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

13 February 2015

CAS Number: 96-23-1

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.

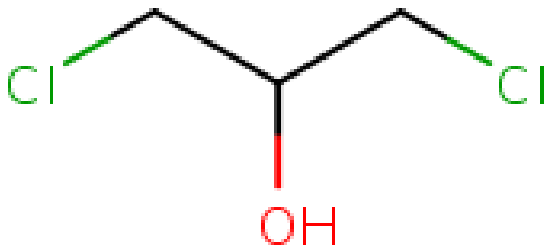
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	1,3-dichloropropan-2-ol 1,3-dichloro-2-hydroxypropane 1,3-dichlorohydrin enodrin 1,3-DCP
Structural Formula	
Molecular Formula	C3H6Cl2O
Molecular Weight (g/mol)	128.99
Appearance and Odour (where available)	Colourless, slightly viscous liquid with an ether-like odour
SMILES	C(O)(CCl)CCl

Import, Manufacture and Use

Australian

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

The chemical has been identified by Food Standards Australia New Zealand (FSANZ) as a chloropropanol formed in foods. Chloropropanols are considered to be contaminants present in foods, formed during the manufacturing process (FSANZ, 2003).

International

The following international uses have been identified through Galleria Chemica; the Substances and Preparations in the Nordic countries (SPIN) database; 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); and International Agency for Research on Cancer (IARC) monographs.

The chemical has reported domestic uses (SPIN):

- in adhesives, binding agents and fillers;

- in paints, lacquers and varnishes; and
- in construction materials.

However, it should be noted that SPIN does not distinguish between direct use of the chemical, or use of the materials that are produced from chemical reactions involving the chemical.

The chemical has reported commercial use in construction materials.

The chemical has reported site-limited uses including:

- as an intermediate in producing epoxide epichlorohydrin;
- as an intermediate in organic synthesis;
- as a precursor in producing synthetic glycerol;
- as a solvent for hard resins and nitrocellulose;
- as a solvent for anti-wrinkle agents and flame retardants in textiles;
- in manufaturing lacquers;
- in manufacturing pulp paper and paper products;
- as a cement for celluloid (a synthetic plastic material); and
- as a binder for watercolour paints.

The chemical has a reported non-industrial use as a percursor in producing the soil fumigant 1,3-dichloropropene.

Restrictions

Australian

The chemical is listed in the Australia New Zealand Food Standards Code, Contaminants and Natural Toxicants—Maximum levels of non-metal contaminants in food (maximum level of 0.005 mg/kg in soy and oyster sauces, calculated on a 40 % dry matter content).

International

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

- EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products;
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain;
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient ‘Hotlist’); and
- 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.

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; R25, Xn; R21 (acute toxicity)
- R45 Carc. Cat 2 (carcinogenicity)

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified for the chemical (Galleria Chemica):

- an exposure limit of 5 mg/m^3 time weighted average (TWA) in Bulgaria and China; and
- 5 mg/m^3 (1 ppm) short-term exposure limit (STEL) in Canada.

Health Hazard Information

Toxicokinetics

The chemical is metabolised in cultured rat hepatocytes and in the rat liver (in vivo) by the cytochrome P450 (CYP) enzyme, CYP2E1. In rats that received the chemical at 50 mg/kg bw by oral gavage for five days, β-chlorolactate was the major metabolite in the urine (5 %), followed by a mercapturic acid conjugate (1 %). In male Wistar rats that received the chemical at 62 mg/kg bw as a single subcutaneous injection, the major urinary metabolites were the chemical itself (2.4 %), 3-chloro-1,2-propanediol (0.35 %) and 1,2-propanediol (0.43 %) (IARC, 2012).

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase ‘Toxic if swallowed’ (T; R25) in the HSIS (Safe Work Australia). The available data support this classification.

Reported median lethal dose (LD50) values ranged from 110–400 mg/kg bw in rats (WHO, 2002; NTP, 2005).

Dermal

The chemical is classified as hazardous with the risk phrase ‘Harmful in contact with skin’ (Xn; R21) in the HSIS) (Safe Work Australia). The available data support this classification.

The dermal LD50 was reported to be 800 mg/kg bw in rabbits (NTP, 2005; HSDB).

Inhalation

The chemical has high acute inhalation toxicity based on the results from animal tests, warranting hazard classification (see **Recommendation** section).

The median lethal concentration (LC50) was reported to be 125 ppm (0.66 mg/L), or between 300 and 1000 ppm (1.58 and 5.28 mg/L) in rats (NTP, 2005).

Observation in humans

Of 12 workers exposed to an unknown concentration of the chemical by inhalation when cleaning a tank that was previously used for manufacturing this chemical, five workers developed acute hepatitis and two of those workers (both middle-aged males) died four and 11 days later (respectively) due to liver failure as a result of hepatocellular necrosis (NTP, 2005; HSDB).

Corrosion / Irritation

Skin Irritation

Based on the available data, the chemical is considered to cause only mild skin irritation.

In an open irritation test exposing rabbit skin to 10 mg of the chemical for 24 hours, mild irritation was observed (NTP, 2005). No further details were available.

Eye Irritation

Based on the limited available data, the chemical is considered to be an eye irritant. The reported data cannot be directly compared with classification criteria but, as reported, the data indicate that irritation is of sufficient severity to require classification (see **Recommendation** section).

Administration of the chemical (dose and duration not available) to rabbits' eyes resulted in severe irritation and damage. An irritation score of 8/10 was reported (Smyth et al., 1962 and Grant, 1974; cited in NTP, 2005). No further details were available.

Sensitisation

Skin Sensitisation

No data are available.

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is considered to cause harmful effects from repeated oral exposure, warranting hazard classification (see **Recommendation** section).

In an oral gavage study in male and female Sprague Dawley (SD) rats exposed to the chemical at doses of 0, 0.1, 1, 10 or 100 mg/kg bw/day five days per week for 13 weeks, the no observed adverse effect level (NOAEL) was reported to be 1 mg/kg bw/day based on liver effects (increased liver weight, histopathological changes and increased liver enzyme activity) and kidney effects (increased kidney weight, histopathological changes and altered urinary parameters) at doses ≥10 mg/kg bw/day (WHO, 2002; NTP, 2005). Further details, including levels of statistical significance and details of histopathological changes, were not available.

Dose-dependent increases in liver and kidney weights were also reported in another 13-week oral gavage study in SD rats exposed to the chemical at doses of 15, 30 or 60 mg/kg bw/day (NTP, 2005).

In a two-week oral gavage study in male and female SD rats exposed to the chemical at doses of 0, 1, 10, 25 or 75 mg/kg bw/day, increased liver weights were reported in males at the 10, 25 and 75 mg/kg bw/day doses and in females at the 25 and 75 mg/kg bw/day doses. Males also had increased kidney weights (NTP, 2005). Details on statistical significance were not available.

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the available data, the chemical is not considered to be genotoxic.

A number of in vitro assays gave positive results for mutagenicity and clastogenicity (NTP, 2005; IARC, 2012):

- mostly positive results in bacterial reverse mutation assays in *Salmonella typhimurium* strains TA100 and TA1535, with or without metabolic activation;
- mostly positive results in bacterial reverse mutation assays in *S. typhimurium* strains TA97 and TA98, with metabolic activation, and negative results without metabolic activation;

- positive results in bacterial forward mutation assay in *S. typhimurium* strain TM677 with metabolic activation, and negative results without metabolic activation;
- positive results in bacterial reverse mutation assays in *Escherichia coli* strains WP2, TM930 and TM1080, with metabolic activation, and negative results without metabolic activation;
- positive results in prophage induction, SOS repair, DNA strand breaks or cross-links assays in *E. coli* strains PM21 and GC4798, with metabolic activation, and negative results without metabolic activation;
- positive results in sister chromatid exchange (SCE) assays in Chinese hamster ovary (CHO) and Chinese hamster lung V79 cells, with or without metabolic activation;
- positive results in a chromosome aberration assay in CHO cells, with or without metabolic activation;
- positive results in gene mutation assays in mouse lymphoma cells, with or without metabolic activation;
- positive results in a gene mutation assay in HeLa S3 cells, with metabolic activation; and
- positive results in a transformation assay in mouse fibroblasts, without metabolic activation.

The following in vivo studies gave negative results for genotoxicity (NTP, 2005; IARC, 2012):

- a somatic mutation assay (wing-spot test) in *Drosophila melanogaster* exposed to the chemical at doses of 0.006–1.3 mg/mL;
- a micronucleus assay in male Han Wistar rat bone marrow exposed to the chemical twice at doses of 25, 50 or 100 mg/kg bw/day; and
- an unscheduled DNA synthesis (UDS) assay in the liver of male Han Wistar rats exposed to the chemical at doses of 40 or 100 mg/kg.

Despite the positive in vitro genotoxicity studies, the available in vivo data were uniformly negative. The positive results observed in the in vitro assays were suggested to be due to the reactions of chemical metabolites with the culture medium used in the in vitro assays (Frei & Wurgler, 1997).

Carcinogenicity

The chemical is classified 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, 2012).

In a two-year study, Wistar rats (n = 80/sex/dose) were exposed to the chemical at 0, 27, 80 or 240 mg/L in drinking water (equivalent to doses of 0, 2, 6 or 19 and 0, 3, 10 or 30 mg/kg bw/day in males and females, respectively). There was an increased incidence of liver tumours (hepatocellular adenoma and carcinoma), tongue tumours (squamous cell papilloma and carcinoma) and thyroid tumours (follicular adenoma and carcinoma) in male and female rats exposed to the chemical at doses ≥6 mg/kg bw/day and 30 mg/kg bw/day, respectively. In male rats, there was also an increased incidence of kidney tumours (renal tubular adenoma and carcinoma). Non-neoplastic changes (dose-dependent increases in relative liver, kidney and brain weights; increased incidence of elevated fat content in liver Kupffer cells; progression of nephrosis; and thyroid follicular cell hyperplasia) were reported at all doses. At the highest dose, there was increased mortality in all rats, and females exhibited signs of hepatotoxicity and nephrotoxicity (NTP, 2005).

Reproductive and Developmental Toxicity

Only limited data are available. No conclusion can be derived on the reproductive and developmental toxicity of the chemical.

There were reduced sperm counts in male Wistar rats six weeks post-exposure to the chemical via an intraperitoneal (i.p.) injection at 44 mg/kg bw. A spermatocoele (cyst of the epididymis containing spermatozoa) was observed in one male albino Wistar rat (n = 10) exposed (by oral gavage) to the chemical at 20 mg/kg bw/day for 14 days (NTP, 2005).

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 (carcinogenicity).

The chemical can also cause harmful effects following repeated oral exposure. It can also cause eye irritation and mild skin irritation.

Public Risk Characterisation

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

Occupational Risk Characterisation

Given the critical health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise 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.

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

NICNAS Recommendation

Assessment of the chemical 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 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)* Harmful in contact with skin (Xn; R21)* Toxic by inhalation (T; R23)	Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Fatal if inhaled - Cat. 2 (H330)
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)
Repeat Dose Toxicity	Harmful: Danger of serious damage to health by prolonged exposure if swallowed (Xn; R48/22)	May cause damage to organs through prolonged or repeated exposure - Cat. 2 (H373)
Carcinogenicity	Carc. Cat 2 - May cause cancer (T; R45)*	May cause cancer - Cat. 1B (H350)

[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, 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 which 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;
- health monitoring for any worker who is at risk of exposure to the chemical, 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 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 [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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