Phosphorous acid, isodecyl diphenyl ester: Human health tier II assessment

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CAS Number: 26544-23-0

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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.

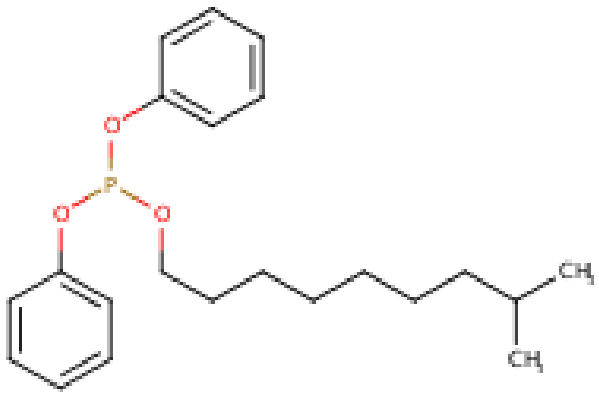
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	diphenylisodecyl phosphite isodecyl diphenyl phosphite isodecyl alcohol, diphenyl phosphite phosclere P26 DPDP
Structural Formula	
Molecular Formula	C22H31O3P
Molecular Weight (g/mol)	374.45
Appearance and Odour (where available)	clear, colourless liquid at room temperature.
SMILES	c1(OP(Oc2ccccc2)OCCCCCCCC(C)C)ccccc1

Import, Manufacture and Use

Australian

The chemical was reported under previous mandatory and/or voluntary calls for information with reported site-limited use as a stabiliser.

The chemical was also reported to have use in process colour and printing ink products.

International

The following international uses have been identified through:

- the European Union (EU) Registration, Evaluation and Authorization of Chemicals (REACH) dossiers;
- Galleria Chemica;
- the Substances and Preparations in Nordic countries (SPIN) database;
- the United States (US) Department of Health and Human Services, Household Products Database (HPD).

The chemical has reported domestic uses including in:

- paints, lacquers and varnishes.

The chemical has reported commercial uses including:

- as a reagent; and
- in lubricants and additives.

The chemical has reported site-limited use as a stabiliser for polyvinyl and polyolefin resins.

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 listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

The chemical phosphorous acid, isodecyl diphenyl ester (commonly known as isodecyl diphenyl phosphite or DPDP) is an alkyl-aryl phosphite and is insoluble in water (US EPA, 2007; REACH). Phosphite esters (with successive changes across the series of aryl to alkyl ester, i.e. alkyl to aryl ratio) are known to cause skin sensitisation (refer to **Sensitisation** section). Although the potency of the sensitisation reaction varies between phosphites, the potential for skin sensitisation is still present. Thus where data are limited, animal studies on other structurally-related phosphites (phenyldiisodecyl phosphite (CAS No. 25550-98-5) and triphenyl phosphite (CAS No. 101-02-0), also known as PDDP and TPP, respectively) are included where relevant (US, EPA 2007; EU CLP; REACH).

Acute Toxicity

Oral

The chemical has low acute oral toxicity based on results from a key study (equivalent to OECD TG 401) and non-guideline animal studies in rats following oral exposure (liquid). The median lethal dose (LD50) was reported to be > 2000 mg/kg bw (3990 and 4060 mg/kg bw in males and female Herman-Wistar rats, respectively; 3840 and 6730 mg/kg bw in male and female Charles River (CD-1) rats, respectively; and 3900 mg/kg bw in both sexes of CFY rats (US EPA, 2007; REACH).

Dermal

The chemical has low acute dermal toxicity based on results from a key study (equivalent to OECD TG 402 with restrictions) in male and female New Zealand White rabbits following dermal exposure (liquid). The median lethal dose (LD50) was reported to be > 5000 mg/kg bw (US EPA, 2007; REACH).

Inhalation

The chemical has low acute inhalation toxicity based on results from a key study (equivalent to OECD TG 403) in male and female Sherman-Wistar rats following inhalation exposure (aerosol). The median lethal concentration (LC50) was reported to be > 8.4 mg/L (US EPA, 2007; REACH).

Corrosion / Irritation

Skin Irritation

Based on the available information, no hazard classification for skin irritation is recommended.

In a non-guideline study, the chemical (purity unspecified) was reported to be slightly irritating to the abraded and unabraded skin of New Zealand White rabbits (six/unspecified sex), following application (liquid) of 0.5 g for twenty-four hours, using an occlusive patch. Animals were observed at 24 hours (immediately after removal of wrap) and at 72 hours (48 hours after the patch was removed). No oedema but slight erythema was reported in all animals. More animals with abraded skin had erythema compared with animals with unabraded skin. The reported primary dermal irritation index (PDII) was reported to be 1 (REACH).

Eye Irritation

Based on the available information, no hazard classification for eye irritation is recommended.

In a non-guideline study, the chemical (purity unspecified) was reported to be slightly irritating to the eyes of New Zealand White rabbits (six/unspecified sex), following application (liquid) of 0.1 g for four days over a four day observation period. Slight redness of the eyes with no significant effects on the iris or cornea were reported (REACH).

Sensitisation

Skin Sensitisation

Limited data are available for this chemical. Based on the weight of evidence and available read-across data on other structurally-related phosphite chemicals (PDDP (CAS No. 25550-98-5) and TPP (CAS No. 101-02-0)), the chemical is considered to be a skin sensitiser (US, EPA 2007; EU CLP; REACH).

Positive results for skin sensitisation were reported in a non-guideline guinea pig maximisation test (GPMT). Male Dunkin-Hartley guinea pigs (10/dose) were administered 0.1 % or 25 % (v/v) of the chemical (as Phosclere P26, a tradename for diphenyl isodecyl phosphite; purity unspecified) by intradermal and epicutaneous induction, respectively (aqueous). The animals were challenged with 10 % (first challenge) or 2 % (second challenge) (v/v) of the chemical and finally rechallenged with 5 % (third challenge) (v/v) of the chemical under occlusive conditions. Skin reactions were reported in 7/10 animals challenged with 10 % of the chemical, 6/10 animals challenged with 2 % of the chemical and 7/10 animals challenged with 5 % of the chemical, when observed 72 hours post-challenge (REACH).

In two studies (OECD TG 429), PDDP and TPP were reported to be positive for skin sensitisation in mouse local lymph node assays (LLNA). The estimated concentration needed to produce a three-fold increase in lymphocyte proliferation (EC3) was reported to be 40.6 % for PDDP (a weak sensitiser at the top two dose levels: 50 and 100 %) and 1.4 % for TPP (a strong sensitiser at all dose levels: 2.5, 5 and 10 %) (REACH).

Repeated Dose Toxicity

Oral

No data are available for this chemical. Based on the available read-across data from other phosphite chemicals (TPP (CAS No. 101-02-0)), the repeat dose oral toxicity is not expected to be high.

In a 16-week combined repeated dose/reproductive oral toxicity study (similar to OECD TG 422 with study deviations), SD rats (10/sex/dose pre-mating exposure for two weeks) were dosed with the analogue chemical TPP daily, seven days a week by oral gavage doses of 0, 5, 15 and 40 mg/kg bw/day. Two 28-day recovery groups (5/sex/dose) from the 0 and 40 mg/kg bw/day dose groups were held without dosing for two weeks after the pre-mating dosing period was completed. Treatment-related effects included decrease in body weight and body weight gains, ataxia and lethargy. The ratio of adrenal gland weight to body weight was significantly increased, while testes weight was decreased. No further study details were reported. The no observed adverse effect level (NOAEL) and the lowest observed adverse effect (LOAEL) were determined to be 15 mg/kg bw/day and 40 mg/kg bw/day, respectively (US EPA, 2007; REACH).

Dermal

No data are available for this chemical.

Inhalation

No data are available for this chemical.

Genotoxicity

Based on the available data, the chemical is not considered to be genotoxic.

Several in vitro assays using the chemical gave negative results (US EPA, 2007; REACH) in the following studies:

- bacterial mutation assays (various *Salmonella typhimurium* strains) with and without metabolic activation at doses of up to 50 µg/plate and 5000 µg/plate; and
- DNA repair-suspension assays (two *Escherichia coli* strains) with and without metabolic activation at doses of up to 50 µg/mL.

The chemical gave a negative result in an in vivo mammalian erythrocyte micronucleus test in CD-1 mouse bone marrow cells at doses up to 9000 mg/kg (REACH; US EPA HVIS).

Carcinogenicity

No data are available for this chemical, although the chemical is not likely to be carcinogenic based on available genotoxicity data (refer to **Genotoxicity** section). Furthermore, the chemical presented no alerts for mutagenicity or carcinogenicity based on its molecular structure as profiled by the OECD Quantitative Structure–Activity Relationship (QSAR) Toolbox v3.3.

Reproductive and Developmental Toxicity

No data are available for this chemical. Based on the available read-across data on other phosphite chemicals (TPP (CAS No. 101-02-0)), hazard classification for reproductive and developmental toxicity is not recommended.

In a combined repeated dose/reproductive and developmental toxicity study (OECD 422) previously described (refer to the **Repeated dose toxicity: Oral** section), SD rats were dosed with the analogue chemical TPP daily, seven days a week by oral gavage doses of 0, 5, 15 and 40 mg/kg bw/day. Fertility effects were not seen at ≥ 40 mg/kg bw/day (the highest dose tested). However, at post natal day 0 a significant decrease in litter sizes was reported. All pups in two litters died at the highest dose. A developmental NOAEL of 15 mg/kg bw/day was reported. The NOAEL for systemic maternal effects was also determined to be 15 mg/kg bw/day. (US EPA, 2007, REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include local effects (skin sensitisation).

Public Risk Characterisation

Although the public could be exposed to the chemical through domestic uses, there are no identified uses in domestic products according to the US Department of Health and Human Services, Household Products Database. The chemical is mainly used commercially as a reagent (refer to **Import, manufacture & use** section) and public exposure is not expected when used as such. Public exposure is considered to be low and the chemical can be managed through appropriate labelling. The chemical is not considered to pose an unreasonable risk to public health.

Occupational Risk Characterisation

During product formulation, dermal 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 could pose an unreasonable risk to workers unless adequate control measures to minimise dermal 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 HSIS is considered appropriate for the chemical.

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

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2015).

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 and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)

[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 consumers

Products containing the chemical should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal 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;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- 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.

References

European Chemicals Agency (ECHA), Classification & Labelling Inventory. Accessed November 2015 at http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database

Galleria Chemica. Accessed November 2015 at https://jr.chemwatch.net/galleria/

Organization for Economic Cooperation and Development (OECD) Quantitative Structure-Activity Relationship (QSAR) Toolbox Version 3.3. Accessed November 2015 at http://www.oecd.org/chemicalsafety/assessmentofchemicals/theoecdqsartoolbox.htm

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Isodecyl diphenyl phosphite (CAS No. 26544-23-0). Accessed November 2015 at http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

SPIN (Substances in Preparations in Nordic Countries) Database. Accessed November 2015 at http://195.215.202.233/DotNetNuke/default.aspx

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2015. Accessed November 2015 at https://www.comlaw.gov.au/Details/F2015L01534

US EPA (2007). United States Environmental Protection Agency, High Production Volume (HPV) Chemical Challenge Program. Robust summaries for Isodecyl/Phenyl Phosphite Category: Phosphorous acid, isodecyl diphenyl ester (CAS No. 26544-23-0). Accessed December 2015 at http://iaspub.epa.gov/oppthpv/public_search.publiclist?wChemicalName=26544-23-0&programFlags=

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