

Human Health Hazard Assessment

**Diisotridecyl phthalate (DITDP)
(CAS No. 68515-47-9)**

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INTRODUCTION

This review of di-isotridecyl phthalate (DITDP) is a health hazard assessment only. For this assessment, an OECD SIDS Initial Assessment Report on High Molecular Weight Phthalate Esters (HMWPE) (OECD, 2004) containing information on DITDP was consulted. This review was updated with relevant studies from more recent literature surveys conducted up to September 2006.

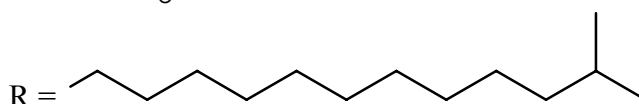
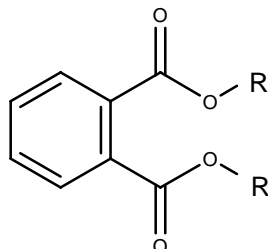
References not marked with an asterisk were examined for the purposes of this assessment. References not examined but quoted from these two reports as secondary citations are also noted in this assessment and marked with an asterisk.

Hazard information from this assessment is published also in the form of a hazard compendium providing a comparative analysis of key toxicity endpoints for 25 phthalates (NICNAS 2007).

1. IDENTITY

1.1 Identification of the Substance

CAS Number:	68515-47-9
Chemical Name:	1,2-Benzenedicarboxylic acid, di-C11-14-branched alkyl esters, C13 rich
Common Name:	Diisotridecyl phthalate (DITDP)
Molecular Formula:	C ₃₄ H ₅₈ O ₄
Structural Formula:	



(based on a di-C13 phthalate ester)

Molecular Weight:	530.8 (based on a di-C13 phthalate ester)
Synonyms:	Di-tridecyl phthalate
Purity/Impurities/Additives:	No data
Note :	DITDP as a C13 isomer is known by the CAS number 27253-26-5.

1.2 Physicochemical Properties

Table 1: Summary of physicochemical properties

<i>Property</i>	<i>Value</i>
Physical state	Colourless liquid
Melting point	-37°C
Boiling point	501°C (calculated) at 101.3 kPa

Density	950 kg/m ³
Vapour pressure	3.63 x 10 ⁻¹¹ kPa (25°C)
Water solubility	7 x 10 ⁻⁸ mg/L
Partition coefficient n-octanol/water (log Kow)	12.1 (25°C)
Henry's law constant	Not available
Flash point	Not available

2. USES

DITDP belongs to a group of phthalates consisting of esters with alkyl carbon backbone of ≥ 7 (High Molecular Weight Phthalate Esters, HMWPEs) (OECD, 2004). According to the European Council for Plasticisers and Intermediates, estimated production of HMWPEs is approximately 60-100 ktonnes per year in Europe. This is likely to represent about one third of world production.

HMWPEs 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.

3. HUMAN HEALTH HAZARD

3.1 Toxicokinetics

No data.

3.2 Acute Toxicity

Previous Evaluations

<i>Study</i>	<i>Species</i>	<i>Result</i>
Oral	Rat	LD ₅₀ > 10,000 mg/kg bw
Dermal	Rabbit	LD ₅₀ > 3.16 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.

3.3 Irritation

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.

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.

3.4 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.

3.5 Repeated Dose Toxicity

No data.

3.6 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.

3.7 Carcinogenicity

No data.

3.8 Reproductive Toxicity

No data.

4. 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 (2007) containing a comparative analysis of toxicity endpoints across 25 phthalates, including DITDP.

DITDP is a member of the High Molecular Weight Phthalate Esters (HMWPEs) Category as defined by the 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 ≥ 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 HMWPEs indicate that they are rapidly metabolised in the gastrointestinal tract to the corresponding monoester, absorbed 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 HMWPEs, DITDP is expected to have low acute inhalation toxicity (NICNAS, 2007). 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 7 phthalates reviewed in the NICNAS Phthalate Hazard Compendium (NICNAS, 2007) 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. Based on similar high molecular weight phthalates, DITDP is unlikely to affect fertility and development.

5. HUMAN HEALTH HAZARD SUMMARY TABLE

<i>Phthalate</i>	<i>Acute Toxicity</i>	<i>Irritation & Sensitisation</i>	<i>Repeated Dose Toxicity</i>	<i>Genetic Toxicity</i>	<i>Carcinogenicity</i>	<i>Fertility</i>	<i>Developmental Toxicity</i>
Diisotridecyl phthalate (DITDP)	Oral Rat: LD50 >10,000 mg/kg bw Dermal Rabbit LD50 >3.16 mg/kg bw	Skin Irritation: ME Eye Irritation: ME Skin Sensitisation: negative	No data	<u><i>In vitro</i></u> Negative in bacterial mutation assays <u><i>In vivo</i></u> No data	No data	No data	No data

ME – minimal effects

6. REFERENCES

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