File No: NA/408

Date: September 1996

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Citmol 316

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For Enquiries please contact the Administration Coordinator at:

Street Address: 92 Parramatta Rd Camperdown, NSW 2050, AUSTRALIA
Postal Address: GPO Box 58, Sydney 2001, AUSTRALIA
Telephone: (61) (02) 9577-9466 **FAX (61) (02) 9577-9465**

Acting Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Citmol 316

1. APPLICANT

Ellis and Associates of 4 William Street MOUNT WAVERLEY VIC 3149 have submitted a standard notification statement accompanying their application for an assessment certificate for Citmol 316.

2. IDENTITY OF THE CHEMICAL

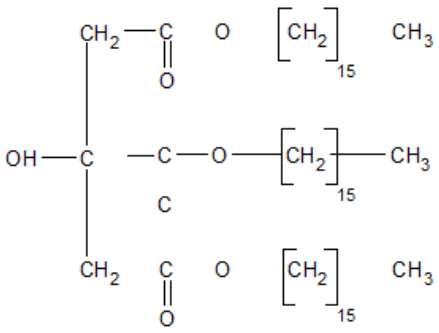
Chemical name: triisocetyl citrate

Chemical Abstracts Service (CAS) Registry No.: 93385-14-9

Trade name: Citmol 316
Bernel Citmol 316

Molecular formula: $C_{54}H_{104}O_7$

Structural formula:



Molecular weight: 864

Method of detection and determination: determination of the acid value; saponification value and determination of the hydroxyl number

Spectral data: infrared; major characteristic peaks were found at: 710, 980, 1170, 1450, 1720, 2900 cm^{-1}

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	clear colourless liquid
Boiling point:	not determined
Specific gravity:	0.908 (at 25°C)
Vapour pressure:	not determined
Water solubility:	insoluble
Partition co-efficient (n-octanol/water):	not determined
Hydrolysis as a function of pH:	stable between pH 3 and pH 10
Adsorption/desorption:	not determined
Dissociation constant:	does not dissociate in water
Flash point:	239°C (closed cup)
Flammability limits:	not determined
Autoignition temperature:	not determined
Explosive properties:	not sensitive to heat, shock or friction
Reactivity/stability:	not reactive; not an oxidiser; stable

Comments on Physico-Chemical Properties

The vapour pressure has not been determined. However, the notifier states that since Citmol 316 contains 54 carbon atoms the vapour pressure is expected to be extremely low.

The notifier states that Citmol 316 is insoluble in water. This is supported by calculation of the log K_{ow} (see below), and the presence of long hydrophobic hydrocarbon chains.

The notifier states that Citmol 316 will hydrolyse into its components above pH = 10 and below pH = 3. Hence hydrolysis of Citmol 316 is not expected to occur within the environmental pH range due to the low solubility.

The partition coefficient (log K_{ow}) for the chemical was not determined by the notifier.

A value of ~21 for log K_{ow} has been calculated using atom/fragment contribution method developed by Syracuse Research Corporation (1).

No information was provided on the adsorption/desorption properties of the chemical. Given the chemical's low water solubility and high partition coefficient it is anticipated that it will strongly adsorb to soil and sediments.

The notified chemical contains no dissociable hydrogens or basic functionalities.

4. PURITY OF THE CHEMICAL

Degree of purity: 99%

Toxic or hazardous impurities: none

Non-hazardous impurities:

Chemical Name	*CAS No.*	*Weight %*
water		0.08
diisocetyl citrate		trace
isocetyl citrate		trace
isocetyl alcohol	369311-34-9	trace

Additives/Adjuvants: none

5. USE, VOLUME AND FORMULATION

The majority of Citmol 316 will be imported as a component (at a concentration of 4%) of skin care lotions. The product will be imported in 200 mL screw top plastic bottles. A smaller amount of the pure chemical will be imported for local formulation into cosmetic products such as lipsticks, lip balm, eye shadows and face powder. The concentration of Citmol 316 in these products will be less than 2%. The pure chemical will be imported in 200 L steel drums and 16 kg plastic drums. The estimated import quantities for the notified chemical for the next 5 years are given below:

Year	Pure chemical (kg)	Chemical (kg) as part of formulation
1996	-	2000
1997	100	3000
1998	150	3500
1999	150	3700
2000	200	4000

6. OCCUPATIONAL EXPOSURE

The notified chemical will be imported in pure form in 200 L steel drums and 16 kg plastic drums. In addition, skin care products containing the notified chemical (at a concentration of 4%) will be imported in fibre board cartons containing 12 screw cap, plastic bottles per carton.

Waterside, transport and warehouse workers are not expected to be exposed to Citmol 316 under normal circumstances.

Dermal exposure to Citmol 316 may occur when workers insert taps into drums containing the notified chemical in order to dispense an appropriate amount of the liquid into a stainless steel container for weighing. The container will be sealed and transferred to the compounding area, where the contents will be poured into a closed mixing vessel with other formulation ingredients. Formulators are expected to spend approximately 3 hours per year working with the notified chemical in its pure form, and a further 18 hours per year in contact with formulations containing the notified chemical. Inhalational exposure is not expected to occur due to the expected low vapour pressure of the notified chemical, and skin and eye exposure will be limited to drips and splashes during the transfer of the chemical from vessel to vessel.

Once the mixing cycle is completed, the formulation will be pumped from the mixing vessel to an automatic, closed filling machine for final packaging. Filling operators are expected to spend 120 hours per year working with the notified chemical, but as the filling process will be closed and automated, workers are only expected to come into contact with the chemical in the event of a spillage or cleaning and maintenance of equipment.

Laboratory workers may be exposed to small amounts of the notified chemical during routine quality control and research work. These workers will spend approximately 50 hours per year during initial trials working with the chemical; this will decrease to approximately 3 hours per year after the first 12 months.

Sales staff may also be dermally exposed to low concentrations (less than 4%) of notified chemical while demonstrating cosmetic products containing Citmol 316.

Occupational exposure to the notified chemical will be further limited by workers wearing gloves and eye protection while handling the pure chemical, and workers cleaning equipment wearing gloves under normal circumstances.

7. PUBLIC EXPOSURE

The notified chemical will be used in cosmetic products including skin care lotions, lipsticks, lip balms, eye shadows and face powder at a concentration of 4%. These products will be directly applied to the skin. Thus the major route of exposure of the public to the notified chemical is expected to be by dermal contact.

Compared to the dermal exposure from cosmetic use, negligible public exposure is

expected to result from reformulation, storage, distribution or disposal of the notified chemical or products containing the notified chemical.

8. ENVIRONMENTAL EXPOSURE

Release

The formulation and packaging of the cosmetics will take place in a closed system, reducing the likelihood of the chemical being released into the environment during routine mixing of formulations and packing of final products. Spillages are to be contained and not released to sewer. Spilled material will be collected using approved absorbents and disposed of in approved landfills. Should a spillage of the notified chemical occur, a maximum of 200 L of the chemical would be released into the environment and will be collected for incineration or to be disposed of in landfill.

The use of products containing the chemical would be widespread but diffuse as they would be applied in small quantities to the skin. Release to the environment may occur to the sewer or to landfill through the removal of the cosmetic product from the skin by washing or wiping, and the disposal of residual quantities of the cosmetics within used containers. In particular it is expected coloured cosmetics will be removed using cleanser on paper towels or cotton wool and disposed of in normal garbage, which will be landfilled. The notifier claims that due to the chemical's strong affinity with the skin not more than 10% of the product will be lost to the sewer through normal use. This would release approx 425 kg of Citmol 316 through washing to effluent. Assuming 1% remains in bottles another 43 kg would be released to the environment through disposal in landfill.

Fate

Citmol 316 is intended for use in cosmetics and, as such, would be expected to be released to the environment via consumer use by landfill of discarded paper or cotton wipes, or through washing the residual chemical off the skin and into the sewerage system.

Taking the worst case assumption that 10% of the chemical to be imported remains suspended in the sewerage system and thus is discharged to receiving waters, a predicted environmental concentration (PEC) for the substance in sewage water across Australia can be estimated from the following assumptions: 4 250 kg maximum annual use, an Australian population of 18 million and a daily per capita waste water discharge (a conservative estimate) of 150 L. This provides a PEC of approximately 0.4 ppb in sewage water.

This neglects adsorption to particles and sediments, which is expected to be extensive. Citmol 316 has a low solubility in water and it will be effectively removed during the water treatment process. Hence it will be handled as part of the normal solid waste recovery and disposed of to approved landfill or incinerated. Thus there is little likelihood of the Citmol 316 entering natural waterways in significant quantities. A small amount (< 43 kg per annum), the residue from drums and 'empty'

cosmetic containers, will go into landfill where it is not expected to be mobile, based on its low water solubility.

No biodegradation data have been provided. The chemical is of a type that could be susceptible to biodegradation since it is composed of long chain aliphatic alcohols esterified with citric acid. However, its low solubility would be likely to inhibit the degradation. The molecular weight and high log K_{ow} of the chemical indicates that it could potentially bioaccumulate. However, the potential for bioaccumulation is decreased by the low water solubility of the chemical and its expected metabolism by aquatic organisms.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of Citmol 316

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 40 000 mg/kg	2
skin irritation	rabbit	non-irritant	3, 4
eye irritation	rabbit	non-irritant	3
skin sensitisation	guinea pig	non-sensitising	5

9.1.1 Oral Toxicity (2)

Species/strain:	albino rats
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	gavage; undiluted
Clinical observations:	in 9 of the 10 animals, hair was matted and moist from 6 hours to 3 days
Mortality:	none
Morphological findings:	none
Test method:	according to Hagan (6)
LD_{50}:	> 40 000 mg/kg
Result:	low oral toxicity in a limit test - single dose of 40 000 mg/kg

9.1.2 Dermal Toxicity

No dermal toxicity study was performed, however, skin irritation tests discussed below (Section 9.1.4.1 and 9.1.4.2) involved both single and repeated dermal application of the notified chemical. Animals were not necropsied at the end of these studies, however systemic toxicity was not apparent based on clinical observation. In addition, a human use-irritancy test was performed (see section 9.4.4 below). Subjects applied a product containing 4% Citmol 316 once daily all over the body following bath or shower for 14 days. While irritancy on use was inconclusive, no signs of systemic toxicity were observed.

9.1.3 Inhalation Toxicity

Not performed

9.1.4 Skin Irritation

9.1.4.1 Skin Irritation Test 1 (3)

Species/strain:	New Zealand White rabbits
Number/sex of animals:	6; sex unspecified
Observation period:	72 hours
Method of administration:	0.5 mL of the test article (25% w/w suspension of the notified chemical in corn oil) was applied to two dorsal test sites, one abraded and one intact; test sites occluded for 24 hours; sites examined 24 and 72 hours after administration and scored according to the method of Draize (7)

Draize Scores (7) (refer to endnote)

	Time after treatment			
	60 min	***1 day***	***2 days***	***3 days***
ERYTHEMA				
1	-	1	*	1
2	-	0	*	0
3	-	1	*	1
4	-	0	*	0
5	-	1	*	0
6	-	0	*	1
OEDEMA				
1	-	0	*	0
2	-	0	*	0
3	-	0	*	0
4	-	0	*	0
5	-	0	*	0
6	-	0	*	0

*since no observation was made for erythema and oedema at 48 hour interval, the notified chemical cannot be classified for skin irritation in accordance with Worksafe Australia's *Approved Criteria for Classifying Hazardous Substances* (Approved Criteria) (16).

Test method: according to Hagen (6)

Result: slightly irritating to rabbit skin

9.1.4.2 Skin Irritation Test 2 (4)
(Non-Occlusive)

Species/strain: albino guinea pig

Number/sex of animals: 3/ sex

Observation period: 15 days (at 24 hour interval)

Method of administration: 0.05 mL of the of the notified chemical was applied on the left flank of each animal at 24 hour intervals for 14 days; sites examined at 24 hour intervals before each application for 15 days and scored according to the method of Draize (8); the right flank of each animal was used as a control

Test method: Safepharm Laboratories (4)

Result: not a skin irritant; no erythema or oedema observed up to 24 hours after application

9.1.5 Eye Irritation (3)

Species/strain:	New Zealand White rabbits
Number/sex of animals:	6; sex unspecified
Observation period:	7 days
Method of administration:	0.1 mL of the test article (25% w/w suspension of the notified chemical in corn oil) was placed in one eye; untreated eye served as control; material remaining in eye after 24 h was washed away
Test method:	according to Draize (7)
Result:	no evidence of irritation; the notified chemical is not an eye irritant in rabbits.

9.1.6 Skin Sensitisation (5)

Species/strain:	guinea pig/ Pirbright (Tif:DHP)
Number of animals:	10 test, 10 control
Induction procedure:	3 pairs of intradermal injections: - Freunds Complete Adjuvant (FCA)/ distilled 1:1 - 0.1 mL (0.1 mg) notified chemical - 0.1 mL notified chemical in FCA/saline 1:1 after one week occluded application of the notified chemical (0.4 mg) for 24 hours with 10% sodium lauryl sulphate applied 24 h prior to application
Challenge procedure:	after 3 weeks occluded administration of 0.4 mL (0.4 mg) notified chemical for 24 hours

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hrs****	***48 hrs****	***24 hrs***	***48 hrs***
0.4 mg (0.4 mL)	0/10**	0/10	0/10	0/10

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

Test method:	according to Sato *et al.* (8)
Result:	not a skin sensitiser in guinea pigs

9.2 Repeated Dose Toxicity

No repeat dose toxicity studies were carried out, however, the second skin irritation test discussed above (Section 9.1.4.2) involved repeated dermal application of the notified chemical for a period of 14 days. Animals were not necropsied at the end of the study, however systemic toxicity was not apparent based on clinical observation. In addition, a human use-irritancy test was performed (see section 9.4.4 below). Subjects applied a product containing 4% Citmol 316 once daily all over the body following bath or shower for 14 days. While irritancy on use was inconclusive, no signs of systemic toxicity were observed.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (9)

Strains:	TA 1535, TA 1537, TA 98 and TA 100; E. coli WP2 *uvrA*
Concentration range:	312.5 - 5000 μg/plate
Test method:	OECD Guidelines for Testing of Chemicals (10)
Result:	not mutagenic in the bacterial strains tested in the presence or absence of metabolic activation provided by rat liver S9 fraction

9.3.2 Cytogenetic Test on Chinese Hamster Cells *In Vitro* (11)

Cell line:	Chinese hamster lung cells
Doses:	625 1250 2500 and 5000 μg/mL for 6 hours (followed by 15 or 39 hours recovery) with metabolic activation provided by rat liver S9 fraction and 18 or 42 hours without metabolic activation
Test method:	OECD Guidelines for Testing of Chemicals (10)
Result:	not clastogenic in mammalian cells *in vitro*

9.4 Human Data

The notifier has provided details of several tests which were carried out to determine the toxicity of the notified chemical in cosmetic preparations. The composition of these formulations varied slightly, however all contained 4% (w/w) of the notified chemical.

9.4.1 Irritancy/Sensitisation Test (12)

Number:	52; ages 18 - 69
Observation period:	24 hours after induction and 24, 48, and 72 hours after challenge
Sample application:	0.2 - 0.3 mL of the test sample (containing 4% Citmol 316) was applied to each subject using a semi occlusive patch; 8 induction applications were made during weeks 1 and 2, followed by a 2 week hiatus; a single challenge application was made on sites adjacent to the induction sites in week 5
Procedure:	each subject was patched with a total of 6 samples on the lateral aspect of the upper arms (3 sites/arm)
Scoring system:	induction and challenge patches were worn for 24 hours and reactions of the test sites were scored according to a pre-determined scoring system
Deviation from protocol:	7 subjects were dropped for reasons unrelated to the study
Test method:	according to Marva (12)
Result:	not a skin irritant/sensitiser in humans

9.4.2 Phototoxicity Test (13)

Number:	28; ages 18 - 69
Observation period:	24 hours after each induction application
Sample application:	0.1 mL of the test sample (containing 4% Citmol 316) was applied to each subject using a semi occlusive patch
Procedure:	24 hours after application irradiated for 20

	minutes with a lamp output range 4.4 mW/cm^2 for UVA exposure
Scoring system:	the reactions of the test sites were examined initially 24 hours after application, soon after irradiation, 24 and 48 hours thereafter and scored according to a pre-determined scoring system; all patches were worn for 24 hours
Deviation from protocol:	1 subject was dropped for reasons unrelated to the study
Test method:	according to Marva (13)
Result:	no phototoxic potential observed under UVA light

9.4.3 Evaluation of Photoallergy and Contact Allergy (14)

Number:	26
Experimental design	
Induction:	12 repetitive applications of the test material (containing 4% Citmol 316) made on duplicate sets of sites for 3 weeks (4 applications per week); ten minutes following removal of the patches, one set of replicate sites was irradiated with UVA and UVB; the second set of sites served as a control
Rest:	two weeks rest period following induction
Challenge:	sets of duplicate contact patches made on previously untreated sites; one of the replicate patch sites in each set was irradiated with UVA (16 - 20 joules)
Rechallenge:	the challenge schedule was repeated in selected subjects
Sample application:	0.2 mL of the test sample was applied on each subject using a semi-occlusive patch
Scoring system:	the reactions of the test sites were examined after induction and challenge

Deviation from protocol:	1 subject was dropped for reasons unrelated to the study
Test method:	according to Laino (14)
Result:	no contact allergy or photoallergy was observed

9.4.4 Use - Irritancy Test (15)

Number:	26; ages 18 - 69 (females)
Observation period:	Study period covered 14 days; subjects' skin examined on days 0, 7 and 14
Sample application:	Product containing 4% Citmol 316 was applied once daily all over the body following bath or shower for 14 days
Procedure:	subjects examined every 7 days
Scoring system:	induction and challenge patches were worn for 24 hours and reactions of the test sites were scored according to a pre-determined scoring system
Deviation from protocol:	one subject was absent for the mid-test exam; 5 subjects used the product more than instructed; one subject discontinued use after 11th application.
Test method:	according to Marva (15)
Result:	irritancy on use was inconclusive

9.5 Overall Assessment of Toxicological Data

The notified chemical exhibited low acute oral (LD_{50} > 40 000 mg/kg) toxicity in rats. It was a slight skin irritant in rabbits, but no skin irritancy was observed in a repeat dermal application test in guinea pigs. Citmol 316 was not an eye irritant in rabbits or a skin sensitiser in guinea pigs. Inhalational toxicity tests were not provided. Dermal toxicity and repeat dose toxicity data were also not provided, however, clinical observation during dermal application irritation studies indicated no signs of systemic toxicity. No mutagenicity was observed in bacteria and no clastogenicity was observed in Chinese hamster cells *in vitro*.

The notified chemical was not a skin sensitiser in humans. No phototoxic

potential, contact allergy, photoallergy or skin irritancy was observed in humans. Several people were observed to have positive irritation and allergic reactions in a use-irritancy test with a formulation containing 4% of the notified chemical, although it is possible that the adverse reactions seen in the use-irritancy test were due to another ingredient in the preparation or factors unrelated to the test product.

Based on the animal and human data provided by the notifier, Citmol 316 would not be classified as hazardous according to Worksafe's *Approved Criteria for Classifying Hazardous Substances* (16).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Data on the ecotoxicity, biodegradation or bioaccumulation of Citmol 316 have not been provided by the notifier, although they are required by the Act.

The notifier is unable to locate any data and has provided arguments based on the chemical's low water solubility, its physical and chemical stability, its lack of toxicity to humans and no reported environmental problems with the use of the chemical in Europe and America over the past 15 years. An invalid argument claiming low ecotoxicity based on translation of mammalian toxicity is also presented. A search of the US EPA's ASTER data base provided no ecotoxicological information.

The very low water solubility suggests that Citmol 316 should not have significant aquatic toxicity.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The hazard posed by the end use product appears to be small in that it will be incorporated at a small percentage (< 4%) in a range of cosmetic products the use of which might be expected to be widespread across Australia. Release of the notified chemical to the environment may occur as a result of formulation and use of the cosmetic products in which it is used. Most of this is expected to be landfilled after removal from the body by paper towels or cotton wool.

As a worst case, an environmental concentration of 0.4 ppb is predicted if 10% of the imported chemical remains suspended in sewage waters (assuming: 4250 kg maximum annual use, an Australian population of 18 million and a daily per capita waste water discharge of 150 L). However, most is expected to adsorb to sewerage sludge which will be landfilled or incinerated. In landfill the substance is not expected to be mobile or degrade due its low water solubility. Little exposure to natural waterways and low aquatic is also expected. Hence, the overall environmental hazard of the chemical can be rated as negligible.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Based on the animal and human data provided by the notifier, Citmol 316 would not be classified as hazardous according to Worksafe's *Approved Criteria for Classifying Hazardous Substances* (16). However, inconclusive results in a use-irritancy test with a formulation containing 4% of the notified chemical and a slight dermal irritation response in rabbits indicates a possible risk of skin irritancy.

The occupational health risk posed by this chemical to transport and warehouse workers is expected to be negligible, due to the low toxicity of the chemical, and the lack of exposure under normal circumstances.

Dermal exposure to the notified chemical may occur when workers dispense the pure chemical, prior to formulation. Dermal exposure to the notified chemical may also occur at other stages of the formulation process, however, the chemical will be at a reduced concentration in formulated products. Due to the low toxicity and low irritancy of the chemical, the occupational risk posed to all workers during the formulation process is expected to be low. The risk to laboratory workers performing quality control or research work is also expected to be low, although impermeable gloves are recommended for all workers when handling the notified chemical in pure form due to the potential skin irritancy.

The occupational risk of skin irritation posed to sales staff is also expected to be low, based on results of tests performed on animals and humans. In addition, they will only be exposed to low concentrations (4% or less) of the notified chemical.

Cosmetic use of the notified chemical will result in considerable direct dermal exposure of the public to the notified chemical. However, the toxicological properties of the notified chemical and the low concentration (up to 4%) present in cosmetic products suggest that such use should present only low risk to public health.

13. RECOMMENDATIONS

To minimise occupational exposure to Citmol 316 the following guidelines and precautions should be observed:

- Workers handling the notified chemical in pure form should wear impermeable gloves conforming to Australian Standard 2161 (17) to reduce risk of dermal irritation;

- Spillage of the notified chemical should be avoided, spillages should be cleaned up promptly with absorbents which should then be put into containers for disposal;

- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the Material Safety Data Sheet (MSDS) should be easily accessible to employees.

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* (18).

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.

Secondary notification will be required if uses are proposed which would lead to more significant exposure to natural waterways. This should include full results of physico-chemical environmental fate and toxicity as required by the schedule to the Act.

16. REFERENCES

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4. Walker DJ, 1991, *Citmol 316 (Tri-Isocetyl Citrate): Fourteen-Day Repeat Application Dermal Irritation Study In The Guinea Pig (Non-Occlusive).* Project number 357/1, data on file, Safepharm Laboratories Limited, Derby.

5. Walker, DJ, 1991, *Citmol 316 (Tri-Isocetyl Citrate): Adjuvant/Patch Contact Sensitisation Study In The Guinea Pig (Sato et al).* Project number 357/2, data on file, Safepharm Laboratories Limited, Derby.

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7. Draize JH, 1959, 'Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics', *Association of Food and Drug Officials of the US,* **49**.

8. Sato Y *et al.,* 1981, 'A modified technique of guinea pig testing to identify delayed hypersensitivity allergens', *Contact Dermatitis,* ***7.***

9. Jenkinson PC, 1991, *Citmol 316 (Tri-Isocetyl Citrate): Reverse Mutation Assay 'Ames Test' Using Salmonella typhimurium And Escherichia coli,* Project number 357/3, data on file, Safepharm Laboratories Limited, Derby.

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13. Marva SK, 1991, *Phototoxicity Study.* Project number: GMEH #2995, data on file, Gillette Medical Evaluation Laboratories.

14. Laino J, 1991, *Evaluation Of Human Photoallergy And Contact Allergy.* Project number 91-4112-74 Revised report 1, data on file, Hill Top Research Inc, New Jersey.

15. Marva SK, 1991, *Use-irritancy Study.* Project number: GMEH #3017, data on file, Gillette Medical Evaluation Laboratories.

16. National Occupational Health and Safety Commission 1994, *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(1994)], Australian Government Publishing Service, Canberra.

17. Standards Australia 1978, *Australian Standard 2161-1978, Industrial Safety Gloves and Mittens (excluding electrical and medical gloves),* Standards Association of Australia Publ., Sydney.

18. National Occupational Health and Safety Commission 1994, *National Code of Practice for the Preparation of Material Safety Data Sheets* [NOHSC:2011(1994)], Australian Government Publishing Service, 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