

Benzene, 1,2-dichloro-4-nitro-: Human health tier II assessment

17 May 2013

CAS Number: 99-54-7



- Preface
- Chemical Identity
- Import, Manufacture and Use
- Restrictions
- Existing Work Health and Safety Controls
- Health Hazard Information
- Risk Characterisation
- NICNAS Recommendation
- References

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.

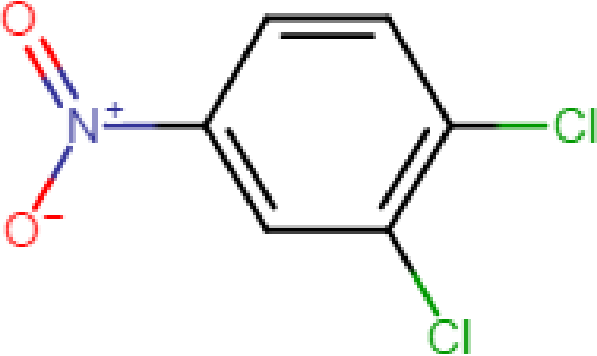
For more detail on this program please visit: www.nicnas.gov.au

Disclaimer

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS using a range of sources, including information from databases maintained by third parties, which include data supplied by industry. NICNAS has not verified and cannot guarantee the correctness of all information obtained from those databases. Reproduction or further distribution of this information may be subject to copyright protection. Use of this information without obtaining the permission from the owner(s) of the respective information might violate the rights of the owner. NICNAS does not take any responsibility whatsoever for any copyright or other infringements that may be caused by using this information.

Acronyms & Abbreviations

Chemical Identity

Synonyms	1,2-dichloro-4-nitrobenzene 3,4-dichloronitrobenzene 1-nitro-3,4-dichlorobenzene Benzene, 1,2-dichloro-4-nitro-
Structural Formula	
Molecular Formula	C6H3Cl2NO2
Molecular Weight (g/mol)	192.0
Appearance and Odour (where available)	Solid
SMILES	<chem>c1(Cl)c(Cl)cc(N(=O)=O)cc1</chem>

Import, Manufacture and Use

Australian

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

International

The following uses have been identified from REACH Dossiers, Chemica Galleria, and Hazardous Substances Data Bank (HSDB):

- Chemical intermediate for dyes; and
- Chemical intermediate for herbicides (eg Propanil) and insecticides.

Restrictions

Australian

No known restrictions have been identified.

International

No known restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not classified on the Hazardous Substances Information System (HSIS) (may be accessed at <http://hsis.safeworkaustralia.gov.au/HazardousSubstance>). This assessment reviews the data to determine whether classification is required.

Exposure Standards

Australian

There are no specific exposure standards for this chemical.

International

There are no specific exposure standard for this chemical.

Health Hazard Information

Toxicokinetics

It is reported in OECD (2003) that the chemical is absorbed from the gastro-intestinal tract. Although there are some species differences in experimental animals, from the available data it can be concluded that the chemical is excreted mainly via urine in the form of the mercapturic acid derivative N-acetyl-S-(2-chloro-4-nitrophenyl)-L-cysteine.

Acute Toxicity

Oral

The chemical was reported to cause acute toxicity via the oral route (mean lethal dose (LD50) in rats = 625 - 950 mg/kg bw) (OECD 2003). Predominant signs of intoxication included lethargy, increasing weakness, collapse and coma.

Dermal

The chemical was reported to cause low acute toxicity via the dermal route (LD50 in rats is > 2000 mg/kg bw) (OECD 2003).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

The chemical gave no skin irritation effects when tested for 4 hours under semi-occlusive conditions according to OECD TG 404 (OECD 2003). It was noted that slight irritation occurred, which disappeared within 72 hours, under occlusive conditions according to the method of Federal Register 38 No. 187.

Eye Irritation

The chemical was reported as slightly irritating to the eyes when tested according to OECD TG 405 (OECD 2003). The average scores for cornea / iris / conjunctivae (redness) / conjunctivae (chemosis) were given as 0 / 0.1 / 1.3 / 0.2. The effects were reversible within 72 hrs.

Sensitisation

Skin Sensitisation

The chemical was not found to induce dermal sensitisation when tested according to OECD TG 406 (OECD 2003).

Observation in humans

In a limited study of 10 female subjects, the single dermal application of a 10 % solution of the chemical in acetone followed by a challenge with a 10 or 0.01 - 1 % solution in acetone on day 28 and 49 was not found to induce dermal sensitisation in humans (OECD 2003).

Repeated Dose Toxicity

Oral

A no observed adverse effect level (NOAEL) of 4 mg/kg bw/d was derived based on changes in red blood cell parameters and haemolytic anemia with microscopic changes in the spleen (OECD 2003; ECHA 2012).

In a repeated dose toxicity study with Wistar rats following the guidelines set out in OECD TG 407, the chemical was administered via gavage to 5 animals/sex/dose at 0, 4, 20 or 100 mg/kg bw/day for 28 days (OECD 2003).

No deaths were observed in either sex during that time. Increased salivation, a slight non-significant increased water intake (in both males and females) and dark yellow discolouration of urine (in males) were observed at dose levels of = 20 mg/kg bw. At dose levels of 100 mg/kg bw/day irregular respiration was seen in both sexes and stilted gait and dark yellow discolouration of urine was observed in females.

Haematological examination revealed significantly reduced haematocrit (mid- and the high-dosed male rats) and significantly increased mean corpuscular volume (MCV-values) and number of reticulocytes, both in high-dosed male rats. Female rats showed significantly increased MCV-values at the mid- and the high-dosage only. At necropsy, increased relative liver weights (males: > 12 % from mid-dose onwards, females: > 22 % at high dose group) and spleen weights (males/females: 41 – 70 % at highest dose group), splenic congestion and increased extramedullary haematopoiesis and haemosiderosis were noted. No histopathology changes were reported for the liver. Marked haemosiderosis was seen in mid and high dose groups.

Dermal

Studies dealing specifically with dermal repeat dose toxicity were not identified.

Inhalation

The no observed adverse effect concentration (NOAEC) following subchronic inhalation exposure study of limited validity (limited documentation) was 0.4 mg/m³ (4 hours per day) (OECD 2003). Given the limited documentation it was difficult to interpret the data in this study.

The chemical was administered via inhalation 0, 0.4, 3.6 or 10 mg/m³ on 4 hrs/day over four months. No deaths were reported. Clinical effects including an increase in methaemoglobinaemia, Heinz bodies and pronounced reticulocytosis and decreases in erythrocyte count and haemoglobin levels at 3.6 mg/m³. At 10 mg/m³ significant increase in serum transaminases, liver catalase and liver diaminoxidase were reported in addition to increased levels of bilirubin in blood and cholesterol in adrenals. There was no histological examination reported in this study.

Observation in humans

It is reported in OECD (2003) that changes in haematological parameters (e.g. methaemoglobinaemia, Heinz bodies) are the main target in the only available report on exposure of the chemical to workers. As these findings relate to mixed exposures they cannot be clearly attributed to the chemical, but would be plausible, because they were also observed in animal experiments.

Genotoxicity

The chemical is not considered genotoxic.

The chemical exhibits mutagenic activity in *Salmonella typhimurium* but not in the HPRT test in Chinese Hamster Ovary (CHO) cells (OECD 2003). The chemical induced chromosomal aberrations in V79 cells with metabolic activation only at the highest concentration, which was cytotoxic. In insects (*Drosophila melanogaster*) the chemical revealed no mutagenic activity in the sex-linked recessive lethal test (SLRL-test) after application over 3 days with slight increased toxicity, but revealed mutagenic activity following a single intraperitoneal injection of a clearly toxic dose (OECD 2003). The chemical also showed no clastogenic activity *in vivo* in a chromosomal aberrations test with rats.

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Any reproductive and developmental effects were only observed secondary to maternal toxicity, so the chemical is not a specific reproductive or developmental toxin (OECD 2003).

In a rat teratology study using Sprague-Dawley rats (n = 25 females per group), the chemical was administered via gavage at 0, 10, 30 or 100 mg/kg bw/d from gestation day (gd) 6 – 15. No deaths were observed. A significant dose-response trend for variations (dilated ureters) was seen in the fetuses of = 30 mg/kg bw/day-groups. However, this occurred in the presence of significantly reduced body weight gain of dams at dose levels of 30 mg/kg bw/day on gd 6 - 10 and with an even stronger effect at 100 mg/kg bw/day. Based on the results reported a NOAEL of 10 mg/kg bw/day was determined for maternal and developmental toxicity.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are repeat dose toxicity and acute toxicity through the oral route.

Public Risk Characterisation

Given the use as an intermediate in the manufacture of dyes and other chemicals it is unlikely that public will be exposed to this chemical. Hence, the public risk from this chemical is low.

Occupational Risk Characterisation

There is concern for worker health and safety given the acute oral toxicity of the chemical and blood effects observed with repeated exposure at low concentrations in animal studies. Airborne concentration of the chemical should be kept as low as reasonably practicable to minimise risk.

The chemical is used as an intermediate in the manufacture of dyes and other chemicals. Available information from international sources indicate the chemical is well controlled in occupational settings given the chemical is processed in closed systems.

The chemical is not currently classified on HSIS. Hence, the chemical should be appropriately classified and labelled to ensure that a person conducting a business or an employee at a workplace has adequate information to determine appropriate controls.

NICNAS Recommendation

The chemical is sufficiently assessed and risk managed provided the current recommendation for classification and labelling is followed.

Regulatory Control

Public Health

Considering the available information to indicate low public exposure from this chemical, no regulatory controls are recommended.

Work Health and Safety

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

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Acute Toxicity	Harmful if swallowed (Xn; R22)	Harmful if swallowed - Cat. 4 (H302)
Repeat Dose Toxicity	Danger of serious damage to health by prolonged exposure (Xn; R48)	May cause damage to organs through prolonged or repeated exposure - Cat. 2 (H373)

^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

Work Health and Safety (WHS) legislation in each Australian state and territory imposes obligations on manufacturers and importers of hazardous chemicals to ensure that the chemicals are correctly classified, correctly labelled and (material) safety data sheets ((m)SDS) are prepared for those chemicals. These include:

- the (m)SDS for the chemical, or products and mixtures containing the chemical, must contain accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of a chemical, as well as instructions on the safe storage, handling, use and disposal of the chemical (a review of physical hazards of the chemical has not been undertaken as part of this assessment); and
- a copy of the (m)SDS must be easily accessible to employees.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals to meet duties under the WHS Regulations are provided in the *Preparation of Safety Data Sheets for Hazardous Chemicals—Code of Practice* and *Labelling of Workplace Hazardous Chemicals—Code of Practice*, respectively.

To comply with the WHS legislation, a person conducting a business or undertaking (PCBU) at a workplace must manage risks arising from storage, handling and use of a hazardous chemical. Other duties may apply to a PCBU involved in the storage, handling and use of hazardous chemicals at a workplace. Refer to the WHS legislation in the relevant jurisdiction for further information.

Guidance on managing risks from hazardous chemicals are provided in the *Managing Risks of Hazardous Chemicals in the Workplace—Code of Practice*.

It is recommended that a PCBU should ensure that:

- equipment be designed, constructed, and operated so that, the person handling the chemical does not come into contact with the chemical and is not exposed to a concentration of the chemical that is greater than the workplace exposure standard for the chemical;
- equipment used to handle the chemical retains the chemical, without leakage, at all temperatures and pressures for which the equipment is intended to be used and dispenses or applies the substance, without leakage, at a rate and in a manner for which the equipment is designed.

References

ChemIDPlus. Cas no: 99-54-7, Accessed 3 October 2012.

ECHA (2012). REACH Dossier for Benzene, 1,2-dichloro-4-nitro- (99-54-7). Accessed October 2012.
<http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances>

Galleria Chemica. Accessed June 2012. <http://jr.chemwatch.net/galleria/>

IARC (1996). Volume 65 - Printing Processes and Printing Inks, Carbon Black and Some Nitro Compounds. WHO International Agency for Research on Cancer. Accessed October 2012. <http://monographs.iarc.fr/ENG/Monographs/vol65/mono65.pdf>

OECD (2003), SIDS 1,2-dichloro-4-nitrobenzene (99-54-7). Accessed October 2012.
<http://www.chem.unep.ch/irptc/sids/OECD/SIDS/99547.pdf>

U.S National Library of Medicine, Hazardous Substances Data Bank, Benzene, 1,2-dichloro-4-nitro- (99-54-7). Assessed September 2012. <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~cnM6rF:1>

Last update 17 May 2013

Share this page