* (15).

The extent of public exposure to the notified chemical will depend on the range of cosmetics into which it is incorporated and the commercial success of these products. Extensive and repeated exposure in individuals using products containing the notified chemical is an inevitable consequence of the nature of those products. The potential for unintentional exposure however, is minimal. The notified chemical is considered to present a low public health hazard, based on its likely use patterns and toxicological characteristics.

The notified chemical is not classified as hazardous according to the Worksafe Australia *Approved Criteria for Classifying Hazardous Substances* (14) on the basis of the toxicity data submitted. It is considered that the risk to workers through occupational exposure to the notified chemical will be low.

13. RECOMMENDATIONS

To minimise occupational exposure to 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1,3 propanedione the following guidelines and precautions should be observed:

- When handling the chemical in powdered formulations, good general and local exhaust ventilation should be provided in weighing areas. Where this is not available then the appropriate respiratory device should be selected and used in accordance with Australian Standard/ New Zealand Standard (AS/ NZS) 1715 (16) and should conform to AS/NZS 1716 (17).

- Safe practices, as should be followed when handling any chemical formulation, should be adhered to - these include:

    - minimising spills and splashes;

    - practising good personal hygiene; and

    - practising good housekeeping and maintenance including bunding of large spills which should be cleaned up promptly with absorbents and put into containers for disposal.

- A copy of the Material Safety Data Sheet (MSDS) should be easily accessible to employees.

  It is expected that, in the industrial environment, protective clothing conforming to and used in accordance with Australian Standard (AS) 2919 (18) and protective footwear conforming to Australian/New Zealand Standard (AS/NZS) 2210 (19) should be worn as a matter of course. In addition it is advisable when handling chemical formulations containing the notified polymer to wear chemical-type goggles (selected and fitted according to AS1336 (20) and meeting the requirements of AS/NZS 1337 (21)), impermeable gloves (AS 2161) (22) should be worn to protect against unforseen circumstances.

In addition:

- If the volume of importation should exceed 1 tonne per annum, the company should resubmit a full submission, including further investigation of biodegradation, and repeating ecotoxicological tests as appropriate to clarify problems encountered with toxicity tests submitted with the current application.
- If therapeutic claim is to be made for any product incorporating the notified chemical, in relation to the advantages or consequences of UV protection for example, a submission will need to be made to the Therapeutic Goods Administration (TGA).

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in accordance with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (23).

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.

15. 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. No other specific conditions are prescribed.

16. REFERENCES

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5. Parcell B I, 1993, Project Number KW930435 - *Pongamol*, *Eye Irritation to the Rabbit*, Huntingdon Research Centre, Huntingdon, UK

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20. Australian Standard 1336-1982, *Recommended Practices for Eye Protection in the Industrial Environment*, Standards Association of Australia Publ., Sydney, 1982.

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22. Australian Standard 2161-1978. *Industrial Safety Gloves and Mittens (excluding Electrical and Medical Gloves)*, Standards Association of Australia Publ., Sydney, 1978.

23. National Occupational Health and Safety Commission (1994). *National Code of Practice for the Completion of Material Safety Data Sheets*, [NOHSC:2011(1994)], AGPS, Canberra.

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