

Organoarsenic compounds: Human health tier II assessment

03 July 2015

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Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Arsonic acid, phenyl-	98-05-5
Arsonic acid, (phenylmethyl)-	620-27-9
Arsonic acid, (4-methylphenyl)-	3969-54-8

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

Grouping Rationale

The chemicals in this group are organic arsenic compounds. The toxicity of the arsenic compound depends on how the chemicals disrupt the complex metabolic reactions in the body that ultimately provide energy in the form of adenosine triphosphate (ATP) (INCHEM, 2001). These chemicals are bonded with other functional groups and cannot react in the same way as inorganic arsenic compounds; hence, organic arsenic compounds are not as toxic as inorganic arsenic compounds.

Based on a review of publicly available hazard information in accordance with the IMAP Framework (NICNAS, 2013), limited or no toxicological data are available for the chemicals in this group. For chemicals with limited data, NICNAS will commonly use the principles of 'read across' in accordance with the Organisation for Economic Co-operation and Development (OECD) *Guidance on grouping of chemicals* (OECD, 2014) based on known properties of similar chemicals (analogues). The quality of the data used depends on how similar the analogues are to the chemicals being assessed. A conservative read across for the chemicals in this group can be undertaken as part of IMAP.

It is possible that the chemicals being assessed are not used for industrial purposes in Australia, or used only in very small quantities. For phenylarsonic acid (CAS No 98-05-5), the available information has indicated site-limited use (INCHEM, 2001; NTP, 2009; Galleria Chemica; HSDB). A common organic arsenic, Roxarsone (4-hydroxy-3-nitrophenylarsonic acid) (CAS No. 121-19-7) is widely used internationally as a feed additive for poultry (ATSDR, 2010). It is also likely that special containment equipment that precludes any human or environmental exposure is used. Information on the use of these chemicals could potentially remove the need to undertake a conservative assessment. Considering that the critical concerns for this group of chemicals relate to acute oral and inhalation toxicity, NICNAS needs to validate that exposure to these chemicals will be negligible, in order to then draw a conclusion that no additional risk management would be required.

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, Authorization and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR); the US National Library of Medicine's Hazardous Substances Data Bank (HSDB) and various international assessments including the International Agency for Research on Cancer (IARC, 2012); World Health Programme on Chemical Safety (INCHEM, 2001) and the National Toxicology Program (NTP, 2009).

The chemical, arsonic acid, phenyl- (CAS No. 98-05-5) has reported site-limited use as an analytical reagent for tin.

Restrictions

Australian

These chemicals, belong to the group entry 'arsenic', are listed in the *Poisons Standard*—the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedule 7 with the below entry for industrial uses:

'Arsenic **except**:

- (a) when separately specified in this Schedule;
- (b) when included in Schedule 4 or 6;
- (c) as selenium arsenide in photocopier drums;
- (d) as 10,10'-oxydiphenoxarsine in silicone rubber mastic containing 120 mg/kg or less of arsenic;
- (e) as 10,10'-oxydiphenoxarsine contained in polyvinyl chloride and polyurethane extruded and moulded articles containing 160 mg/kg or less of arsenic other than when included in articles:
- (i) in contact with food stuffs, animal feeds or portable water;
- (ii) of clothing and footwear in contact with the skin;
- (iii) used as infant wear; or
- (iv) intended for use as packaging materials;
- (f) in animal feeds containing 75 g/tonne or less of arsenic; or
- (g) in paints containing 0.1 % or less of arsenic calculated on the non-volatile content of the paint.'

Schedule 7 chemicals are labelled with 'Dangerous Poison'. These are substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special regulations restricting their availability, possession, storage or use may apply.

The chemicals are listed under 'arsenic and its compounds' as restricted hazardous chemicals under Schedule 10 (Prohibited carcinogens, restricted carcinogens and restricted hazardous chemicals) of the Work Health and Safety (WHS) regulation (WHS, 2011). Specifically, use is restricted in:

- abrasive blasting at a concentration of greater than 0.1 % as arsenic; and
- spray painting.

International

The chemicals belong to the group entry arsenic and soluble compounds (as arsenic) and are listed on the following (Galleria Chemica):

- EU Cosmetics Directive 76/768/EEC Annex II—List of substances which must not form part of the composition of 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
- ASEAN Cosmetic Directive Annex II Part 1: List of substances which must not form part of the composition of cosmetic products.

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are classified under the group entry 'Arsenic compounds, with the exception of those specified elsewhere in HSIS' as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- T; R23/25 (acute toxicity)

Exposure Standards

Australian

The chemicals in this group belong to the group entry arsenic and soluble compounds (as arsenic), which have an exposure standard of 0.05 mg/m³ time weighted average (TWA).

International

The following exposure standards are identified for arsenic and soluble compounds (as arsenic) (Galleria Chemica):

An exposure limit of 0.01–0.5 mg/m³ TWA in different countries such as Canada, Egypt, Argentina and South Africa and 0.01–0.5 mg/m³ occupational exposure limit (OEL) in different countries such as the United Arab Emirates, Thailand and Ireland.

Temporary Emergency Exposure Limits (TEELs), as defined by the US Department of Energy (DOE) for phenylarsonic acid are reported as :

- TEEL-1 = 3.4 mg/m³;
- TEEL-2 = 3.4 mg/m³; and
- TEEL-3 = 20 mg/m³.

The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV) of 0.5 mg/m³ for arsenic and its soluble compounds in countries such as Austria, Belgium, Finland, Japan and Holland; and 0.3 mg/m³ in Russia, Romania and Switzerland.

Health Hazard Information

Limited data are available for the chemicals in this group. The available information suggests that the organic arsenic compounds are less extensively metabolised than inorganic arsenic compounds and are rapidly eliminated in animals and humans.

This group of chemicals is classified as hazardous with the risk phrases 'Toxic if swallowed' (T; R25) and 'Toxic by inhalation' (T; R23) in the HSIS (Safe Work Australia).

The HSDB reported that acute exposure to high levels of phenylarsonic acid resulted in an inability to control body and limb movements and ataxia in laboratory animals. Paralysis and erythema were also observed a few days after the acute exposure. In other studies, the lowest oral median lethal dose (LD50) in mice was 270 µg/kg and the LD50 intravenous in rabbits was 16 mg/kg (HSDB).

In an acute inhalation toxicity study in rats and mice, the median lethal concentration (LC50) for mice was >6.4 mg/L in mice and >6.9 mg/L and >3.9 mg/L in male and female rats respectively. Observed clinical effects in both species included respiratory distress, rhinorrhoea and porphyrin-like encrustation of the eyes. Other effects observed in female rats at necropsy were an impacted caecum, blood in the intestine and bright red lungs with dark spots (INCHEM, 2001).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute effects (acute toxicity from oral or inhalation exposure). Other health hazards have not been characterised.

Public Risk Characterisation

The chemicals are currently listed on Schedule 7 of the SUSMP. Schedule 7 chemicals are not available for general public use.

Occupational Risk Characterisation

During product formulation, oral 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. Worker exposure to the chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

There is insufficient information regarding the use of these chemicals in Australia and their safety as used. Therefore, a Tier III assessment may be required (see **NICNAS Recommendation**).

NICNAS Recommendation

It is recommended that NICNAS undertake further consultation to determine to what extent these chemicals have industrial uses, and the control/regulatory measures that could be required based on the pattern use.

Should the consultation identify additional evidence pertaining to the use of the chemicals that could pose a risk to workers and/or the public, a Tier III assessment should be undertaken to characterise the risk and recommendations may be made if considered appropriate.

Regulatory Control

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
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Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Acute Toxicity	Toxic if swallowed (T; R25)* Toxic by inhalation (T; R23)*	Toxic if swallowed - Cat. 3 (H301) Toxic if inhaled - Cat. 3 (H331)

^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

References

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International Agency for Research on Cancer (IARC, 2012) Monographs on the Evaluation of Carcinogenic Risk to Humans. A Review of Human Carcinogens: Arsenic, Metals Fibers and Dusts. Volume 100C. Accessed June 2015 at <http://monographs.iarc.fr/ENG/Monographs/vol100C/index.php>.

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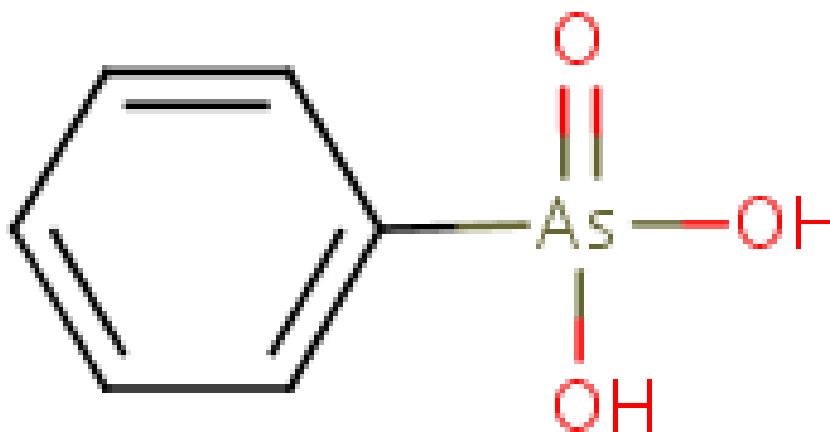
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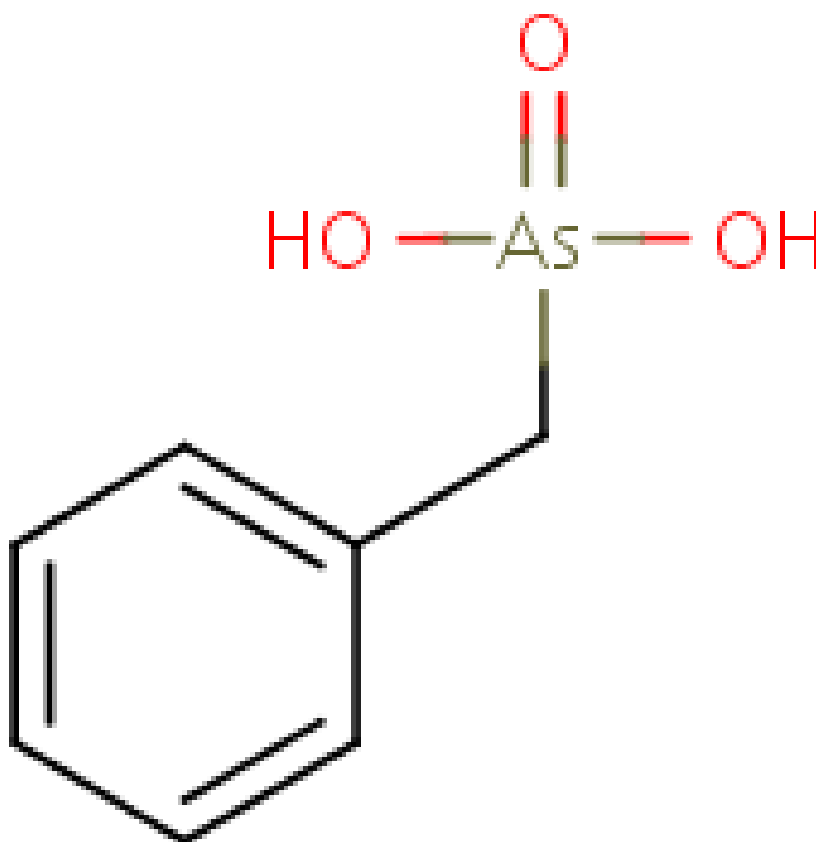
Chemical Identities

Chemical Name in the Inventory and Synonyms	Arsonic acid, phenyl- arsonic acid monophenylarsonic acid phenylarsonic acid
CAS Number	98-05-5
Structural Formula	



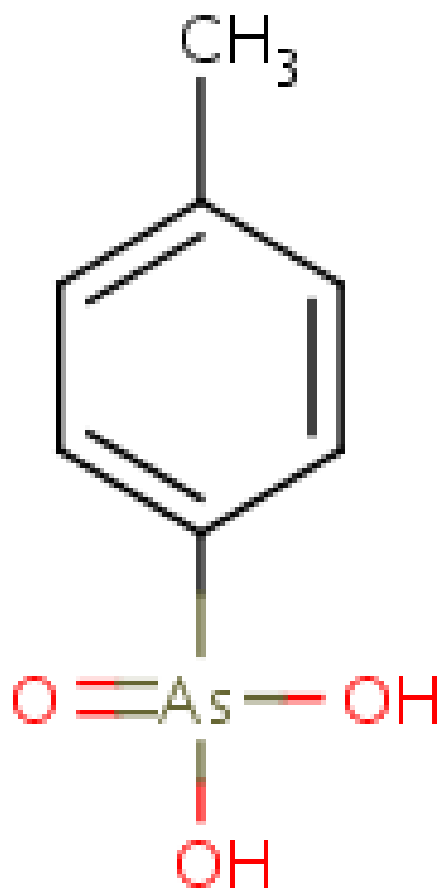
Molecular Formula	C6H7AsO3
Molecular Weight	202.0

Chemical Name in the Inventory and Synonyms	Arsonic acid, (phenylmethyl)- .alpha.-tolueneearsonic acid methaneearsonic acid, phenyl- benzylarsonic acid
CAS Number	620-27-9
Structural Formula	



Molecular Formula	C7H9AsO3
Molecular Weight	216.0

Chemical Name in the Inventory and Synonyms	Arsonic acid, (4-methylphenyl)- p-tolyarsonic acid p-methylbenzenearsonic acid 4-tolyarsonic acid
CAS Number	3969-54-8
Structural Formula	



Molecular Formula	C ₇ H ₉ AsO ₃
Molecular Weight	216.07

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