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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

CS-8203

This Assessment has been compiled in accordance with the provisions of *the Industrial Chemicals (Notification and Assessment) Act 1989* (the Act), and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by Worksafe Australia which also conducts the occupational health & safety assessment. The assessment of environmental hazard is conducted by the Department of the Environment, Sport, and Territories and the assessment of public health is conducted by the Department of Health and Family Services

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

CS-8203

1. APPLICANT

Hanimex Pty Limited of 108 Old Pittwater Road BROOKEVALE, NSW 2100 has submitted a limited notification statement in support of their application for an assessment certificate for CS-8203.

CS-8203 has been classified as hazardous in accordance with Worksafe Australia's *Approved Criteria for Classifying Hazardous Substances* due to its severe eye irritation properties. However, for commercial reasons, the chemical identity, chemical composition, spectral data and import quantities have been granted exemption from publication in the Full Public Report and Summary Report. The conditions of this being permitted are:

- A descriptive generic name be used to identify the substance in public reports and the Material Safety Data Sheet (MSDS),
- The relevant employee unions shall be informed of the conditions of use of CS-8203,
- The full chemical name shall be provided to any health professionals in the case of a legitimate need where exposure to the chemical may involve a health risk,
- The full chemical name shall be provided to those on site who are using the chemical and to those who are involved in planning for safe use, etc. in the case of a legitimate need,
- The Director of NICNAS will release the full chemical name etc. in the case of a request from a medical practitioner,
- Confidentiality will expire after a 3 year period,
- The chemical be identified as an eye irritant in the Health Effects Section of the MSDS, and that reference to its assessment by NICNAS be made on the MSDS,

These conditions shall be published in the Chemical Gazette

Trade Name:	CS-8203
Method of Detection and Determination:	the chemical is separated by high performance liquid chromatography and detected by ultraviolet/visible, infrared (IR) and nuclear magnetic resonance spectroscopy

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	white powder
Odour:	unknown
Melting Point:	decomposes at 158-164°C
Boiling Point:	not applicable (substance decomposes upon melting)
Density:	1500 kg/m^3 at 23°C
Vapour Pressure:	0.2 kPa at 20°C 0.35 kPa at 25°C
Water Solubility:	704 mg/L at 20°C at pH 4.7
Hydrolysis as a Function of pH:	hydrolytically stable at pH 4, 7 and 9 at 50°C.
Partition Coefficient (n-octanol/water):	log P_{ow} 2 at 20°C
Adsorption/Desorption:	adsorption coefficients - sandy loam 0.8, sandysilt loam 0.5, clay loam 3.3
Dissociation Constant:	pK_a not determined
Flammability Limits:	not flammable
Autoignition Temperature:	not auto-flammable
Explosive Properties:	not explosive
Reactivity/Stability:	not oxidising

Particle Size Distribution: range - > 400 μm 16.3%
400-125 μm 80.3%
125-75 μm 3.3%
75-30 μm < 0.1%
30-10 μm < 0.1%
< 10 μm < 0.1%

Comments on Physico-Chemical Properties

The boiling point was unable to be determined as decomposition occurred on melting.

No dissociation constant was determined when the test was conducted by a titrimetric method over the pH range 2 to 11. This would be expected as there are no readily ionisable hydrogen components on the molecule.

The adsorption coefficients for the chemical indicate that it would have high mobility in sandy soils and medium mobility in clay loam soil.

4. PURITY OF THE CHEMICAL

Degree of Purity: 99%

Lower Limit: 95%

Upper Limit: 100%

Toxic or Hazardous Impurities: none

Non-Hazardous Impurities:

Chemical name:	ammonium chloride
CAS No.:	12125-02-9
Weight percentage:	0-5%

Additives/Adjuvants: none

5. INDUSTRIAL USE, VOLUME AND FORMULATION

CS-8203 will be imported into Australia, as a component of a photographic processing reagent. The estimated quantities to be imported during 1996-99 being approximately 1 tonne.

6. OCCUPATIONAL EXPOSURE

The notified chemical will be imported in an aqueous solution (N3R) at a concentration of 1.2% in sealed 2 litre plastic bottles secured with a screw type plastic top. The bottles are packed into inner cartons which are repacked into outer cartons. The cartons are palletised and wrapped in a plastic film. From the wharf palletised cartons are transported by road to a warehouse. The product containing the notified chemical is sold in carton quantities and transported by road to mainland customers and by sea to non-mainland customers.

The notified chemical will be initially used in about 25 Fuji automated photographic film processing laboratories in Australia. This number is expected to increase as more machines are imported. N3R is used without dilution in the fixer tank of the film processing machine. At each site, exposure to the notified chemical will be limited to:

. one worker for 0.2 hours/day, approximately 125 days/year, while

charging the machine; and

. 2.5 workers for 8 hours/day, approximately 250 days/year, during machine operation.

The film processing takes place in a closed system. There is possible exposure during charging and emptying the fixer tank and local exhaust ventilation will be used at these stages.

Expected exposure to the notified chemical is approximately 0.024 kg per batch.

7. PUBLIC EXPOSURE

During the charging of the developing machine public exposure is likely to be negligible. However following completion of processing there is residual compound remaining on the film surface which is capable of being removed by contact. This is estimated as 4-6 mg/m^2 of film or 0.16-0.24 μg/roll of film (35mm x 24 exposures). The general public will handle the processed film and therefore be potentially exposed (via dermal contact) to this quantity of notified chemical. Ocular contact and oral ingestion may also result from accidental transfer of chemical from hands to eyes and mouth. Minor public exposure may result from accidental spillage of the notified chemical during transport or storage.

8. ENVIRONMENTAL EXPOSURE

Release

There is currently only one model of film processor in Australia which can use this chemistry, and some 25 photolabs have this model. No environmental exposure during transport of the chemical is expected. In the event of accidental spillages, environmental exposure would be minimal due to the small container size. Also there are adequate instructions on the MSDS to deal with spillage situations.

All photolabs have two processing machines, one being for paper processing, and the other for film processing. Within the film processing machines, there are generally five chemical tanks which are replenished from holding tanks. Any resulting overflow is collected for disposal along with the waste from other machines within the photolab, and sink wastes.

It is standard practice to rinse freshly emptied chemical containers with water and add the resulting rinsate to the chemical mix in the processor. The plastic containers are recyclable, or will be landfilled.

The concentration of the chemical in the N3R solution is approximately 1.2%. Of the photographic film and paper process chemical waste, overflow of this solution accounts for about 5%. This waste is then further diluted with water and allowed to enter the sewerage drainage system at an estimated concentration of 182 ppm.

Fate

All photographic chemical wastes are to be disposed in accordance with P.U.R.E. guidelines (Photographic Uniform Regulations for the Environment guidelines) (1). This involves disposal to sewer as the preferred option, however, where a discharger is unable to meet the requirements, or chooses not to install the necessary pre-treatment facilities, waste photographic chemicals are to be carted off site by a licensed transporter to an approved liquid waste disposal depot. Disposal to sewer usually involves dilution with other photo chemicals and water, balancing with other photo chemicals and then desilvering.

A modified Sturm Test on CS-8203 (EC Directive 92/69/EEC) to determine ready biodegradation showed it did not readily biodegrade, with 5% CO_2 production over 28 days. Its inherent biodegradability cannot be ascertained from this test.

Bioaccumulation is not expected due to its low Log P_{ow} and high water solubility (2).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of ammonium methanethiosulfinate

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat (M)	LD_{50} > 2,000 mg/kg	(3)
acute oral toxicity	rat (F)	LD_{50} > 2,000 mg/kg	(3)
acute dermal toxicity	rat (M)	LD_{50} > 2,000 mg/kg	(4)
acute dermal toxicity	rat (F)	LD_{50} > 2,000 mg/kg	(4)
eye irritation	rabbit	severe irritant	(5)
skin sensitisation	guinea pig	not sensitising	(6)

9.1.1 Oral Toxicity (3Ref No:3332)

After an initial dose-ranging study, groups of CD rats (5 per sex; approximately 5 weeks old) were administered a single gavage dose of 2,000 mg/kg of the notified chemical in aqueous suspension. Clinical signs were recorded daily and the animals were sacrificed and necropsied on day 15. Body weight was determined pre-treatment and on days 1, 2, 3, 4, 8 and 15.

There were no deaths during the study. Clinical signs observed within three hours after dosing were restricted to underactivity while piloerection and hunched posture were evident on day 2. There was bodyweight loss in 2/10 animals up to day 3 but not thereafter. Necropsy revealed no significant macroscopic signs of toxicity. The acute oral LD_{50} of the notified chemical was greater than 2,000 mg/kg in male and female rats.

9.1.2 Dermal Toxicity (4)

A dose of 2,000 mg/kg of the notified chemical in aqueous suspension was applied for 24 hours to the clipped, intact skin of CD strain rats (5 per sex, approximately 7-11 weeks old) under an occlusive dressing. Clinical signs were recorded daily and the animals were sacrificed and necropsied on day 15. Body weight was determined pre-treatment and on days 1, 8 and 15.

There were no deaths during the study. There were no clinical signs of toxicity observed at any period and bodyweight gains were normal. Necropsy revealed no significant macroscopic signs of toxicity in 8/10 animals but enlarged mandibular lymph nodes in two female animals. The acute dermal LD_{50} of the notified chemical was greater than 2,000 mg/kg in male and female rats.

9.1.3 Inhalation Toxicity

Not done. Considered not necessary.

9.1.4 Skin Irritation

Not done. Irritation was not seen in acute dermal toxicity study but was observed in the skin sensitisation study.

9.1.5 Eye Irritation (5)

In a sighting study a 0.1g sample of the notified chemical was instilled into the right conjunctival sac of one female New Zealand White rabbit. The eyes were not flushed.

At one and 24 hours after instillation the treated eye showed a diffuse beefy-red conjunctival appearance, moderate discharge, slight chemosis, iritis and corneal opacity. At 24 hours there was also areas of haemorrhage on the nictitating membrane and upper and lower eyelids. The study was terminated after 24 hours due to the severity of the reaction and no further animals were committed to the test.

9.1.6 Skin Sensitisation (6)

Groups of Dunkin-Hartley strain guinea pigs (6-8 weeks old) were divided into a treatment group (10 per sex) and a control group (5 per sex). An induction dose of 0.1 mL of Freunds Complete Adjuvant (FCA), 5% w/v ammonium methanethiosulfonate in water or 5% w/v ammonium methanethiosulfonate in FCA were injected intradermally. On day 8, 0.6 mL of 10% w/v ammonium methanethiosulfonate in water was applied to the skin over the injection sites and the area occluded for 48 hours. The control group were similarly treated, except the test material was replaced by vehicle in all cases.

On day 22, the animals were challenged by occluded application of water to the left flank, 10% w/v ammonium methanethiosulfonate and 3% w/v ammonium methanethiosulfonate to the right flank. The occlusive dressings were removed after

24 hours and the test sites assessed 24 and 48 hours later. In addition, body weights were determined at the beginning and at the completion of the study.

Bodyweight gains were normal throughout the study. A significant dermal response (slight erythema or above) was seen in 2/10 controls and 5/20 test animals subjected to challenge with 10% w/v ammonium methanethiosulfonate. No control or test animals showed dermal response to 3% w/v ammonium methanethiosulfonate challenge. These responses were regarded as indicative of primary irritation and not sensitisation. The notified chemical did not cause skin sensitisation in the guinea pig.

9.2 Repeated Dose Toxicity (7)

Groups of CD rats (5/sex/dose) received ammonium methanethiosulfonate by gavage at 0, 30, 150 or 1000 mg/kg/day in aqueous suspension for four weeks. Clinical signs of toxicity were assessed daily and bodyweight and food consumption calculated weekly. Blood samples for haematology and clinical chemistry were taken before sacrifice at day 29. Necropsy included macroscopic pathology, organ weights and histology.

There were no deaths during the study. Clinical signs were restricted to post-dose salivation in 1000 mg/kg/day rats from week 2. Food consumption, food conversion ratio and bodyweight were unaffected by treatment. Haemoglobin(Hb) concentrations, erythrocyte numbers and mean cell Hb concentrations were reduced, and mean cell volumes were increased in 1000 mg/kg/day rats. Platelet counts of 1000 mg/kg/day female rats were lower than controls. Plasma creatinine and total bilirubin concentrations were elevated and plasma sodium levels decreased compared to controls in the 1000 mg/kg/day male rats. Absolute kidney weights were increased in the 1000 mg/kg/day animals and relative liver weights in males and relative adrenal weights in females were also increased in these animals. There were no significant macroscopic pathology findings but histology revealed splenic congestion and/or extramedullary haemopoesis in all males and 1/5 females in the 1000 mg/kg/day group.

In conclusion the notified chemical appeared to cause slight anaemia and reactive spleen changes in the 1000 mg/kg/day animals but no other significant toxic effects.

9.3 Genotoxicity

Summary of genotoxicity studies of ammonium methanethiosulfonate

STUDY TYPE	*TEST STRAINS*	*CONCENTRATION*	*RESULT*	*REF*
Reverse mutation	*S. typhimurium* strain TA(98,100, 1535, 1537)	50-5,000 mg/plate (+/- S9)	-ve	8
Clastoge-nicity	Cultured Human Lymphocytes	15.6-5000 mg/mL (+/- S9)	-ve	9

9.4 Overall Assessment of Toxicological Data

The studies demonstrated that the notified chemical (ammonium methanethiosulfonate) has low acute oral and dermal toxicity, is a severe eye irritant, is possibly a skin irritant and does not cause dermal sensitisation. A 28-day oral repeat dose study in rats revealed induction of mild anaemia at the highest dose of 1000 mg/kg/day. The compound showed no genotoxic activity in reverse mutation tests in bacteria (Ames test) nor direct clastogenic activity in human lymphocytes at non-toxic doses.

On the basis of submitted data, the notified chemical would be classified as hazardous in accordance with Worksafe Australia's *Approved Criteria for Classifying Hazardous Substances* with respect to eye irritation.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Results of ecotoxicity tests are summarised. While the chemical can be classified as non-toxic to fish and algae, it is slightly toxic to water fleas, with a 21 day EC_{50} of 31.8 mg/L. Also, the chemical does not appear to inhibit the activity of bacteria in aerobic sludge. This observation was made during the conduct of the ready biodegradation test.

All ecotoxicity tests were performed to test methods following the EC Directive 92/69/EEC.

Ecotoxicity test results

Species	***Test***	***Concentrations*** [a] *(mg/L)*	***Result*** *(mg/L)*
Rainbow Trout	96 h acute	92.3	LC_{50} > 92.3 NOEC > 92.3
Water Flea (*Daphnia magna)*	48 h acute	6.08, 12.2, 26, 50.9, 105	EC_{50} = 67.6
Water Flea (*Daphnia magna*)	21 d	5.9, 12.0, 24.7, 48.7, 101	EC_{50} = 36.8 EC_{50} (reproduction) = 31.8 & 33.3
Algae (*Selenastrum capricornutum*)	96 h growth	97.2	NOEC > 97.2
Aerobic Sludge	5 d	10	NOEC > 10

a All concentrations are mean measured test concentrations except for aerobic sludge which was not measured.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The chemical will be distributed to 25 different processing laboratories throughout the country.

The greatest potential for environmental exposure from CS-8203 will result from the disposal of the overflow to sewer.

The notified chemical is present in a concentration of approximately 1.2% in the fixing solution. Film fix overflow accounts for about 5% of the total photographic film and paper process chemical waste, which at the highest importation rate, will be approximately 7 kg per year, or 20 g per day. In a worst case, if all the predicted country's overflow entered the sewage system in one large country town, in one day (around 5 megalitres), the chemical would be present at a concentration of 4 ppb. Several orders of magnitude therefore exists between the worst case estimated environmental concentration (4 ppb) and the most sensitive effects concentration (21 day EC_{50} = 31.8 ppm for water fleas), and the environmental hazard of the chemical can be rated as negligible.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

CS-8203 is stable, non-flammable and is expected to exhibit low volatility. Based on the submitted data, the major toxicological concerns associated with CS-8203 will be its potential severe eye irritation.

The notified chemical is classified hazardous according to Worksafe Australia's *Approved Criteria for Classifying Hazardous Substances*, but the imported chemical mixture, containing the notified chemical at a concentration of 1.2% is not classified hazardous (10).

The most likely worker exposure will be inhalation (due to aerosol formation) or dermal exposure during charging and emptying the solution containing the notified chemical. During these operations the use of local exhaust ventilation would minimise exposure due to aerosol spray. However, should ventilation methods be inadequate, exposure may be further controlled with personal protective equipment. Once the notified chemical is incorporated into the photographic film, no additional worker exposure will take place.

Given the low concentration of the notified chemical in the formulation together with expected low exposure, the occupational health risk arising from transport, storage and use is expected to be minimal.

The use of the chemical will be restricted to a small number of automated photographic film processing laboratories. Following completion of processing there is residual compound remaining on the film surface which is capable of being removed by contact. This is estimated as 0.16-0.24 ug/roll of film(35 mmx24 exposures). The general public may handle the processed film and therefore be exposed to this minute quantity of notified chemical. The notified chemical has low

acute oral and dermal toxicity and does not cause dermal sensitisation but is a severe eye irritant. The amount of chemical that could be ingested by hand to mouth contact is of no concern. The potential for eye irritation from hand to eye contact does exist but appears small. Minor public exposure may result from accidental spillage of the notified chemical during transport or storage. In conclusion the use of CS-8203 in the proposed manner is not expected to result in significant adverse public health effects.

13. RECOMMENDATIONS

To minimise occupational exposure to CS-8203 the following guidelines and precautions should be observed during usage of the formulation:

- safe practices, as should be followed when handling any chemical formulation, should be adhered to - these include:

  - minimising spills and splashes;

  - practising good personal hygiene; and

  - practising good housekeeping and maintenance including bunding of large spills which should be cleaned up promptly with absorbents and put into containers for disposal.

In addition personal protective equipment such as eye protection, impervious gloves and protective clothing should be worn.

- if the concentration of the notified chemical, CS-8203 is to be imported in a formulation at a concentration that exceeds 5%, then the Director should be advised in writing.

14. MATERIAL SAFETY DATA SHEET

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

This MSDS was provided by the applicant as part of their notification statement. The accuracy of this information remains the responsibility of the applicant.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989*, secondary notification of CS-8203 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. P.U.R.E. *Photographic Uniform Regulations for the Environment*. *Photographic Industry Code of Practice*, March 1993.

2. Connell DW 1989. *General characteristics of organic compounds which exhibit bioaccumulation. In Bioaccumulation of Xenobiotic Compounds*, DW Connell (ed). CRC Press, Boca Raton, USA. Chapter 3.

3. M-3217A: *Acute oral toxicity study in the rat. PB Rees, Pharmaco LSR Ltd, England. Report no.: 94/FIT370/0409,* December 1994. QA; GLP.

4. M-3217A: *Acute percutaneous toxicity study in the rat. PB Rees, Pharmaco LSR Ltd, England. Report no.: 94/FIT372/0387,* December 1994. QA; GLP.

5. M-3217A: *Acute eye irritation test in the rabbit.* PB Rees, Pharmaco LSR Ltd, England. Report no.: 94/FIT373/0399, November 1994. QA; GLP.

6. M-3217A: *Delayed contact hypersensitivity study in the guinea pig. PB Rees, Pharmaco LSR Ltd, England. Report no.: 94/FIT374/0562,* November 1994. QA;GLP

7. M-3217A: *Four-week oral toxicity study in the rat. IR Johnson, Pharmaco LSR Ltd, England. Report no.: 94/FIT375/0889,* January 1995. QA; GLP.

8. M-3217A: *Assessment of mutagenic potential in histidine auxotrophs of Salmonella typhimurium* (the Ames test). K May, Pharmaco LSR Ltd, England. Report no.: 94/FIT376/0491, October 1994. QA; GLP.

9. M-3217A: *An in vitro test for induction of chromosome damage: cytogenetic study in cultured human peripheral lymphocytes.* CN Edwards, Pharmaco LSR Ltd, England. Report no.: 94/FIT377/0810, December 1994. QA; GLP

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

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