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May 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

CIN 10066831

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Director
Chemicals Notification and Assessment

TABLE OF CONTENTS

FULL PUBLIC REPORT

CIN 10066831

1. APPLICANT

Kodak Australasia Pty Ltd of 173 Elizabeth St COBURG VIC 3058 has submitted a standard notification statement in support of their application for an assessment certificate for CIN 10066831.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, molecular and structural formulae, spectral data, details of non-hazardous impurities and details of formulation of the notified chemical have been exempted from publication in the Full Public Report and the Summary Report.

Marketing Name: CIN 10066831

Molecular Weight: 898.12

3. PHYSICAL AND CHEMICAL PROPERTIES

Data on two different samples of the notified chemical were provided as part of the notification statement - HAEL# 97-0042 and HAEL# 96-0040. Both are commercial grades of the notified chemical, containing respectively 81.4 % and approximately 80 % notified chemical.

All physical and chemical properties testing was performed on sample HAEL# 97-0042 – see Section 4 below.

Appearance at 20°C & 101.3 kPa: green to black solid

Melting Point: decomposes above 234°C (OECD TG102)

Specific Gravity: 1.5482 at 20°C (OECD TG109)

Vapour Pressure: $< 2.9 \times 10^{-8}$ kPa at 25°C (OECD TG104)

Water Solubility: 67800 mg/L at 30°C (OECD TG105)

Particle Size: Size Range (μm) Mass %

		29.45
	< 38	15.96
Inspirable range:	38 - 53	14.86
	53 - 75	25.23
	75 - 106	9.32
	106 – 150	
		0.91
	150 - 212	0.41
	212 - 300	0.48
	300 - 420	0.50
	420 - 595	0.80
	595 - 850	1.03
	850 - 1190	0.64
	1190 - 1680	0.89
	1680 - 2360	0.66
	> 2360	
	median size 59.8 μm (OECD TG110)	

Partition Co-efficient (n-octanol/water):	log K_{ow} = 0.82 (OECD TG117)
Hydrolysis as a Function of pH:	$T_{1/2}$ at pH 4.0 = 8431 hours at 25°C $T_{1/2}$ at pH 9.0 = 4550 hours at 25°C (OECD TG111)
Adsorption/Desorption:	K_{oc} range from 37.7 to 126.4 (OECD TG 106)
Dissociation Constant:	pK_a = 5.07 (Method OECD TG110)
Flash Point:	not applicable for solids of low vapour pressure
Flammability Limits:	not highly flammable (92/69 EEC, A.10)
Autoignition Temperature:	no self-ignition to 400°C (92/69 EEC, A.16)
Explosive Properties:	not explosive
Reactivity/Stability:	not oxidising; not expected to be reactive under normal environmental conditions

3.1 Comments on Physico-Chemical Properties

Water solubility was determined by the shake flask method and using High Performance Liquid Chromatography (HPLC) for detection.

The potential of the notified chemical to undergo hydrolytic degradation in an aquatic environment was determined using a preliminary test at 50°C to calculate the change in the test substance concentration over time. Concentrations were analysed by HPLC/UV. Greater than 10 % hydrolysis was observed in the pH 4 and pH 9 buffers after 120 hours, but as < 10 % hydrolysis occurred in the pH 7 system, no further testing was necessary. This was

performed on 15 mg/L concentrations of the substance in pH 4 and 9 buffers at 60, 70 and 80°C. The test solutions were analysed using HPLC/UV and the half lives of the substance at pH 4 and 9 were calculated from these results.

Experimental determination of the n-octanol/water partition coefficient was made by HPLC, based on a reverse-phase HPLC separation procedure. The measured retention time of the substance was used to estimate the log K_{ow} from a previously established linear regression equation.

Adsorption/desorption data was derived using both the preliminary and definitive parts of OECD TG 106. The adsorption phase was performed on three soil types: Spodosol, Alfisol and Entisol. The three soil types were mixed with 20 mL of the test solution, in triplicate, (12.8 mg/L notified chemical in 0.01 M $CaCl_2$), mixed for 18.5 hours at 22.8°C, centrifuged and analysed using HPLC/Vis. The desorption phase was performed by adding 20 mL of 0.01 M $CaCl_2$ to each adsorption soil sample, mixing for 19.5 h at 23.1°C, centrifuging and analysing by HPLC (desorption wash 1). This method was repeated to produce desorption wash 2. Results are as follows:

Soil Type	*pH*	*Organic Carbon %*	*Mean % Adsorbed*	*Mean % Desorbed*	*Mean % Retained*	*Mean K*	*Mean Koc*
Spodosol	4.7	2.4	30.1	60.7	39.3	2.5	104.2
Alfisol	6.5	3.0	38.9	-2.73	103	3.8	126.4
Entisol	7.5	1.2	7.4	38.6	61.4	0.45	37.7

The pKa for the sample HAEL# 97-0042 was determined by titration by sodium hydroxide. No endpoints were detected for the substance when analysed with 0.1000 N hydrochloric acid by potentiometric titration. This is not consistent with the expected structure of the compound, which should have basic but not acidic properties as notified, and could be due to the presence of acetic acid, present as an impurity, causing protonation of the basic site.

4. PURITY OF THE CHEMICAL

Degree of Purity:

HAEL# 96-0040	81.4 %
HAEL# 97-0042	approximately 80 %

Hazardous Impurities:

Chemical name:	acetic acid
Weight percentage:	HAEL# 97-0042 10 %
CAS No.:	64-19-7
Regulatory Controls:	National exposure standard 10 ppm TWA, 15 ppm STEL (NOHSC, 1995)
Toxic Properties:	at 10 %, R36/38 Irritating to eyes and skin (NOHSC, 1999b)

Chemical name:	2,4-dinitroaniline
Synonym:	benzenamine, 2,4-dinitro-
CAS No.:	97-02-9
Weight percentage:	HAEL# 97-0042 1.66 % (the notifier has indicated that the concentration is lower, generally < 0.6 %, in production batches)
Toxic properties:	at a concentration of 1.66 %, this chemical is classified as hazardous with the risk phrases: R23/24/25 Toxic by inhalation, in contact with skin and if swallowed R33 Danger of cumulative effects (NOHSC, 1999b)
Non-hazardous Impurities (> 1% by weight):	identities of non-hazardous impurities have been exempted from publication in the Full Public Report
Additives/Adjuvants:	none

5. USE, VOLUME AND FORMULATION

The notified chemical will be used in the manufacture of photographic film and paper.

The notified chemical will not be manufactured in Australia. It will be imported as a powder in plastic bags inside cardboard cartons, each containing 6 kg of notified chemical. The import volume for the notified chemical is estimated to be approximately 1.2 tonnes in the first year and 1.5 tonnes per annum during the next four years of importation.

6. OCCUPATIONAL EXPOSURE

Transport and Storage
Transport and storage workers are not likely to be exposed to the notified chemical except in the case of an accident involving damage to the packaging. No details of occupational exposure were provided by the notifier.

Formulation
The appropriate amount of the notified chemical, in powdered form, will be added directly from the imported bags to mix tanks with other substances to form aqueous solutions (< 10 % notified chemical) in multi-batch runs, many times per year. Addition to the mix tanks will be performed manually. Batches will comprise around 400 L of solution. The addition of the notified chemical will take approximately 5 minutes per batch. A sample of the solution will be taken for laboratory testing. Inhalation and eye exposure to the powdered form of the notified chemical may occur because adding to the mix tank is an open process. Dermal contact with the powdered substance or the solution is also possible.

Addition of the notified chemical to the mix tank will be conducted under local exhaust ventilation. Workers handling the dry powder are to wear company provided overalls, safety

glasses, disposable vinyl gloves, and a half face respirator with particle filter.

The notifier indicates that 6 operators will be involved in producing the aqueous solutions.

The aqueous solution will be transported to the coating area in tanks. The solution will then be transferred to automated processing equipment, where the notified chemical will be incorporated into photographic films and paper. No details of the manner of transfer of the aqueous solutions from the mix tank to transfer tanks, and then to the automated system, were provided by the notifier. It is probable that dermal exposure could occur during these processes. Intermittent dermal exposure to the notified chemical is also possible during cleaning of automated processing equipment.

The notifier indicates that 27 operators and 4 technicians will be involved in handling the aqueous solutions.

End Use
The notifier indicates that the notified chemical will be under overcoat layers in the finished articles. Therefore no exposure of end users who handle the film or paper, such as photographers, is likely. During developing, normally carried out in minilabs, and dermal contact with solutions containing the notified chemical in dilute form (maximum 0.17 g/L) is possible. Minilab operators are advised to wear protective clothing including goggles and nitrile gloves when handling the solutions, according to the technical advice from the processing chemical manufacturers (see, for example, Kodak (1999)) and the Material Safety Data Sheets (MSDS) for the processing chemicals.

7. PUBLIC EXPOSURE

The notified chemical will be used only within an industrial environment prior to incorporation in photographic film and paper. These will be sold to the public and therefore there will be widespread availability of the notified chemical in the public domain in these forms. However, once incorporated onto photographic film or paper, the gelatin dispersion containing the notified chemical will reside beneath several overcoat layers, which limits the possibility of dermal contact. The notified chemical will be washed out during minilab processing and disposed of to the sewer. Little public contact with the notified chemical is expected during the processing operations.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Some chemical is likely to be left in the imported bags after they have been emptied. The company estimates that 4.0 kg per year of the chemical will be left as residues when the import containers are emptied and 0.8 kg per year will be trapped in the filters used in the dust extraction equipment. These residues will be disposed to landfill as will any reject dye batches (< 0.1 % of import volume). The company also indicated that around 0.025 % of the chemical may be released in the aqueous solution from the mix tank, and that this would be

released to the sewerage system, and discharged to the sea after treatment at a sewage treatment plant. This amounts to an estimated total release from the paper manufacturing process of around 6.7 kg each year, of which 6.3 kg will go to landfill and 0.4 kg to the sewers.

The notifier indicates that due to its water solubility, they expect the notified chemical to wash out of the photographic paper into the photoprocess chemicals in the minilab operation. The minilab procedure involves processing the paper through a developer solution, a bleach-fix solution and a stabiliser/wash solution. The total process time is around 3 minutes. They claim that it will predominantly wash out in the developer tank but small amounts could also be in the bleach-fix and stabiliser wash solutions.

The notifier has given a Predicted Environment Concentration (PEC) calculation that suggests a nationwide release of the chemical of only 343 g/day of the chemical. This would mean a total release of < 120 kg/annum. This figure appears rather low when the very high water solubility of 67800 mg/L and the import volume of 1500 kg/annum is taken into account. The notifier has not estimated what percentage of the dye will wash from the paper during the developing process but, noting the water solubility, at least 50 % seems an appropriate estimate. Approximately 192.3 kg of the chemical will be lost in the paper manufacturing process, leaving 1307.7 kg adhering to the paper which will undergo the developing process in minilabs, of which 50 % (653.9 kg) may be released to the sewers in the minilab effluent.

There is generally no pre-treatment of the waste developer solutions before it is released to the sewers. Some minilab operators may collect and dispose of wastes via waste disposal contractors.

While the compound is not readily biodegradable under environmental conditions, the notifier has provided data to show that the half-life of the dye in the developing solution is less than one hour.

Eventual disposal of old photographs and negatives is likely to be through deposition into landfill where very slow release could be expected as the old photographs become degraded. Some old photographs and films may be incinerated, which would destroy the chemical, producing water vapour and oxides of nitrogen and sulphur, and hydrogen chloride.

8.2 Fate

The notifier included reports on a Biochemical Oxygen Demand (BOD) (Steinbugler, 1997a) and a Chemical Oxygen Demand (COD) (Steinbugler, 1997b) determination. The BOD of the chemical was measured in compliance with "OECD Principles of Good Laboratory Practice", [C(81) 30(Final)], Annex 2 using Method C.5. "Degradation, Biochemical Oxygen Demand". The mean of the two 5-day results was found to be 0.071 g/g of the test substance The mean of the two 20-day results was 0.16 g/g of test substance.

The COD was measured in compliance with "OECD Principles of Good Laboratory Practice", [C(81) 30(Final)], Annex 2 using Method C.6. "Degradation, Chemical Oxygen Demand". The mean of three measurements was 1.09 g COD/g test substance. The BOD_5/COD ratio was found to be 0.065.

The notified chemical was examined for biodegradation potential using EEC Directive 92/69, Part C.4-C (Modified Sturm Test), and OECD Test Guideline 301B (Berlinger & Ruffing, 1997b), with substance added directly to test carboys due to sparing solubility. Over the 28 day test, biodegradation showed 7 % (Vessel 1) and 8 % (Vessel 2). The control solutions were found to have 77 % degradation over the 28 days. These results indicate that the notified chemical is not readily biodegradable.

The very high water solubility and low value for the n-octanol/water partition coefficient indicate that residues released directly to the aquatic compartment, for example from minilab effluent, are likely to remain in solution.

While the compound is not readily biodegradable under environmental conditions, the notifier has provided a test report that indicates that the half-life of the dye in the developing solution is less than one hour. No details of the authorship of the report were provided. The test involved dissolving 0.2 g of the chemical in 1 L of the developer solution, diluting aliquots of the stock by 1:25 and recording the absorbances at 667 nm and 458 nm with a spectrophotometer. One sample was kept at room temperature while the other was heated to 38°C and the absorbances read at various time intervals.

Some of the material disposed of into landfill (eg residues in empty bags) is expected to leach out of the landfill site due to its high water solubility and high soil mobility (K_{oc} range 37.7 to 126.4) and become mobile in the water compartment.

Photographs and films which are discarded would most probably be placed into landfill where the chemical is expected to be slowly released as the film and emulsion are degraded. It is expected that released compound would become mobile in the soils and leach out into the water compartment. Some photographs and films may be incinerated which would result in complete destruction of the compound with formation of oxides of nitrogen and sulphur, and hydrogen chloride.

The high molecular weight, low partition coefficient (log K_{ow} = 0.82) and high water solubility (67800 mg/L) of the notified chemical indicate that significant bioaccumulation is not likely (Connell, 1990).

9. EVALUATION OF TOXICOLOGICAL DATA

Two different samples of the notified chemical were used for toxicology testing - HAEL# 97-0042 and HAEL# 96-0040. As discussed above, the former sample contains the hazardous impurity 2,4-dinitroaniline at 1.66 % and acetic acid at approximately 10 %, while the latter sample contains no hazardous impurities. Both are commercial grades of the notified chemical, containing respectively 81.4 % and approximately 80 % notified chemical.

Sample HAEL# 97-0042 was used for the acute oral toxicity, acute eye irritation, skin sensitisation and 28-day oral toxicity studies; sample HAEL# 96-0040 was used for the acute dermal toxicity, acute skin irritation, bacterial point mutation and *in vitro* chromosomal aberration studies.

9.1 Acute Toxicity

Summary of the acute toxicity of CIN 10066831

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} > 2000 mg/kg	(Shepard, 1997)
acute dermal toxicity	rat	LD_{50} > 2000 mg/kg	(Bernard, 1997b)
skin irritation	rabbit	non-irritating	(Bernard, 1997a)
eye irritation	rabbit	moderate irritant	(Bernard, 1997c)
skin sensitisation	guinea pig	non-sensitising	(Jessup, 1997)

9.1.1 Oral Toxicity (Shepard, 1997)

Species/strain:	rat/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Test Substance:	HAEL# 97-0042
Method of administration:	gavage; limit dose of 2000 mg/kg as a 20 % suspension in vehicle (0.5 % w/v carboxymethyl-cellulose in water)
Test method:	OECD TG 401
Mortality:	no mortality was noted during the study
Clinical observations:	abnormal clinical signs were limited to discolouration (blue) of the excreta, skin, eyes, and mucus membranes, and staining of the skin which came in contact with the discoloured urine and faeces by day 8, no further discolouration or staining was evident, and all animals appeared clinically normal for the remainder of the study
Morphological findings:	no treatment-related changes were observed at necropsy
Comment:	all animals gained weight during both weeks of the study
LD_{50}:	> 2000 mg/kg
Result:	the notified chemical was of very low acute oral toxicity in rats

9.1.2 Dermal Toxicity (Bernard, 1997b)

Species/strain:	rat/Sprague-Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Test Substance:	HAEL# 96-0040
Method of administration:	test substance, moistened with water, was applied to shaved dorsal skin under occlusive dressing for 24 hours
Test method:	OECD TG 402
Mortality:	all animals survived to the termination of the study
Clinical observations:	abnormal clinical signs were limited to staining (blue) by the test substance at the application site for all animals following dosing through to termination of the study
Morphological findings:	no treatment-related changes were observed at necropsy
Comment:	all animals gained weight over the study period
LD_{50}:	> 2000 mg/kg
Result:	the notified chemical was of low dermal toxicity in rats

9.1.3 Inhalation Toxicity

No study was supplied by the notifier, who stated that the test was not relevant having regard to the nature of the chemical and its mode of use. As the notified chemical is to be handled in the form of a powder containing a large respirable component (> 29 % is of particle size smaller than 38 μm, the smallest sieve size used in analysis), inhalation is a possible mode of exposure and, in the absence of inhalation toxicity data, a high level of respiratory protection should be provided to workers who handle the powdered substance.

9.1.4 Skin Irritation (Bernard, 1997a)

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	3 (sex not specified)
Observation period:	3 days

Test Substance:	HAEL# 96-0040
Method of administration:	0.5 g test substance, moistened in water, was applied under occlusive conditions to shaved dorsal skin for 4 hours
Test method:	OECD TG 404
Comment:	slight staining by the test substance was evident at the application site of all animals throughout the study; this did not interfere with the observations no irritant response or serious lesion was noted during the 72-hour observation period; all Draize scores (Draize, 1959) were zero no mortality occurred during the study
Result:	the notified chemical was non-irritating to the skin of rabbits

9.1.5 Eye Irritation (Bernard, 1997c)

Species/strain:	rabbit/New Zealand White
Number/sex of animals:	6 (sex not specified)
Observation period:	7 days
Test Substance:	HAEL# 97-0042
Method of administration:	a single dose of 0.1 g of test substance was placed in the conjunctival sac of one (right) eye of each of the six test animals; the treated eyes of three animals were immediately washed with running distilled water; the eyes of the other three animals were not irrigated; the untreated eye served as control
Test method:	OECD TG 405

Draize scores (Draize, 1959) of unirrigated eyes:

	Time after instillation				
Animal	***1 hour***	***1 day***	***2 days***	***3 days***	***7 days***
Cornea	***o***	***o***	***o***	***o***	***o***
1	0[1]	0	0	0	0
2	0	1	1	0	0
3	0	1	1	1	0
4i	0	0	0	0	0

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

[1] see Attachment 1 for Draize scales
i = irrigated
b = blue staining by the test substance prevented evaluation of effects
o = opacity a = area r = redness c = chemosis d = discharge

Comment:

mean ocular scores for non-irrigated eyes were as follows:
corneal opacity: 0, 0.67, 1
iris: 0, 0.33, 0.67
redness: 1, 1.67, 2
chemosis: 0, 1.67, 3

mean ocular scores for irrigated eyes were as follows:
corneal opacity:0, 0, 0
iris: 0, 0, 0
redness: 0.33, 0.33, 0.33
chemosis: 0.33, 0, 0

blue staining of the conjunctivae, nictitating membrane, and cornea by the test substance was observed at the 1-hour examination for all unwashed eyes; this blue staining hindered examination for redness in all unwashed eyes and the iris for two of the three unwashed eyes at the 1-hour examination

staining of the conjunctivae, nictitating membrane, and cornea was evident for two of three unwashed eyes (animals #2 and #3) when tested with fluorescein dye 24 hours after administration of the test substance; no other lesions were noted for the unwashed or washed eyes during the 7-day

observation period; immediate irrigation of the eyes caused a large reduction in the severity of the effects observed

Result: The notified chemical was moderately irritating to the eyes of rabbits

9.1.6 Skin Sensitisation (Jessup, 1997)

Species/strain: guinea pig/Crl:(HA)BR VAF/Plus®

Number of animals: males: 20 test and 10 control animals

Test Substance: HAEL# 97-0042

Induction procedure:

Day 0
on a prepared area of skin from the shoulder region of test animals, three pairs of intradermal injections were administered as follows:

1. 0.1 mL of 5 % test substance in corn oil;
2. 0.1 mL 5 % test substance in Freund's Complete Adjuvant (FCA) and distilled water (1:1);
3. 0.1 mL of test substance in FCA

for control animals the injections were as follows:

4. 0.1 mL of corn oil;
5. 0.1 mL FCA and distilled water (1:1);
6. 0.1 mL of corn oil in FCA (1:1)

Day 6
local irritation was induced at the shaved test site for both test and control groups by application of 0.5 mL of 10 % sodium lauryl sulphate in petrolatum

Day 7
a 25 % concentration of the test substance in petrolatum (approximately 2 g) was painted on the same site that received the intradermal injections and secured by a patch for 48 hours; application sites were observed for irritation 24 hours subsequently

for the control animals, petrolatum only was used in this phase

Challenge procedure:

Day 20
a patch of approximately 2 cm square was fully loaded with 1 g of a 25 % concentration of the test substance in petrolatum and applied to the shaved left flank of each animal; 100 % petrolatum was applied to the shaved right

	flank patches were secured to the torso with bandages for 24 hours and dermal reactions were scored at 24 and 48 hours (Days 22 and 23) after patch removal
Test method:	OECD TG 406; Magnusson and Kligman maximisation test
Comment:	approximately 15 min following the intradermal injections, all animals in the treated group had blue skin, eyes, and mucous membranes, as well as blue urine for approximately 3 hours post-injection; after the challenge dose, no dermal reactions were noted for the test animals; control animals responded appropriately
Result:	the notified chemical was non-sensitising to the skin of guinea pigs

9.2 Repeated Dose Toxicity (Gearhart & Faber, 1998)

Species/strain:	rat/Sprague-Dawley
Number/sex of animals:	5/sex/group
Test Substance:	HAEL# 97-0042
Method of administration:	gavage
Dose/Study duration:	1000, 300, 100 and 0 mg/kg/day for 29 days; vehicle corn oil
Test method:	OECD TG 407
Mortality:	all animals survived to the termination of the study

Clinical observations:
Blue discolouration of the urine was observed for all treated animals, with colour intensity being minor for the 1000 mg/kg/day groups, and minimal for the 300 and 100 mg/kg/day groups, beginning on Day 0 and continuing for the duration of the study. All treated animals had blue discolouration of the faeces from Day 1 through study termination except for one or two days for the 300 and 100 mg/kg/day groups. Systemic blue discolouration including the skin, eyes, mouth, and/or mucous membranes due to absorption of the test substance was observed for all treated groups following administration of the test substance.

No toxicologically significant alterations were observed in the functional observational battery. On Day 14, 300 mg/kg/day males had a significantly higher incidence of constricted pupils compared with the control group, although this observation was not

considered to be treatment related as it was not seen in females or at the higher dose.

There were no significant differences in mean body weight or feed consumption among the groups.

There were no significant differences in either mean total motor activity counts or mean total ambulations for male rats. Total motor activity counts were significantly lower for 1000 and 300 mg/kg/day females, although this was attributable to unusually low values in the controls prior to dosing, and higher than normal values in the controls at day 28.

Clinical chemistry/Haematology
Light blue serum was observed for all 1000 mg/kg/day animals and eight 300 mg/kg/day animals. Mean potassium concentrations were significantly lower for the 1000 and 100 mg/kg/day male groups when compared with the control group. Mean potassium concentrations for the 100 mg/kg/day females were significantly higher when compared with the control group. Mean blood urea nitrogen concentrations were significantly higher for the 1000 mg/kg/day females when compared with the control group. There were no other differences in clinical chemistry parameters among the groups.

Target cells were observed in one to three males per group, including the control group, and two females in the 300 mg/kg/day group. Minimal poikilocytosis was observed in one 300 mg/kg/day male and one control female. A minimal decrease in blood platelet counts was observed for one 1000 mg/kg/day rat and two control females. One 1000 mg/kg/day male had a severely decreased platelet count but because this animal had a normal prothrombin time and no other indications of pathology with clotting mechanisms, the finding was considered to be spurious. There were no other differences in cell morphology among the groups.

Organ weights:
All mean absolute and relative (to body weight) organ weights for male and female treated groups were comparable to those of the respective controls.

Gross pathology:
Gross lesions in treated groups included systemic blue discolouration of the skin for all 1000 mg/kg/day animals and three 300 mg/kg/day animals. There was also blue discolouration of the tongue, oesophagus, kidneys and bladder, with both the incidence and severity being dose-related.

Blue discolouration of the stomach, duodenum, jejunum, ileum, caecum, colon, rectum and/or contents was observed for all treated groups, also in a dose-related pattern.

Thymus haemorrhage was observed for four animals in the 1000 mg/kg/day group, three in the 300 mg/kg/day group, and one in the 100 mg/kg/day group. One rat in the 100 mg/kg/day group had focal red discolouration of the lungs. Two females each in the 1000 and 100 mg/kg/day groups had hydrometra of the uterus.

Histopathology:
Incidental lesions were found in the stomach, colon, thymus, kidneys, urinary bladder, prostate, uterus, liver, lungs, and cervical lymph nodes of males and/or females in both the control and treated groups, or the control group only. Lesions observed only in the treated

groups included minimal to mild mononuclear cell infiltrates in the liver for one male and one female in the 1000 mg/kg/day group. One 1000 mg/kg/day male had minimal metaplastic ossification of the lungs. One 1000 mg/kg/day female had a mild ultimobranchial cyst in the thyroid gland, and one 1000 mg/kg/day female had mild sinus erythrocytosis of the mediastinal lymph node. No dose-related microscopic findings were observed for any group.

Comment:
The presence of blue discolouration of various organs and tissues at each dose level meant that no no-observed-effect-level (NOEL) could be determined.

Apart from blue discolouration, all findings were slight and within normal control ranges, or scattered at low incidence with no evident dose-response. The thymus haemorrhage was minimal in the majority of cases and the notifier has indicated that it is related to the use of CO_2 anaesthesia, rather than to treatment with the test substance.

Result:
No signs of systemic toxicity were observed upon treatment of male and female rats with up to 1000 mg/kg/day for 29 days and, accordingly, the no-observed-adverse-effect-level (NOAEL) was established at 1000 mg/kg/day.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Lawlor, 1996)

Strains:	*Salmonella typhimurium* TA98, TA100, TA1535 and TA1537; *Escherichia coli* WP2uvrA(pKM101)
Metabolic activation:	10% rat liver S9 fraction (Aroclor1254-induced) in standard cofactors
Test Substance:	HAEL# 96-0040
Concentration range:	5 000, 3 330, 1 000, 333, and 100 µg/plate, dissolved in deionised water and plated as a 200 µL aliquot
Positive controls:	with S9: 2-aminoanthracene TA98, TA100, TA1535, TA1537: 2.5 µg/plate WP2*uvr*A: 5 µg/plate without S9 TA98: 2-nitrofluorene 1.0 µg/plate TA100,TA1535: sodium azide 2.0 µg/plate TA1537: ICR-191 2.0 µg/plate WP2*uvr*A: 4-nitroquinoline-N-oxide 2 µg/plate
Test method:	OECD TG 471 (plate incorporation method)

Comment:	all concentrations were tested in triplicate and concurrent positive and negative controls responded appropriately in the initial mutagenicity assay, there was a 2.6-fold increase in the number of revertants per plate with TA98 in the presence of S9; no positive increases were observed with any of the other tester strains, either in the presence or absence of S9 in the confirmatory assay, there was a 1.9-fold increase in revertants with TA98 in the presence and absence of S9; negative responses for other strains/conditions were confirmed to investigate the weak mutagenic activity in TA98, a third experiment produced a 1.8-fold increase with S9, and a 1.9-fold increase in the absence of S9 the testing laboratory claimed that the test substance was not mutagenic because the positive effect (2.6-fold increase) seen with TA98 in the initial experiment was not reproduced in the two subsequent experiments; the report stated that increases of 1.9 and 1.8-fold with TA98 did not meet the 2-fold criteria required for a positive evaluation this conclusion by the testing laboratory is not accepted because, firstly, the increases in revertants over the concentration range are dose-related and reproducible (three times) and, secondly, the criteria for a positive response has always been intended to be arbitrary and not absolute; on this basis, the 1.8 and 1.9-fold increases seen with TA98 are considered, in practical and relative terms, to satisfy the condition that a 2-fold has been achieved
Result:	the notified chemical was weakly mutagenic under the conditions of the test

9.3.2 Chromosomal Aberration Assay in Chinese hamster ovary (CHO) cells (Murli, 1996)

Cells:	Chinese hamster ovary (CHO) cells
Metabolic activation system:	15 μL/mL rat liver S9 fraction (Aroclor1254-induced) in standard cofactors
Test Substance:	HAEL# 96-0040
Dosing schedule:	schedule in hours following treatment with test substance

	wash	colcemid	fixation
initial test			
-S9	17.8	18	20
+S9	3.0	18	20
confirmatory test			
-S9	17.8	18.1	20.1
+S9	3.0	18.1	20.1
-S9	41.8	42.0	44.0
+S9	3.0	42.0	44.0

concentrations tested were 496,1240, 2480, 3720 and 4960 μg/mL in the initial test and 500, 1250, 2500, 3750 and 5000 μg/mL in the confirmatory test

in the initial test, chromosomal aberrations were analysed from cultures dosed with 1240, 2480, 3720 and 4960 μg/mL

in the confirmatory test, for the 20.1 hour assay chromosomal aberrations were analysed from cultures dosed with 1250, 2500, 3750 and 5000 μg/mL; for the 44.0 hour assay, doses were 500, 1250, 2500 and 3750 μg/mL

Test method: Similar to OECD guidelines

Comment: the test substance was considered to be negative for inducing chromosomal aberrations in CHO cells with and without metabolic activation; results were confirmed in an independent test; the assays were validated by positive and negative controls which produced appropriate responses

Result: the notified chemical was non clastogenic under the conditions of the test

9.4 Overall Assessment of Toxicological Data

The notified chemical, CIN 10066831, was of very low oral toxicity (LD_{50} > 2000 mg/kg) and low dermal toxicity (LD_{50} > 2000 mg/kg) in rats. No evidence of skin irritation was seen in a study with rabbits. No skin sensitisation was observed in an adjuvant study in guinea pigs.

In an eye irritation study, the notified chemical produced more severe reactions in unwashed eyes compared to irrigated eyes. Blue staining of the conjunctivae, nictitating membrane, and cornea by the test substance was observed at the 1-hour examination for all unwashed eyes. Staining of the conjunctivae, nictitating membrane, and cornea persisted in two animals for 24 hours after administration of the test substance. Corneal and iris effects persisted in one animal to the 72 hour observation, and in another to the 48 hour observation. Conjunctival redness, chemosis and discharge persisted to the 72 hour observation time in both these animals. The eye irritation was therefore classed as moderate. Immediate irrigation of the

eyes caused a large reduction in the severity of the effects observed.

A four week oral toxicity study of the notified chemical was conducted in rats. Blue discolouration of the urine and faeces was observed for all treated animals for the duration of the study. Systemic blue discolouration including the skin, eyes, mouth, and/or mucous membranes due to absorption of the test substance was observed for all treated groups following administration of the test substance. Gross lesions in treated groups included systemic blue discolouration of the skin for all 1000 mg/kg/day animals and three 300 mg/kg/day animals. There was also blue discolouration of the tongue, oesophagus, kidney and bladder, in a dose-related pattern.

Blue discolouration of internal digestive organs was observed for all treated groups, also in a dose-related pattern. All other lesions from the various groups were considered to be incidental due to their limited incidence or occurrence in both high dose (1000 mg/kg/day) and control animals, with no clear increases in incidence in the high dose groups. No treatment-related microscopic findings were observed for any group. The thymus haemorrhage was minimal in the majority of cases and the notifier has indicated that it is related to the use of CO_2 anaesthesia, rather than to treatment with the test substance. The presence of blue discolouration of various organs and tissues at each dose level meant that no no-observed-effect-level (NOEL) could be determined. Treatment of male and female rats with up to 1000 mg/kg/day for 29 days did not result in signs of systemic toxicity and, accordingly, the no-observed-adverse-effect-level (NOAEL) was established at 1000 mg/kg/day. The test substance for this study contained the hazardous impurity, 2,4-dinitroaniline.

The notified chemical did not induce chromosomal aberrations in Chinese hamster ovary cells but was considered to be a weak mutagen in *Salmonella typhimurium* TA 98, even though the testing laboratory claimed that the notified chemical was negative in this assay. In an initial test the notified chemical induced a 2.6 fold increase in TA98 revertants in the presence of metabolic activation, and in two subsequent assays the increases were 1.9- and 1.8-fold. Although borderline, these increases were considered to be biologically relevant because they were dose related and reproducible. Increases of 1.9-fold were also observed in two later assays with TA98 in the absence of S9 mix. The test substance in this study did not include the hazardous impurity, 2,4-dinitroaniline. This evidence alone is insufficient for the notified chemical to meet the criteria for an R40 classification ("Possible risk of irreversible effects"), but further investigations using *in vivo* assays are strongly indicated.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The notifier supplied the following ecotoxicity data in support of the application. The test data were generated according to OECD protocols.

Test	Species	Results (nominal)
Acute Toxicity to Fish [OECD 203]	Fathead minnow *Pimephales promelas*	LC_{50} (96 h) > 105.2 mg/L
Acute Immobilisation to Fresh water invertebrates [OECD 202]	*Daphnia magna*	EC_{50} (48 h) > 102.5 mg/L
Inhibition of Algal growth [OECD TG 201]	*Selenastrum capricornutum*	EbC_{50} (72 h) = 8.29 mg/L ErC_{50} (72 h) = 41.0 mg/L
Respiration Inhibition of Activated Sludge Bacteria [OECD TG 209]	Activated sludge bacteria	EC_{50} (3h) > 1000 mg/L

Fish
Two replicate solutions containing 105.2 mg/L CIN 10087680 (HAEL# 97-0042) were prepared by adding the appropriate amount of the chemical to 20 L of dilution water (Light, 1998b). The vessels were stirred for 1 hour using a stir plate then allowed to settle for 1 hour. The test solutions appeared dark blue throughout the test so the fish could not be observed in the intermediate times and were netted and removed at 96 hours for observation. Following preparation of the test media 7 fathead minnows were added to each of the vessels. As a control, 7 fish were also placed in a separate test vessel to which no test compound had been added. Temperature was maintained at 20±1.0°C, pH values were between 7.4 to 8.4 and dissolved oxygen levels were between 6.8 and 8.5 mg/L.

No mortality or aberrant behaviour was observed in any of the test specimens or in the control fish. From these observations, it was concluded that the new compound is not toxic to this species up to the limits of this test.

Invertebrates
An acute toxicity test of the notified chemical (HAEL# 97-0042) against *Daphnia magna* was conducted using a static methodology (Light, 1998a). As with the fish test, the media was made up by adding the appropriate amount of the chemical to two 20 L glass vessels of dilution water, stirring for 1 hour and allowing to settle for 1 hour. Aliquots were then transferred to the 250 mL test vessels. Again the test solutions were a dark blue colour and no intermediate observations could be made. The test organisms were observed at test end by pouring the solutions into Petri dishes.

Ten daphnia were placed in the duplicate test vessels. Temperature was maintained between 20 and 21°C, pH values were between 7.4 to 8.5 and dissolved oxygen levels were between 7.7 and 8.5 mg/L.

No immobility or mortality was observed in the test media or control solutions throughout the test. Consequently it was concluded that the new compound is not toxic to *Daphnia magna* up to the limits of this test.

Algae
A 72-hour algal growth inhibition test was performed on cultures of algae in five concentrations (0.92, 2.63, 9.26, 28.4 and 92.9 mg/L) of the chemical (HAEL# 97-0042) (Morris, 1997). The dark blue colour of the chemical remained throughout the 72 hours of the

test so algistatic effects due to light attenuation were expected. Throughout the study, the flasks were shaken at 100 rpm, the temperature was maintained at 25°C and the pH ranged from 7.51 to 7.85. Observations were made at 0, 24, 48 and 72 hours.

The EbC_{50} (72 h) was estimated to be 8.29 mg/L while the ErC_{50} (72 h) was estimated to be 41.0 mg/L. The No Observed Effect Concentration (NOEC) (72 h) for both biomass and growth rate was 2.63 mg/L.

After the test period aliquots of the 92.9 mg/L test concentration were taken, resuspended in algal growth medium, diluted to 2 mg/L, 5 mg/L and 10 mg/L and cultured for five days. Normal growth was seen at all three concentrations which supports the theory that effects were algistatic and growth was inhibited by light absorption rather than toxicity.

Sewage Bacteria
The 3 hour test was performed using activated sludge from a domestic waste water treatment plant (Berlinger & Ruffing, 1997a). The sludge was exposed to five concentrations (25, 50, 100, 500 and 1000 mg/L) of the notified chemical (HAEL# 97-0042). The respiration rate was measured following the 3 hour exposure period, and compared with that in a control vessel. None of the samples indicated any significant inhibition of bacterial respiration compared with the controls, and it was concluded that the new chemical is not toxic to sewage bacteria up to a nominal concentration of 1000 mg/L.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The new chemical is not considered to pose a hazard to the environment when used as a component of photographic papers and films in the manner indicated by the company.

As a result of the disposal of industrial wastes from the production of the photographic papers and films, it is estimated that up to 0.4 kg of the chemical could be released into the Melbourne sewage system each year.

Total influent to the Werribee sewage treatment plant is around 500,000,000 litres per day (180×10^9 L per year), and consequently the Predicted Environmental Concentration (PEC) of the compound in the sewage is then 0.4 (kg)/180×10^9 (L) = 0.002 µg/L.

As a result of the disposal of developing solution wastes from minilabs, approximately 650 kg/annum of the notified chemical may be expected to enter the sewers and treatment plants throughout Australia. Therefore the daily release of the chemical would be approximately 1.8 kg. Sewer output for Australia is based on 18 million people, averaging 150 L/day, giving a daily sewer output of 2700 ML. The PEC for the notified chemical released through minilab operations would be 1.8 kg/2.7×10^9 L = 0.6 µg/L.

The chemical is not toxic to those species of fish or daphnia against which it has been tested. Also, the new compound does not inhibit the respiration of sewage bacteria. However, it showed slight to moderate toxicity to algae, apparently caused mainly by inhibiting algal growth through light absorption. Nevertheless, hazard is low as there is a large safety margin between the PEC of 0.6 µg/L and the toxicity value of 8.29 mg/L, in the region of four orders of magnitude.

The chemical is not readily biodegradable, but is unlikely to bioaccumulate due to its high water solubility, low partition coefficient and high molecular weight. It will be expected to remain in the water compartment and quickly be diluted to environmentally negligible levels.

Up to 0.1 % (1.5 kg) of the notified chemical may be disposed to landfill as reject dye batches and approximately 4.8 kg per year of the compound is expected to remain as residues in the empty bags and air filters used in the dust extraction system to be disposed similarly. Chemical released from these sources will become associated with the aquatic compartment as a proportion leaches from the landfill sites and will remain mobile as it is diluted to negligible levels.

The remainder of the chemical is expected to be retained in the developed photographs and films, which are likely to be eventually discarded into landfill. Here the chemical is expected to be slowly released as the photographs degrade, and will then become associated with aquatic compartment due to its high water solubility. Some photographs may be incinerated which will completely destroy the compound with production of water vapour and oxides of nitrogen and sulphur, and hydrogen chloride.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical does not meet the criteria for classification as a hazardous substance according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999a).

The acute oral toxicity of CIN 10066831 is very low (LD_{50} > 2000 mg/kg) and the acute dermal toxicity is low (LD_{50} > 2000 mg/kg). It is not an irritant to the skin of rabbits, but is a moderate irritant to rabbit eyes. It was not a skin sensitiser in guinea pigs in an adjuvant type test. The notified chemical did not induce chromosomal aberrations in Chinese hamster ovary cells but there was evidence of mutagenicity in *Salmonella typhimurium* TA 98, warranting further investigation of the mutagenic potential. No study reports on inhalation toxicity were provided by the notifier, although this is a possible mode of exposure in light of the particle size for the commercial product.

The major hazards from acute exposure arise from the eye irritant effects and from the presence of the hazardous impurity, 2,4-dinitroaniline. The imported substance is classified with the risk phrase R23/24/25 ‘Toxic by inhalation, in contact with skin and if swallowed’ and R33 ‘Danger of cumulative effects’ due to the concentration of this impurity.

For longer-term systemic effects, in a 28 day oral study in rats, no treatment related effects were observed apart from blue staining of skin and internal digestive and excretory organs. Based on the absence of toxicologically significant findings at any dose, the NOAEL was found to be 1000 mg/kg/day.

Occupational Health and Safety
Occupational exposure to the notified chemical can be divided into exposure to the powdered solid, the gelatin dispersions, and the finished photographic film and paper. The dust includes a high proportion (> 95 %) in the inspirable range, and 29.5 % of the particles are below 38 μm, indicating that a significant proportion is within the respirable range. Inhalation exposure should therefore be considered an important risk for workers handling the powdered solid. Workers will handle the powdered solid for short periods during weighing and addition

to the mix tanks where the gelatin dispersion is produced. Exposure may occur many times throughout the year. There is also a risk of eye irritation on acute exposure to dust from the chemical.

The risk of adverse health effects will be reduced by local exhaust ventilation during the processes which involve handling the powdered solid. The wearing of overalls, protective gloves, glasses and respiratory protection while weighing and mixing the powdered solid will also be required. Disposable vinyl gloves should not be used, as these tear easily and do not provide sufficient protection against the hazardous impurity, 2,4-dinitroaniline.

The handling of the gelatin dispersions, containing less than 10 % notified chemical, is a potential hazard by dermal exposure, particularly during cleaning of equipment. The risk will be lower than that associated with the powdered solid, because of the lower concentration of 2,4-dinitroaniline. At the concentration of notified chemical in the dispersion, and with the lower level of this impurity (< 0.6 %) in production batches compared with the test sample, the dispersions will not be classified as hazardous substances. Standard procedures require the use of gloves, overalls and protective glasses by workers handling the gelatin dispersions. After incorporation in articles, the potential hazard should be negligible as the notified chemical will be beneath several overcoat layers.

There may be exposure to the notified chemical for workers involved in processing the film containing the notified chemical, for example minilab operators, but the risk is expected to be low in view of the low concentration (maximum 0.017 %) of notified chemical expected in the used processing solutions.

Public Health

Photographic film and/or paper containing the notified chemical will be sold to the public; consequently there will be widespread availability in the public domain. Once incorporated onto photographic film and paper, the gelatin dispersion containing the notified chemical will reside beneath several overcoat layers, which limits the possibility of dermal contact. Little public exposure is expected to arise from notified chemical washed out of film during processing.

Consequently the potential for public exposure to the notified chemical during all phases of its life cycle is considered to be low and the notified chemical is not expected to pose a significant hazard to public health when used in the proposed manner.

13. RECOMMENDATIONS

To minimise occupational exposure to CIN 10066831 the following guidelines and precautions should be observed:

- Where engineering controls are insufficient to reduce the atmospheric concentration of dust to very low levels, respiratory protection according to Australian Standard (AS) 1716 (Standards Australia/Standards New Zealand, 1994a) should be used while handling the powdered chemical;

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand

Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992); industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987) and AS 3765.2 (Standards Australia, 1990); all occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994b); impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia/Standards New Zealand, 1998) and disposable gloves should not be used;

- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;
- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the MSDS should be easily accessible to employees.

14. MATERIAL SAFETY DATA SHEET

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

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 may be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

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Attachment 1

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

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

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

CORNEA

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

CONJUNCTIVAE

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