File No: NA/37

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

N,N-Bis(carboxymethyl)-ß-alanine
(Also known as ADA)

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

N,N-Bis(carboxymethyl)-ß-alanine
(Also known as ADA)

1. APPLICANT

AGFA-GEVAERT Limited, 372 Whitehorse Road, Nunawading, Victoria 3131.

2. IDENTITY OF THE CHEMICAL

Trade Name: ADA

Based on the nature of the chemical and the data provided, solutions containig < 5% ADA are not considered to be hazardous substances. The notifier has applied for exemption from publication of the chemical name, CAS number, molecualar formula, molecular weight, structure and spectral data for the chemical.

3. PHYSICAL AND CHEMICAL PROPERTIES

ADA has the following physical and chemical properties.

Melting point: 190°C (decomposition)

Density: 550 kg/m^3

Autoignition temperature: Negative at 194°C

Flash point: 155°C

Explosion potential: ADA dust may be explosive in the presence of a spark, however ADA will be imported and used in the form of a liquid concentrate so that there is no risk of dust formation.

Reactivity: ADA is stable and is not expected to undergo polymerization. Under thermal decomposition, nitrogen oxides, carbon monoxide and carbon dioxide are possible products. ADA does not possess any oxidizing properties.

Dissociation constants: $pK_1 = 2.1$, $pK_2 = 3.7$, $pK_3 = 9.6$

Water solubility: 9 g/L at 20°C

Particle size: 3 - 100 µm

Comments on physico-chemical properties: The hydrolysis as a function of pH was not determined. Since ADA has a significant level of water solubility, the hydrolytic potential would normally be required. However, the ADA molecule does not contain any potentially hydrolysable functional groups. While soil adsorption data were not provided, ADA can be expected to prove mobile in soils by comparison with analogous compounds.

The lower end of the particle size range (3 - 7 µm) would be respirable. However, since ADA will be imported in solution form, the respirability is not of concern.

4. METHODS OF DETECTION AND DETERMINATION

Ultraviolet (UV), infrared (IR) and nuclear magnetic resonance (NMR) spectroscopic methods can be used to identify ADA. The degree of purity can be estimated by a high performance liquid chromatography (HPLC) method.

5. PURITY OF THE CHEMICAL

Degree of purity: 100% ADA

Toxic or hazardous impurities: None

6. INDUSTRIAL USES

ADA will be used as an ingredient in liquid bleach solutions, 70 Light BL-J and 70 Light BL-R, which will be used in the developing and fixing of photographic film and paper. The import volume of ADA is expected to be less than 1 tonne per year from 1992-1996.

7. PUBLIC AND OCCUPATIONAL EXPOSURE

ADA will be imported as a component (about 3%) of photographic liquid bleach concentrates. From the point of importation, it will be transported and stored in small, tightly sealed plastic bottles (size not reported) packed in fiberboard cartons. Therefore, the risk of an accidental spill is minimal. Workers involved in transport and storage will use fork lifts or manual handling to load, unload and store cartons. The average exposure during these activities is 30 min per day for 40 days per year.

During the photographic processing workers will unpack the cartons and dilute the bleach concentrates with water to make a working solution of the bleaches (containing approx. 15 g/L of ADA). As standard procedure, the workers will wear protective eye goggles, gloves and clothing. The average exposure during this activity is 4 hours per day for 80 days per year.

The disposal of the used bleach solution will be via local water authority drains after treatment, or it will be collected by a waste disposal company for incineration or land fill. The waste collection may be by pumping from an underground tank directly into a bulk tanker vehicle or it may be done manually using sealed containers. The average exposure time for each laboratory will be 10 days per year.

8. ENVIRONMENTAL EXPOSURE

Environmental Release

. Formulation, handling and disposal

ADA will be imported as an ingredient of the bleach solutions 70 Light BL-J and 70 Light BL-R, and will not be subject to any reformulation until it reaches the user, where it will be diluted with water to make a working solution. Barring accidents during transport, formulation and handling are not expected to release significant amounts of ADA to the environment. The principal route of environmental exposure will be through disposal of spent solutions, either directly to sewer or to landfill following collection.

. Use

The bleach concentrate containing ADA will be diluted with water and loaded into a film or paper processing machine. Approximately ninety five photographic laboratories will use the bleach, each processing an average of 30 rolls of film daily and consuming 22 mL of the bleach per film. The concentration of ADA in the bleach is about 3% and release to the sewer may occur through discharge of spent bleach solutions or wash water, or both, depending on the process involved. Bleach solution overflows (20.5 mL per film) may be discharged directly to sewer, collected for disposal, or continuously recycled. Wash water (a total of 4.2 L per film, containing 1.5 mL bleach solution) will be discharged directly to sewer, except in laboratories using a super stabiliser which does not require preliminary washes following bleaching and fixing. Releases from the various processes are tabulated below.

No of labs	**Overflow**	**Wash water**	**Release to sewer**
20-25	Collected	To sewer	45 mL/lab/day
3	To sewer	To sewer	660 mL/lab/day
30-35	Recycled	To sewer	45 mL/lab/day
20-25	Recycled	None	Nil
12-15	Collected	None	Nil

Environmental Fate

Biodegradability testing is not required for small volume notifications. However, the results from OECD screening tests which showed 95% loss in 14 days with the adapted and 96% in 28 days with the unadapted microorganism, and those from a Zahn-Wellens test which showed >98% degradation after 28 days were provided. These results indicate that ADA should largely degrade in sewage treatment plants. This is supported by data for the analogous compound nitrilotriacetic acid (NTA), for which removal efficiencies in full scale wastewater treatment plants at low ppm concentrations are typically of the order of 90%, although transient decreases in efficiency are observed when loadings are increased.

Solutions of ADA will also enter the environment when they are landfilled. The high water solubility and low partition

coefficient indicate that ADA is likely to leach readily from less secure landfill sites and enter the wider environment in solution. However, significant accumulation of residues is not expected as the closely related compound and its metal chelates are rapidly biodegraded in a variety of aquatic and terrestrial ecosystems, including wastewater treatment systems, soils, surface waters, groundwater aquifers and both aerobic and anaerobic subsurface soil systems. Bioaccumulation is similarly unlikely because of the high water solubility and low partition coefficient.

In contrast to NTA (and by analogy ADA), the standard bleaching agent ferric EDTA depends on photochemical transformation rather than metabolism for its degradation in the environment, and passes through sewage works essentially unchanged (1).

9. TOXICOLOGICAL DATA

There is no requirement for supplying toxicological data for low volume notifications. However, since the data was available the notifier submitted the following studies.

9.1 Acute Toxicity

Table 1: Summary of acute toxicity of ADA

Test	Species	Dose	Outcome	Reference
Oral	Rat	2200 mg/kg	LD50 > 2200 mg/kg	3
Skin Irritation	Rabbit	0.5 g	Slight irritation	4
Eye Irritation	Rabbit	37 mg/0.1 mL	Severe irritation	5

9.1.1 Oral (2)

The acute oral toxicity of ADA was studied in Wistar rats. The rats (5/sex) were treated with a single oral dose of an aqueous solution of ADA at a dose of 2200 mg/kg by gavage. The animals were observed for a period of 14 days after dosing. There were no deaths. There were no treatment-related clinical signs and at necropsy there were no pathological changes. Therefore, the oral LD50 in rats is >2200 mg/kg indicating that ADA has a low acute oral toxicity.

9.1.2 Skin Irritation (3)

The skin irritation potential of ADA was investigated in Vienna white rabbits. Three male rabbits were treated with ADA (0.5 g) moistened with water and applied to shaved skin under semiocclusive bandage. The skin at the application site was examined at 1, 24, 48 and 72 hours after application of the test substance. Only very slight erythema was observed in 2/3 animals at the 1 hour investigation and the erythema had disappeared by 24 hours. Therefore, ADA appears to be slightly irritating to the skin.

9.1.3 Eye Irritation (5)

The eye irritation potential of ADA was investigated in Vienna white rabbits. Two male rabbits and one female rabbit had 0.1 mL of an aqueous solution of ADA (about 37 mg) placed in the conjunctival sac of one eye of each rabbit. The untreated eye of each animal served as a negative control. The eyes were examined at 1, 24, 48, 72 hours and at 8 days after treatment. At the 1 hour investigation, two of the animals had moderate opacity of the cornea, erythema and chemosis of the conjunctiva, and an increase in discharge. The pupil was contracted and there was some loss of corneal tissue in these two animals. The third animal had only a slight opacity of the cornea, but moderate erythema and chemosis of the conjunctiva. These changes were still present on day 8. Circum-corneal injection (congestion) of the iris was apparent in 2 out of 3 animals at 48 hours, and in all animals from 72 hours onwards. One animal had iritis on day 8. Therefore, ADA was shown to be severely irritating to the eye under these experimental conditions.

9.1.4 Overall Assessment of Toxicological Data

ADA was tested for acute oral toxicity in rats and was found to have a low acute oral toxicity with the LD50 being >2200 mg/kg. The skin and eye irritation potential of ADA was studied in white rabbits. ADA was shown to be a slight skin irritant and a severe eye irritant.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

As ADA is highly soluble in water and will be imported in solution, environmental exposure will mainly involve the aquatic compartment. The results submitted for the ferric salt of ADA (see NA/15) indicate it to be practically nontoxic to aquatic fauna, and ADA would be expected to have a similar profile. Aquatic toxicity testing is not required for low volume chemicals.

The aquatic toxicological profile of NTA has been studied for a wide range of freshwater and marine species, including algae, with EC_{50}s obtained in acute tests ranging between 10^2 and 10^4 $mg.L^{-1}$ (5). Toxicity is reduced in hard water, and especially in sea water, because of complexation with metal ions. In view of the close structural similarity, ADA is not expected to have any significant aquatic toxicological characteristics.

11. ENVIRONMENTAL HAZARD

Under worst case conditions in the three laboratories which discharge spent ADA directly to sewer, the daily release from the processing machine will amount to about 20 g in around 120 L of wash water, or a concentration in the region of 200 ppm in machine effluent. Assuming this becomes part of an influent stream to sewage treatment works of 5 ML (typical of smaller inland facilities), the concentration will be reduced below 4 ppb. Dilution by receiving waters, and microbial degradation during sewage treatment, would be expected to reduce this concentration further. As noted above, the other ninety or so laboratories will discharge ADA to sewer at much lower levels, if at all. ADA has low acute toxicity and minimal bioaccumulation potential in the aquatic environment, and the analogous chemical NTA is readily biodegraded in a variety of environmental systems. Accordingly, the environmental hazard arising from the proposed use of ADA appears minimal.

ADA performs the same function as EDTA in photographic processing. In view of the resistance of EDTA to microbial degradation, its substitution by ADA may entail a reduction in environmental hazard. As the use of EDTA in Australia is not subject to any specific controls, except when used for human therapy, there appears to be no need to apply restrictions on the use of ADA in photographic processing.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY

Since ADA will be imported and used in solution form, the most likely route of exposure is dermal. ADA was shown to be a severe eye irritant and, therefore, precautions should be taken to avoid contact with the eyes. Under normal conditions of use, the potential for public and occupational exposure is minimal.

13. RECOMMENDATIONS FOR SAFETY PROCEDURES TO CONTROL OCCUPATIONAL EXPOSURE

To minimise public and worker exposure to ADA, the following guidelines and precautions should be observed:

. good housekeeping practices should be used and precautions taken to minimise splashes and spills,

. workers handling the chemical should be made familiar with emergency procedures,

. workers handling the chemical should wear PVC gloves (AS 2161, 7), goggles (AS 1337, 8) and a PVC apron,

. MSDS for all products containing ADA should be readily available to workers,

. areas where products containing ADA are handled should have good general ventilation or local ventilation.

14. MATERIAL SAFETY DATA SHEET

The Material Safety Data Sheet for ADA and products containing ADA are presented in the Worksafe Australia format (9).

15. SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989*, (the Act) secondary notification of ADA shall be required if:

1. ADA is imported in concentrations of 5% or greater, and

2. any of the circumstances stipulated under subsection 64(2) of the Act arise.

REFERENCES

1. Frank, R. and Rau H., *Ecotoxicology and Environmental Safety*, **19**, 1990, pp. 55-63.

2. *Study on the Acute Oral Toxicity of ADA in Rats*, Project No. 10A0202/911036, BASF, Switzerland, 1991

3. *Report on the Acute Dermal Irritation/Corrosivity to Intact Dorsal Skin of ADA in White Rabbits*, Project No. 18H0202/912057, BASF, Switzerland, 1991.

4. *Report on the Acute Irritation to the Eye of ADA in White Rabbits*, Project No. 11H0202/912058, BASF, Switzerland, 1991.

5. Australian Standard 2161-1978, "Industrial Safety Gloves and Mittens (Excluding Electrical and Medicinal Gloves)", Standards Association of Australia Publ., Sydney, 1978.

6. Australian Standard 1337-1984, "Eye protectors for Industrial Applications", Standards Association of Australia Publ., Sydney, 1984.

7. National Occupational Health and Safety Commission, *Guidance Note for the Completion of Material Safety Data Sheet*, 2nd edition, AGPS, Canberra, 1990