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NATIONAL INDUSTRIAL CHEMICALS
NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

C-1658

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

C# 1658

1. APPLICANT

Kodak Australasia Pty Ltd of 173 Elizabeth St., Coburg, Victoria.

2. IDENTITY OF THE CHEMICAL

Trade Name: C-1658

Molecular weight: 979.6

Method of detection and determination: High Pressure Liquid Chromatography.

Spectral data: UV-VIS, Infrared and Nuclear Magnetic Resonance spectra were provided.

Based on the nature of the chemical and the data provided, C-1658 is considered to be non-hazardous. Therefore, the following details have been exempted from publication: chemical name, Chemical Abstract Services (CAS) number, molecular and structural formulae, spectral data and precise use of the chemical.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance (20°C & 101.3 kPa): cream coloured solid

Melting Point:	96°C
Density:	1,245 kg/m^3 at 23°C
Vapour Pressure:	< 0.26 Pa at 30°C (Gas saturation method)
Water Solubility:	1.3 ppb (calculated)
Fat Solubility:	129 mg/100 g of fat at 37°C

Partition Co-efficient: (n-octanol/water)	Log Kow = 7.5
Hydrolysis as a function of pH:	not provided
Adsorption/Desorption:	not provided
Dissociation Constant:	not provided
Flash Point:	not provided. The substance has a low vapour pressure.
Flammability:	combustible.
Combustion products:	oxides of carbon, nitrogen and sulphur and hydrochloric acid.
Autoignition Temperature:	did not autoignite up to melting point.
Explosive Properties:	this material, like most organic materials in powder form, is capable of creating a dust explosion.
Reactivity/Stability:	stable at room temperature and atmospheric pressure. Incompatible with strong oxidizing agents, acids and bases.
Particle size distribution:	range -38 to >2360 µm mean - 685 µm

Comments on Physico-Chemical Properties

The initial water solubility value submitted by the notifier was <0.1 mg.L^{-1}, the detection limit of the analytical method used (OECD TG 105). The Department of the Arts, Sport, the Environment and Territories (DASET) indicated that a water solubility of this level may still be environmentally significant and that the limit value precludes an accurate assessment of the chemical's fate in the water compartment. DASET suggested that this situation could be rectified through the use of a more sensitive HPLC detection limit or use of the HPLC method in OECD

Test Guideline 117 to determine log P, which in turn would allow calculation of a more accurate water solubility. Kodak responded by providing an estimated value of the partition coefficient according to the procedures outlined in OECD Test Guideline 117. From this value, Kodak calculated the water solubility using the equation:

log (1/S) = 1.339 log Kow -0.978; where S is in moles/L. (1).

No data were provided for hydrolysis on the grounds that the test could not be performed on the substance due to its low water solubility and lack of sufficiently sensitive analytical methods. The substance contains an ester and several other potentially hydrolysable functionalities but hydrolysis is expected to be slow under environmental conditions.

The adsorption-desorption test was not conducted as the notifier was unable to measure the test substance in aqueous solution with sufficient sensitivity. However, the notifier indicated that the substance was observed to adhere to surfaces in vessels in which the limit of solubility was exceeded, and that it would be likely to adsorb on to solid materials. The high log P is indicative of strong adsorption (1).

No data were provided for the dissociation constant on the grounds that results were not measurable on compounds with low water solubility. The substance contains several amino functionalities but it is unclear whether these are acidic or basic.

4. PURITY OF THE CHEMICAL

Degree of purity: 98-100%

Impurities:

.Chemical name:	amine salt of a heterocyclic compound
Weight percentage:	0-2%
Additives/Adjuvants:	None

5. INDUSTRIAL USES

C-1658 will be used in the manufacture of photographic film and paper. Approximately 1.2 tonnes of the chemical will be imported per year.

5.1 Reformulation

C-1658 powder will be reformulated into a dispersion containing 40 g/kg of the chemical. The powder will be added, without reweighing, to mixing tanks and mixed with other chemicals. The resultant dispersion will be chilled and stored for up to several weeks in closed plastic bags in a cold storage area on site. Reformulation will be carried out approximately 25 times per year.

5.2 Use

The dispersion, containing C-1658, will be taken from storage and added to melt tanks together with other chemicals and then pumped to closely-controlled automated processing equipment for incorporation into photographic film and paper products.

6. OCCUPATIONAL EXPOSURE

The notified chemical will be reformulated and used at only one site in Australia. C-1658 powder will be imported in pre-weighed units. The units will be stored on site in a sealed shipping container. Worker exposure during transport and storage of the powder or dispersion should be minimal under normal conditions.

6.1 Reformulation

During reformulation, worker exposure to C-1658 may occur when the powder is added to the mixing tanks. Inhalation is the major route of potential exposure to the powder. Local exhaust ventilation will be fitted close to the mixing tanks. The notifier states that workers handling the powder will wear protective clothing, safety glasses, surgical gloves and disposable dust masks.

6.2 Use

During use, worker exposure may occur when the dispersion is added to the mixing tanks. The major route of potential exposure for the dispersion is dermal. The notifier states that workers handling the dispersion will wear protective clothing, safety glasses, surgical gloves and disposable dust masks. Once C-1658 becomes an integral part of an article there will be no potential exposure to the chemical.

7. PUBLIC EXPOSURE

Under the stated conditions of reformulation, use and release to the environment, the potential for public exposure is negligible.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

The company states that there are no anticipated releases to the environment of C-1658 powder. Approximately 10% (amount to be confirmed) of the dispersion containing C-1658 could be released to the municipal sewer. Further losses of about 10% are encountered when the dispersion is added to the emulsion and the film is coated. However, this waste is routed through the Port Kembla silver recovery plant and from its physico-chemical properties the C-1658 is likely to be adsorbed to the removed solids from which silver (approx. 10%) is recovered and the remainder incinerated. The company is presently undertaking some analytical testing of the initial effluent, the recovered cake and the filtrate to confirm this. The municipal sewer flow is routed for secondary treatment at Werribee treatment facility. Less than 1% of wastes may be sent to a secured landfill.

8.2 Fate

C-1658 will mainly enter the environment when the dispersion containing the notified substance is discharged to the sewer. It would appear unlikely that C-1658 would undergo significant microbial or chemical breakdown in the sewerage system. Three treatment systems are combined throughout the course of a year at the Werribee treatment complex, land filtration in summer and grass filtration and lagoon treatment in winter (2). Its most likely fate would appear to be sorption onto suspended solids and settling out over the land or into lagoon sludge, as sewage

inflow passes through the filtration systems at Werribee. This may result in the accumulation of C-1658 in the soil, but prospects of leaching to any appreciable extent appear minimal, in view of the low water solubility and expected strong adsorption.

. Biodegradation

Ready biodegradability was investigated using the modified Sturm test (OECD Guideline 301B) with measurement of evolved carbon dioxide. The extent of biodegradation amounted to 8% in 28 days at a nominal concentration of 10 ppm and 9% at 20 ppm. The results indicate that C-1658 is not readily biodegradable.

. Bioaccumulation

C-1658 has a low water solubility and is not readily biodegraded and therefore may bioaccumlate. However, the high molecular weight and relatively large molecular size may preclude this (3). Further, as the log Pow value has been estimated as 7.5, these considerations taken together would indicate that C-1658's bioaccumulation potential is likely to be low. The molecule is also not very fat soluble.

The possibility of soil accumulation needs consideration. However, C-1658 contains linkages such as the ester and amide which would be expected to be vulnerable to microbial cleavage in the soil. Thus significant accumulation is not expected.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Table 1: Summary of the acute toxicity of C-1658:

Test	Species	Dose	Outcome	Ref.
Oral Toxicity	Rat	5000 mg/kg	LD_{50} >5000 mg/kg	4
Dermal Toxicity	Rat	2000 mg/kg	LD_{50} >2000 mg/kg	5
Skin Irritation	Rabbit	0.5 g	non-irritant	6
Eye Irritation	Rabbit	0.1 g	non-irritant	7
Skin Sensitisation	Guinea Pig	0.5 g	non-sensitising	8

9.1.1 Oral Toxicity (5)

This limit test was performed according to the OECD Guidelines for Testing Chemicals, Section 4: Health Effects, Guideline 401, 1981.

A single 5000 mg/kg dose of C-1658 was administered by gavage to 5 male and 5 female CD(SD)BR rats. The chemical was suspended in 1/2% Jaguar guar gum. The animals were observed for 14 days post-treatment. The animals were killed after 14 days and necropsy performed. All animals gained weight during the study and no abnormal clinical signs or gross pathological changes were noted. The acute oral rat LD_{50} was greater than 5000 mg/kg under the conditions of the study.

9.1.2 Dermal Toxicity (6)

This limit test was performed according to the OECD Guidelines for Testing Chemicals, Section 4: Health Effects, Guideline 402, 1981.

A 2000 mg/kg dose of C-1658 was applied to the clipped backs of 5 male and 5 female CD(SD)BR rats. The chemical was placed on the skin under a fibre pad and covered with an occlusive wrap for 24 hours. The treated skin was washed with water after removal of the wrap and the animals were observed for 14 days. All animals gained weight during the study, no abnormal clinical signs were noted and no macroscopic organ changes were observed at necropsy. The acute dermal rat LD_{50} was greater than 2000 mg/kg under the conditions of the study.

9.1.3 Skin Irritation (7)

This study was performed according to the OECD Guidelines for Testing Chemicals, Section 4: Health Effects, Guideline 404, 1981.

A 0.5g dose of C-1658 was moistened with water and applied under an occlusive wrap to the clipped backs of 3 New Zealand White rabbits. The wraps were removed after 4 hours and the treated skin washed with water. The animals were observed at 1 hour, and 1, 2, 3, 7 and 14 days after removal of the wrap. There were no signs of erythema or oedema in any of the treated animals. Under the conditions of the study, C-1658 is not a skin irritant in rabbits.

9.1.4 Eye Irritation (8)

This study was performed according to the OECD Guidelines for Testing Chemicals, Section 4: Health Effects, Guideline 405, 1981.

A single 0.1 g dose of C-1658 was instilled into the conjunctival sac of one eye of each of six New Zealand White rabbits. Three of the eyes were immediately washed with water. The eyes were observed at 1, 24, 48 and 72 hours post-instillation. At the 24 hour observation, fluorescein was added to the treated eyes to determine corneal integrity. Erythema was noted in all eyes at 1 hour but had subsided by the 24 hour observation. This effect is likely due to mechanical abrasion of the eye by the powder. Under the conditions of the study C-1658 was not an eye irritant in rabbits.

9.1.5 Skin Sensitisation (9)

This skin sensitisation study was performed according to the OECD Guidelines for Testing Chemicals, Section 4: Health Effects, Guideline 406, 1981. The study was conducted with CRL:(HA)BR Hartley Guinea Pigs using the Buehler method.

Preliminary study

A primary irritation study was initially carried out by applying 0.5 g of C-1658 to the clipped backs of 3 guinea pigs. The test material was held in place under an occlusive wrap for 6 hours. The guinea pigs were observed at 24 and 48 hours after the wrap was removed. No signs of erythema or oedema were noted.

Induction and challenge study

As in the preliminary study, 0.5 g of C-1658 was applied to the clipped backs of 10 guinea pigs (5 female and 5 male). This procedure was repeated weekly for 3 weeks. Two weeks after the third induction exposure the guinea pigs were challenged by similarly applying 0.5 g to the opposite side of their backs. To differentiate irritation and sensitisation, 10 untreated guinea pigs were challenged at this time. Both groups were observed at 24 and 48 hours after removal of the wrap. No erythema was observed in any of the treated animals. Slight oedema was noted in 3/10 animals in the induced group at either 24 hours or 48 hours after challenge. In this study, C-1658 was not considered a sensitiser in guinea pigs.

9.2 Short-term 28-day Repeated Dose Oral Toxicity (10)

CD(SD)BR rats were fed diets of C-1658 in corn oil for 28 days. Four groups of five males were fed C-1658 at dose levels of 0, 80, 240 or 1052 mg/kg/day and four groups of five females were fed C-1658 at dose levels of 0, 88, 268 or 1146 mg/kg/day. The animals were killed on day 29 of the study and necropsy performed. No deaths occurred during the study and bodyweight gain was normal. In the highest dose group, yellow discolouration of the hair was seen in all animals and was presumed to be due to contact between the hair coat and metabolites excreted in the urine. There were no treatment related effects in food consumption, hematology, clinical chemistry or organ weights. Gross and histopathology were unremarkable.

Results from this 28-day study indicate that C-1658 has no significant toxicological effects in rats at the dose levels tested.

9.3 Genotoxicity

9.3.1 Salmonella typhimurium, Reverse Mutation Assay (11)

C-1658 was tested in two independent Ames tests for mutagenicity using *Salmonella typhimurium* strains TA-1535, TA-1537, TA-1538, TA-98 and TA-100. The tests were performed at concentrations of 1, 10, 100, 500, 1000, 2500, 5000 and 10000 µg per plate, both in the presence and absence of mammalian microsomal enzyme activation (S9 liver mix). Solvent controls, both in the presence and absence of S9 mix, were used as negative controls. Positive controls included sodium azide, 2-nitrofluorene and quinacrine mustard without microsomal activation and 2-anthramine with microsomal activation. No dose-related increase in the number of revertant colonies was observed in any of the strains exposed to C-1658 or the negative controls. In contrast, the positive controls showed marked increases in the number of revertant colonies. C-1658 did not produce mutations in *Salmonella typhimurium* under the conditions of the study.

9.3.2 *In Vivo* Micronucleus Test (12)

C-1658 in corn oil, at concentrations of 1250, 2500 or 5000 mg/kg, was administered by oral gavage to groups of ICR mice (15 males and 15 females per group). Corn oil was used as the negative control and was administered by oral gavage to 15 male and 15 female mice at a volume of 25 ml/kg. Ten animals (5 males and 5 females) were killed at 24, 48 and 72 hours after administration of the test article. The positive control, triethylenemelamine, at a concentration of 1.5 mg/kg was administered intraperitoneally to 5 male and 5 female mice. The positive control group was killed 24 hours after administration. The bone marrow was collected for micronuclei analysis. Neither C-1658 or the corn oil control was associated with an increase in the number of micronucleated polychromatic erythrocytes (PCEs). In contrast, the marrow of the positive controls showed significant increases in micronucleated PCEs.

9.4 Overall Assessment of Toxicological Data

Results of toxicity studies indicate that C-1658 has low acute oral and dermal toxicity (rats), is not an eye or skin irritant (rabbits) and is not a skin sensitiser (guinea pigs). A 28-day repeat-dose oral toxicity study in rats showed no significant toxicological effects. C-1658 was found to be non-genotoxic in an Ames test and in an *in vivo* micronucleus test.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Test	Species	Result
Acute toxicity	Fathead minnow	96h LC50 > 59 $mg.L^{-1}$ NOEC > 59 $mg.L^{-1}$
Acute toxicity	*Daphnia magna*	48h EC50 > 59 $mg.L^{-1}$ NOEC = 0.59 $mg.L^{-1}$

Concentrations tested (0.59, 5.9 and 59 $mg.L^{-1}$) for fathead minnows and *Daphnia* all exceeded the aqueous solubility of C-1658 and undissolved material was observed throughout in all solutions. Although the actual concentrations are unclear, fathead minnows and *Daphnia* are unlikely to suffer acute effects up to the limit of solubility (calculated as 1.3 ppb) of C-1658.

The above results indicate that C-1658 is practically non-toxic to aquatic fauna. While reproduction tests for daphnids were not conducted, the apparent lack of acute toxicity and the probability C-1658, given its relatively high molecular weight and complex functionality, will not be absorbed by living cells, indicate that reproductive effects are unlikely to be observed.

Algal tests were similarly conducted, but significant exposure of algae is not expected given the substance will be discharged to the Melbourne sewerage system and is expected to become associated with the soil compartment at Werribee.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

Up to 0.24 tonne (to be confirmed) of C-1658 may be discharged to sewage treatment works per annum where it is likely to adsorb to sludge or soil. It should be noted that several new chemicals,

used for the same purpose and with similar physico-chemical properties, will also be used during the one product run, resulting in Kodak releasing approximately 3.6 tonne of these chemicals per annum to the sewer. This is a worse case assuming 20% is discharged to the sewer. Discussions with the company as well as Melbourne Water, including a site visit, has indicated that the company has initiated an active program aimed at identifying and reducing the amount of these discharged chemicals. This includes a renegotiation with Melbourne Water of the amount of treated effluent allowed to be discharged.

The dispersion is made up approximately 25 times per year. Assuming that equal lots of 20 kg per batch are discharged, the following "worst case" calculation, using company estimates, indicates that the final concentration reached will be 0.6 ppb.

concentration in dispersion	=	40 $g.kg^{-1}$
rate of dilution in Kodak sewer	=	10^{-4}
concentration in sewer as it leaves Kodak	=	4 ppm
flow rate of Kodak sewer at exit point	=	4 x 10^5 L/day
flow rate (average) into Werribee	=	5 x 10^8 L/day
concentration reaching Werribee	=	3.2 ppb
rate of dilution in receiving waters	=	5 - 25 times
final concentration	=	0.6 - 0.2 ppb

This calculation assumes that there will be no losses due to adsorption to sediment etc. The concentration is of a similar order of magnitude as the calculated water solubility. While aquatic organisms were exposed to levels several orders of magnitude higher than this with no apparent chemical effects, this was largely due to undissolved material and the real level of exposure is unclear. However, the substance is likely to remain with the Werribee sewerage complex, adsorbed to either sediments or soil, and the expected exposure to natural organisms and bioaccumulation is likely to be low. Therefore, C-1658 is likely to present a low hazard to the environment.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Under the use pattern outlined by the notifier, the potential for public exposure to C-1658 is negligible. Once C-1658 is incorporated into photographic film or paper it is protected by

several layers of overcoat. Therefore, public and worker exposure to C-1658 in the finished product will be negligible.

Workers who add the powder to the mixing tank, pack the dispersion, add the dispersion, clean equipment and clean up spills may come into contact with the notified chemical and should take personal protective measures. The major route of potential exposure to the powder is inhalation. Also, C-1658 is combustible and is capable of a dust explosion. Therefore, adequate engineering controls should be implemented to minimise both worker exposure and the possibility of a dust explosion. Under normal use conditions, occupational exposure to C-1658 is expected to be low.

C-1658 has extremely low volatility and the particle size of the dye is well above the respirable size of 7 µm (12). Acute toxicity tests indicate that C-1658 has low acute oral and dermal toxicity and is non irritating to the skin and eye.

Therefore, due to its low exposure under normal use conditions, low acute toxicity and physico-chemical properties, C-1658 is unlikely to pose a significant health and safety hazard to the public and workers.

13. RECOMMENDATIONS

To minimise public and worker exposure to C-1658 the following guidelines and precautions should be observed:

. the workplace should be well ventilated and engineering controls such as local exhaust ventilation should be employed where the powder is handled and mixed;

. workers who may come into contact with C-1658 should

  - wear protective clothing;

  - observe good personal hygiene practices.

. in areas where the powder is handled and mixed and the ventilation is insufficient, workers should also:

  - wear a respirator complying with Australian Standard AS 1716 (13) and chosen and used in accordance with Australian Standard AS 1715 (14); and

- wear safety glasses or goggles complying with Australian Standard AS 1337 (15) and chosen and used in accordance with Australian Standard AS 1336 (16).

. good work practices should be implemented to avoid the generation of a dust cloud, spillages and splashings;

. all sources of ignition, hot surfaces or high temperatures should be eliminated in areas where the powder is handled. Electrical fittings, machinery and equipment should be earthed and dust-proof;

. a copy of the Material Safety Data Sheet should be easily accessible to employees; and

. disposal of C-1658 should be in accordance with local regulations.

It is recommended that the company, in conjunction with Melbourne Water, continue to look at ways of minimising the amount of C-1658 discharged.

14. MATERIAL SAFETY DATA SHEET

The Material Safety Data Sheet (MSDS) for C-1658 is provided at Attachment 1. This MSDS was provided by Kodak Australasia as part of their notification statement. They are reproduced here as a matter of record. The accuracy of this information remains the responsibility of Kodak Australasia.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act), secondary notification of C-1658 shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

16. REFERENCES

1. Lyman, W.J. et al, *Handbook of Chemical Property Estimation Methods*, McGraw-Hill, 1982, pp. 2-15 and pp. 4-9.

2. *Australian Sewage Profile*, Department of the Arts, Sport, the Environment and Territories internal report, 1988.

3. Connell, D.W., *Bioaccumulation of Xenobiotic Compounds*, CRC Press, 1990, p. 56.

4. *Acute Oral Toxicity of C-1658,* HAEL Report No. TX-87-17. Data on file, Eastman Kodak Company, Rochester, NY, 1987.

5. *Acute Dermal Toxicity of C-1658*, HAEL Report No. TX-87-18. Data on file, Eastman Kodak Company, Rochester, NY, 1987.

6. *Acute Skin Irritation of C-1658*, HAEL Report No. TX-87-19. Data on file, Eastman Kodak Company, Rochester, NY, 1987.

7. *Acute Eye Irritation of C-1658*, HAEL Report No. TX-87-20. Data on file, Eastman Kodak Company, Rochester, NY, 1987.

8. *Skin Sensitization Study (Buehler Method) of C-1658*, HAEL Report No. TX-87-21. Data on file, Eastman Kodak Company, Rochester, NY, 1987.

9. *Four Week Oral Toxicity Study of C-1658 in the Rat*, HAEL Report No. TX-87-62. Data on file, Eastman Kodak Company, Rochester, NY, 1987.

10. *Mutagenicity Evaluation of C-1658 in the Ames Salomella/Microsome Reverse Mutation Assay*, Hazleton Laboratories, HAL Project No. 20988. Data on file, Eastman Kodak Company, Rochester, NY, 1987.

11. *Mutagenicity Test on C-1658 the In Vivo Mouse Micronucleus Assay,* Hazelton Laboratories, HAL Project No. 20996. Data on file, Eastman Kodak Company, Rochester, NY, 1987.

12. National Occupational Health and Safety Commission, *Exposure Standards for Atmospheric Contaminants in the Occupational Environment*, AGPS, Canberra, 1990.

13. Standards Australia, AS 1716 *Respiratory Protective Devices*, Standards Australia, Sydney, 1991.

14. Standards Australia, AS 1715 *Selection, Use and Maintenance of Respiratory Protective Devices*, Standards Australia, Sydney, 1991.

15. Standards Australia, AS 1337 *Eye Protectors for Industrial Applications*, Standards Australia, Sydney, 1984.

16. Standards Australia, AS 1336 *Recommended Practices for Eye Protection in the Industrial Environment*, Standards Australia, Sydney, 1982.