Existing Chemical Hazard Assessment Report

Australian Government
Department of Health and Ageing
NICNAS

Dinonyl Phthalate

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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME
GPO Box 58, Sydney NSW 2001, Australia **www.nicnas.gov.au**

Preface

This report was compiled under the National Industrial Chemicals Notification and Assessment Scheme (NICNAS). This Scheme was established by the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act), which came into operation on 17 July 1990.

The principal aim of NICNAS is to aid in the protection of people at work, the public and the environment from the harmful effects of industrial chemicals.

NICNAS assessments are carried out in conjunction with the Department of the Environment, Water, Heritage and the Arts, which carry out the environmental assessment for NICNAS. NICNAS has two major programs: the assessment of the health and environmental effects of new industrial chemicals prior to importation or manufacture; and the other focussing on the assessment of chemicals already in use in Australia in response to specific concerns about their health/or environmental effects.

There is an established mechanism within NICNAS for prioritising and assessing the many thousands of existing chemicals in use in Australia.

For the purposes of Section 78(1) of the Act, copies of assessment reports for New and Existing Chemical assessments are freely available from the web (www.nicnas.gov.au). Summary Reports are published in the *Commonwealth Chemical Gazette* (http://www.nicnas.gov.au/publications/#gazette), and are available to the public on line at www.nicnas.gov.au.

Copies of this report and other NICNAS reports are available on the NICNAS website. Hardcopies are available from NICNAS at the following address:

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Other information about NICNAS (also available on request) includes:

- NICNAS Annual Reports.
- NICNAS Service Charter.
- Brochure on NICNAS Registration.

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Overview

This review of dinonyl phthalate (DNP) is a health hazard assessment only. The review was prepared using information from the Hazardous Substances Data Bank (HSDB) and literature surveys conducted up to September 2006. No international assessment reports were available.

Structurally, phthalate esters are characterized by a diester structure consisting of a benzenedicarboxylic acid head group linked to two ester side chains. DNP possesses 2 linear ester side chains each with a backbone of 9 carbons (C9). DNP is considered to belong to the High Molecular Weight Phthalate Esters (HMWPE) Category as defined by the American Chemistry Council Phthalate Esters Panel HPV Testing Group and OECD. The HMWPE group includes chemically similar substances produced from alcohols having backbone carbon lengths of ≥ C7.

According to the European Council for Plasticisers and Intermediates, estimated production of HMWPE is approximately 60-100 ktonnes per year in Europe. This is likely to represent about one third of world production.

There was no published information on the use of DNP. HMWPE are used primarily as industrial chemicals associated with polymers, mainly as additives to impart flexibility in polyvinyl chloride (PVC) resins, but are also used as synthetic base stocks for lubricating oils. Polymer applications can be divided into PVC-related uses and uses involving other non-PVC polymers. PVC-containing phthalate esters applications can include wire and cable insulation, furniture and automobile upholstery, flooring, wall coverings, coil coatings, pool liners, roofing membranes, and coated fabrics. Polymer-containing phthalate ester applications that are non-PVC based include thermoplastics, rubbers and selected paints and adhesives.

In Australia, DNP is imported for distribution to various institutions and laboratories for analytical, pharmaceutical and biotechnological research.

There was little toxicity information for DNP. For individual health endpoints with missing or incomplete data, information from structurally similar phthalates, where available, was used to extrapolate potential toxicity. Relevant read-across information was obtained from other NICNAS hazard assessment reports for phthalates and the NICNAS Phthalates Hazard Compendium, which contains a comparative analysis of toxicity endpoints across 24 ortho-phthalates, including DNP.

Data were not available on the toxicokinetics of DNP. However, studies on HMWPE indicate that they are rapidly absorbed and metabolised to the corresponding monoester in the gastrointestinal tract, and excreted primarily in the urine.

DNP has low acute oral and intraperitoneal toxicity.

Based on data for the HMWPE Category as a whole, DNP is expected to have low acute dermal and inhalation toxicity with minimal or no irritating or sensitising effects. DNP is also unlikely to be genotoxic. For repeat dose toxicity, liver and kidney effects would be expected, particularly at high doses. However, the severity of these effects as well as carcinogenic potential for DNP is difficult to predict.

Although DNP may also be similarly considered to induce no or minimal fertility or developmental effects, data were insufficient to establish definitively the toxicity potential of DNP for these reproductive endpoints.

Table of Contents

Acronyms and Abbreviations

bw	body weight
C	Celsius
CAS	Chemical Abstracts Service
DNP	dinonyl phthalate
g	gram
HMWPE	High Molecular Weight Phthalate Esters
ip	intraperitoneal
kg	kilogram
kPa	kilopascals
L	litre
LC50	median lethal concentration
LD50	median lethal dose
mg	milligram
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
OECD	Organisation for Economic Cooperation and Development
PVC	polyvinyl chloride
w/w	weight per weight
µ	Micro

1. Introduction

This review of dinonyl phthalate (DNP) is a health hazard assessment only. The review was prepared using information from the Hazardous Substances Data Bank (HSDB) and literature surveys conducted up to September 2006. No international assessment reports were available.

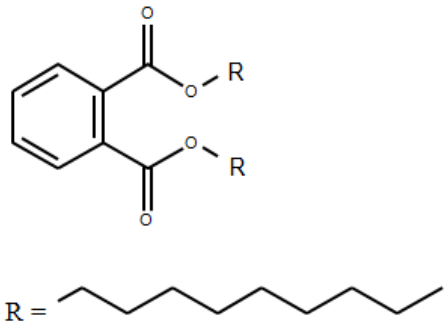
Information on Australian uses was compiled from data supplied by industry in 2004 and 2006.

References not marked with an asterisk were examined for the purposes of this assessment. References not examined but quoted from the key reviews as secondary citations are also noted in this assessment and marked with an asterisk.

Hazard information from this assessment is published also in the form of a hazard compendium providing a comparative analysis of key toxicity endpoints for 24 *ortho*-phthalates (NCNAS, 2008).

2. Identity

2.1 Identification of the substance

CAS Number:	84-76-4
Chemical Name:	1,2-Benzenedicarboxylic acid, dinonyl ester
Common Name:	Dinonyl phthalate (DNP)
Molecular Formula:	$C_{26}H_{42}O_4$
Structural Formula:	
Molecular Weight:	418.60
Synonyms:	Di-*n*-nonyl phthalate; Dinonyl o-phthalate; Phthalic acid, dinonyl ester; Ditrimethylhexyl phthalate
Purity/Impurities/Additives:	Purity: 98% w/w Impurity: not available Additives: not available

2.2 Physicochemical properties

Table 1: Summary of physicochemical properties

Property	Value
Physical state	Colourless oily liquid
Melting point	No data
Boiling point	413ºC
Density	972 kg/m^3 (20ºC)
Vapour pressure	1.33×10^{-2} kPa (205ºC)
Water solubility	Insoluble
Partition coefficient n-octanol/water (log Kow)	>2.12
Henry's law constant	Not available
Flash point	No available

Source: HSDB (2006)

3. Uses

There is no published information on the use of DNP.

DNP has a linear backbone length of C9 and hence is expected to belong to the High Molecular Weight Phthalate Esters (HMWPE) Category as defined by the American Chemistry Council Phthalate Esters Panel HPV Testing Group (2001) and OECD (2004). The HMWPE group includes chemically similar substances produced from alcohols having backbone carbon lengths of ≥ C7. According to the European Council for Plasticisers and Intermediates, estimated production of HMWPE is approximately 60-100 ktonnes per year in Europe (OECD, 2004). This is likely to represent about one third of world production.

HMWPE are used primarily as industrial chemicals associated with polymers, mainly as additives to impart flexibility in polyvinyl chloride (PVC) resins, but are also used as synthetic base stocks for lubricating oils (OECD, 2004). Polymer applications can be divided into PVC-related uses and uses involving other non-PVC polymers. PVC-containing phthalate esters applications can include wire and cable insulation, furniture and automobile upholstery, flooring, wall coverings, coil coatings, pool liners, roofing membranes, and coated fabrics. Polymer-containing phthalate ester applications that are non-PVC based include thermoplastics, rubbers and selected paints and adhesives.

In Australia, DNP is imported for distribution to various institutions and laboratories for analytical, pharmaceutical and biotechnological research.

4. Human Health Hazard

4.1 Toxicokinetics

No data.

4.2 Acute toxicity

Oral

Study	Species	Results (LD50/LC50)	References
Oral	Rat	>2000 mg/kg bw	Patty, 1963
	Mouse, Rat, & Guinea pig	18000-21500 mg/kg bw	Timofievskaya et al., 1980*

Source: HSDB (2006)

Intraperitoneal (ip)

The LD50 in male TCR mice following a single intraperitoneal (ip) dose of DNP was >100000 mg/kg bw (Lawrence et al., 1975).

Conclusion

DNP has low acute oral and intraperitoneal toxicity in laboratory animals. No acute toxicity data from dermal or inhalation exposure or human studies were available for DNP.

4.3 Irritation

4.3.1 Skin irritation

Skin irritation was not observed after intradermal injection of undiluted DNP in mice but details of the test conditions were not available (Lawrence et al., 1975).

Conclusion

Data are insufficient to determine skin irritation effects of DNP.

4.3.2 Eye irritation

Eye irritation was not observed after instillation of undiluted DNP in rabbits but details of the test conditions were not available (Lawrence et al., 1975).

Conclusion

Data are insufficient to determine eye irritation effects of DNP.

4.3.3 Respiratory irritation

No data.

4.4 Sensitisation

No data.

4.5 Repeated dose toxicity

DNP administered orally, inhalationally or topically to mice in subacute and chronic experiments produced toxicity with demyelination, paralysis, disturbances of central and peripheral nervous systems and cachexia observed. No other details were available (Timofievskaya et al., 1973*).

Rats exposed to saturated vapours of DNP at 28ºC for 6 hr/d for 12 days showed no effect (Patty, 1963).

Conclusion

Only poorly detailed repeat dose studies are available. In one study, inhalation exposure for 12 days showed no effect in rats, while central and peripheral nervous system effects and cachexia were noted following repeat oral, inhalational or topical doses. Overall, data are insufficient to determine effects from repeated exposure to DNP.

4.6 Genetic toxicity

No data.

4.7 Carcinogenicity

No data.

4.8 Reproductive toxicity

No data.

5. Hazard Characterisation

There is little toxicity information for DNP. For individual health endpoints with missing or incomplete data, information from structurally similar phthalates, where available, was used to extrapolate potential toxicity. Relevant read-across information was obtained from other NICNAS assessment reports for relevant phthalates and the NICNAS Phthalates Hazard Compendium (NICNAS, 2008), which contains a comparative analysis of toxicity endpoints across 24 *ortho*-phthalates, including DNP.

DNP has an alkyl carbon backbone of C9 and is considered to be a member of the High Molecular Weight Phthalate Esters (HMWPE) Category as defined by the American Chemistry Council Phthalate Esters Panel HPV Testing Group (2001) and OECD (2004). Due to their similar chemical structure, category members are generally similar with respect to physicochemical, biological and toxicological properties or display an expected trend. Thus, read-across for toxicity endpoints is an appropriate approach to characterise selected endpoints for members of this category.

Data are not available on the toxicokinetics of DNP. However, studies on HMWPE indicate that they are rapidly absorbed and metabolised to the corresponding monoester in the gastrointestinal tract, and excreted primarily in the urine.

DNP has low acute oral and intraperitoneal toxicity. Other toxicological properties of DNP are based on data for the HMWPE Category as a whole, including data on the high molecular weight phthalates reviewed in the NICNAS Phthalate Hazard Compendium (NICNAS, 2008) and other high molecular weight phthalates reviewed by the Phthalate Esters Panel HPV Testing Group (2001) and OECD (2004). DNP is expected to have low acute dermal and inhalation toxicity with minimal or no irritating or sensitising effects. DNP is also unlikely to be genotoxic. For repeat dose toxicity, liver and kidney effects would be expected, particularly at high doses. However the severity of these effects as well as carcinogenic potential for DNP is difficult to predict. Although DNP may also be similarly considered to induce no or minimal fertility or developmental effects, data are insufficient to establish definitively the potential of DNP for these reproductive endpoints.

6. Human Health Hazard Summary Table

Phthalate	**Acute Toxicity**	**Irritation & Sensitisation**	**Repeated Dose Toxicity**	**Genetic Toxicity**	**Carcinogenicity**	**Fertility**	**Developmental Toxicity**
Dinonyl phthalate (DNP)	Oral Rat: LD50 >2000 mg/kg/bw Dermal No data Inhalation No data	Skin irritation: Insufficient data Eye irritation: Insufficient data Respiratory irritation: No data Skin sensitisation : No data	Insufficient data	No data	No data	No data	No data

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Timofievskaya LA et al. (1973) Vopr Gig Tr Profpatol Toksikol Proizvod Ispolz Fosfororg Plastif, 83-86. Cited in HSDB (2006), op.cit.

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