Acetamide, 2,2-dibromo-2-cyano-: Human health tier II assessment

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Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

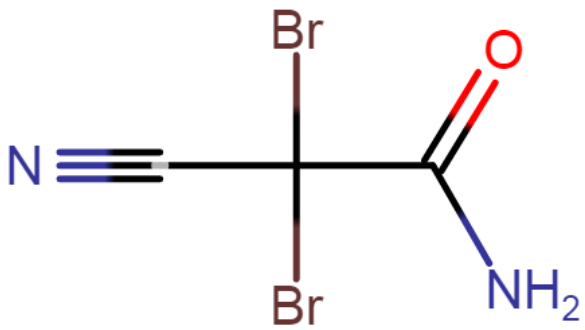
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:www.nicnas.gov.au

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	2,2-dibromo-3-nitrilopropionamide (DBNPA) dibromocyanoacetamide 2,2-dibromo-2-cyanoacetamide
Structural Formula	
Molecular Formula	C3H2Br2N2O
Molecular Weight (g/mol)	241.87
Appearance and Odour (where available)	White to yellow powder with a mild odour
SMILES	C(N)(=O)C(Br)(Br)C#N

Import, Manufacture and Use

Australian

The chemical has site-limited, non-industrial use to remove membrane biofouling in water distribution systems (Department of Health WA, 2015). The chemical has reported use in cleaner and polish products at low concentrations.

International

The following international uses have been identified through: Galleria Chemica; California Environmental Protection Agency; the United States Environmental Protection Agency (US EPA); and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic uses as a biocide/antimicrobial agent, and as a preservative.

The chemical has reported domestic use, including as a preservative enhancer in finished products such as adhesives and paper products.

The chemical has reported commercial uses as a biocide/antimicrobial agent in water processing and/or recycling systems and as a preservative enhancer in finished products such as metalwork cutting fluid, emulsions and polymers.

The chemical has reported site-limited use in hydraulic fracturing operations.

Restrictions

Australian

The chemical is listed in *Materials and Substances in Contact with Drinking Water* under Schedule 8: *Chemicals and Procedures used to Maintain Water Treatment and Distribution Systems,* with applicable operational conditions (Department of Health, 2015).

International

No known restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Acute Toxicity

Oral

Based on the available data, the chemical has high acute toxicity based on the results from animal tests following oral exposure, waranting hazard classification.

The median lethal dose (LD50) values of 235 mg/kg bw and 178 mg/kg bw were reported for male and female rats, respectively. For both female guinea pigs and rabbits, an LD50 value of 118 mg/kg bw was reported. Reported sublethal effects included depression, prostration, and laboured breathing (US EPA, 1994).

Dermal

Based on the available data, the chemical is expected to have low toxicity following acute dermal exposure. An LD50 value of 2000 mg/kg was reported for male rabbits. In other dermal studies, although no mortalities have occurred, dermal irritation was observed (US EPA, 1994). In the absence of more comprehensive information, classifying the chemical for this particular endpoint is not warranted.

Inhalation

Based on the available data, the chemical has high acute toxicity based on the results from animal tests following inhalation exposure, warranting hazard classification.

A median lethal concentration (LC50) value of 0.32 mg/L in rats was determined in a four-hour exposure study. Corneal opacity was also noted in the surviving animals (US EPA, 1994).

Corrosion / Irritation

Skin Irritation

The chemical is reported to be a slight to moderate skin irritant in animal studies (see **Acute toxicity − dermal** and **Repeat dose toxicity − dermal** sections). The effects reported were not sufficient to warrant hazard classification.

Eye Irritation

The chemical is considered to be a severe eye irritant.

Studies conducted in rabbits have shown that the chemical caused severe corneal damage and corneal opacity within one hour of treatment. Another study conducted in rabbits resulted in severe and permanent corneal damage. No further details were provided (US EPA, 1994). Severe ocular effects were also reported in an acute inhalation study (see **Acute Toxicity – Inhalation** section).

Sensitisation

Skin Sensitisation

Based on the information available from animal studies, the chemical may be a weak skin sensitiser. However, the information available is not sufficient to warrant hazard classification.

The chemical was found to be a weak sensitiser based on two dermal studies in guinea pigs (US EPA, 1994). However, study details were not provided.

Repeated Dose Toxicity

Oral

While minor adverse effects were seen at low doses in the available studies, repeated oral exposure to the chemical is not considered to cause serious damage to health.

In a 90-day study conducted in Sprague Dawley (SD) rats (n=20/sex/dose), the chemical was administered by oral gavage at doses of 0, 5, 13 or 35 mg/kg bw/d. However, the dose was reduced to 30 mg/kg bw/d due to dyspnoea in high dose group observed after four days. Increased mortality was observed in the high dose group. The high dose group showed increased adrenal weights, plasma urea and creatinine concentration, as well as tympanism of the digestive tract (swelling of the abdomen due to gas in the intestinal or peritoneal cavity), haemorrhage of the lungs, acute tracheitis, and depressed lymphoreticular system. Dyspnoea and increased urine volume were observed at doses of 13 and 35 mg/kg bw/d. A no observed effect level (NOEL) and a lowest observed effect level (LOEL) of 5 mg/kg bw/d and 13 mg/kg bw/d, were determined, respectively (CEPA, 2007; US EPA, 1994).

In another 90-day study conducted in SD rats (n=10/sex/dose), the chemical was administered in drinking water at concentrations of 0, 20, 100 or 500 ppm. The chemical was reported to be unstable at pH 8; therefore, exposure to breakdown products of the chemical was also considered. The only effect reported was minimal renal tubular alterations of the kidneys in the high dose group. The NOEL of 100 ppm was determined in this study (equivalent to 8 mg/kg bw/d for males or 15.9 mg/kg bw/d for females) (CEPA, 2007).

Dermal

Based on the data available, repeated dermal exposure to the chemical is not considered to cause serious damage to health.

In a 90-day dermal study in Fischer 344 (F344) rats (10 animals/sex/group), the chemical was administered under patch occlusion at doses of 0, 103, 309, or 1031 mg/kg bw/d for six hours per day, five days per week. No mortalities or systemic toxicity effects were reported in this study. Dermal irritation was reported in the 309 mg/kg bw/d and 1031 mg/kg bw/d dose groups. In the 309 mg/kg bw/d group, only transient dermal irritation was observed while in the high dose group, erythema, oedema, scabs, hyperkeratosis, and inflammation were observed. The NOEL and LOEL values were determined to be 309 mg/kg bw/d and 1031 mg/kg bw/d, respectively (CEPA, 2007; US EPA, 1994).

Inhalation

No data are available.

Genotoxicity

The chemical is not considered to be genotoxic. Negative results are reported for the following *in vitro* assays (CEPA, 2007):

- Ames tests in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538, and in *Escherichia coli* strain WP2uvrA, with or without metabolic activation;

- forward mutation assay of the hypoxanthine-guanine phosphoribosyltransferase (*hgprt*) locus in Chinese hamster ovary (CHO) cells;
- chromosome aberration assay in cultured human peripheral human lymphocytes;
- unscheduled DNA synthesis in primary hepatocytes from male rats; and
- sister chromatid exchange in CHO cells, with or without metabolic activation.

A negative result was reported for an *in vivo* micronucleus test in mice bone marrow (CEPA, 2007).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Based on the data available, the chemical is not expected to cause reproductive and developmental effects.

In a study conducted in female New Zealand White rabbits (14 animals/dose), the chemical was administered via gavage at doses of 0, 2, 10, 30 or 60 mg/kg bw/d from gestation day (GD) 7 through 19. In the high dose group, observed maternal effects includes mortality, decreased food consumption, and reduced body weight gain. Foetal effects were observed in the 30 and 60 mg/kg bw/d groups, including increased incidence of reduced ossification of the ribs (sternebrae and xiphisternum) and long bone epiphyses. The developmental delays were considered secondary to maternal toxicity. The maternal and developmental NOEL was determined to be 30 mg/kg bw/d and 10 mg/kg bw/d, respectively (CEPA, 2007; US EPA, 1994).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute effects (acute toxicity from oral and inhalation exposure) and severe eye irritation.

Public Risk Characterisation

Given the uses identified for the chemical in Australia, it is unlikely that the public will be exposed to the chemical at high concentrations. Hence, the public risk from this chemical is not considered to be unreasonable.

Occupational Risk Characterisation

During product formulation, oral, ocular and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical (acute/local) health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2016).

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25) Toxic by inhalation (T; R23)	Toxic if swallowed - Cat. 3 (H301) Toxic if inhaled - Cat. 3 (H331)
Irritation / Corrosivity	Risk of serious eye damage (Xi; R41)	Causes serious eye damage - Cat. 1 (H318)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing the chemical should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, ocular and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

References

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed at http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/258/ApprovedCriteria_Classifying_Hazardous_Substances_NOHSC1008-2004_PDF.pdf

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