Chrysene: Human health tier II assessment

13 February 2015

CAS Number: 218-01-9

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

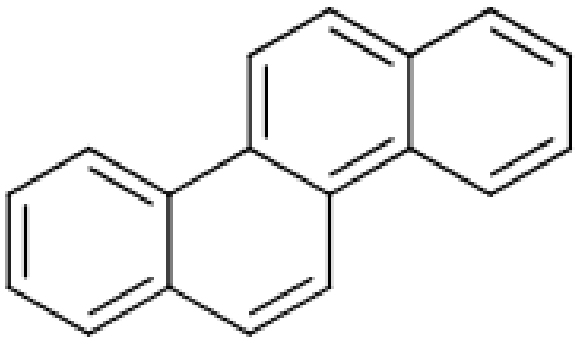
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	1,2-Benzphenanthrene 1,2,5,6-Dibenzonaphthalene Benzo(a)phenanthrene Coal tar pitch volatiles: chrysene
Structural Formula	
Molecular Formula	C18H12
Molecular Weight (g/mol)	228.3
Appearance and Odour (where available)	Red, blue, fluorescent odourless crystals.
SMILES	c12c(c3c(c4c(cccc4)cc3)cc1)cccc2

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; and the United States (US) National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported site-limited use in organic synthesis of other products.

Restrictions

Australian

The chemical is covered under polycyclic aromatic hydrocarbons listed in Schedule 4 (Hazardous chemicals requiring health surveillance under National Code of Practice) of the Work Health and Safety Regulations (WHS, 2011).

International

Chrysene is listed on the following (Galleria Chemica):

- Association of South East Asian Nations (ASEAN) Cosmetic Directive Annex II Part 1: List of substances which must not form part of the composition of cosmetic products;
- Council of Europe Regulation AP (92)2 on control of aids to polymerisation for plastic materials and articles-limits for finished articles;
- EU Cosmetics Regulation 1223/2009 Annex II-List of substances prohibited in cosmetic products; and
- New Zealand Cosmetic Products Group Standard-Schedule 4: Components cosmetic products must not contain.

Existing Work Health and Safety Controls

Hazard Classification

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

- R45 Carc. Cat. 2 (carcinogenicity)
- R68 Mut. Cat. 3 (mutagenicity)

Exposure Standards

Australian

The chemical is known to be carcinogenic and it is not possible to assign an appropriate exposure standard. Exposure should be controlled to the lowest practicable level.

International

The following exposure standards are identified (Galleria Chemica).

An exposure limit of 0.2 mg/m^3 time weighted average (TWA) in different countries such as Argentina, Iceland and China and 0.6–700 mg/m^3 temporary emergency exposure limit (TEEL) in the USA.

Health Hazard Information

The chemical belongs to a group of chemicals known as polycyclic aromatic hydrocarbons (PAHs). PAHs are a group of chemicals formed during the incomplete burning of coal, oil, gas, wood, garbage, or other organic substances. PAHs occur naturally and can be manufactured as individual compounds for industrial purposes.

Genotoxicity and carcinogenicity are the endpoints of concern for this chemical (refer **Genotoxicity** and **Carcinogenicity** sections). The chemical is expected to have low reactivity, and structurally similar chemicals such as anthracene and phenanthrene have low acute toxicity and irritancy. In the absence of relevant reliable data for the other endpoints in this report, the focus of the hazard assessment is on genotoxicity and carcinogenicity.

Toxicokinetics

Chrysene is absorbed through oral and dermal exposure. The peak concentration of chrysene is reached within an hour in the blood and liver. It concentrates in the adipose and mammary tissues and is predominantly eliminated through faeces with up to 41–79 % as an intact chemical. The chemical is completely eliminated within two days (IARC 1983; HSDB).

Chrysene is one of the PAHs where the structure has a "bay-region" and this gives rise to specific metabolic reactions resulting in DNA binding. The chemical is converted to a dihydrodiol, which is further metabolised to a diol epoxide metabolite which is not readily decomposed and can bind to DNA and form DNA adducts (HSDB).

Mixed function oxidases metabolise the bay-region in the chrysene structure to reactive bay-region diol epoxides that are mutagenic in bacteria and tumorigenic in mouse skin-painting assays (Levin et al., 1978; Nordqvist et al., 1981; Slaga et al., 1980; Wood et al., 1977 & 1979).

Genotoxicity

The chemical is classified as hazardous—Category 3 mutagenic substance—with the risk phrase ‘Possible risk of irreversible effects’ (Xn; R68) in the HSIS (Safe Work Australia). The available data support this classification.

In several studies, the chemical was mutagenic to *Salmonella typhimurium* (TA100 & TM677) in the presence of a metabolic activation system. It did not induce unscheduled DNA synthesis in primary rat hepatocytes when tested up to 100 nmol/ml, or mutations in Chinese hamster V79 cells when tested up to 10 µg/ml. It was positive in a mammalian cell transformation assay with Syrian hamster embryo cells when tested at 10 µg/ml, but was negative in mouse prostate C3HG23 cells when tested up to 10 µg/ml (IARC, 1983).

In one in vivo study, chromosomal aberrations were observed in NMRI mice treated with 450 mg/kg bw orally. In another study, the chemical induced sister chromatid exchange in Chinese hamster bone-marrow cells when administered with two doses of 450 mg/kg bw intraperitoneally (IARC, 1983).

Carcinogenicity

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

In a one year skin painting study, 20 female Swiss mice were dermally exposed to a 1 % solution of chrysene in acetone three times/week. Of the 20 mice, nine developed skin papillomas and eight developed skin carcinomas. Only six animals were alive at the end of 12 months. While no controls were used, it was concluded that "it is unlikely such a high incidence of carcinomas would occur spontaneously in this strain" (IARC, 1983; NIOSH, 2009).

One squamous-cell carcinoma was induced after 31 weeks when 15 CD-1 rats were treated twice weekly by applying a 0.2 % solution of chrysene in acetone to the skin (IARC, 1983).

In a study investigating cancer-initiating potential of the chemical, 1 mg of chrysene in 0.4 mL acetone was applied to the shaved backs of 20 female ICR/HA Swiss strain mice. Following 13–21 days of chrysene treatment, all animals were exposed to 25 mg of croton resin (a known tumour promoter) in 0.1 mL acetone three times weekly. Two out of the 20 mice developed carcinomas and 16/20 mice developed papillomas. Control mice receiving only croton resin showed five incidences of benign tumours and one malignant tumour (IARC, 1983; NIOSH, 2009).

In other studies, local tumours were observed after mice were subcutaneously injected with chrysene. An increased incidence of liver tumours was observed after mice were administered chrysene (perinatally) by subcutaneous or intraperitoneal (i.p.)injection (IARC, 1983).

IARC (1983) concluded that there is limited evidence that the chemical is carcinogenic to laboratory animals.

Risk Characterisation

Critical Health Effects

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

Public Risk Characterisation

Use of the chemical in Australia is unknown. Overseas, the chemical is used for site-limited organic synthesis. 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

During use, dermal, ocular and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. 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 could pose an unreasonable risk to workers unless adequate control measures to minimise occupational 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.

Based on the available data, the hazard classification in the HSIS (Safe Work Australia) is considered appropriate.

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 Globally Harmonised System of Classification and Labelling of Chemicals (GHS) as below. This assessment does not consider classification of physical and environmental hazards.

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

[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 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;
- 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.

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