

File No: NA/534

November 1997

**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION
AND ASSESSMENT SCHEME**

FULL PUBLIC REPORT

LR-147

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 and the assessment of public health is conducted by the Department of Health and Family Services.

For the purposes of subsection 78(1) of the Act, copies of this full public report may be inspected by the public at the Library, Worksafe Australia, 92-94 Parramatta Road, Camperdown NSW 2050, between the following hours:

Monday - Wednesday	8.30 am - 5.00 pm
Thursday	8.30 am - 8.00 pm
Friday	8.30 am - 5.00 pm

Copies of this full public report may also be requested, free of charge, by contacting the Administration Coordinator on the fax number below.

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

Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT**LR-147****1. APPLICANT**

Tektronix Australia Pty Limited of 80 Waterloo Road NORTH RYDE NSW 2113 has submitted a standard notification statement in support of their application for an assessment certificate for LR-147.

2. IDENTITY OF THE CHEMICAL

LR-147 is not considered to be hazardous based on the nature of the chemical and the data provided. Therefore the chemical name, CAS number, molecular and structural formulae, molecular weight, spectral data and details of exact import volume have been exempted from publication in the Full Public Report and the Summary Report.

Trade Name:	LR-147
Other Names:	charge control agent (0-2%) in QTC-29DE
Method of Detection and Determination:	ultraviolet/visible (UV/Vis) spectrophotometry, infrared (IR) spectroscopy and nuclear magnetic resonance (NMR) spectroscopy

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	white powder
Melting Point:	decomposes without melting at 355°C
Specific Gravity:	1.3735
Vapour Pressure:	$< 1.3 \times 10^{-9}$ kPa at 25°C (estimate)
Water Solubility:	4 380 mg.L ⁻¹ at 20°C and pH 4
Partition Co-efficient (n-octanol/water):	$\log P_{ow} = 0.0611$ at 24°C

Hydrolysis as a Function of pH:	$T_{1/2}$ at pH 4.0, 7.0 and 9.0 > 1 year
Adsorption/Desorption:	$\log K_{oc} < 2.41$ at 20°C
Dissociation Constant:	not determined
Surface Tension:	65.6 mN.m ⁻¹ at 22°C for a 1 010 mg.L ⁻¹ solution
Fat Solubility:	7.7 mg per 100 g fat at 37°C
Particle Size:	mass median diameter 20.65 µm
Flash Point:	not determined
Flammability Limits:	not highly flammable
Autoignition Temperature:	> 400°C
Explosive Properties:	not explosive
Reactivity/Stability:	the notified chemical does not have oxidising properties

Comments on Physico-Chemical Properties

Tests were performed according to EEC/OECD test guidelines (1, 2) at facilities complying with OECD Principles of Good Laboratory Practice.

The physico-chemical properties provided by the notifier are in full accord with expectations for a chelate compound of the indicated chemical structure. The compound is highly water soluble, stable to hydrolysis in the environmentally significant pH range and partitions mainly into the water phase. The compound is not surface active and fat solubility is low.

4. PURITY OF THE CHEMICAL

Degree of Purity: high

5. USE, VOLUME AND FORMULATION

The notified chemical will not be manufactured in Australia. LR-147 will be imported as a component (at a concentration of 2%) of a fully formulated toner product ready for use in photocopying, printing and facsimile equipment. Less than one tonne of the notified chemical will be imported per annum for each of the first five years.

6. OCCUPATIONAL EXPOSURE

Toner products containing the notified chemical will be imported in the form of pre-packed cartridges containing 210 g of toner. Waterside, warehouse and transport workers are unlikely to be exposed to the notified chemical under normal circumstances.

Office workers may be minimally exposed to the notified chemical during the operation and maintenance of photocopiers, facsimile machines and laser printers which use toner containing the notified chemical. The pre-packaged cartridges are sealed and worker exposure to the contained product should be minimised through use of the replacement procedures recommended by the manufacturer. The toner cartridges are designed so that no release of the contents can occur until a shutter or seal tape is removed, however, dermal exposure may occur if toner containing the notified chemical is spilled while changing cartridges. While replenishing the toner in office equipment, the operator fits the cartridge to the machine and opens the shutter which allows transfer of the contents to storage within the machine. Inhalation exposure to the notified chemical is expected to be low, as the notified chemical makes up less than 2% of the final toner product. In addition, the mass median diameter of the particles of the notified chemical is just over 20 μm , which falls outside the range considered respirable (cited in (3)). Contact with paper printed with the toners containing the notified chemical is unlikely to result in dermal exposure, as the notified chemical will be fixed to the paper as part of the toner product.

Office equipment repair personnel have the potential to come into contact with the notified chemical more often than office workers, although exposures are still expected to be minimal, due to the design of the toner cartridges.

7. PUBLIC EXPOSURE

End users of the product containing the notified chemical will have minimal exposure since the cartridge is sealed and will be inserted directly into the photocopier or printer. Contact with the cured toner containing the notified chemical can occur when handling printed paper, but exposure is not expected, as the notified chemical will be bound to the paper. Dermal exposure to the toner containing the notified chemical may occur during servicing or clearing paper jams, but this would occur infrequently. In addition, dermal adsorption should be minimal considering the relatively large particle size and low octanol/water partition coefficient of the notified chemical.

8. ENVIRONMENTAL EXPOSURE

Release

There are two principal pathways of release of the notified substance into the environment. Firstly residual unused toner - *ie* that remaining in the spent cartridges after most of the material has been used - will be disposed of as office waste and will be either incinerated or disposed of to landfill. In the normal course of usage, this should be minimal, since it is expected that only between 5 and 20 g of toner product (*ie* between 2.5 and 10%) would remain in the spent cartridges, and since the notified chemical constitutes only 2% of the product it is estimated that each spent cartridge has the potential to contribute from between 0.1 and 0.4 g of the notified compound to the environment via this route. It is anticipated that the spent toner cartridges would be disposed of into landfill. However, release of the residual toner should occur only after destruction of the integrity of the cartridge.

In normal use the product will be incorporated into a thermo-cured resin (*ie* the print) and firmly bound to the paper substrate, and hence would be released to the environment through disposal of the waste paper. The anticipated fate of the material would be associated with that of the paper, and is described below.

Fate

The majority of the notified chemical will be associated with the print and bound strongly to paper. Waste paper disposal is effected either through high temperature incineration, recycling or deposition into landfill.

High temperature incineration would destroy the compound with evolution of oxides of carbon and production of boron oxides which would be assimilated into ash. Similarly, it is expected that during the repulping and bleaching procedures employed during paper recycling the material would be either destroyed chemically or be incorporated into waste sludge, although since the compound has appreciable water solubility some may remain with aqueous waste streams generated during recycling. Waste sludge from the recycling plants would be either incinerated or disposed of to landfill, while aqueous waste would be comprehensively treated prior to discharge.

Some waste paper may be disposed of directly to landfill, and although only slowly hydrolysable and not readily bio-degradable, it is anticipated that prolonged residence in an active landfill environment would eventually degrade the notified substance.

The material is not readily biodegradable, and the ready biodegradability test of OECD Guideline 301D (2) indicated only 27% degradation after 28 days.

Despite the low molecular weight, the ionic nature of the substance, relatively high water solubility and low oil/water partition coefficient indicate that the compound will not accumulate appreciably in biological tissue.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of LR-147

<i>Test</i>	<i>Species</i>	<i>Outcome</i>	<i>Reference</i>
acute oral toxicity	rat	LD ₅₀ > 2 000 mg.kg ⁻¹	(4)
acute dermal toxicity	rat	LD ₅₀ > 2 000 mg.kg ⁻¹	(5)
skin irritation	rabbit	slight irritant	(6)
eye irritation	rabbit	slight irritant	(7)
skin sensitisation	guinea pig	non-sensitiser	(8)

9.1.1 Oral Toxicity (4)

<i>Species/strain:</i>	rat/Sprague-Dawley
<i>Number/sex of animals:</i>	5/sex
<i>Observation period:</i>	14 days
<i>Method of administration:</i>	gavage
<i>Clinical observations:</i>	common signs of systemic toxicity noted were hunched posture and lethargy with additional signs of decreased respiratory rate; surviving animals recovered 24 hours after dosing
<i>Mortality:</i>	one male died on the day of dosing
<i>Morphological findings:</i>	no abnormalities were noted for animals that survived the dosing; the animal that died on the day of dosing had haemorrhagic lungs, dark liver, dark kidneys and haemorrhage of the gastric mucosa
<i>Test method:</i>	similar to OECD guidelines (2)
<i>LD₅₀:</i>	> 2 000 mg.kg ⁻¹
<i>Result:</i>	the notified chemical is of low acute oral toxicity to rats

9.1.2 Dermal Toxicity (5)

<i>Species/strain:</i>	rat/Sprague-Dawley
<i>Number/sex of animals:</i>	5/sex
<i>Observation period:</i>	14 days
<i>Method of administration:</i>	dose of 2 000 mg.kg ⁻¹ of the notified chemical was applied to an area of shaved skin for 24 hours under an occlusive dressing
<i>Clinical observations:</i>	no signs of systemic toxicity were observed; desquamation was noted at the treatment sites of four females three to six days after dosing and persisted in two females seven days after dosing
<i>Mortality:</i>	nil
<i>Morphological findings:</i>	nil
<i>Test method:</i>	similar to OECD guidelines (2)
<i>LD₅₀:</i>	> 2 000 mg.kg ⁻¹
<i>Result:</i>	the notified chemical is of low acute toxicity when applied dermally to rats

9.1.3 Inhalation Toxicity

This information was not provided by the notifier

9.1.4 Skin Irritation (6)

<i>Species/strain:</i>	rabbit/New Zealand White
<i>Number/sex of animals:</i>	3 males
<i>Observation period:</i>	72 hours
<i>Method of administration:</i>	0.5 g of the test material, moistened with 0.5 mL distilled water was applied under a gauze patch for a period of 4 hours
<i>Test method:</i>	similar to OECD guidelines (2)
<i>Draize scores (9) (see Attachment 1 for Draize</i>	one animal developed erythema and oedema (Draize score of 1) by the 24 hour

scales): reading;

oedema had cleared by 48 hours and erythema had disappeared by day 7

Result: the notified chemical is a slight irritant to the skin of rabbits

9.1.5 Eye Irritation (7)

Species/strain: rabbit/New Zealand White

Number/sex of animals: 3 males

Observation period: 72 hours for two of the animals, 7 days for the third animal.

Method of administration: 0.1 mL of the test solution was placed into the conjunctival sac of the right eye; the left eye was used as a control; animals 2 and 3 were administered one drop of local anaesthetic (ophtaine) into each eye 1-2 minutes before dosing

Draize scores (9) of unirrigated eyes:

	Time after instillation														
Animal	1 hour		1 day		2 days		3 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	0	0	1	3	1	2	1	1	0	0					
2	0	0	0	0	0	0	0	0	-	-					
3	0	0	0	0	0	0	0	0	-	-					
Iris															
1		1		1		1		0		0					
2		0		0		0		0		-					
3		0		0		0		0		-					
Conjunctiv a	r ^c	c ^d	d ^e	r ^c	c ^d	d ^e	r ^c	c ^d	d ^e	r ^c	c ^d	d ^e	r ^c	c ^d	d ^e
1	2	2	3 ^f	2	2	3	2	2	1	1	1	0	0	0	0
2	1	1	1 ^f	1	0	0	0	0	0	0	0	0	-	-	-
3	1	0	1 ^f	0	0	0	0	0	0	0	0	0	-	-	-

¹ see Attachment 1 for Draize scales

^a opacity ^b area ^c redness ^d chemosis ^e discharge

^f residual test material around the treated eye

Test method: similar to OECD guidelines (2)

Result: the notified chemical was a slight irritant to the rabbit eye

9.1.6 Skin Sensitisation (8)

Species/strain: guinea pig/Dunkin-Hartley

Number of animals: 20 test; 10 control

Induction procedure: day 0 - intradermal induction: three pairs of injections (0.1 mL) were made on the shoulder region of each animal:

- aqueous v/v Freund's Complete Adjuvant (FCA)(1:1)
- 0.5% (w/v) of notified chemical in arachis oil BP
- 0.5% (w/v) of notified chemical in arachis oil BP/FCA mixture (1:1);

day 7 - topical induction; occluded application of 0.2-0.3 mL of notified chemical with arachis oil (50% w/w) for 48 hours

Challenge procedure: day 21 - 0.1 - 0.2 mL of the notified chemical in arachis oil BP (10 and 25% (w/w)) was applied to the shaved right flank of each animal by means of an occluded patch

Comments: one test animal was found dead on day 13; the cause of death was not determined but was considered to be unrelated to treatment with the test material

Challenge outcome:

Challenge concentration	Test animals		Control animals	
	24 hours*	48 hours*	24 hours	48 hours
10%	0/19**	0/19	0/10	0/10
25%	0/19	0/19	0/10	0/10

* time after patch removal

** number of animals exhibiting positive response

Test method: similar to OECD guidelines (2)

Result: the notified chemical was not a skin sensitiser when tested in guinea pigs

9.2 Repeated Dose Toxicity (10)

Species/strain: rat/Sprague-Dawley

Number/sex of animals: 5/sex

Method of administration: oral; gavage

Dose/Study duration:: three dose groups were used; vehicle was arachis oil BP; duration was 28 days

control: 0 mg.kg⁻¹.day⁻¹
low dose: 150 mg.kg⁻¹.day⁻¹
mid dose: 400 mg.kg⁻¹.day⁻¹
high dose: 1 000 mg.kg⁻¹.day⁻¹

an additional 10 animals (5/sex) included in the control and high dose groups were maintained for a further 14-day recovery period prior to sacrifice

Clinical observations: mid and low dose animals showed no signs of toxicity during the study; high dose animals of either sex showed isolated incidents of increased salivation after day 5, together with fur wetting and red/brown staining of the external body surface; one high dose female developed hunched posture, pilo-erection, decreased respiratory rate, lethargy and ptosis by day 27; following dosing, deterioration continued and the animal was killed *in extremis*

Clinical chemistry/Haematology mid and low dose animals showed no treatment-related changes in blood chemistry or haematological parameters; high dose animals showed increases in plasma alkaline phosphatase; male animals in this group showed increases in aspartate aminotransferase and bilirubin while both cholesterol and triglycerides were slightly elevated in females; plasma alanine aminotransferase was also slightly raised in all animals in the high dose group;

treatment-related changes had regressed completely after 14 days without treatment; all animals showed a reduction in haemoglobin concentration and haematocrit; reductions in mean corpuscular haemoglobin and mean corpuscular volume suggest that the anaemia was microcytic and hypochromic in nature; cessation of treatment resulted in complete recovery by day 14

Histopathology:

high dose animals of either sex had a statistically significant increase in both absolute and relative liver weight compared with controls; several animals had a pale liver at the end of the treatment period; treatment-related hepatic changes were observed including hepatocyte enlargement and increased hepatocyttoplasmic density; these changes were considered to be adaptive in nature and regressed upon cessation of treatment

females in the high dose group also exhibited thickening of the glandular region of the stomach and high dose males showed a slight but statistically significant increase in spleen weight (relative to body weight)

Test method:

similar to OECD guidelines (2)

Result:

daily oral administration of the notified chemical for a 28-day period resulted in mild anaemia in high dose groups (1 000 mg.kg⁻¹.day⁻¹) and adaptive liver changes in all dose groups; these effects were no longer apparent following a 14-day recovery period

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (11, 12)

Strains:

TA1535, TA1537, TA98 and TA100, *Escherichia coli* WP2uvrA (both tests)

Concentration range:

0 - 5000 µg per plate; assays were carried out in the presence or absence of rat liver S9 fraction

<i>Test method:</i>	similar to OECD guidelines (2)
<i>Result:</i>	the notified chemical was not mutagenic in either of the assays in the bacterial strains tested; the presence or absence of metabolic activation provided by rat liver S9 fraction was tested in both assays

9.3.3 Chromosomal Aberration Assay in Chinese hamster lung cells (13)

<i>Dosing schedule:</i>	cells without S9 metabolic activation were exposed to four dose periods (6, 12, 24 and 48 hour) of the notified chemical
	cells with S9 metabolic activation were exposed to two dose periods (4 and 6 hour) of the notified chemical, followed by 18 hour and 8 hour incubation periods, respectively
	three dose levels from each treatment case were evaluated for chromosomal aberrations
<i>Test method:</i>	similar to OECD guidelines (2)
<i>Result:</i>	the notified chemical was not clastogenic in Chinese hamster lung cells <i>in vitro</i>

9.4 Overall Assessment of Toxicological Data

The notified chemical was of low oral ($LD_{50} > 2\,000\text{ mg.kg}^{-1}$) and dermal ($LD_{50} > 2\,000\text{ mg.kg}^{-1}$) toxicity when tested in rats. When tested in rabbits it was a slight irritant to both the skin and the eye. The notified chemical was not a skin sensitiser in guinea pigs.

A 28-day repeat dose oral toxicity study showed that at high dose levels ($1\,000\text{ mg.kg}^{-1}.\text{day}^{-1}$) induced mild anaemia. Hepatic effects were also seen at all dose levels, although these were considered to be adaptive in nature, as there were no corresponding signs of degeneration.

In the presence or absence of metabolic activation, the notified chemical was not mutagenic in bacteria and it did not produce chromosomal aberrations in the Chinese hamster lung cells *in vitro*

On the basis of the submitted data, the notified chemical would not be classified as hazardous in accordance with the *Approved Criteria for Classifying Hazardous Substances* (14).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The following ecotoxicity studies have been supplied by the notifier - tests were carried out using OECD Test Guideline Methods (2).

Test	Species/ Method	Results (Concentrations cited are nominal)
Acute Toxicity (static test)	Rainbow Trout (method C1 OECD TG 203)	LC ₅₀ (96 hour) > 100 mg.L ⁻¹
Acute Immobilisation (static test)	<i>Daphnia magna</i> . (method C2 OECD TG 202)	Immobilisation: EC ₅₀ (48 hour) > 100 mg.L ⁻¹
Growth Inhibition (Biomass)	Algae <i>Scenedesmus subspicatus</i> (method C3 OECD TG 201)	E _b C ₅₀ (72 hour) > 100 mg.L ⁻¹
Respiration Inhibition (static test)	Aerobic Waste Water Bacteria (method OECD TG 209)	IC ₅₀ (3 hour) > 1000 mg.L ⁻¹

In the case of the fish toxicity tests, the NOEC (96 hour) was greater than 100 mg.L⁻¹. For toxicity to water fleas, the NOEC (48 hour) was greater than 100 mg.L⁻¹, and similarly in tests on inhibition of algal biomass the NOEC (72 hour) was greater than 100 mg.L⁻¹. In tests of effects of the compound on respiration inhibition of sewage sludge, a 38% decrease in respiration was observed at 3 hours at an exposure to 1 000 mg.L⁻¹ of the test substance. The notified substance is practically non toxic to the range of aquatic organisms tested against.

For all the above biological tests, the indicated concentrations of the test substance were near nominal concentrations.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The environmental hazard from the notified chemical appears to be minimal, and in light of the ecotoxicological data provided, even gross spillage of the individual toner containing cartridges (eg transport related accident) should cause little environmental damage from the contained LR-147 material.

In the event of accidental spillage or release of the toner, the clean-up operation would probably entail disposal to landfill.

The 'long term' fate of the majority of the notified material is expected to be either through paper recycling, landfill disposal or incineration of waste paper. In all three cases it is anticipated that the material would be destroyed either through the action of a vigorous chemical environment or through (admittedly slow) biological or abiotic processes. Even in the absence of substantial degradation, the relatively

low usage rate and diffuse nature of disposal patterns would indicate very slow release into the wider environment, and this at low concentrations.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Waterside, warehouse and transport workers will be only be exposed to the notified chemical in the event of an accident or damage to packaging. The occupational health risk to these workers is negligible, particularly considering the low concentration of the notified chemical in toner products and the low hazard presented by the chemical.

Office workers are not expected to come into contact with the notified chemical under normal circumstances. The design of the toner cartridges is such that exposure to the notified chemical should be minimal, even when changing toner cartridges. Minor dermal exposure may occur if a small quantity of toner is spilt while changing cartridges. If eye contact occurs, the notified chemical or other toner components may cause mild eye or skin irritation. There may be a low level of toner dust in the immediate vicinity of photocopiers, facsimile machines and laser printers when they are operating, although inhalation exposure to the notified chemical (which is at a concentration of < 2% within toners) is expected to be negligible. Exposure to the notified chemical is not expected to occur once the toner is bound to paper. Based on the low toxicological hazard presented by the chemical and the expected very low exposures, the health risk posed to office workers is negligible.

A low occupational health risk exists for repair workers, who may be dermally or inhalationally exposed to low concentrations of the notified chemical (possibly more frequently than office workers) when repairing office equipment.

Infrequent dermal exposure of end users to the toner containing the notified chemical may occur during servicing or clearing paper jams, but the relatively large particle size and low octanol/water partition coefficient of the notified chemical indicate that dermal absorption would be minimal. As discussed above, although the notified chemical causes slight skin irritation in rabbits, the level of the notified chemical in the toner is low and the minor dermal exposure during servicing or clearing paper jams is unlikely to cause irritation to the skin. Public exposure to the notified chemical is possible in the event of an accident during transport and storage, but the likelihood of a substantial spill occurring is low in view of the packaging. Based on the information provided and the intended use, the notified chemical does not appear to pose a significant risk to public health.

13. RECOMMENDATIONS

To minimise occupational exposure to LR-147 the following guidelines and precautions should be observed:

- Work areas around photocopiers, facsimile machines and laser printers should be well ventilated and good work practices should be implemented to avoid the generation of dusts;
- Spillage of toner products should be avoided and good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the Material Safety Data Sheet (MSDS) and/or information about the toners containing LR-147 should be easily accessible to employees.

14. MATERIAL SAFETY DATA SHEET

The MSDS for a product containing the notified chemical was provided in accordance with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (15).

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

1. European Economic Community (EEC) 1992, 'Methods for the Determination of Physico-Chemical Properties', in *EEC Directive 92/69, Annex V, Part A, EEC Publication No. L383*, EEC.
2. Organisation for Economic Co-operation and Development 1995-1996, *OECD Guidelines for the Testing of Chemicals on CD-Rom*, OECD, Paris.
3. National Occupational Health and Safety Commission 1995, 'Adopted National Exposure Standards for Atmospheric Contaminants in the Occupational Environment, [NOHSC:1003(1995)]', in *Exposure Standards for Atmospheric Contaminants in the Occupational Environment: Guidance Note and National Exposure Standards*, Australian Government Publishing Service, Canberra.
4. Tuffnell, P. 1992, *LR-147: Acute Oral Toxicity (Limit Test) in the Rat*, Project no., 256/38, Safepharm Laboratories Limited, UK.

5. Tuffnell, P. 1992, *LR-147: Acute Dermal Toxicity (Limit Test) in the Rat*, Project no., 256/39, Safepharm Laboratories Limited, UK.
6. Tuffnell, P. 1992, *LR-147: Acute Dermal Irritation Test in the Rabbit*, Project no., 256/40, Safepharm Laboratories Limited, UK.
7. Tuffnell, P. 1992, *LR-147: Acute Eye Irritation Test in the Rabbit*, Project no., 256/43, Safepharm Laboratories Limited, UK.
8. Tuffnell, P. 1992, *LR-147: Magnusson and Kligman Maximisation Study in the Guinea Pig*, Project no., 256/41, Safepharm Laboratories Limited, UK.
9. Draize, J.H. 1959, 'Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics', *Association of Food and Drug Officials of the US*, vol. 49, pp. 2-56.
10. Wragg, M. 1993, *LR-147: Twenty-eight Day Sub-Acute Oral (Gavage) Toxicity Study in the Rat*, Project no., 256/52, Safepharm Laboratories Limited, UK.
11. Nishiuchi, M. 1991, *Ames Salmonella/Microsome Plate Test - Chemical: LR-147*, Project no., MG0030, Hist Science Laboratories Co Ltd, Japan.
12. Thompson, P. 1993, *LR-147: Reverse Mutation Assay 'Ames Test' Using Salmonella typhimurium and Escherichia coli*, Project no., 256/53, Safepharm Laboratories Limited, UK.
13. Wright, N. 1993, *LR-147: Metaphase analysis in CHL Cells in vitro*, Project no., 256/54, Safepharm Laboratories Limited, UK.
14. National Occupational Health and Safety Commission 1994, *Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(1994)]*, Australian Government Publishing Service, Canberra.
15. 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