Cyclopentanone, phenylhydrazone: Human health tier II assessment

28 June 2019

CAS Number: 1132-58-7

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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

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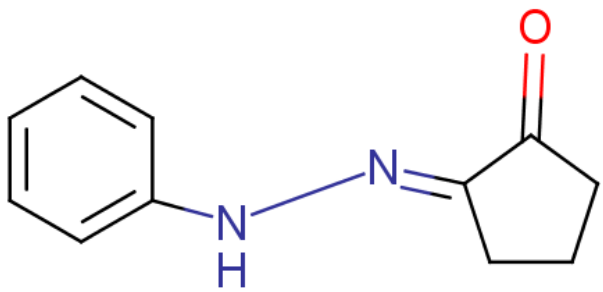
Acronyms & Abbreviations

Chemical Identity

Synonyms	pentanone phenylhydrazone cyclopentanon-phenylhydrazon
Structural Formula	
Molecular Formula	C11H14N2
Molecular Weight (g/mol)	174.2
Appearance and Odour (where available)	colourless liquid with peppermint like odour
SMILES	c1(NN=C2CCCC2)ccccc1

Import, Manufacture and Use

Australian

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

International

No specific international use, importation, or manufacturing information has been identified.

The parent chemical, phenylhydrazine (CAS No. 100-63-0), has reported site-limited uses, including:

- as intermediates for organic synthesis (including dyes);
- in photography (NICNASa).

Cyclopentanone, phenylhydrazine is expected to have use as a source of phenylhydrazine and; therefore, similar uses are expected.

Restrictions

Australian

No known restrictions have been identified for the chemical.

International

No known restrictions have been identified for the chemical.

The parent chemical, phenyl hydrazine is subject to restrictions under the group entry 'Hydrazine (CAS No. 302-01-2), its derivatives and their salts' in the European Union (EU) Cosmetics Regulation 1223/2009 Annex II—List of susbtances in cosmetic products (CosIng, Galleria Chemica).

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

The chemical is a derivative of phenylhydrazine (CAS No. 100-63-0). Cyclopetanone phenylhydrazone undergoes Fischer Indole Synthesis and Schiff base reactions in the body, resulting in formation and release of phenylhydrazine in the body (McIsaac et al, 1958; Moldoveanu, 2019). Cyclopentanone was evaluated by NICNAS (NICNASb) and is not expected to be harmful to the same extent as phenylhydrazine. Therefore, the main concerns regarding effects on human health and toxicity is expected to be entirely driven by phenylhydrazine (NICNASa). While there is no health hazard or toxicokinetic data available on the specific chemical, the health hazard information of the parent chemical, phenylhydrazine, has been evaluated by NICNAS (NICNASa) and is considered relevant to this assessment.

Phenylhydrazine is considered hazardous for acute toxicity, irritation, sensitisation, repeat dose toxicity, genotoxicity and carcinogenicity. The available data supports all of the existing hazard classifications, including evidence for carcinogenicity and genotoxicity. These data and recommendations are considered relevant to cyclopetanone phenylhydrazone (see **Recommendation** section).

The Tier II Human health assessment for phenylhydrazine (the parent chemical) is available at: www.nicnas.gov.au. The report should be read in conjunction with this Tier II Human Health assessment.

Risk Characterisation

Critical Health Effects

Based on the information available for the parent chemical, phenyl hydrazine (CAS No. 100-63-0), this chemical's (CAS No. 1132-58-7) critical health effects for, the risk characterisation include:

- systemic long-term effects (carcinogenicity, mutagenicity);
- systemic acute effects (from oral, dermal and inhalation exposure); and
- local effects (skin sensitisation, skin and eye irritation).

The chemical may also cause harmful effects following repeated oral, dermal and inhalation exposure.

Public Risk Characterisation

Given the site-limited uses identified for the parent chemical, it is unlikely that the public will be exposed to the chemical. The public risk from the chemical is not considered to be unreasonable.

Occupational Risk Characterisation

During product formulation, oral, dermal, ocular and inhalation exposure may occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could 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 may 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.

Based on available read-across data, hazard classification is recommended (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 aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Not Applicable	Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Toxic if inhaled - Cat. 3 (H331)
Irritation / Corrosivity	Not Applicable	Causes serious eye irritation - Cat. 2A (H319) Causes skin irritation - Cat. 2 (H315)
Sensitisation	Not Applicable	May cause an allergic skin reaction - Cat. 1 (H317)
Repeat Dose Toxicity	Not Applicable	Causes damage to organs through prolonged or repeated exposure - Cat. 1 (H372)
Genotoxicity	Not Applicable	Suspected of causing genetic defects - Cat. 2 (H341)
Carcinogenicity	Not Applicable	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 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;
- 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 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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