Existing Chemical Hazard Assessment Report

Australian Government
Department of Health and Ageing
NICNAS

Diisoundecyl Phthalate

June 2008

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

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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.

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GPO Box 58
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AUSTRALIA
Attention: Office Manager
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Overview

This review of diisoundecyl phthalate (DIUP) is a health hazard assessment only. For this assessment, the Organisation for Economic Cooperation and Development, Screening Information Data Set (OECD SIDS) Initial Assessment Report on High Molecular Weight Phthalate Esters (HMWPE) was consulted. Information from this report was supplemented with literature surveys conducted up to September 2006.

Structurally, phthalate esters are characterized by a diester structure consisting of a benzenedicarboxylic acid head group linked to two ester side chains. DIUP possesses 2 branched and/or linear ester side chains each with a backbone of predominantly 10 carbons (C10). DIUP is considered to belong to the 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.

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, DIUP is imported in automotive sealant/adhesives and flame resistant plastics.

Toxicity data for DIUP were not available for the majority of health endpoints. For 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 DIUP.

Data were not available on the toxicokinetics of DIUP. 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.

Although there were no acute toxicity or irritation studies, DIUP is expected to exhibit low acute oral, dermal and inhalation toxicity and have none or minimal skin or eye irritant effects based on data obtained on other HMWPE. DIUP was not a skin sensitiser in a guinea pig test.

DIUP has not been tested for genotoxicity. However, DIUP is considered unlikely to be genotoxic based on the negative mutagenicity data for the HMWPE Category as a whole.

No repeated dose toxicity studies on DIUP were available. For those phthalates currently with no information, the severity of effects expected from repeat dose exposure is difficult to predict. However, liver and kidney effects would be expected, particularly at high doses.

No in vivo carcinogenicity data are available for DIUP. In vitro, DIUP was considered inactive in an in vitro mouse cell transformation assay. Due to insufficient testing on other phthalates, it is not possible to extrapolate carcinogenic potential for DIUP.

DIUP has not been tested for reproductive or developmental toxicity. However, none of the other studies of HMWPE (except diisononyl phthalate, DINP) reviewed by NICNAS revealed effects on fertility or other aspects of the male reproductive system. DIUP therefore may be similarly considered not to show significant effects on fertility. The HMWPE appear generally to induce slight developmental effects at high doses. Increased frequencies of skeletal variations, common variations seen in developmental studies, were observed following gestational exposure to some HMWPE at high doses. Therefore, exposure to DIUP may have similar slight adverse developmental effects at high doses.

Table of Contents

Acronyms and Abbreviations

bw	body weight
C	Celsius
CAS	Chemical Abstracts Service
DIUP	diisoundecyl phthalate
DUP	Diundecyl phthalate
g	gram
HMWPE	High Molecular Weight Phthalate Esters
ip	intraperitoneal
kg	kilogram
kPa	kilopascals
L	litre
LD50	median lethal dose
mg	milligram
mL	millilitre
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
OECD	Organisation for Economic Cooperation and Development
PVC	polyvinyl chloride
SIDS	Screening Information Data Set
w/w	weight per weight
µ	micro

1. Introduction

This review of diisoundecyl phthalate (DIUP) is a health hazard assessment only. For this assessment, the Organisation for Economic Cooperation and Development, Screening Information Data Set (OECD SIDS) Initial Assessment Report on High Molecular Weight Phthalate Esters (HMWPE) (OECD, 2004) was consulted. Information from this report was supplemented with literature surveys conducted up to September 2006.

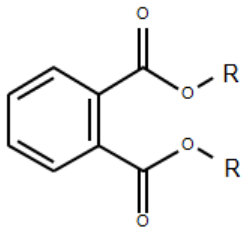
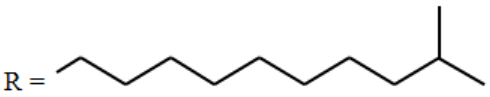
Information on Australian uses was compiled from data supplied by industry in 2004 and 2006.

References not marked with an asterisk were examined for the purposes of this assessment. References not examined but quoted from the key report 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 (NICNAS, 2008).

2. Identity

2.1 Identification of the substance

CAS Number:	85507-79-5
Chemical Name:	1,2-Benzenedicarboxylic acid, diundecyl ester, branched and linear
Common Name:	Diisoundecyl phthalate (DIUP)
Molecular Formula:	$C_{30}H_{50}O_4$
Structural Formula:	  (branched only shown)
Molecular Weight:	474.7 (based on a di-C11 phthalate ester)
Synonyms:	Diundecyl phthalate, branched and linear
Purity/Impurities/Additives:	Purity: >99.5% w/w Impurity: 0.1-0.2% w/w anti oxidant Additives: none

2.2 Physicochemical properties

Table 1: Summary of physicochemical properties

Property	Value
Physical state	Colourles s liquid
Melting point	-9°C
Boiling point	501°C (101.3 kPa)
Density	964 kg/m^3
Vapour pressure	4.97 x 10^{-10} kPa (25°C)
Water solubility	4.41 x 10^{-9} g/L
Partition coefficient n-octanol/water (log Kow)	10.3
Henry's law constant	Not avail able
Flash point	Not avail able

Source: OECD (2004)

3. Uses

DIUP belongs to a group of phthalates consisting of esters with alkyl carbon backbone of ≥ 7 (High Molecular Weight Phthalate Esters, HMWPE) (OECD, 2004). 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.

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, DIUP is imported in automotive sealant/adhesives and flame resistant plastics.

4. Human Health Hazard

4.1 Toxicokinetics

Previous evaluations

No data.

Data not reported in previous evaluations

No data.

Conclusion

No toxicokinetic studies were available for assessment.

4.2 Acute toxicity

Previous evaluations

In an acute oral study in rats a LD50 >15800 mg/kg bw was reported for a di-C11 phthalate ester (whether DUP, CAS No. 3648-20-2 or DIUP, CAS No. 85507-79-5 was not specified) (Krauskopf, 1973*).

In an intraperitoneal (ip) toxicity study in mice, DIUP (100000 mg/kg bw) did not cause any deaths. No significant signs of toxicity were noted, and necropsy findings were normal at the end of the 7-day observation period. The ip LD50 in mice was >100000 mg/kg bw (Lawrence et al., 1975*).

In another ip toxicity study in mice a di-C11 phthalate ester (whether DUP or DIUP was not specified) at a dose of 2400 mg/kg bw did not cause any deaths (Nematollahi et al., 1967*).

Data not reported in previous evaluations

No data.

Conclusion

The acute oral toxicity for a di-C11 phthalate ester is low, with LD50 >15800 mg/kg bw. However, the CAS No. was not available to determine whether the data was for DUP (CAS No. 3648-20-2) or DIUP (CAS No. 85507-79-5). No acute toxicity data from inhalation or dermal exposure or human studies were available for DIUP.

4.3 Irritation

4.3.1 Skin irritation

Previous evaluations

No data.

Data not reported in previous evaluations

No data.

Conclusion

No skin irritation studies were available for assessment.

4.3.2 Eye irritation

Previous evaluations

No data.

Data not reported in previous evaluations

No data.

Conclusion

No eye irritation studies were available for assessment.

4.3.3 Respiratory irritation

Previous evaluations

No data.

Data not reported in previous evaluations

No data.

Conclusion

No respiratory irritation studies were available for assessment.

4.4 Sensitisation

Previous evaluations

In a Buehler study, DIUP did not cause skin sensitisation in guinea pigs (Huntingdon Research Center, 1994*).

Data not reported in previous evaluations

No data.

Conclusion

DIUP did not induce dermal sensitisation in guinea pigs.

4.5 Repeated dose toxicity

Previous evaluations

No data.

Data not reported in previous evaluations

No data.

Conclusion

No repeated dose toxicity studies were available for assessment.

4.6 Genetic toxicity

Previous evaluations

No data.

Data not reported in previous evaluations

No data.

Conclusion

No genotoxic studies were available for assessment.

4.7 Carcinogenicity

Previous evaluations

In an in vitro cell transformation assay, DIUP was not active in Balb/c-3T3 mouse cell lines at concentrations of 400-40000 nL/mL (CMA 1985*; Barber et al., 2000*). Testing was conducted without metabolic activation. DIUP did not significantly increase transformed loci and was considered inactive at concentrations at or below its solubility limit.

Data not reported in previous evaluations

No data.

Conclusion

DIUP was inactive in an in vitro mouse cell transformation assay. No in vivo carcinogenicity data were available for DIUP.

4.8 Reproductive toxicity

Previous evaluations

No data.

Data not reported in previous evaluations

No data.

Conclusion

Effects on fertility

No reproductive toxicity studies were available for assessment.

Effects on development

No developmental toxicity studies were available for assessment.

5. Hazard Characterisation

Toxicity data for DIUP were not available for the majority of health endpoints. For 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 DIUP.

DIUP is a C10 phthalate and 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). The HMWPE group includes chemically similar substances produced from alcohols having backbone carbon lengths of ≥ C7. 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 DIUP. 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.

Although there are no acute toxicity or irritation studies, DIUP is expected to exhibit low acute toxicity and have none or minimal irritant effects based on data obtained on other HMWPE. DIUP was not a skin sensitiser in a guinea pig test.

DIUP has not been tested for genotoxicity. However, DIUP is considered unlikely to be genotoxic based on the negative mutagenicity data for the HMWPE Category as a whole, including data on the 7 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). The outcome of this read-across approach to characterise the genotoxicity potential for high molecular weight phthalates is in accordance with the general understanding that chemicals with bulky substituents and high molecular weight are likely to be of lower genotoxic potential than their smaller counterparts because they are less effective in interacting with DNA.

No repeated dose toxicity studies on DIUP are available. For those phthalates currently with no information such as DIUP, the severity of effects expected from repeat dose exposure is difficult to predict. However, liver and kidney effects from repeat doses would be expected, particularly at high doses.

No in vivo carcinogenicity data are available for DIUP. In vitro, DIUP was considered inactive in an in vitro mouse cell transformation assay. Due to insufficient testing on other phthalates, it is not possible to extrapolate carcinogenic potential for DIUP.

DIUP has not been tested for reproductive or developmental toxicity. However, none of the other studies of high molecular weight phthalates (except diisononyl phthalate, DINP) reviewed by NICNAS revealed effects on fertility or other aspects of the male reproductive system. DIUP therefore may be similarly considered not to show effects on fertility. The high molecular weight phthalates appear generally to induce slight developmental effects at high doses (NICNAS, 2008). Increased frequencies of skeletal variations, common variations seen in developmental studies, were observed following gestational exposure to some high molecular weight phthalates at high doses. Therefore, exposure to DIUP may have similar slight adverse developmental effects at high doses.

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6. Human Health Hazard Summary Table

Phthalate	**Acute Toxicity**	**Irritation & Sensitisation**	**Repeated Dose Toxicity**	**Genetic Toxicity**	**Carcinogenicity**	**Fertility**	**Developmental Toxicity**
Diisoundecyl phthalate (DIUP)	Oral Rat: LD50 >15800 mg/kg bw Dermal No data Inhalation No data	Skin irritation: No data Eye irritation: No data Respiratory irritation: No data Skin sensitisation: Negative	No data	No data	In vitro: Negative in cell transformation assay In vivo: No data	No data	No data

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