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August 1998

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

LR-147

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

LR-147

1. APPLICANT

Minolta Business Equipment Australia Pty Ltd of Unit 9, 372 Eastern Valley Way CHATSWOOD NSW 2067 and Lexmark International Inc of 12A Rodborough Road FRENCHS FOREST NSW 2086 have submitted a limited 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 toxicological 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 products containing LR-147 include M32F, M32F-Y, M32F-M and M32F-C
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 at 23°C
Vapour Pressure:	< 1.3×10^{-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:	$T_{1/2}$ > 1 year at 25°C, less than 10% hydrolysis after 5 d at 50°C at pH 4.0, 7.0 and 9.0
Adsorption/Desorption:	log K_{oc} ≤ 2.41 at 20°C
Dissociation Constant:	not determined due to complex mode of dissociation
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 mean diameter 19.04 µm; mass median diameter 20.65 µm; 10.6% w/w < 10.3 µm
Flash Point:	not applicable
Flammability Limits:	not highly flammable (in EC Flammability of solids test) combustible
Autoignition Temperature:	> 400°C
Explosive Properties:	not explosive
Reactivity/Stability:	stable, no oxidising properties

Comments on Physico-Chemical Properties

Tests were performed according to OECD/EEC (European Economic Community (EEC), 1992) (Organisation for Economic Co-operation and Development, 1995-1996) test guidelines at facilities complying with OECD Principles of Good Laboratory Practice (GLP).

Full study reports were submitted. The physico-chemical properties provided by the notifier are consistent 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
Toxic or Hazardous Impurities:	none known

5. USE, VOLUME AND FORMULATION

The notified chemical will not be manufactured in Australia. LR-147 will be imported as a component (less than 1%) 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 the first five years.

Only one cartridge design will be imported, although other types may be introduced in the future for different copier machines or printers.

The individual colour cartridges will be interchanged with spent ones in electrophotocopying machines, presumably in the main by office staff. The toner cartridges are sealed and designed so that no release of the contents can occur till the shipping tape is removed.

6. OCCUPATIONAL EXPOSURE

Toner products containing the notified chemical will be imported in the form of pre-packed cartridges containing 210-220 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 spilt while changing cartridges. Spent cartridges are expected to retain approximately 50 g of toner. 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. The mass mean diameter of particles of the notified chemical is 20.65 μm, however, approximately 10% of particles are less than 10 μm in diameter, that is, approximating the respirable range of 0 to 7 μm (National Occupational Health and Safety Commission, 1995). Particle size data on the product has not been provided, however, as the formulated toner product contains less than 2% of the notified chemical, inhalational exposure to the notified chemical is expected to be low. 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 controlled, due to the design of the toner cartridges.

7. PUBLIC EXPOSURE

The notified chemical is imported as a component of an ink preparation contained in toner cartridges for use by the public in photocopying machines or printers. There is no human exposure to the notified chemical during normal use of the photocopier or printer, however

intermittent exposure of the public or trained engineers to the toner containing the notified chemical is possible during the clearing of paper jams and during servicing. Toner is melted by the heat roller and is absorbed into the paper, where it sticks. No public exposure is expected from handling of the printed sheets as the toner is bound in the structure of the paper. The amount of notified chemical that may be lost to the environment during handling and use is minimal.

8. ENVIRONMENTAL EXPOSURE

Release

The notifier states that the toner (with the notified chemical) will be fused to the paper in a water insoluble matrix during copying. This use offers little potential for release into the environment, other than through the disposal of waste paper. When the copier requires more toner of a particular colour, the cartridge is simply replaced. The exchange process is designed to minimise toner losses.

The majority of the notified chemical will be associated with the fused toner and will be strongly bound to the paper. Its release will be associated with the fate of the waste paper.

The majority of emptied cartridges are expected to be disposed of with general office waste and placed into landfill. Release of toner, albeit minimal, will only occur after destruction of the integrity of the cartridge. The notifier has estimated the amount of toner in the cartridge when it is replaced to be approx. 50 g, or approximately 0.35 g of notified chemical.

Fate

Waste paper disposal is effected either through incineration, recycling or deposition into landfill. Incineration will destroy the compound with evolution of oxides of carbon and production of boron oxides that will be assimilated into ash.

The notifier has provided no data on the likely behaviour of the polymer during the paper recycling process. During such processes, waste paper is repulped using a variety of alkaline, dispersing and wetting agents, water emulsifiable organic solvents and bleaches. These agents enhance fibre separation, ink detachment from the fibres, pulp brightness and the whiteness of paper. It is expected that during the repulping and bleaching procedures employed during paper recycling, the chemical will be either destroyed chemically or be incorporated into waste sludge. However, as the chemical has appreciable water solubility, some may remain with aqueous waste streams generated during recycling. Waste sludge from the recycling plants will be either incinerated or disposed of to landfill, while aqueous waste should 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 (see below), it is anticipated that prolonged residence in an active landfill environment will eventually degrade the notified substance.

The material is not readily biodegradable, with the ready biodegradability test (OECD Test Guideline 301D: Closed bottle test) indicating only 27% degradation after 28 days (Sewell, 1992).

Despite the low molecular weight, the chemical should not accumulate appreciably in biological tissue due to the ionic nature of the substance, relatively high water solubility and low octanol/water partition coefficient (Connell, 1989).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of LR-147

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 2 000 $mg.kg^{-1}$	(Tuffnell, 1992a)
acute dermal toxicity	rat	LD_{50} > 2 000 $mg.kg^{-1}$	(Tuffnell, 1992b)
skin irritation	rabbit	slight irritant	(Tuffnell, 1992c)
eye irritation	rabbit	slight irritant	(Tuffnell, 1992d)
skin sensitisation	guinea pig	non-sensitiser	(Tuffnell, 1992e)

9.1.1 Oral Toxicity (Tuffnell, 1992a)

Species/strain:	rat/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	gavage
Clinical observations:	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
Mortality:	one male died on the day of dosing
Morphological findings:	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

Test method:	similar to OECD TG 401 (Organisation for Economic Co-operation and Development, 1995-1996)
LD_{50}:	> 2 000 $mg.kg^{-1}$
Result:	the notified chemical is of low acute oral toxicity in rats

9.1.2 Dermal Toxicity (Tuffnell, 1992b)

Species/strain:	rat/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	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
Clinical observations:	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
Mortality:	nil
Morphological findings:	nil
Test method:	similar to OECD TG 402 (Organisation for Economic Co-operation and Development, 1995-1996)
LD_{50}:	> 2 000 $mg.kg^{-1}$
Result:	the notified chemical is of low acute toxicity when applied dermally to rats

9.1.3 Inhalation Toxicity

No study was provided by the notifier.

9.1.4 Skin Irritation (Tuffnell, 1992c)

Species/strain:	rabbit/New Zealand White

Number/sex of animals:	3 males
Observation period:	72 hours
Method of administration:	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
Test method:	similar to OECD TG 404 (Organisation for Economic Co-operation and Development, 1995-1996)
Draize scores (Draize, 1959) (see Attachment 1 for Draize scales)*:*	one animal developed erythema and oedema (Draize score of 1) by the 24 hour 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 (Tuffnell, 1992d)

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 into each eye 1-2 minutes before dosing

Draize scores (Draize, 1959) of 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			-	
Conjunctiva	***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 TG 405 (Organisation for Economic Co-operation and Development, 1995-1996)

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

9.1.6 Skin Sensitisation (Tuffnell, 1992e)

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:

	Test animals		***Control animals***	
Challenge concentration	***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:	Magnusson and Kligman maximisation study similar to OECD TG 406 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	the notified chemical was not a skin sensitiser when tested in guinea pigs

9.2 Repeated Dose Toxicity (Wragg, 1993)

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 both sexes showed isolated incidents of increased salivation after day 5, together with fur wetting and red/brown staining of the external body surface; one high does 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 of both sexes and mid-dose males 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 high-dose 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
Terminal studies, including histopathology:	high dose animals of both sexes 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 hepatocytoplasmic density but no evidence of hepatocellular degeneration; the brain and kidney weights in high-dose males were increased and ovary weight in high-dose females was decreased; 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; high dose males showed a slight but statistically significant increase in spleen weight (relative to body weight)
Test method:	similar to OECD TG 407 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	under the conditions of the study, the NOEL is 150 $mg.kg^{-1}.d^{-1}$ based on the increase in the plasma level of alkaline phosphatase in males at 400 $mg.kg^{-1}.d^{-1}$; statistically significant changes in liver weight and haematological parameters were observed at 1 000 $mg.kg^{-1}.d^{-1}$

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Nishiuchi, 1991)

Strains:	*S. typhimurium* TA1535, TA1537, TA98 and TA100; *Escherichia coli* WP2*uvrA*
Concentration range:	0 - 5000 µg per plate; assays were carried out in the presence or absence of rat liver S9 fraction
Test method:	similar to OECD TG 471 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	the notified chemical was not mutagenic in either of the assays in the bacterial strains tested either with or without metabolic activation provided by rat liver S9 fraction

9.3.2 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Thompson, 1993)

Strains:	*S. typhimurium* TA1535, TA1537, TA98 and TA100; *Escherichia coli* WP2*uvrA*
Concentration range:	0 - 5000 µg per plate; assays were carried out in the presence or absence of rat liver S9 fraction
Test method:	similar to OECD TG 471 (Organisation for

Economic Co-operation and Development, 1995-1996)

Result: the notified chemical was not mutagenic in either of the assays in the bacterial strains tested either with or without metabolic activation provided by rat liver S9 fraction

9.3.3 Chromosomal Aberration Assay in Chinese Hamster Lung Cells (Wright, 1993)

Dosing schedule: cells without S9 metabolic activation were exposed to four dose periods (6, 12, 24 and 48 hour) dose rates were 0 – 234.4 $\mu g.mL^{-1}$ 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; dose rate were 0 – 468.75 $\mu g.mL^{-1}$

three dose levels from each treatment case were evaluated for chromosomal aberrations

solvent treatment groups were used as the negative controls; the positive controls included mitomycin C (MMC) at 75 $ng.mL^{-1}$ for cultures treated for 12, 24 or 48 hours in the absence of metabolising enzymes and cyclophosphamide (CP) at 10 $\mu g.mL^{-1}$ for cultures treated for 6 hours both with and without S9 mix and the 12 hour culture with S9 mix

Test method: similar to OECD TG 473 (Organisation for Economic Co-operation and Development, 1995-1996)

Result: one of the positive controls (CP) did not show a significant increase in aberrations in two of the dosing regimes, one with S9 and one without S9; however, as LR-147 did not induce any dose-related increases in cell aberration frequency or polyploid cell numbers at any of the six dose/time levels, it can be concluded that, under the conditions of the study, the notified chemical was not clastogenic to CHL cells *in vitro*

9.4 Toxicological Studies on M32F, M32F-Y, M32F-M and M32F-C

M32F, M32F-Y, M32F-M and M32F-C are some of the products containing the notified chemical. Acute oral toxicity and skin sensitisation studies on M32F, and *Salmonella typhimurium* reverse mutation assays on M32F-Y, M32F-M and M32F-C were included in the submission and summarised below.

Test	*Species*	*Product*	*Outcome*	*Reference*
acute oral toxicity	rat	M32F	LD_{50} > 2 000 $mg.kg^{-1}$	(Allen, 1996a)
skin sensitisation	guinea pig	M32F	non-sensitiser	(Allen, 1996b)

9.4.1 Oral Toxicity of M32F (Allen, 1996a)

Species/strain:	rat/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	gavage (vehicle: arachis oil)
Clinical observations:	no signs of systemic toxicity
Mortality:	none
Morphological findings:	no abnormalities were noted
Test method:	limit test, based on OECD TG 401 (Organisation for Economic Co-operation and Development, 1995-1996)
LD_{50}:	> 2 000 $mg.kg^{-1}$
Result:	M32F was of low acute oral toxicity in rats

9.4.2 Skin Sensitisation Study on M32F (Allen, 1996b)

Species/strain:	guinea pig/Dunkin-Hartley
Number of animals:	20 test; 10 control
Induction procedure:	day 1 – M32F (0.5 mL, 50% in arachis oil) was applied to the shorn left flank and covered with a strip of surgical adhesive tape and aluminum foil for 6 hours this induction was repeated on days 7 and 14

Challenge procedure: day 28 – M32F (0.5 mL, 25% or 50% in arachis oil) was applied to the shorn flank and covered with a strip of surgical adhesive tape and aluminum foil for 6 hours

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
25%	0/20**	0/20	0/10	0/10
50%	0/20	0/20	0/10	0/10

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

Test method: Buehler delayed contact hypersensitivity study based on OECD TG 406 (Organisation for Economic Co-operation and Development, 1995-1996)

Result: M32F was not a skin sensitiser when tested in guinea pigs

9.4.3 *Salmonella typhimurium* Reverse Mutation Assay on M32F-Y (Thompson, 1996a)

Strains: *S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100

Concentration range: 0 – 5 000 µg per plate; assays were carried out in the presence or absence of rat liver S9 fraction

Test method: similar to OECD TG 471 (Organisation for Economic Co-operation and Development, 1995-1996)

Result: M32F-Y was not mutagenic in either of the assays in the bacterial strains tested either with or without metabolic activation provided by rat liver S9 fraction

9.4.4 *Salmonella typhimurium* Reverse Mutation Assay on M32F-Y (Thompson, 1996b)

Strains: *S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100

Concentration range:	0 – 5 000 µg per plate; assays were carried out in the presence or absence of rat liver S9 fraction
Test method:	similar to OECD TG 471 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	M32F-M was not mutagenic in either of the assays in the bacterial strains tested either with or without metabolic activation provided by rat liver S9 fraction

9.4.5 *Salmonella typhimurium* Reverse Mutation Assay on M32F-C (Thompson, 1996c)

Strains:	*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100
Concentration range:	0 – 5 000 µg per plate; assays were carried out in the presence or absence of rat liver S9 fraction
Test method:	similar to OECD TG 471 (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	M32F-C was not mutagenic in either of the assays in the bacterial strains tested either with or without metabolic activation provided by rat liver S9 fraction

9.5 Overall Assessment of Toxicological Data

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

In a 28-day oral rat study, the NOEL was 150 $mg.kg^{-1}.d^{-1}$, based on an increase in the plasma level of alkaline phosphatase in males at 400 $mg.kg^{-1}.d^{-1}$. Treatment with LR-147 at the high dose (1 000 $mg.kg^{-1}.d^{-1}$) induced mild anaemia and statistically significant liver effects. Minor adaptive changes to the liver were observed at all dose levels. In general, treatment-related effects regressed after 14 days without treatment.

In the presence or absence of metabolic activation, the notified chemical was not mutagenic in bacteria and it did not produce chromosomal aberrations in 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 NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1994a).

Several studies on products containing LR-147, were provided by the notifier. M32F was of low acute oral toxicity (LD_{50} > 2 000 mg.kg^{-1}) in rats and was not a skin sensitiser in guinea pigs. In three Ames tests, the products M32F-Y, M32F-M and M32F-C were not mutagenic in bacteria in the presence or absence of metabolic activation.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

While not required for chemicals to be imported in quantities less than one tonne per annum, the following ecotoxicity studies have been supplied by the notifier. The tests were carried out according to OECD Test Guidelines and Principles of Good Laboratory Practice.

Test	Species	Results (Nominal)	Reference
Acute Toxicity 96 h Static-renewal OECD TG 203	Rainbow trout *(Oncorhynchus mykiss)*	LC_{50} > 100 mg.L^{-1}	(Handley et al., 1992a)
Acute Immobilisation 48 h Static OECD TG 202	Water Flea *(Daphnia magna)*	EC_{50} > 100 mg.L^{-1}	(Handley et al., 1992b)
Growth Inhibition (b=biomass, r=growth) 72 h Static OECD TG 201	Algae *(Scenedesmus subspicatus)*	E_bC_{50} > 100 mg.L^{-1} E_rC_{50}† > 100 mg.L^{-1}	(Handley et al., 1994)
Respiration Inhibition 3 h Static OECD TG 209	Aerobic Waste Water Bacteria	IC_{50} > 1 000 mg.L^{-1}	(Mead, 1995)

†. 24-48 hour

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

In the case of the fish toxicity tests, the 96 h NOEC was ≥ 100 mg.L^{-1}. There were no mortalities or behavioural reactions at this concentration. For toxicity to the water flea, the 48 h NOEC was ≥ 100 mg.L^{-1}, and similarly in tests on inhibition of algal biomass the 72 h NOEC was > 100 mg.L^{-1} (only 4% inhibition observed at 100 mg.L^{-1}). There were no immobilised daphnids or other adverse reactions observed up to the maximum concentration tested, i.e. 100 mg.L^{-1}.

In the initial range-finding test to determine the effects of the chemical on respiration inhibition of sewage sludge, a 38% decrease in respiration was observed after 3 hours at an exposure of 1000 mg.L^{-1} of the test substance. However, the second range-finding study showed that increasing the test concentration to 1 800 mg.L^{-1} did not result in greater than 50% inhibition of respiration after 3 hours. The result quoted in the above table is that of the definitive study.

It can be concluded that the notified chemical is practically non-toxic to fish, aquatic invertebrates, algae and waste water treatment micro-organisms.

11. ENVIRONMENTAL HAZARD

The environmental exposure from the notified chemical is expected to be low, and considering the ecotoxicological data provided, even gross spillage of the individual toner containing cartridges, e.g. transport related accident, should cause little environmental damage from the contained notified chemical.

The majority of notified chemical should not enter the environment until it is incorporated into a polymer matrix when the toner is cured and fixed to paper. Disposal of the waste paper containing the cured toner is normally through landfill, incineration or recycling. In all three cases it is anticipated that the chemical will be destroyed either through the agency of a vigorous chemical environment, or through (admittedly slow) biological or abiotic processes. Even in the absence of substantial degradation, the diffuse nature of disposal patterns would indicate slow release into the wider environment.

Accidental spillage of the toner, e.g. during transport, should result in powder wastes being sent to either landfill or incineration facilities. Empty colour cartridges containing small volumes of toner will also be sent to landfill or for incineration. Any movement of the chemical in landfill should not present a significant environmental hazard due to the low ecotoxicity and expected diffuse disposal pattern.

Considering the above, the overall environmental hazard is expected to be low.

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. Infrequent dermal exposure of end users to the toner containing the notified chemical may occur during servicing or clearing paper jams, but the relatively low octanol/water partition coefficient of the notified chemical indicates 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. If eye contact occurs, the notified chemical or other toner components may cause mild 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 minimal. 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 by the notified chemical is very low. Similarly, a low occupational health risk exists for repair workers, who are likely to be exposed to the notified chemical via the skin and respiratory tract, more frequently than office workers.

Some toxicological data was available for products containing the notified chemical. Based on this data and the expected low exposures, the health risk to workers resulting from normal handling and use of the products would be expected to be low.

There is negligible potential for public exposure to the notified chemical arising from its use as a component in ink toner cartridges for photocopiers and printers. There may be widespread public contact with the notified chemical from handling of the printed paper sheets, however the toner is bound in the structure of the paper, the notified chemical is at low concentration in the toner and has a low toxicological hazard, and the pattern of exposure would be intermittent.

13. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical and the products containing the chemical were provided. The MSDS for LR-147 submitted by the applicant is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

14. 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. Workers using the product should implement good work practices to avoid spills and the generation of dusts;
- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the Material Safety Data Sheet (MSDS) for LR-147 and/or information about the toners containing LR-147 should be easily accessible to employees.

If products containing the notified chemical are hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1994a), then workplace practices and control procedures consistent with State and territory hazardous substances regulations must be in operation.

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

Allen D (1996a) M32F: Acute oral toxicity (Limit test) in the rat, Project No. SPL 635/043, SafePharm Laboratories Limited, Derby, UK.

Allen D (1996b) M32F: Buehler delayed contact hypersensitivity study in the guinea pig, Project No. SPL 635/045, SafePharm Laboratories Limited, Derby, UK.

Connell DW (1989) General characteristics of organic compounds which exhibit bioaccumulation. In: D. W. Connell ed. Bioaccumulation of Xenobiotic Compounds. CRC Press, Boca Raton, .

Draize JH (1959) Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. Association of Food and Drug Officials of the US, **49**: 2-56.

European Economic Community (EEC) (1992) EEC Directive 92/69. Methods for the determination of physico-chemical properties.

Handley J, Grant-Salmon D & Bartlett A (1992a) The acute toxicity of LR-147 to rainbow trout (Oncorhynchus mykiss), Project No. 256/35, SafePharm Laboratories Limited, Derby, UK.

Handley J, Grant-Salmon D & Bertlett A (1992b) The acute toxicity of LR-147 to Daphnia magna, Project No. 256/34, SafePharm Laboratories Limited, Derby, UK.

Handley J, Mead C & Bartlett A (1994) LR-147: Algal inhibition test, Project No. 594/21, SafePharm Laboratories, Derby, UK.

Mead C (1995) LR-147: Assessment of the inhibition effect on the respiration of activated sewage sludge, Project No. 256/74, SafePharm Laboratories Limited, Derby, UK.

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

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

Nishiuchi M (1991) Ames Salmonella/Microsome plate test - Chemical: LR-147, Project No. MG0030, Hist Science laboratories Co Ltd, Japan.

Organisation for Economic Co-operation and Development (1995-1996) OECD Guidelines for the Testing of Chemicals on CD-Rom. Paris, OECD.

Sewell I (1992) Assessment of the Ready Biodegradability (Closed Bottle Test), Project No. 256/17, SafePharm Laboratories Limited, Derby, UK.

Thompson P (1993) LR-147: Reverse mutation assay "Ames Test" using salmonella typhimurium and Escherichia coli, Project No. 256/53, SafePharm Laboratories Limited, Derby, UK.

Thompson P (1996a) M32F-Y: Reverse mutation assay 'Ames test' using Salmonella typhimurium, Project No. SPL 635/046, SafePharm Laboratories Limited, Derby, UK.

Thompson P (1996b) M32F-M: Reverse mutation assay 'Ames test' using Salmonella typhimurium, Project No. SPL 635/047, SafePharm Laboratories Limited, Derby, UK.

Thompson P (1996c) M32F-C: Reverse mutation assay 'Ames test' using Salmonella typhimurium, Project No. SPL 635/048, SafePharm Laboratories Limited, Derby, UK.

Tuffnell P (1992a) LR-147: Acute oral toxicity (Limited Test) in the rat, Project No. 256/38, SafePharm Laboratories Limited, Derby, UK.

Tuffnell P (1992b) LR-147: Acute dermal toxicity (Limited Test) in the rat, Project No. 256/39, SafePharm Laboratories Limited, Derby, UK.

Tuffnell P (1992c) LR-147: Acute dermal irritation test in the rabbit, Project No. 256/40, SafePharm Laboratories Limited, Derby, UK.

Tuffnell P (1992d) LR-147: Acute eye irritation test in the rabbit, Project No. 256/43, SafePharm Laboratories Limited, Derby, UK.

Tuffnell P (1992e) LR-147: Magnusson and Kligman maximisation study in the guinea pig, Project No. 256/41, SafePharm Laboratories Limited, Derby, UK.

Wragg M (1993) LR-147: Twenty-eight day sub-acute oral (gavage) toxicity study in the rat, Project No. 256/52, SafePharm Laboratories Limited, Derby, UK.

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.
		Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
Diffuse beefy red	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