

# Existing Chemical Hazard Assessment Report



Australian Government  
Department of Health and Ageing  
NICNAS

## Diisotridecyl Phthalate

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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](http://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](http://www.nicnas.gov.au).

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

- NICNAS Annual Reports.
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# Overview

This review of diisotridecyl phthalate (DITDP) 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. DITDP possesses 2 branched ester side chains each with a backbone of predominantly 12 carbons (C12). DITDP 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  $\geq$  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.

Information on Australian uses was compiled from data supplied by industry in 2004 and 2006. In Australia, DITDP is used as a component of air compressor lubricants.

Toxicity data for DITDP were not available for the majority of health endpoints. 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 containing a comparative analysis of toxicity endpoints across 24 *ortho*-phthalates, including DITDP.

Data were not available on the toxicokinetics of DITDP. 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.

DITDP has low acute oral and dermal toxicity. Data on acute inhalation toxicity were not available but based on data for other HMWPE, DITDP is expected to have low acute inhalation toxicity. DITDP caused minimal skin and eye irritation in animals. No skin irritation was reported in humans. DITDP did not cause skin sensitisation in animals or humans.

DITDP was shown to be non-mutagenic in two bacterial mutagenicity assays. No in vitro mammalian mutation, cytogenetic or in vivo genotoxicity data were available. However, based on the negative mutagenicity data for the HMWPE Category as a whole, including data

on the seven phthalates reviewed in the NICNAS Phthalate Hazard Compendium and other HMWPE reviewed by Phthalate Esters Panel HPV Testing Group and OECD, DITDP is unlikely to be genotoxic.

Data for DITDP for repeat dose toxicity, carcinogenicity or reproductive toxicity were not available. Based on data for the HMWPE Category as a whole, liver and kidney effects from repeat doses of DITDP would be expected, particularly at high doses. Due to insufficient testing on other phthalates, it is not possible to extrapolate carcinogenic potential for DITDP. 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. DITDP 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 DITDP may have similar slight adverse developmental effects at high doses.

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# Acronyms and Abbreviations

bw	body weight
C	Celsius
CAS	Chemical Abstracts Service
DEHP	diethylhexyl phthalate
DITDP	diisotridecyl phthalate
f	female
g	gram
h	hour
HMWPE	High Molecular Weight Phthalate Esters
kg	kilogram
kPa	kilopascals
L	litre
LC50	median lethal concentration
LD50	median lethal dose
LOAEL	lowest-observed-adverse-effect level
m	male
mg	milligram
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NOAEL	no-observed-adverse-effect level
OECD	Organisation for Economic Cooperation and Development
ppm	parts per million
PVC	polyvinyl chloride
SIDS	Screening Information Data Set
μ	micro



# 1. Introduction

This review of diisotridecyl phthalate (DITDP) 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.

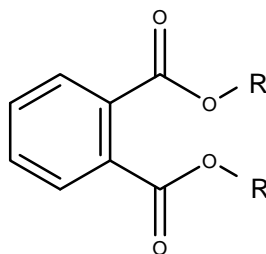
References not marked with an asterisk were examined for the purposes of this assessment. References not examined but quoted from these two reports as secondary citations are also noted in this assessment and marked with an asterisk.

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).

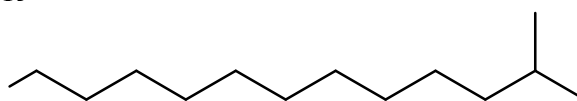
## 2. Identity

### 2.1 Identification of the substance

CAS Number:	68515-47-9
	Note: DITDP as a C13 isomer is known by the CAS number 27253-26-5.
Chemical Name:	1,2-Benzenedicarboxylic acid, di-C11-14-branched alkyl esters, C13 rich
Common Name:	Diisotridecyl phthalate (DITDP)
Molecular Formula:	C <sub>34</sub> H <sub>58</sub> O <sub>4</sub>
Structural Formula:	



R =



(based on a di-C13 phthalate ester)

Molecular Weight:	530.8 (based on a di-C13 phthalate ester)
Synonyms:	Ditridecyl phthalate
Purity/Impurities/Additives:	No data

### 2.2 Physicochemical properties

**Table 1: Summary of physicochemical properties**

Property	Value
Physical state	Colourless liquid
Melting point	-37°C
Boiling point	501°C (calculated) at 101.3 kPa
Density	950 kg/m <sup>3</sup>
Vapour pressure	3.63 x 10 <sup>-11</sup> kPa (25°C)
Water solubility	7 x 10 <sup>-11</sup> g/L
Partition coefficient n-octanol/water (log Kow)	12.1 (25°C)
Henry's law constant	Not available
Flash point	Not available

### 3. Uses

DITDP belongs to a group of phthalates consisting of esters with alkyl carbon backbone of  $\geq 7$  (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, DITDP is used as a component of air compressor lubricants.

## 4. Human Health Hazard

### 4.1 Toxicokinetics

No data.

### 4.2 Acute toxicity

#### Previous evaluations

Study	Species	Result (LD50)
Oral	Rat	>10000 mg/kg bw
Dermal	Rabbit	>3160 mg/kg bw

Source: OECD (2004)

#### Data not reported in previous evaluations

No data.

#### Conclusion

DITDP was shown to be of low toxicity in an oral and dermal study. No acute inhalation toxicity data were reported.

### 4.3 Irritation

#### 4.3.1 Skin irritation

#### Previous evaluations

DITDP was found to be non-irritating to rabbits with a Primary Irritation Index of 0.21 on a scale of 0-8 (Huels, 1984a\*). DITDP was used in human studies in a Human Repeated Insult Patch Test (HRIPT) in which 15 subjects were treated with the undiluted test substance applied to the skin under occluded patch for 24 hours. The test areas were examined at 30 minutes and at 24 hours after removal of each patch and no evidence of skin irritation were observed (Medeiros et al., 1999\*).

#### Data not reported in previous evaluations

No data.

#### Conclusion

DITDP causes minimal skin irritation in rabbits. No skin irritation was reported in humans.

### **4.3.2 Eye irritation**

#### **Previous evaluations**

Three separate studies have been performed on DITDP. The earliest by Lawrence et al. (1975\*) showed the mixture to be non-irritating to rabbit eyes. The second study (Bio/dynamics Inc, 1981c\*) indicated that slight conjunctival irritation was produced in the eyes of rabbits, but that this generally cleared within 72 hours. The maximum total Draize score observed was 14 on a scale of 0 to 110. Group mean scores at 24, 48 and 72 hours were 1.0, 0.33 and 0 for conjunctival redness and 0.67, 0 and 0 for chemosis. No iridial or corneal effects were noted. The most recent study (Huels, 1984b\*) showed the C13-rich mixture to be non-irritating to rabbit eyes, with a Draize score of 2.17 on a scale of 0 to 110. Conjunctival redness and chemosis were 0.33 and 0.0 respectively and no effects were observed in the cornea or iris.

#### **Data not reported in previous evaluations**

No data.

#### **Conclusion**

DITDP causes minimal eye irritation in rabbits.

### **4.4 Sensitisation**

#### **Previous evaluations**

Two Buehler studies (Huntington Research Centre, 1994b\* and Huels, 1993\*) showed that DITDP did not cause skin sensitisation in guinea pigs.

A modified Draize procedure was used in a Human Repeated Insult Patch Test (HRIPT) was conducted in a 104-person panel exposed to C6-C13 phthalate esters, including DITDP. No indication of sensitisation was noted from any of the substances tested (Medeiros et al., 1999\*).

#### **Data not reported in previous evaluations**

No data.

#### **Conclusion**

DITDP did not cause skin sensitisation in guinea pigs or humans.

### **4.5 Repeated dose toxicity**

No data.

### **4.6 Genetic toxicity**

#### **Previous evaluations**

Two studies have shown that DITDP was non-mutagenic in the Ames test using *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1538. In the first study, conducted by Zeiger et al. (1985\*), a pre-test for toxicity was conducted to

determine the high dose level on TA100 in the presence and absence of S-9. No mutagenic activity was observed at doses up to 10 mg/plate in any of the strains with or without metabolic activation.

The most recent study (Huels, 1988\*) was done using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 at concentrations of up to 5000 µg/plate and also showed the test substance to be non mutagenic, either with or without metabolic activation.

#### **Data not reported in previous evaluations**

Nil

#### **Conclusion**

DITDP was negative in bacterial mutation assays. No in vitro mammalian mutation, cytogenetic and in vivo genotoxicity data are available for DITDP.

#### **4.7 Carcinogenicity**

No data.

#### **4.8 Reproductive toxicity**

No data

## 5. Hazard Characterisation

There is incomplete toxicity information for DITDP. 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, 200) containing a comparative analysis of toxicity endpoints across 24 *ortho*-phthalates, including DITDP.

DITDP is 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  $\geq 7$ . 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 DITDP. 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.

DITDP has low acute oral and dermal toxicity. Data on acute inhalation toxicity were not available but based on data for other HMWPE, DITDP is expected to have low acute inhalation toxicity (NICNAS, 2008). DITDP caused minimal skin and eye irritation in animals. No skin irritation was reported in humans. DITDP did not cause skin sensitisation in animals or humans.

DITDP was shown to be non-mutagenic in two bacterial mutagenicity assays, with or without metabolic activation. No *in vitro* mammalian mutation, cytogenetic or *in vivo* genotoxicity data were available. However, based on the negative mutagenicity data for the HMWPE Category as a whole, including data on the seven phthalates reviewed in the NICNAS Phthalate Hazard Compendium (NICNAS, 2008) and other high molecular weight phthalates reviewed by Phthalate Esters Panel HPV Testing Group (2001) and OECD (2004), there is a low likelihood that DITDP is genotoxic.

Data for repeat dose toxicity, carcinogenicity or reproductive toxicity were not available. Based on data for the HMWPE Category as a whole, liver and kidney effects from repeat doses of DITDP would be expected, particularly at high doses. Due to insufficient testing on other phthalates, it is not possible to extrapolate carcinogenic potential for DITDP. 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. DITDP 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 DITDP 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
Diisotridecyl phthalate (DITDP)	<p>Oral Rat: LD50 &gt;10000 mg/kg bw</p> <p>Dermal Rabbit: LD50 &gt;3160 mg/kg bw</p> <p>Inhalation No data</p>	<p>Skin Irritation: ME</p> <p>Eye Irritation: ME</p> <p>Skin Sensitisation: negative</p>	No data	<p>In vitro: Negative in bacterial mutation assays</p> <p>In vivo: No data</p>	No data	No data	No data

ME – minimal effects

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