Benzene, (dichloromethyl)-: 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.

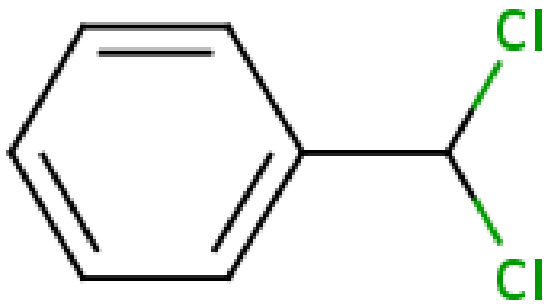
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	benzal chloride benzyl dichloride benzylidene chloride chlorobenzal a,a-dichlorotoluene
Structural Formula	
Molecular Formula	C7H6Cl2
Molecular Weight (g/mol)	161.03
Appearance and Odour (where available)	Colourless oily liquid with a faint aromatic odour
SMILES	c1(C(Cl)Cl)ccccc1

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 the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and assessments from the International Agency for Research on Cancer (IARC).

The chemical has reported site-limited uses, including in:

- manufacture of benzoyl chloride, benzaldehyde and cinammic acid; and
- dyes.

Restrictions

Australian

No known restrictions have been identified.

International

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

- 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');
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain; 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):

- Xn; R22 (acute oral toxicity)
- T; R23 (acute inhalation toxicity)
- Xi; R37/38-41 (irritation)
- R40 Carc. Cat 3 (carcinogenicity)

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica).

An exposure limit of 0.1 mg/m^3 (0.0015 ppm) time weighted average (TWA) in Switzerland, and a TWA of 0.5 mg/m^3 in Latvia and Russia.

Health Hazard Information

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase 'Harmful if swallowed' (Xn; R22) in the Hazardous Substances Information System (HSIS) (Safe Work Australia). Some of the available data in rats and mice support this classification.

The available data indicate moderate to low acute oral toxicity in rats and mice (study details are not available). Oral median lethal dose (LD50) values of 1400 mg/kg bw were reported in rats and mice (RTECS). Other reported oral LD50 values were 3250 mg/kg bw in male Sprague Dawley (SD) rats and 2460 mg/kg bw in male CF-1 mice (IARC, 1982; HSDB; REACH).

Dermal

No data are available.

Inhalation

The chemical is classified as hazardous with the risk phrase ‘Toxic by inhalation’ (T; R23) in the HSIS (Safe Work Australia). The available data from the 4-hour exposure study in rats support a lower hazard classification, although 2-hour exposure studies are consistent with a higher hazard classification. Considering the variability of available data, the existing hazard classification in the HSIS is not recommended to be amended.

Median lethal concentration (LC50) values of 0.4 mg/L/2-hours (61 ppm/2-hours) in rats and 0.21 mg/L/2-hours (32 ppm/2-hours) in mice were reported (IARC, 1982; REACH). An LC50 of 4.3 mg/L/4-hours in rats was also reported (REACH).

Reported signs of toxicity include central nervous system (CNS) excitation, eye irritation, respiratory irritation and hyperaemia (excess blood flow) of the extremities (IARC, 1982; REACH).

Corrosion / Irritation

Respiratory Irritation

The chemical is classified as hazardous with the risk phrase 'Irritating to respiratory system' (Xi; R37) in the HSIS (Safe Work Australia). Only limited data are available to support this classification.

In a carcinogenicity study in female ICR mice, the chemical dissolved in benzene was applied to shaved skin. Respiratory irritation was reported in the first few minutes after administration (IARC, 1982; REACH), which is likely due to vapour release following the dermal application.

In a study in male Swiss Webster mice (n = 4/dose) exposed to the chemical vapour at four different concentrations (not reported) for 10 minutes, the concentration required to reduce respiration by 50 % (a marker of sensory irritation) was determined to be approximately 27 ppm (REACH).

Skin Irritation

The chemical is classified as hazardous with the risk phrase 'Irritating to skin' (Xi; R38) in the HSIS (Safe Work Australia). Only limited data are available to support this classification.

In a carcinogenicity study in female ICR mice, the chemical dissolved in benzene (which is itself classified as a skin irritant in the HSIS) was applied to shaved skin. Irritation was reported due to the presence of redness and swelling. These effects occurred in the first few minutes after administration of the chemical and were described as 'rather severe' (IARC, 1982; REACH).

The chemical was also reported to be 'highly irritating' (REACH). No further data are available.

Eye Irritation

The chemical is classified as hazardous with the risk phrase 'Risk of serious damage to eyes' (Xi; R41) in the HSIS (Safe Work Australia). Only limited data are available to support this classification.

In a carcinogenicity study in female ICR mice, the chemical dissolved in benzene (which is itself classified as an eye irritant in the HSIS) was applied to shaved skin. Eye irritation was reported in the first few minutes after administration (IARC, 1982; REACH), which is likely due to vapour release following the dermal application.

The chemical was also reported to be 'slightly irritating' (REACH). No further details are available.

Sensitisation

Skin Sensitisation

No data are available.

Repeated Dose Toxicity

Oral

No data are available.

Dermal

Only limited data are available, showing local skin effects following repeated dermal exposure. No systemic toxicity effects were reported.

In a carcinogenicity study in female ICR mice, the chemical dissolved in benzene was applied to shaved skin for up to 50 weeks. Long-term skin irritation effects with repeated dosing included alopecia (spot balding) and induration (fibrous tissue formation, loss of elasticity). In some animals, there was also marked keratinisation, ulceration and/or necrosis (IARC, 1982; REACH).

Inhalation

No data are available.

Genotoxicity

The limited data available are insufficient to make a conclusion on the genotoxicity of the chemical.

The chemical induced mutations in *Escherichia coli* strain WP2 and *Salmonella typhimurium* strain TA100, in reverse mutation assays with metabolic activation (not tested without metabolic activation); and caused DNA damage in *Bacillus subtilis* in a recombination assay without metabolic activation (not tested with metabolic activation) (IARC, 1999; REACH).

The chemical was negative in mutagenicity tests in larva or adult *Drosophila melanogaster*. Insects were exposed to 1 mg of the chemical in feed for up to 10 days or exposed to 10 mg chemical vapour for up to five days, and mutation frequencies were not significantly different compared with controls (HSDB).

Carcinogenicity

The chemical is classified as hazardous—Category 3 carcinogenic substance—with the risk phrase ‘Limited evidence of carcinogenic effect’ (Xn; R40) in the HSIS (Safe Work Australia). The limited available data from a dermal carcinogenicity study support this classification.

The IARC has classified combined exposures to a-chlorinated toluenes (including the chemical) as ‘Probably carcinogenic to humans’ (Group 2A) (IARC, 1999).

In a carcinogenicity study, female ICR mice (n = 19) were dermally administered the chemical (25 µL of a 9.2 % solution of the chemical in benzene) or neat benzene (n = 20) twice weekly for 50 weeks. There was increased mortality in mice exposed to the chemical (74 %), compared with mice exposed to benzene (20 %) at the end of the study. Tumour incidences were also increased in mice exposed to the chemical, with nine squamous cell carcinomas, two skin fibrosarcomas, and one lymphoma reported. No skin tumours were reported in the benzene control mice. There were 2/20 and 5/20 lung adenomas in control and treated mice, respectively (IARC, 1982; REACH).

No animal carcinogenicity studies are available for the oral or inhalation routes of exposure.

Reproductive and Developmental Toxicity

No data are available.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include:

- carcinogenicity (systemic long-term effect); and
- skin, eye and respiratory irritation.

The chemical can also cause systemic acute effects from oral and inhalation exposure.

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 oral, 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.

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

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety, and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

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	Harmful if swallowed (Xn; R22)* Toxic by inhalation (T; R23)*	Harmful if swallowed - Cat. 4 (H302) Toxic if inhaled - Cat. 3 (H331)
Irritation / Corrosivity	Risk of serious eye damage (Xi; R41)* Irritating to skin (Xi; R38)* Irritating to respiratory system (Xi; R37)*	Causes serious eye damage - Cat. 1 (H318) Causes skin irritation - Cat. 2 (H315) May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)
Carcinogenicity	Carc. Cat 3 - Limited evidence of a carcinogenic effect (Xn; R40)*	Suspected of causing cancer - Cat. 2 (H351)

[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 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;
- 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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