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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

MHD-64

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health and Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment, Water, Heritage and the Arts.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

This Full Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Sony Australia Ltd (ABN: 59 001 215 354)
33-39 Talavera Road
North Ryde NSW 2113

NOTIFICATION CATEGORY
Limited-small volume: Chemical other than polymer (1 tonne or less per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Chemical Name, Other Names, CAS Number, Molecular Formula, Structural Formula, Molecular Weight, Purity, Non-Hazardous Impurities, Import Volume, Identity of Recipients.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
EU (1998), TSCA, Switzerland (2007), Japan (2003)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
MHD-64 (concentration of <1% in imported product)
Marketing names of the imported ink ribbon products include:
2UPC-R154(H,H/1,PC,HF,PF), 2UPC-R155(H,H/1), 2UPC-R156(H,H/1,HF,PF), 2UPC-R46A, 2UPC-R57A, 2UPC-R68A, 2UPC-C14, 2UPC-C15, UPC-21L, UPC-21S, 10UPC-X34/0, 10UPC-X46/0

MOLECULAR WEIGHT
< 500 Da

ANALYTICAL DATA
Reference NMR, IR, HPLC, UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY >95%

HAZARDOUS IMPURITIES
None

ADDITIVES/ADJUVANTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: Dark red powder

Property	Value	Data Source/Justification
Melting Point	191 ± 1°C	Measured
Boiling Point	The notified chemical decomposed prior to boiling.	Measured
Density	1185 kg/m^3 at 20 ± 0.5°C	Measured
Vapour Pressure	< 3.1 x 10^{-8} kPa at 25°C	Measured
Water Solubility	< 5 × 10^{-5} g/L at 20.0°C	Estimated
Fat (or n-octanol) Solubility	146mg/100g standard fat at 37.0°C	Measured
Hydrolysis as a Function of pH	Potentially hydrolysable at pH 4	Based on the functional group chemistry of the notified chemical.
Partition Coefficient (n-octanol/water)	log P_{ow} > 4.2 at 21.0°C	Estimated
Adsorption/Desorption	log K_{oc} > 5.63 at 20°C	Estimated
Dissociation Constant	pK_a = 3.67	Calculated
Particle Size	Inhalable fraction (<100 μm): ~80% Respirable fraction (<10 μm): 11.74% MMAD* = 34.158 μm	Measured
Flash Point	Not determined	Low vapour pressure solid.
Flammability	Not highly flammable	Measured
Autoignition Temperature	>191°C	Measured
Explosive Properties	Not explosive	Measured
Oxidising Properties	Oxidising	Measured

* MMAD = Mass Median Aerodynamic Diameter

DISCUSSION OF PROPERTIES

For full details of tests on physical and chemical properties, please refer to Appendix A.

Reactivity

The notified chemical is expected to be stable and not to react with air or water under normal conditions.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

The notified chemical will be imported into Australia as a component of an ink ribbon product at inclusion levels of <1% in the ink.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	<1	<1	<1	<1	<1

PORT OF ENTRY

Sydney

TRANSPORTATION AND PACKAGING

Printer ink ribbons will either be contained within a polypropylene bag inside a cardboard box or within rigid plastic cassettes. It will be transported in Australia mainly by truck.

USE

The notified chemical will be a component of dye for use in colour dye sublimation printing (eg. photographs). These printers will be used by both office workers, such as those in digital photo printing shops, and members of the public.

OPERATION DESCRIPTION

The notified chemical will be supplied as a component of printer ink ribbons (inclusion levels of <1%). The ink ribbons will be fitted directly into dye sublimation printers by office workers. The printer ink ribbon consists of a polyester sheet with the notified chemical coated on one side. The dye will be transferred onto the substrate sheets by heat (approximately 200°C). Finally a clear film overlay will be applied to the receiving sheet from the printer ribbon, prior to the printed product being automatically expelled from the printer.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency (days/year)*
Ink ribbon changes (operator in digital photo printing shop)	1	Minimal	26

EXPOSURE DETAILS
Dermal exposure of workers to the notified chemical may occur infrequently by direct contact with the ink ribbon that is coated with the notified chemical (inclusion levels of <1%) during fitting or replacement of the ribbon into the printer. Such exposure is expected to be negligible, as the ribbon is likely to be contained within rigid plastic cassettes and only coats the notified chemical on one side. In addition, the wearing of gloves is recommended during handling of the ink ribbon, further reducing the possibility for exposure.

Exposure to the notified chemical during printing processes, including inhalation exposure, is unlikely to occur as it is contained within the printer and is localised in nature.

Dermal exposure to the notified chemical from handling of printed sheets is unlikely to occur as the notified chemical will be covered with a clear film overlay (this film may not be cured upon exit from the printer, taking several hours or days, but is expected to prevent direct exposure to the notified chemical).

6.1.2. Public exposure
The exposure of the public to the notified chemical is expected to be identical or of a lesser extent than that experienced by workers using the same products, due to the likely lower frequency of use.

6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	Low toxicity LD50 >5000 mg/kg bw
Rat, acute dermal toxicity	Low toxicity LD50 >2000 mg/kg bw
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Mutagenicity – bacterial reverse mutation	non mutagenic

Toxicokinetics, metabolism and distribution
Many azo dyes are unlikely to be absorbed through the skin because of their size and polarity (Øllgaard, 1998). Smaller species may undergo percutaneous absorption, depending on their properties. There was no evidence from the toxicological investigations to suggest that the notified chemical was absorbed following dermal exposure. Absorption through the skin is not expected to be significant, given its low water solubility (<1 mg/L), and relatively high partition coefficient (log P>4).

The azo linkage is the most labile portion of an azo dye molecule, and it is readily enzymatically metabolised in mammals, including man (SCCNFP, 2002). Liver azo reductase enzymes reductively cleave the molecule into

component amines. Some metabolism may also occur in the cells of the bladder wall, and during percutaneous absorption. Anaerobic intestinal bacteria are also capable of catalysing reductive cleavage of the azo bond. In addition, bacterial skin microflora have been reported to be able to break down azo dyes into smaller amine species through azo reduction, and these may be readily absorbed (SCCNFP, 2002). As such, azo dyes should be assessed for toxicity on the basis of their component amines.

The particle size of the notified polymer indicates that a significant portion of the notified chemical will be inspirable with a small portion also respirable. It the notified chemical is inhaled at low levels, it is likely to be cleared from the upper respiratory tract readily through mucociliary action. Small proportions of the notified chemical may reach the lower respiratory tract, but it should still be readily cleared from the lungs unless high levels are inhaled. When high concentrations of the notified chemical are inhaled, it is likely to be cleared from the lungs, but this may be slower and temporary respiratory impairment is possible.

General toxicity
The notified chemical was of low acute oral and dermal toxicity in rats (LD50 >2,000 mg/kg bw), and no treatment-related effects were observed. The notified chemical was found to be slightly irritating to the eyes and skin.

Sensitisation
Whilst the notified chemical was negative in a skin sensitisation test, its possible degradation products/metabolites contain structural moieties that are known to be alerts for sensitisation (Barratt *et al*, 1994). A number of azo dyes have been demonstrated to be skin sensitisers in humans, using clinical patch tests, and others have been associated with causing allergic contact dermatitis (Øllgaard *et al*, 1998). Therefore, the potential for the notified chemical to induce skin sensitisation upon exposure to humans cannot be completely ruled out.

Mutagenicity
Azo dyes as a class are a concern for their potential induction of mutagenicity and carcinogenicity. Reductive cleavage or degradation into component aromatic amines is perhaps the most important mechanism leading to the genotoxicity of azo dyes (SCCNFP, 2002). This mechanism is thought to contribute to the carcinogenicity of many azo dyes.

The notified chemical is not expected to be reductively cleaved to release any of the restricted aromatic amines specified in either the Appendix to EC Directive 76/769/EEC (EC, 2004) or the annexes of EU SCCNFP/0495/01 (SCCNFP, 2002). However, the notified chemical can be cleaved by azo reduction into arylamine species, each of which potentially could be mutagenic.

The notifier has supplied test results showing that the notified chemical was not mutagenic in bacteria. The Ames test performed was a standard test, according to OECD Test Guideline 471. However, this test guideline strongly recommends the use of alternative procedures for the detection of mutagenicity of azo dyes, as it is recognised that the standard procedure may not be sufficiently sensitive for these chemicals. Modified tests, such as that of Prival and Mitchell, utilise a reductive pre-incubation step (during which the azo dye is reduced to amine species) before the test is carried out (Prival and Mitchell, 1982). This modified test is thought to yield a greater detection of mutagenic azo dyes. As such, mutagenicity of the notified chemical cannot be ruled out.

Overall, these results do not rule out the notified chemical as a possible mutagen or carcinogen, as reductive metabolism may be significant *in vivo*. It is also noted that, in general, the degree of correlation between mutagenicity study results and the carcinogenicity of azo dyes as a class is poor, likely due to their complex metabolism *in vivo* (Brown and DeVito, 1993, referenced in Øllgaard, 1998).

Classification
Based on the available data the notified chemical can not be classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human health risk characterisation

6.3.1. Occupational health and safety
Workers contacting the notified chemical during handling of printer ink ribbons or printed sheets will only be

exposed to concentrations of <1% infrequently and for relatively short time periods and thus exposure is expected to be minimal. In addition, under normal circumstances, workers are unlikely to make deliberate contact with the notified chemical. Accidental exposure is likely to involve low level contact with inks on the fingertips. As such, the risk of irritancy effects resulting from dermal exposure to the notified chemical are unlikely. At such low levels of exposure, the risk of skin sensitisation is also unlikely.

In conclusion, the occupational health and safety risk associated with the notified polymer is considered to be low, assuming that exposure is of low frequency and short duration.

6.3.2. Public health

The risk to the health of the public during the use of dye sublimation printers containing the notified chemical are expected to be identical or similar to that experienced by office workers, and therefore is expected to be low.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The importation of the notified chemical as a minor component of printer ribbons contained within rigid plastic cassettes will limit any potential environmental releases to those arising from accidental breakages of the cassettes. It is expected that cassettes broken during importation, transport, or storage will be sent either to recyclers of plastic printing components or to landfill.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be used exclusively in the production of photographic images on paper. In the production of these digital photographic prints, the transfer of the notified chemical from the printer ribbon to the receiving paper occurs within the printer. This thermally activated process takes place in close proximity to the receiving paper and no fugitive releases of the notified chemical are expected from this application method. The clear plastic film that is overlaid on the image formed on the receiving sheet will prevent release of the notified chemical from the final photographic sheet until the photograph degrades.

A small fraction of the initial quantity of notified chemical may remain on spent printer ribbons. The used cassettes containing the spent ribbons (and hence the residual notified chemical) will be sent either to recyclers of plastic printing components or to landfill. This small residual quantity of notified chemical may slowly leach from spent printer ribbons in landfill, but it will adsorb strongly to soil and will not be mobile.

RELEASE OF CHEMICAL FROM DISPOSAL

The majority of the imported quantity of notified chemical will be disposed of in the form of discarded photographs. As photographs are unsuitable for paper recycling, it is expected that most photographs and hence the major proportion of imported notified chemical will be disposed of in landfill sites. The notified chemical may be slowly released by decomposing photographic prints, but it will adsorb strongly to soil and will not be mobile. A small proportion of photographs maybe incinerated in domestic situations. The incineration of photographs with residues of the notified chemical will release oxides of carbon and nitrogen, and water.

7.1.2 Environmental fate

The notified chemical is insoluble in water with a very strong tendency to partition onto soil. The notified chemical will therefore not be mobile in either aquatic or terrestrial eco-systems. The notified chemical is not readily biodegradable but, as indicated in Appendix C, it is inherently biodegradable. Based on its chemical structure, the notified chemical is expected to be degraded by abiotic process including hydrolysis under acidic conditions. The notified chemical will therefore degrade in the environment by both biotic and abiotic processes.

7.1.3 Predicted Environmental Concentration (PEC)

The notified chemical is not expected to be released to aquatic environments. Hence, no PEC was calculated.

7.2. Environmental effects assessment

No ecotoxicity data were submitted.

7.2.1 Predicted No-Effect Concentration

As no ecotoxicology data are available for the notified chemical, no PNEC has been calculated.

7.3. Environmental risk assessment

The low quantities of notified chemical introduced, the distributed disposal pattern, and the very limited possibility for environmental release indicates that there will be no significant exposure of aquatic and terrestrial biota to this chemical. Therefore, the risk of an adverse effect on the environment from the intended use of the notified chemical is considered low.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

Based on the available data the notified chemical cannot be classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

Human health risk assessment

Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unacceptable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unacceptable risk to public health.

Environmental risk assessment

On the basis of the proposed use pattern and the low potential for environmental exposure, the notified chemical is not considered to pose a risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid contact with eyes and skin.

- Service personnel should wear cotton or disposable gloves when removing spent printer cartridges containing the notified chemical and during routine maintenance and repairs.

- A copy of the MSDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Public Health

- The following measures should be taken to minimise public exposure to the notified chemical:
  – Avoid skin contact with ink.

Environment

- The notified chemical should be disposed of by landfill.

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- the importation volume exceeds one tonne per annum notified chemical;
- the notified chemical is imported in any form other than on printer ribbons;
- additional information related to the mutagenicity/carcinogenicity of the notified chemical becomes available.

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from being a component of dye for use in colour dye sublimation printing, or is likely to change significantly;
- the amount of chemical being introduced has increased from 1 tonne per annum, or is likely to increase, significantly;
- if the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

No additional secondary notification conditions are stipulated.

Material Safety Data Sheet
The MSDS of products containing the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point 191 ± 1ºC

Method EC Directive 84/449/EEC A.1 Melting/Freezing Temperature.
Test Facility SafePharm (1991a)

Boiling Point

Remarks The notified chemical was observed to decompose prior to boiling at atmospheric pressure and also at reduced pressure.
Test Facility SafePharm (1992)

Density 1185 kg/m^3 at 20 ± 0.5ºC

Method EC Directive 84/449/EEC A.3 Relative Density.
Air comparison pycnometer
Test Facility SafePharm (1992)

Vapour Pressure < 3.1 x 10^{-8} kPa at 25ºC

Method EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks The vapour pressure at 25ºC was extrapolated from measurements taken with a vapour pressure balance.
Test Facility University of Leeds (1991)

Water Solubility < 5 × 10^{-5} g/L at 20.0ºC

Method EC Directive 84/449/EEC A.6 Water Solubility.
Remarks The water solubility of the notified chemical at pH 6.1 was evaluated by a shake-flask method. The saturation concentration of the notified chemical was below the limit-of-detection of the spectrophotometric analytical technique employed and the reported water solubility is therefore an estimated upper limit.
Test Facility SafePharm (1992)

Fat (or n-octanol) Solubility 146 mg/100 g standard fat at 37.0°C

Method EC Directive 84/449/EEC A.7 Fat Solubility.
Remarks The concentration of notified chemical dissolved in standard fat was determined spectrophotometrically. The measured solubility in 12 replicate tests spanned a range from 62.7 to 218 mg/100 g fat and the reported value is the mean of these results.
Test Facility SafePharm (1992)

Hydrolysis as a Function of pH Not determined

Remarks The functional group chemistry of the notified chemical indicates that it may hydrolyse at pH 4. However, the rate of this process will be limited by the low water solubility of the notified chemical.

Partition Coefficient (n-octanol/water) log P_{ow} > 4.2 at 21.0ºC

Method EC Directive 84/449/EEC A.8 Partition Coefficient.
Shake flask method
Remarks The concentration of notified chemical in the aqueous and n-octanol phases was determined spectrophotometrically. The concentration in the aqueous phase was beneath the limit-of-detection and the quoted partitioning constant is therefore a lower limit.
Test Facility SafePharm (1992)

Adsorption/Desorption log K_{oc} > 5.63 at 20°C

Method OECD TG 121 Estimation of the Adsorption Coefficient (K_{oc}) on Soil and Sewage Sludge using High Performance Liquid Chromatography (HPLC)
Remarks The adsorption coefficient for the notified chemical is a lower limit based on the longer retention time of this substance as compared with a reference compound.
Test Facility NOTOX B.V. (2007)

Dissociation Constant $pK_a = 3.67$

Method Calculated by the Perrin method.
Remarks Could not be determined experimentally because of the low water solubility.
Test Facility NOTOX B.V. (2007)

Particle Size

Method OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions.
Laser diffraction (BS ISO 13320-1 : 1999)
Results

Range (μm)	*Mass (%)*
<9.012	10
<31.377	50
<287.527	90

11.74% by volume of sample was <10 μm
Mass Median Aerodynamic Diameter (MMAD) = 34.158 μm
Test Facility Chilworth (2007)

Flammability Not highly flammable

Method EC Directive 84/449/EEC A.10 Flammability (Solids).
Test Facility SafePharm (1992)

Autoignition Temperature >191°C

Method EC Directive 84/449/EEC A.16 Relative Self-Ignition Temperature for Solids.
Test Facility SafePharm (1992)

Explosive Properties Not explosive

Method EC Directive 92/69/EEC A.14 Explosive Properties.
Test Facility Nobel (1991)

Oxidizing Properties Oxidising

Method EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Remarks The notified chemical is considered to have oxidising properties, as its maximum burning rate with cellulose mixtures was significantly greater than that of the reference mixtures.
Test Facility SafePharm (1992)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 401 Acute Oral Toxicity – Limit Test. EC Directive 84/449/EEC B.1 Acute Toxicity (Oral) – Limit Test.
Species/Strain	Rat/Sprague-Dawley
Vehicle	Arachis oil BP
Remarks - Method	No significant protocol deviations
RESULTS	
LD50	>5000 mg/kg bw
Remarks - Results	No mortality, signs of toxicity, or adverse effects in organs were observed at the dose level of 5000 mg/kg bw.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	SafePharm (1991b)

B.2. Acute toxicity – dermal

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test. EC Directive 84/449/EEC B.3 Acute Toxicity (Dermal) – Limit Test.
Species/Strain	Rat/Sprague-Dawley
Vehicle	Arachis oil BP
Type of dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations
RESULTS	
LD50	>2000 mg/kg bw
Remarks - Results	No mortality, signs of toxicity, or adverse effects in organs were observed at the dose level of 2000 mg/kg bw.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	SafePharm (1991c)

B.3. Irritation – skin

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Directive 84/449/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	2M, 1F
Vehicle	Distilled water
Observation Period	7 days
Type of Dressing	Semi-occlusive
Remarks - Method	No significant protocol deviations.
RESULTS	

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0.7	0.7	1.3	2	< 7 days	0
Oedema	0.3	0.3	0.7	1	< 72 hr	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results: Very slight erythema was observed on all animals one hour after patch removal and on two animals at 24 and 48 hour observation times. Well defined erythema was noted on one animal at 24 hour, and very slight erythema on the same animal at the 48 and 72 hour time point. Very slight oedema was noted at all treated sites at the 24 hour observation and persisted at one site at the 48 hour observation.

CONCLUSION: The notified chemical is slightly irritating to the skin.

TEST FACILITY: SafePharm (1991d)

B.4. Irritation – eye

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 84/449/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain: Rabbit/New Zealand White
Number of Animals: 3
Observation Period: 72 hr
Remarks - Method: No significant protocol deviations.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.3	0	0.3	1	< 48 hr	0
Conjunctiva: chemosis	0	0	0	1	< 4 hr	0
Conjunctiva: discharge	0	0	0	2	< 24 hr	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	1	< 24 hr	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results: None

CONCLUSION: The notified chemical is slightly irritating to the eye.

TEST FACILITY: SafePharm (1991e)

B.5. Skin sensitisation

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 406 Skin Sensitisation – Magnusson and Kligman Maximisation Test.
EC Directive 84/449/EC B.6 Skin Sensitisation - Magnusson and Kligman Maximisation Test.

Species/Strain: Guinea pig/Albino Dunkin-Hartley
PRELIMINARY STUDY: Maximum Non-irritating Concentration:

	intradermal: 10% topical: 25%
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 10
INDUCTION PHASE	Induction Concentration: intradermal: 10% topical: 25%
Signs of Irritation	Following topical induction, dark red staining caused by the test material was noted at all treatment sites. This prevented accurate evaluation of skin reactions.
CHALLENGE PHASE	
1st challenge	topical: 25%
Remarks - Method	No significant protocol deviations.

RESULTS

Remarks - Results	Slight red coloured staining caused by the test material was noted at all treatment sites following topical challenge. This did not prevent evaluation of erythema. No adverse reactions or sensitisation responses were observed.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	SafePharm (1991f)

B.6. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 84/449/EEC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1538, TA1535, TA1537, TA98, TA100
Metabolic Activation System	S9 mix from Sprague-Dawley rat liver induced with Aroclor 1254
Concentration Range in Main Test	a) With metabolic activation: 8-5000 µg/plate b) Without metabolic activation: 8-5000 µg/plate
Vehicle	Dimethyl sulfoxide
Remarks - Method	An *E.coli* WP2 strain was not used in this test. Some of the positive controls used in the absence of metabolic activation were not those recommended by the OECD Test Guideline.

RESULTS

Remarks - Results	No significant increases in the number of revertant colonies were observed during the test. Cytotoxicity was not observed at the concentrations tested. Precipitation of the test substance was observed at and above the dose level of 1000 µg/plate.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	SafePharm (1991g)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 D Ready Biodegradability: Closed Bottle Test
Inoculum	Activated sludge bacteria from the aeration stage of a municipal sewage treatment plant treating predominantly domestic sewage.
Exposure Period	28 days
Auxiliary Solvent	None. The required quantity of notified chemical was loaded onto glass filter paper supports and placed in the test bottles.
Analytical Monitoring	The oxygen concentration was determined electrochemically.
Remarks - Method	The biodegradation of the notified chemical was evaluated at a nominal test concentration of 1.5 mg/L. The theoretical oxygen demand for the notified chemical is 2.91 mg O_2 per mg. The positive control test was performed on test solutions containing 3 mg/L sodium benzoate and 2 mg/L aniline. A toxicity control test was not performed.

RESULTS

Test substance		*Sodium benzoate*		*Aniline*
Day	*% Degradation*	*Day*	*% Degradation*	*% Degradation*
5	21	5	78	40
15	36	15	88	59
28	37	28	92	68

Remarks - Results	The degradation of sodium benzoate reached the pass value within 5 days of test initiation. The degradation of aniline did not reach the pass value within the permitted 14-day window, but exceeded the pass value after 28 days. The other requirements for test validity were satisfied and the test is therefore considered valid. The biodegradation of the notified chemical did not reach the 60% pass value after 28 days and it is therefore not classified as readily biodegradable according to the test guidelines.
CONCLUSION	The notified chemical is not readily biodegradable
TEST FACILITY	SafePharm (1991h)

C.1.2. Bioaccumulation

REMARKS	The relatively high estimated log K_{ow} of the notified chemical (> 4.2), its low water solubility, and relatively low molecular weight, indicate that this substance might partition into biological membranes. However, the apparently low solubility of this substance in fat indicates that the notified chemical is unlikely to accumulate in lipids. The risk of bioaccumulation is further reduced by the very limited exposure of aquatic organisms to this notified chemical arising from its use in photographic image production, and the strong tendency of the chemical to bind to soil.

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