Ethane, hexachloro-: Human health tier II assessment

27 November 2014

CAS Number: 67-72-1

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.

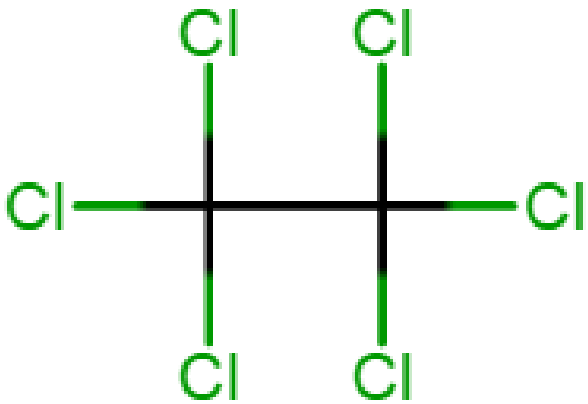
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	1,1,1,2,2,2-hexachloroethane ethane hexachloride ethylene hexachloride Distopan
Structural Formula	
Molecular Formula	C2Cl6
Molecular Weight (g/mol)	236.74
Appearance and Odour (where available)	Colourless crystals with characteristic odour
SMILES	C(Cl)(Cl)(Cl)C(Cl)(Cl)Cl

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; Substances and Preparations in the Nordic countries (SPIN) database; the US Environmental Protection Agency's Aggregated Computational Toxicology Resource (ACToR); and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported commercial use including:

- as a camphor substitute in nitrocellulose explosives, pyrotechnics and smoke devices;
- as a lubricating oil additive;
- in fluxes;
- in fire extinguishing fluids; and
- as a plasticiser for cellulose esters.

The chemical has reported site-limited use including:

- as a solvent in organic synthesis;
- as a polymerisation catalyst;
- as a vulcanising agent; and
- in metallurgy for refining aluminium alloys, recovering metal from ores, or smelting products.

The chemical has reported non-industrial use including:

- as a retarding agent in fermentation;
- in insecticides; and
- in veterinary medicine.

Restrictions

Australian

No known restrictions have been identified.

International

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

- 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;
- European Union (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
- Phillipines Restricted Ingredients for Use in Cosmetics.

The chemical is also restricted by Annex XVII to Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) Regulation. 'The chemical shall not be placed on the market, or used, as substance or in mixtures, where the substance or mixture is intended for the manufacturing or processing of non-ferrous metals.'

Existing Work Health and Safety Controls

Hazard Classification

The chemical is listed in the Hazardous Substances Information System (HSIS) (Safe Work Australia), but there are no risk phrases assigned to the chemical.

Exposure Standards

Australian

The chemical has an exposure standard of 9.7 mg/m^3 (1 ppm) time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica):

TWA:

- 2–10 mg/m^3 (~1 ppm) in Canada (Alberta, British Columbia, Quebec, Saskatchewan, Yukon), China, Denmark, Germany, Spain, Switzerland, the United States of America (USA) (California, Hawaii, Minnesota, Vermont, Washington); and
- 50 mg/m^3 (5 ppm) in Greece and South Africa.

Short-term exposure limits (STEL):

- 20–30 mg/m^3 (2–3 ppm) in Canada (Saskatchewan, Yukon), Poland, Switzerland and the USA (Washington); and
- 6–10 mg/m^3 (respirable fraction) in Canada (Saskatchewan) and the USA (Washington).

Health Hazard Information

Toxicokinetics

Animal studies have shown that the chemical can be absorbed following oral and inhalation exposure. Varied amounts of absorption were detected in the gastrointestinal tract; 40–50 % in rabbits and 62–88% in rats and mice. Dermal absorption across human skin is perceived to be low, based on calculated dermal penetration rates from in vitro testing (0.023 mg/cm^2/hour) (ATSDR, 1997).

Following oral exposure, the chemical was found to be distributed preferentially to the adipose tissues, kidneys, liver and blood. Smaller amounts were detected in the brain, lungs and muscle. In rats, the highest concentration of the chemical was found in male kidneys (4–45 % more than that in female kidneys). Concentrations in the mouse liver were observed to be twice that of the rat liver following intraperitoneal administration (ATSDR, 1997; US EPA, 2011).

The chemical is metabolised in the liver by a two-step reduction process, initially by cytochrome P450 (CYP450), followed by either nicotinamide adenine dinucleotide phosphate (NADPH) or cytochrome *b*5. The primary metabolites generated from the first and second reaction were the pentachloroethyl radical (pentachloroethane as the minor product) and tetrachloroethene, respectively. These primary metabolites are then oxidised to form trichloroethanol and trichloroacetic acid (TCA), identified as the major urinary metabolites in rodents. The chemical is also excreted in exhaled air (65–70 % in rodents, 14–25 % in rabbits) and in the faeces (ATSDR, 1997; US EPA, 2011).

Acute Toxicity

Oral

The chemical is reported to have low acute toxicity in animal tests following oral exposure.

The median lethal dose (LD50) ranged from 4460–7690 mg/kg bw in rats and 4970 mg/kg bw in male guinea pigs. Observed sublethal signs in rats were hepatic effects (increased liver weights, elevated serum liver enzyme levels, centrilobular necrosis, fatty degeneration and haemorrhage), reduced body weight gain, and neurological effects (tremor, decreased motor activity). Renal effects were observed in male rats but were minimal (ATDSR, 1997; US EPA, 2011; HSDB).

Dermal

Data on the acute dermal exposure is limited to one irritation study. Based on the result, the chemical has low acute toxicity following dermal exposure.

The chemical (0.5 g) was applied as a paste (in water) to the intact and abraded skin of six male New Zealand White rabbits for 24 hours. Slight redness occurred but disappeared 72 hours after treatment. The dermal LD50 was reported to be ≥32000 mg/kg bw (ATDSR, 1997; HSDB).

Inhalation

Based on the available information, the chemical is considered to have low acute inhalation toxicity.

Due to the physicochemical properties of the chemical (sublimation at ambient air temperatures, saturated vapour at concentrations of 670–700 ppm (6487–6778 mg/m^3) at 20 °C), the vapour concentrations used in inhalation studies are limited. Above the saturation threshold, the animals are exposed to both microcrystalline and volatilised forms of the chemical (ATDSR, 1997).

In an acute inhalation study, male Sprague Dawley (SD) rats were exposed to 2500 or 57000 mg/m^3 for eight hours, and 17000 mg/m^3 for six hours and observed for 14 days. No adverse effects were observed in rats exposed to 2500 mg/m^3. At high concentrations (57000 mg/m^3), the chemical vapour became supersaturated and formed particles. Respiratory effects (interstitial pulmonary pneumonitis), reduced body weight gain and staggered gait were observed and mortalities (2/6) occurred

at the end of eight hours. Rats exposed to 17000 mg/m^3 for six hours showed reduced body weight gain and staggered gait (2/6). No exposure-related gross or histopathological changes in the liver or kidneys were observed (ATSDR, 1997; IARC, 1999; US EPA, 2011; HSDB). No median lethal concentration (LC50) could be determined.

Corrosion / Irritation

Respiratory Irritation

The available data indicate irritant effects in the respiratory tract, although not sufficient to warrant a hazard classification.

Irritation of the respiratory tract in animals appeared to worsen upon prolonged or repeated inhalation exposure. However, the effects were reversible once exposure ceased (ATDSR, 1997).

Respiratory tract irritation was observed following acute inhalation exposure to the chemical vapour at concentrations that resulted in condensation (see **Acute toxicity: Inhalation**).

Skin Irritation

The available information indicates that the chemical is not a skin irritant.

In a dermal study (non-guideline), the chemical (0.5 g solid) was applied on the intact and abraded skin of male New Zealand White rabbits (n = 6) for 24 hours, with observation up to seven days. No primary irritation was observed at 24 or 72 hours, or at seven days. When the chemical was applied as a paste (see **Acute toxicity: Dermal**), no oedema and very mild erythema were observed on intact skin at 24 hours. On abraded skin, one rabbit displayed moderate to severe erythema reactions which disappeared after 72 hours (ATSDR, 1997; US EPA, 2011). The mean scores over 24 and 72 hours for intact skin were 1.0 and 0.33, respectively for erythema, and zero for oedema at both time points (Weeks and Thomasino, 1978).

Eye Irritation

Although limited data are available, the chemical had been reported to be an eye irritant and warrants hazard classification.

In an eye irritation study (non-guideline), the chemical (0.1 g solid) was applied to one eye of each of six male New Zealand White rabbits for 24 hours. Observations were made at 24, 48, and 72 hours, and thereafter for seven days. Moderate corneal damage, iritis and conjunctivitis were observed in 5/6 rabbits within 72 hours after exposure. All effects were reversible within seven days. The mean scores (for 24, 48 and 72 hours) were 0.83 for corneal damage; 0.27 for iritis; and 3.5 for conjunctivitis. Based on the conjunctival effects observed, the chemical is considered to be an eye irritant (Weeks and Thomasino, 1978; US EPA, 2011).

Sensitisation

Skin Sensitisation

Based on the limited data available, the chemical is not considered to be a skin sensitiser.

In an old skin sensitisation study (non-guideline), male guinea pigs (n = 10/dose) were injected intradermally with 0.1 % of the chemical and followed by a challenge dose of 0.1 % after two weeks. The chemical did not produce any sensitising effect (Weeks and Thomasino, 1978).

Repeated Dose Toxicity

Oral

Based on the available data, repeated oral exposure to the chemical may cause serious damage to health, (e.g. liver and kidney effects at doses above 62 mg/kg bw/day in female rats) and warrants classification under the GHS.

The kidneys and liver appear to be the main target organs in animal studies following repeated oral exposure. Rats were more sensitive to the chemical than rabbits. Renal effects in male rats were more severe than for females (US EPA, 2011). In two-year chronic/carcinogenic studies, toxic tubular nephropathy was observed in both rats and mice (see **Carcinogenicity**).

In two subchronic oral toxicity studies, Fischer 344 (F344/N) rats (n = 10/sex/dose) were exposed to the chemical by gavage at doses of 0, 34, 67, 134, 268 or 536 mg/kg bw/day for 13 weeks, or in the diet at doses of 1, 15 or 62 mg/kg bw/day for 16 weeks. Mortalities occurred at 536 mg/kg bw/day in both males (5/10) and females (2/10). The males were observed to be more susceptible to kidney effects (increased kidney weights, hyaline droplet formation, atrophy and degeneration of renal tubules) at ≥15 mg/kg bw/day. The females were more susceptible to liver effects (with significant increase in relative liver weights at ≥62 mg/kg bw/day and a dose-response increase in hepatocellular necrosis from ≥134 mg/kg bw/day). Kidney effects (atrophy and degeneration of tubules) were also observed in the females at higher doses (≥62 mg/kg bw/day). The no observed adverse effect levels (NOAELs) were established as 1 mg/kg bw/day (males) and 15 mg/kg bw/day (females) based on renal tubule toxicity observed at 15 and 62 mg/kg bw/day respectively (IARC, 1999; US EPA, 2011; HSDB).

In a short-term study where F344/N rats (n = 5/dose) were exposed to the chemical (gavage) up to doses of 2250 mg/kg bw/day for 16–21 days, all rats died during the dosing period ≥1125 mg/kg bw/day (NTP, 1989). Effects on the kidneys (hyaline droplet formation, tubular cell regeneration, granular casts) and urinalysis parameters were observed in male rats at the lowest dose of 140 mg/kg bw/day. The NOAEL was 281 mg/kg bw/day in female rats based on decreased body weights at 563 mg/kg bw/day (NTP, 1989; US EPA, 2011).

In a 12-day oral gavage study in New Zealand White male rabbits, liver effects (degeneration and necrosis) and effects on kidneys (tubular nephrosis and nephrocalcinosis) were observed at 320 mg/kg bw/day. The NOAEL was established as 100 mg/kg bw/day (US EPA, 2011).

Dermal

No data are available.

Inhalation

Repeated inhalation exposure studies are limited due to the vapour saturation threshold of the chemical at room temperature (see **Acute toxicity: Inhalation**). At very high doses, transient signs of neurotoxicity were observed in dogs and rats, but not at lower doses. Based on the available data, the chemical is not considered to cause serious health effets following repeated inhalation exposure.

In a repeated inhalation study (non-guideline), SD rats (n = 25/sex/dose), male beagle dogs (n = 4/dose), male Hartley guinea pigs (n = 10/dose), and female Japanese quails (n = 20/dose) were exposed to the chemical vapour at concentrations of 15, 48 or 260 ppm (145, 465 or 2517 mg/m^3), six hours/day, five days/week for six weeks. At the highest dose level, signs of neurotoxicity (tremors, facial muscular fasciculations, head bobbing, hypersalivation) were observed in dogs and at a lesser extent in rats during the exposure period (recovery seen during the 12 week post-exposure period). At the highest dose, increased relative kidney, spleen and testes weights in male rats and increased liver weights in female rats were observed. The guinea pigs showed body weight reduction and increased relative liver weights at the highest dose. No toxic effects were observed in quails. No treatment-related effects were observed in any species at the two lower doses. There were mortalities at ≥2517 mg/m^3 within the exposure period in dogs (1/4), rats (2/50) and guinea pigs (4/10). The no observed adverse effect concentration (NOAEC) was established as 465 mg/m^3 based on effects at the highest dose (ATDSR. 1997; IARC, 1999; US EPA, 2011).

Observation in humans

Eleven munition workers exposed to the chemical (10–20 mg/m^3) for more than five weeks reported incidences of irritation (dry skin and mucous membranes). The workers were wearing protective equipment including compressed air-fed visors or full facepiece masks with combination filters. The clinical examinations did not reveal any abnormalities in the respiratory system, haematological parameters or in the liver or kidneys. The investigators postulated the principal exposure route was dermal, and the observed irritation effects were a result of a local trauma effect from the protective equipment (ATSDR, 1997).

Genotoxicity

Based on the weight of evidence from the available data, the chemical is not considered to be genotoxic. However, binding of the chemical to DNA may be possible under certain circumstances.

In vitro genotoxicity studies conducted in microorganisms (bacterial systems and yeast) and cultured mammalian cells were mostly negative, with or without metabolic activation (IARC, 1999; US EPA, 2011).

In vivo studies in animals are limited and gave predominantly negative results (mammalian bone marrow micronucleus test in mice, hepatocyte replicative DNA synthesis assay in mice). However, in one study, male BALB/c mice and Wistar rats that received a single intraperitoneal (i.p.) injection of the chemical at ~1 mg/kg bw showed binding of the chemical (22 hours after injection) to DNA, ribonucleic acid (RNA) and protein in the isolated liver, kidneys, lungs and stomach. Mice exhibited the highest levels of DNA and protein binding in the liver (nine times greater than in rats). However, adducts were not identified. The study was further evaluated in vitro in the microsomal and cytosolic fractions from the same organs. There was no clear evidence of DNA-adduct formation in vitro (IARC, 1999; US EPA, 2011; Health Canada, 2014).

It was reported that the chemical was not significantly genotoxic in rats, and that carcinogenicity in some target tissues occurred though a process other than induced mutations (NTP, 1989; US EPA, 2011).

Modelled predictions of the genotoxicity of the chemical have been reported as generally negative (Health Canada, 2014).

Carcinogenicity

Based on the available animal data, the chemical is considered to be a carcinogen and warrants classification.

After evaluating the available data, the International Agency for Research on Cancer (IARC) (1999) classified the chemical as ‘possibly carcinogenic to humans’ (Group 2B). IARC (1999) concluded that ‘There is *inadequate evidence* in humans for the carcinogenicity of hexachloroethane. There is *sufficient evidence* in experimental animals for the carcinogenicity of hexachloroethane.' The US Environmental Protection Authority (EPA) classified the chemical as a ‘possible human carcinogen’ (Group C) (US EPA, 2011). A recent National Toxicology Program (NTP) report listed it as 'reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in experimental animals' (NTP, 2014).

In a chronic toxicity/carcinogenicity study, B6C3F1 mice (n = 50/sex/dose) were administered the chemical at doses of 0, 590 or 1179 mg/kg bw/day (doses were adjusted to 0, 360 or 722 mg/kg bw/day to reflect continuous exposure—US EPA 2011) for five days/week up to 78 weeks. Increased incidence of hepatocellular carcinoma was observed in all exposed groups. Histopathological results showed that hepatocellular carcinomas occurred in low- and high-dose males at 15/50 and 31/49 respectively (compared with 1–3/18–20 controls); in low- and high-dose females at 20/50, 15/49 respectively (compared with 0–2/18–20 controls). Toxic tubular nephropathy (>92 %) was also observed in all treated animals (NCI, 1978; US EPA, 2011).

In the same study, Osbourne–Mendel rats (n = 50/sex/dose) were administered the chemical (oral gavage) at doses of 0, 212 or 423 mg/kg bw/day (doses were adjusted to 0, 113 or 227 mg/kg bw/day to reflect continuous exposure—US EPA, 2011) for five days/week up to 78 weeks. Mortality occurred early at both doses in both sexes (by week 15 for males and by week 25 for females). Increased incidences of renal tubular cell adenomas was observed in males, and only significant at the low dose (US EPA, 2011).

In another carcinogenicity study, F344/N rats (n = 50/sex/dose) were administered the chemical (by gavage) at 0, 10 or 20 mg/kg bw/day (males) and at 0, 80 or 160 mg/kg bw/day (females), five days/week up to two years. The males displayed an increased incidence (7/50 compared with 1/50 controls) of renal tubular adenomas or carcinomas at 20 mg/kg bw/day, and

pheochromocytomas (26/45 compared with 14/50 controls) of the adrenal gland at 10 mg/kg bw/day. Three carcinomas were observed at the high dose, and 1/3 metastasised. The NTP concluded that there was evidence of carcinogenicity in male rats in this study, based on a comparison with the historical controls of renal tubular cell neoplasms (10/1943) in NTP studies. Females did not develop renal tumours or pheochromocytomas despite being exposed to doses eight times higher than males (160 mg/kg bw/day) (NTP, 1989; IARC, 1999; US EPA, 2011).

A two-stage initiation–promotion assay was conducted in male rats to evaluate the development of liver foci, relevant for the prediction of liver tumour development. The rats were exposed (by gavage) to the chemical at a single dose of 500 mg/kg bw, followed by a promoting agent, 0.05 % phenobarbital (dietary), for seven weeks. No increase in preneoplastic lesions (liver foci) was observed. The results indicated that the chemical is a promoter of carcinogenicity rather than an initiator (ATSDR, 1997; IARC, 1999; US EPA, 2011).

The induction of kidney tumours in male rats has been postulated to be associated with an $\alpha 2\mu$-globulin mediated mode of action, which was considered not relevant for humans. However, the applicability of this mechanism in this case has not been established. Furthermore, dose-related increased incidence and severity of nephropathy reported in mice and female rats implies adverse effects occur in the kidney through a different mechanism (NTP, 1989; US EPA, 2011). The chemical also generates the metabolite pentachloroethane (CAS No. 76-01-7) (see **Toxicokinetics**), which is a classified carcinogen in HSIS and induces hepatocellular neoplasms in mice.

In one cohort study of Swedish workers at aluminium production sites (n = 1880), no significant association was observed between exposure to the chemical and incidences of anorectal, liver or lung cancer, or malignant lymphomas (IARC, 1999).

Reproductive and Developmental Toxicity

No reproductive toxicity studies are available. The available information indicate that the chemical does not cause developmental toxicity. Any adverse foetal effects observed were secondary to maternal toxicity.

Data are limited to only developmental toxicity studies. Two oral studies and one inhalation study have been conducted on pregnant female rats.

In a developmental toxicity study, pregnant female SD rats (n = 22/dose) were administered (by gavage) the chemical at doses of 0, 50, 100 or 500 mg/kg bw/day for six hours/day, on gestation days (GD) 6–16. A maternal lowest observed adverse effect level (LOAEL) of 500 mg/kg bw/day was determined based on decreased body weight gains. Fertility (increased resorptions and decreased litter size) was adversely affected at this dose, but the foetuses did not display any skeletal or soft tissue anomalies (IARC, 1999; US EPA, 2011).

In another developmental toxicity study, pregnant female Wistar rats (n = 21/dose) were exposed (oral) to the chemical at doses of 0, 56, 167 or 500 mg/kg bw/day on GD 7–17. The maternal NOAEL was reported as 56 mg/kg bw/day based on decreased body weight gain, subcutaneous haemorrhage and neurotoxicity effects (decreased motor activity and piloerection) observed at this dose level. The developmental NOAEL was 167 mg/kg bw/day based on decreased foetal body weight gains, skeletal variations (rudimentary lumbar ribs) and delayed ossification observed at this dose. However, no skeletal malformations were observed (ATSDR, 1997; US EPA, 2011).

In a developmental inhalation toxicity study, female SD rats (n = 22/dose) were exposed to 0, 145, 465 or 2517 mg/m^3 during GD 6–16. The maternal NOAEC was established as 465 mg/m^3 based on decreased body weight gain and tremors observed on GD 12–16. No effects were observed in the foetuses up to the highest concentration tested (ATDSR, 1997; US EPA, 2011).

Other Health Effects

Neurotoxicity

Although neurological symptoms were evident in several animal toxicity studies, it is unclear whether these effects were caused by the parent compound or its metabolites (ATSDR, 1997; US EPA, 2011). The exposure levels that caused neurotoxicity in animals were higher than the exposure levels that require classification of the chemical for neurotoxic effects.

Acute and intermediate (six-week) inhalation exposure to the chemical have caused staggering gait (>57000 mg/m^3), tremors and ruffled pelt (>2517 mg/m^3) in rats. The rats that inhaled the chemical repeatedly showed no changes in motor activity or avoidance behaviour. However, decreased motor activity and tremors were observed in pregnant rats, following gestational exposure to the chemical at doses ≥167 mg/kg bw/day (oral) and ≥2517 mg/m^3 (inhalation) (see **Reproductive and developmental toxicity**) (US EPA, 2011).

Dogs appear to be more susceptible to neurological effects following repeated inhalation exposure, compared with rats (see **Repeated toxicity: Inhalation**). They exhibited symptoms including tremors, ataxia, hypersalivation, severe head bobbing and facial fasciculations. They recovered overnight after exposure ceased (ATSDR, 1997; US EPA, 2011).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (carcinogenicity).

The chemical can also cause eye irritation and other harmful effects (see **Repeated toxicity: Oral**) following repeated oral exposure.

Public Risk Characterisation

Given the uses identified for the chemical, it is unlikely that the public will be exposed.

Occupational Risk Characterisation

During product formulation, ocular and inhalation exposure of workers to the chemical might occur, particularly where manual or open processes are used. These can include transfer and blending activities, quality control analysis, and cleaning and maintenance of equipment. Worker exposure to the chemical at lower concentrations may 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 health effects, the chemical might pose an unreasonable risk to workers unless adequate control measures to minimise ocular exposure to the chemical 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 appropriate controls.

The data available support an amendment to the hazard classification in HSIS (refer to **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 hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)
Repeat Dose Toxicity		May cause damage to organs through prolonged or repeated exposure through the oral route - Cat. 2 (H373)
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, 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 may 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;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- 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 assist with meeting 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

Agency for Toxic Substances and Disease Registry (ATSDR) 2010. Toxicological Profile for Hexachloroethane. Accessed October 2014 at http://www.atsdr.cdc.gov/toxprofiles/tp97.pdf

Aggregated Computational Toxicology Resource (ACToR), US EPA. CAS No. 67-72-1, Accessed October 2014 at http://actor.epa.gov/actor/GenericChemical?casrn=67-72-1

ChemIDPlus, CAS No. 67-72-1. Accessed September 2014 at http://chem.sis.nlm.nih.gov/chemidplus.

Galleria Chemica. Accessed October 2014 at https://jr.chemwatch.net/galleria/

Hazardous Substances Data Bank (HSDB). National Library of Medicine. Accessed on October 2014 at http://toxnet.nlm.nih.gov.

Health Canada (2014). Draft Screening Assessment Report for Hexachloromethane. Accessed October 2014 at http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=CD3BB2EB-1

International Agency for Research on Cancer (IARC) (1999). IARC Monographs on the evaluation of carcinogenic risks to humans. Volume 73 Some Chemicals that Cause Tumours of the Kidney or Urinary Bladder in Rodents and Some Other Substances. Accessed October 2014 at http://monographs.iarc.fr/ENG/Monographs/vol73/mono73-15.pdf

National Toxicology Program (NTP) 1989. Toxicology and Carcinogenesis Studies of Hexachloroethane (CAS No. 67-72-1) in F344/N rats. Accessed October 2014 at http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr361.pdf

National Toxicology Program (NTP) 2014. Report on Carcinogens, Thirteenth Edition. Hexachloroethane (CAS No. 67-72-1). Accessed October 2014 at http://ntp.niehs.nih.gov/ntp/roc/content/profiles/hexachloroethane.pdf#search=hexachloroethane

Nationcal Cancer Institute (NCI) 1978. Bioassay of hexachloroethane for possible carcinogenicity (CAS No. 67-72-1). Technical Report Series No. 68 (NCI-CG-TR-68). U.S. Department of Health, Education, And Welfare. Accessed October 2014 at http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr068.pdf

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed October 2014 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

Substances in Preparations in Nordic Countries (SPIN). Accessed October 2014 at http://195.215.202.233/DotNetNuke/default.aspx

US EPA 2011. Toxicological Review of Hexachloroethane. Accessed October 2014 via the US EPA Integrated Risk Information System (IRIS) http://www.epa.gov/iris/toxreviews/0167tr.pdf

Weeks M& Thomasino J 1978. Assessment of acute toxicity of hexachloroethane in laboratory animals. Aberdeen Proving Ground, MD: U.S. Army Environmental Hygiene Agency.

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