# 1-Propanol, 2,3-dibromo-: Human health tier II assessment

**13 February 2015**

## CAS Number: 96-13-9



## 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.

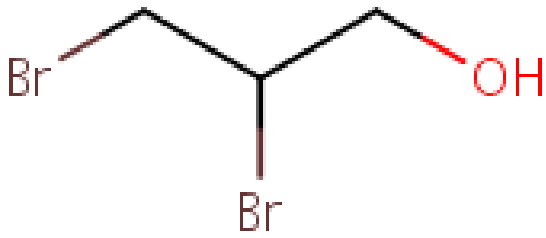
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

**Disclaimer**

Acronyms & Abbreviations

## Chemical Identity

| | |
|---|---|
| Synonyms | 1,2-dibromopropan-3-ol<br>DBP<br>2,3-DBP |
| Structural Formula |  |
| Molecular Formula | C3H6Br2O |
| Molecular Weight (g/mol) | 217.89 |
| Appearance and Odour (where available) | Colourless liquid |
| SMILES | C(Br)(CO)CBr |

## Import, Manufacture and Use

### Australian

No specific Australian use, import, or manufacturing information has been identified.

### International

The following international uses have been identified through Galleria Chemica; the United States (US) Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR); the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); the International Agency for Research on Cancer (IARC) monographs; and National Toxicology Program (NTP) technical reports.

The chemical has reported commercial uses as a:

- package moulding and sealing agent; and
- flame retardant.

The chemical has reported site-limited use as an intermediate in flame retardant preparation.

The chemical has reported non-industrial use as an intermediate in preparing insecticides and pharmaceuticals.

# Restrictions

## Australian

No known restrictions have been identified.

## International

The chemical is listed on the following (Galleria Chemica):

- European Union (EU) Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products;
- Health Canada List of Prohibited and Restricted Cosmetic Ingredients (The Cosmetic Ingredient "Hotlist");
- Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex II Part 1: List of substances which must not form part of the composition of cosmetic products; and
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components Cosmetic Products Must Not Contain.

# Existing Work Health and Safety Controls

## Hazard Classification

The chemical is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- T; R24, Xn; R20/22 (acute toxicity)
- T; R45 Carc. Cat. 2 (carcinogenicity)
- T; R62 Repr. Cat. 3 (reproductive toxicity)

## Exposure Standards

### Australian

No specific exposure standards are available.

### International

The following exposure standards are identified (Galleria Chemica):

An exposure limit of 0.5 mg/m$^3$ time weighted average (TWA) in Russia.

# Health Hazard Information

## Toxicokinetics

Oral administration of the chemical to male Sprague Dawley (SD) rats at a dose of 50 mg/kg bw yielded two mercapturic acid conjugates and β-bromolactate in urine. Intraperitoneal (i.p.) injection of 10 µg/kg bw of the chemical in rats also yielded 2-bromoacrylic acid in urine, most likely via 2-bromoacrolein—a highly reactive and unstable intermediate. These metabolites are formed via oxidation and dehydrohalogenation, followed by glutathione conjugation (NTP, 1993; IARC, 2000).

## Acute Toxicity

### Oral

The chemical is classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in the HSIS (Safe Work Australia). Based on the available data, the chemical is considered to have high acute oral toxicity, warranting a higher hazard classification (see **Recommendation** section).

The median lethal dose (LD50) was determined to be between 177 and 375 mg/kg bw in Fischer 344/N (F344/N) rats (NTP, 1993). However, another study reported an LD50 value of 681 mg/kg bw in rats (RTECS).

### Dermal

The chemical is classified as hazardous with the risk phrase ‘Toxic in contact with skin’ (T; R24) in the HSIS (Safe Work Australia). While the NTP data support a lower hazard classification, other data (from RTECS) support the existing hazard classification. Considering the worst case, the existing hazard classification is supported.

An LD50 value of 316 mg/kg bw was reported in rats (RTECS). However, based on single-dose studies conducted by the NTP, a dermal LD50 of between 750 and 1500 mg/kg bw in F344/N rats was determined (NTP, 1993).

### Inhalation

The chemical is classified as hazardous with the risk phrase ‘Harmful by inhalation’ (Xn; R20) in the HSIS (Safe Work Australia). The available data support this classification.

A median lethal concentration (LC50) of 9.92 mg/L was reported in rats exposed to the chemical for four hours (RTECS).

## Corrosion / Irritation

### Skin Irritation

No data are available.

### Eye Irritation

No data are available.

## Sensitisation

### Skin Sensitisation

No data are available.

## Repeated Dose Toxicity

### Oral

No data are available.

### Dermal

Based on the available data, the chemical is not considered to cause severe effects from repeated dermal exposure.

In a 13-week study, F344/N rats (n = 10/sex/dose) were dermally exposed to the chemical (on subscapular skin) at doses of 0, 44, 88, 177, 375 or 750 mg/kg bw/day for five days per week. The no observed adverse effect level (NOAEL) was determined to be 177 mg/kg bw/day, based on increased

incidence (minimal severity) of nephropathy observed in male rats at 375 mg/kg bw/day, as well as the presence of mild hepatocellular necrosis in all female rats at 750 mg/kg bw/day (NTP, 1993).

A dermal study exposed B6C3F1 mice (n = 10/sex/dose) to the chemical (on subscapular skin) at doses of 0, 44, 88, 177, 375 or 750 mg/kg bw/day, five days per week for 13 weeks. The no observed effect level (NOEL) was determined to be 44 mg/kg bw/day based on an increased incidence of bronchiole pleomorphism (altered shape and size) in the lungs of male mice at doses ≥88 mg/kg bw/day and increased incidence of hepatocellular necrosis in the liver of female mice at doses ≥177 mg/kg bw/day. There was also an increased incidence of lung necrosis and liver centrilobular necrosis in male mice at 750 mg/kg bw/day, and increased incidence of bronchiole pleomorphism in female mice at doses ≥375 mg/kg bw/day. The severity of all reported lesions was not significantly increased compared with control mice (NTP, 1993).

### Inhalation

No data are available.

## Genotoxicity

Based on the available data, the chemical is considered to have genotoxic potential, warranting hazard classification (see **Recommendation** section). Although the sex-linked recessive lethal mutation test in *Drosophila melanogaster* gave positive results for germ cell mutations, a higher hazard classification is not recommended as there were no positive mammalian in vivo genotoxicity tests with the chemical. However, considering that a metabolite of the chemical, 2-bromoacrolein (see **Toxicokinetics** section), is a highly reactive intermediate and a direct-acting mutagen, this supports the mutagenicity classification.

Several in vitro assays gave mainly positive results for mutagenicity and clastogenicity (IARC, 2000):

- positive bacterial reverse mutation assays with and without metabolic activation in *Salmonella typhimurium* strains TA100 and TA1535;
- positive bacterial reverse mutation assays with metabolic activation in *S. typhimurium* strains TA98, TA102 and TA2638, but negative or not tested without metabolic activation;
- negative bacterial reverse mutation assays with and without metabolic activation in *S. typhimurium* strains TA1537 and TA1538;
- positive bacterial reverse mutation assays with metabolic activation in *Escherichia coli* strain WP2, but not tested without metabolic activation;
- positive sister chromatid exchange (SCE) assay with and without metabolic activation in Chinese hamster ovary (CHO) cells;
- positive chromosomal aberration assay in CHO cells with and without metabolic activation; and
- positive gene mutation assays in mouse lymphoma or Chinese hamster lung V79 cells.

Negative results in a bone marrow micronucleus formation assay were reported in male B6C3F1 mice when exposed to the chemical via i.p. injection at 100 mg/kg bw/day for three days. However, most of the in vivo assays in *Drosophila melanogaster* gave positive results for genotoxicity (IARC, 2000):

- weakly positive results for aneuploidy in *D. melanogaster* exposed to the chemical at 0.5 mg/mL in feed;
- negative results for aneuploidy in *D. melanogaster* exposed to the chemical at 50 mg/mL in feed (but positive in the DNA repair-deficient strain Mei-9);
- positive results for reciprocal translocations in *D. melanogaster* exposed to the chemical at 400 ppm in feed;
- loss of heterozygosity by mitotic recombination in *D. melanogaster* exposed to the chemical at 21.8 µg/mL in feed; and
- positive results in the sex-linked recessive lethal mutation test in *D. melanogaster* exposed to the chemical at 500 ppm in feed.

## Carcinogenicity

The chemical is classified as hazardous as a Category 2 carcinogen with the risk phrase ‘May cause cancer’ (T; R45) in the HSIS (Safe Work Australia). The available data support this classification.

The IARC has classified the chemical as 'Possibly carcinogenic to humans' (Group 2B), based on inadequate evidence for carcinogenicity in humans, but sufficient evidence for carcinogenicity in animals (IARC, 2000).

In long-term studies, F344/N rats (n = 50/sex/dose) and B6C3F1 mice (n = 50/sex/dose) were dermally exposed to the chemical (in 95 % ethanol), at doses of 0, 188 or 375 mg/kg bw/day for 48–55 weeks and 0, 88 or 177 mg/kg bw/day for 36–42 weeks, respectively. These studies were intended to continue for two years, but were terminated early due to increased mortality in the high-dose rat/mice groups due to chemical-induced neoplasms (NTP, 1993). 'In mice, it produced tumours of the skin at the site of application and forestomach in both males and females and tumours of the liver in males. In rats, it produced tumours of the skin at the site of application and of the digestive tract including the mouth, oesophagus, forestomach and intestines, nasal mucosa and Zymbal gland in both males and females, and tumours of the liver, mammary gland and clitoral gland in females' (IARC, 2000).

Terminal body weights of male and female rats were significantly reduced by 23 % and 48 %, respectively; mouse body weights were not significantly different for the duration of the study. Non-neoplastic lesions occurred mainly in high-dosed rats and mice. These included hyperkeratosis (thickening) and hyperplasia of the skin at the site of application and in the oesophagus; nasal, lung and forestomach epithelium dysplasia (abnormal cell growth and differentiation); and renal tubule cell hyperplasia and nuclear enlargement (NTP, 1993).

### Reproductive and Developmental Toxicity

The chemical is classified as a hazardous substance toxic to reproduction (Category 3), with the risk phrase 'Possible risk of impaired fertility' (Xn; R62) in the HSIS (Safe Work Australia). The available data support this classification.

Only limited data are available. Male F344/N rats dermally exposed to the chemical at 188 or 375 mg/kg bw/day for 13 weeks had reduced testes and epididymides weights, and reduced sperm density, compared with control animals (NTP, 1993).

## Risk Characterisation

### Critical Health Effects

The critical health effects for risk characterisation include:

- systemic acute effects from oral, dermal and inhalation exposure; and
- systemic long-term effects (mutagenicity and carcinogenicity).

The chemical might also cause fertility effects.

### Public Risk Characterisation

Given the uses identified for these chemicals, it is unlikely that the public will be exposed. Hence, the public risk from these chemicals is not considered to be unreasonable.

### Occupational Risk Characterisation

Given the critical health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise exposure are implemented. The chemicals 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.

The data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (see **Recommendation** section).

## NICNAS Recommendation

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendment to the 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

Work Health and Safety

The chemicals are 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 in contact with skin (T; R24)* Harmful by inhalation (Xn; R20)* | Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Toxic if inhaled - Cat. 3 (H331) |

| Hazard | Approved Criteria (HSIS)[a] | GHS Classification (HCIS)[b] |
|---|---|---|
| Genotoxicity | Muta. Cat 3 - Possible risk of irreversible effects (Xn; R68) | Suspected of causing genetic defects - Cat. 2 (H341) |
| Carcinogenicity | Carc. Cat 2 - May cause cancer (T; R45)* | May cause cancer - Cat. 1B (H350) |
| Reproductive and Developmental Toxicity | Repro. Cat 3 - Possible risk of impaired fertility (Xn; R62)* | Suspected of damaging fertility - Cat. 2 (H361f) |

[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 industry

***Control measures***

Control measures to minimise the risk from oral, dermal and inhalation exposure to the chemicals 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 chemicals are used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemicals, if valid techniques are available to monitor the effect on the worker's health;
- 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 chemicals.

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 chemicals 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 these chemicals has not been undertaken as part of this assessment.

## References

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