Existing Chemical Hazard Assessment Report



Australian Government Department of Health and Ageing NICNAS

# **Diisooctyl Phthalate**

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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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- NICNAS Annual Reports.
- NICNAS Service Charter.
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# Overview

This review of diisooctyl phthalate (DIOP) is a health hazard assessment only. For this assessment, a British Industrial Biological Research Association (BIBRA) Toxicity Profile and an International Uniform Chemical Information Database (IUCLID) dataset on DIOP were consulted. Information from these documents 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. DIOP possesses 2 branched ester side chains each with a backbone of 7 carbons (C7). DIOP 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.

Little use information was available for DIOP. In Australia, DIOP is imported in rubber compounds for the manufacture of automotive hoses and parts. The chemical is also distributed to various institutions and laboratories for biotechnological and pharmaceutical research.

Toxicity data for DIOP were not available for all 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 DIOP.

DIOP is metabolised and cleared rapidly following ingestion in humans and eliminated in urine in part as monooctyl phthalate. Near complete excretion of DIOP in the urine and faeces was noted between 4 and 21 days following dietary administration in rats, dogs and pigs. No significant tissue accumulation of DIOP was found in experimental animals.

DIOP has low acute oral and dermal toxicity. No inhalation toxicity studies were available for DIOP. Based on data for other HMWPE, DIOP is expected to have low acute inhalation toxicity. DIOP causes minimal irritation when applied dermally to rabbits and reportedly does not cause irritation to rabbit eyes, however no details were available. Based on results from other phthalates, DIOP is unlikely to cause skin sensitisation.

Poorly detailed summaries of studies in rats and dogs noted that short-term repeated oral exposure (up to 1000 mg/kg bw/d) to DIOP is not associated with any apparent changes of toxicological significance. The lack of details from these summaries does not allow the determination of a repeated dose NOAEL or LOAEL for DIOP.

DIOP gave equivocal results in in vitro bacterial mutation assays. Its closely related analogue, a linear C8 phthalate, di-n-octyl phthalate (DnOP), is negative in mutation and DNA damage assays. In addition, based on the negative mutagenicity data for the HMWPE Category as a whole, DIOP is considered unlikely to be genotoxic.

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

No data were available for reproductive toxicity for DIOP. None of the studies of the other HMWPE (except diisononyl phthalate, DINP) reviewed by NICNAS revealed effects on fertility or other aspects of the male reproductive system. In this respect, DIOP may be similarly considered not to show significant effects on fertility. However, data are insufficient to establish definitively the potential for fertility effects.

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 DIOP may have similar slight adverse developmental effects at high doses.

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# Acronyms and Abbreviations

BBP	butylbenzyl phthalate
bw	body weight
С	Celsius
CAS	Chemical Abstracts Service
d	day
DBP	dibutyl phthalate
DEHP	diethylhexyl phthalate
DINP	diisononyl phthalate
DIOP	diisooctyl phthalate
DNA	deoxyribonucleic acid
ECB	European Chemicals Bureau
f	female
g	gram
h	hour
HMWPE	High Molecular Weight Phthalate Esters
IUCLID	International Uniform ChemicaL Information Database
kg	kilogram
kPa	kilopascals
L	litre
LC50	median lethal concentra tion
LD50	median lethal dose
LOAEL	lowest-observed-advers e-effect level
m	male
mg	milligram
mL	millilitre
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NOAEL	no-observed-adverse-eff ect level
OECD	Organisation for Economic Cooperation and Development
ppm	parts per million
PVC	polyvinyl chloride
w/w	weight per weight
μ	micro

# 1. Introduction

This review of diisooctyl phthalate (DIOP) is a health hazard assessment only. For this assessment, a British Industrial Biological Research Association Toxicity Profile (BIBRA, 1989) and an International Uniform Chemical Information Database (IUCLID) dataset (ECB, 2000) on DIOP were consulted. Information from these documents 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. It should be noted that the data in the IUCLID are data reported by the European Chemicals Industry and have not undergone review by the European Commission.

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*-phthalate esters (NICNAS, 2008a).

# 2. Identity

# 2.1 Identification of the substance

CAS Number: Chemical Name: Common Name:

Molecular Formula:

Structural Formula:

1,2-Benzenedicarboxylic acid, diisooctyl ester Diisooctyl phthalate (DIOP)  $C_{24}H_{38}O_4$ 



**R** =

27554-26-3

Molecular Weight:	390.62
Synonyms:	Diisooctyl 1,2-benzenedicarboxylate; Phthalic acid, diisooctyl ester
Purity/Impurities/Additives:	Technical grade reagent: 99%, mixture of C8 isomers, ≤ 2% dioctyl phthalate

# 2.2 Physicochemical properties

### Table 1: Summary of physicochemical properties

Property	Value
Physical state	Oily liqui d
Melting point	-45°C
Boiling point	230°C (0.53 kPa)
Density	986 kg/m <sup>3</sup> (20°C)
Vapour pressure	1.33 kPa (200°C)
Water solubility	<0.1 g/L (20°C)
Partition coefficient n-octanol/water (log Kow)	Not avail able
Henry's law constant	Not avail able
Flash point (closed cup)	227°C

Source: BIBRA (1989) and ECB (2000)

# 3. Uses

Overseas use information was not available.

In Australia, DIOP is imported in rubber compounds for the manufacture of automotive hoses and parts. The chemical is also distributed to various institutions and laboratories for biotechnological and pharmaceutical research.

# 4. Human Health Hazard

# 4.1 Toxicokinetics

#### **Previous evaluations**

Ikeda et al. (1978) showed complete excretion of <sup>14</sup>C-DIOP in the urine and faeces within 4 to 21 days following dietary administration in rats, dogs and pigs. In the study, male rats, dogs and miniature pigs were given 50 mg/kg bw/d DIOP in the diet for 21-28 days before oral administration (by stomach tube) of a single radioactively labelled dose. In the rat, approximately half the labelled compound was excreted in the urine and half in the faeces, with 85% of the dose excreted after 24 h and virtually all of it within 4 days. In the dog, 69-80% appeared in the faeces, whilst in pigs 65-86% was eliminated in the urine. Only about 50% had been excreted by the dogs and pigs after 24 hours, and complete elimination by dogs took 4 days and by pigs took 21 days. A small distribution to body fat occurred in all 3 species, and the investigators suggested that a slower release of DIOP from body fat and subsequent metabolism may have accounted for the slower excretion rate in pigs (Ikeda et al., 1978).

### Data not reported in previous evaluations

The metabolism of DIOP was monitored in humans by administering a single isotope-labelled dose containing butylbenzyl phthalate (BBP), dibutyl phthalate (DBP), diethylhexyl phthalate (DEHP), and diisooctyl phthalate (DIOP) to 24 volunteers. Eight volunteers received control, eight received low dose (including DIOP, 168  $\mu$ g), and eight received high dose (including DIOP, 336  $\mu$ g). Urine samples were collected at 1 day before dosing and 1, 2, 6 days after the dose was administered. The bulk of all labelled phthalates were eliminated in urine as the respective monoester metabolites within the first 24 hours. Approximately, 14 and 12% of the low and high dose was excreted as monooctyl phthalate, respectively (Anderson et al., 2001), as measure of DEHP and DIOP metabolism.

#### Conclusion

In humans, DIOP is in part eliminated in urine in the form of its monoester, monooctyl phthalate. Near complete excretion of DIOP in the urine and faeces was noted between 4 and 21 days following dietary administration in rats, dogs and pigs. Apart from a small amount distributed to fat within this timeframe, no significant tissue accumulation of DIOP was found in experimental animals.

### 4.2 Acute toxicity

#### **Previous evaluations**

Study	Species	Results (LD50/LC50)	References
Oral	Rat	>22000 mg/kg bw	WR Grace & ( o., 1948*; Tatsuno, 1975*
	Mouse	>26000 mg/kg bw	Tatsuno, 1975*
Dermal	Rabbit	>3160 mg/kg bw	Biodynamics Inc, 1981

\* From BIBRA (1989)

#### Data not reported in previous evaluations

No data

#### Conclusion

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

### 4.3 Irritation

#### 4.3.1 Skin irritation

#### **Previous evaluations**

No data.

#### Data not reported in previous evaluations

DIOP was reported to be slightly irritating to the rabbit skin in an unpublished study (ICI Chemical & Polymers, 1965\*, cited in ECB, 2000), however no information on dosage or time of exposure was available.

Also in another unpublished skin irritation study (ICI Chemicals & Polymers, 1958\*, cited in ECB, 2000), dermal application of undiluted DIOP to male rats for 24 hours, plus 6 applications on alternate days caused no skin irritation. No information on dose was available.

Doses of 50, 200, 794 and 3160 mg/kg bw DIOP were applied to the exposed skin of NZ White Albino rabbits (2/sex/dose). The application site was occluded for a total exposure of 24 hours. Observations for erythema or other evidence of skin irritation or injury were made approximately 30 minutes after removal of the occlusive wrapping and again at day 3, 7, 10 and 14. There were no signs of skin irritation in almost all animals at 50 and 200 mg/kg bw. Most animals at the 794 mg/kg dose level exhibited well defined erythema at 24 h only. At 3160 mg/kg dose level, very slight to severe skin irritation was noted in all animals at 24 h and on day 3, and two animals continued to exhibit very slight erythema on day 7 but not subsequently.

Only one animal at the highest dose exhibited slight oedema (on day 3) (Biodynamics Inc, 1981).

#### Conclusion

DIOP caused minimal skin irritation in rabbits.

### 4.3.2 Eye irritation

### **Previous evaluations**

No data.

#### Data not reported in previous evaluations

An unpublished study in rabbits (ICI Chemicals & Polymers, 1958\*, cited in ECB, 2000) stated that one drop of undiluted DIOP compound applied to the conjunctival sac did not cause irritation.

#### Conclusion

DIOP is reported not to cause eye irritation in rabbits, no further details available.

#### 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**

No data.

### Data not reported in previous evaluations

No data.

#### Conclusion

No sensitisation studies were available for assessment.

# 4.5 Repeated dose toxicity

#### **Previous evaluations**

No data.

### Data not reported in previous evaluations

Several unpublished studies for repeated dose toxicity in experimental animals were reported in the IUCLID database (ECB, 2000) and the available details are listed in the table below.

#### Human studies

BIBRA (1989) notes a Russian study (Milkov et al., 1973\*) describing exposure of leather workers to mixed phthalates, including periodically DIOP. Complaints of pain, numbness and spasms in hands of feet, polyneuritis and ear effects in of workers employed for 6 or more years were noted. Ambient air concentrations of phthalate mixtures were reported as 1.7 to 66 mg/m<sup>3</sup>. No further details were provided from which to determine DIOP-specific effects.

#### Conclusion

In poorly detailed summaries, repeated dose exposure to DIOP was not associated with any apparent changes of toxicological significance in rats and dogs. A multigenerational study in rats noted no effects on growth. Short-term 7-8 day studies in rats noted no abnormalities including a lack of effects on mortality, growth, blood profile or histological findings.

The lack of details from these animal studies does not allow the determination of a repeated dose NOAEL or LOAEL for DIOP.

Exposure Routes, Species & Duration	Doses (mg/kg bw/d)	Remarks	References
Oral, Rat, 4 weeks	0, 100	Reported NOAEL of 100 mg/kg bw/d No further data available	Shibko & Blumenthal, 1973
Oral, Rat, 15-21 months, 3-5 generations	0, 100, 300, 500	No effects on growth	Lefaux, 1972*
Oral, Rat, 8 days	0, 1000	No effects or deaths reported. No abnormalities observed following blood, post mortem and histological examination.	ICI Chemicals & Polymers, 1958*
Oral, Dog, 14 weeks	0, 100	Reported NOAEL of 100 mg/kg bw/d No further data available	Shibko & Blumenthal, 1973
Subcutaneous, Rat, 7 days	0, 1000	No adverse effects other than some swelling at the site of injection. No abnormalities observed following blood, post mortem and histological examination.	ICI Chemicals & Polymers, 1958*

Table 2: Details of unpublished studies for repeated dose toxicity in experimental animals reported in the IUCLID database (ECB, 2000).

# 4.6 Genetic toxicity

### **Previous evaluations**

DIOP was weakly mutagenic in the presence, but not in the absence, of a liver metabolic activation system in a modified Ames test using *S. typhimurium* (strains not specified). The results were considered equivocal as no consistent dose-related response was seen and the mutagenic activity only occurred within a narrow concentration range (Grasso, 1978\*).

# Data not reported in previous evaluations

No mutagenic activity was detected in an Ames test using *S. typhimurium* (TA98, 100, 1535, and 1537) at DIOP concentrations of 10 to 2000  $\mu$ g/plate, with and without metabolic activation (USS Chemical, year not stated\*).

### Conclusion

DIOP tested negative in one Ames study (with and without metabolic activation) and weakly positive in another (with metabolic activation). Results of the latter test were considered equivocal as no consistent dose-related response was seen and the mutagenic activity only occurred within a narrow concentration range.

No in vitro cytogenetic, mammalian mutation and in vivo genotoxicity data were available for DIOP.

# 4.7 Carcinogenicity

#### **Previous evaluations**

No data.

# Data not reported in previous evaluations

DIOP was tested in an in vitro Balb/3T3 mammalian cell transformation assay. DIOP did not induce the appearance of a significant number of transformed foci over the concentration range of 0.13  $\mu$ L/mL to 42.4  $\mu$ g/mL and was considered to be inactive under the condition of this test (Litton Bionetics, 1981).

#### Conclusion

DIOP was inactive in a single in vitro mammalian cell transformation assay. No in vivo carcinogenicity data were available for DIOP.

# 4.8 Reproductive toxicity

# **Previous evaluations**

No data.

#### Data not reported in previous evaluations

No data.

# Mode of action

DIOP was negative for oestrogenic activity in a yeast 2-hybrid assay (Nishihara et al., 2000).

# 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 DIOP were not available for many 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 (2008a) which contains a comparative analysis of toxicity endpoints across 24 *ortho*-phthalates, including DIOP.

DIOP has a straight-chain carbon backbone of 7 and 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 (2001) and OECD (2004). The HMWPE group includes chemically similar substances produced from alcohols having backbone carbon lengths of  $\geq$  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.

DIOP is metabolised and cleared rapidly following ingestion in humans and eliminated in urine in part as monooctyl phthalate. Near complete excretion of DIOP in the urine and faeces was noted between 4 and 21 days following dietary administration in rats, dogs and pigs. No significant tissue accumulation of DIOP was found in experimental animals.

DIOP has low acute oral and dermal toxicity. No inhalation toxicity studies are available for DIOP. Based on data for other HMWPE, DIOP is expected to have low acute inhalation toxicity. DIOP causes minimal irritation when applied dermally to rabbits and reportedly does not cause irritation to rabbit eyes, however no details were available. Based on results from other phthalates, DIOP is unlikely to cause skin sensitisation.

Poorly detailed summaries of studies in rats and dogs noted that short-term repeated oral exposure (up to 1000 mg/kg bw/d) to DIOP is not associated with any apparent changes of toxicological significance. A multigenerational study in rats noted no effects on growth. Short-term 7-8 day studies in rats noted no abnormalities including a lack of effects on mortality, growth, blood profile or histological findings. The lack of details from these summaries does not allow the determination of a repeated dose NOAEL or LOAEL for DIOP.

DIOP tested negative in one Ames study (with and without metabolic activation) and weakly positive in another (with metabolic activation). Results of the latter test were considered equivocal. Its closely related analogue, a linear C8 phthalate DnOP, is negative in mutation and DNA damage assays (NICNAS, 2008b). In addition, 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, 2008a) and other high molecular weight phthalates

reviewed by the Phthalate Esters Panel HPV Testing Group (2001) and OECD (2004), DIOP is considered unlikely to be genotoxic.

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

None of the studies of the other high molecular weight phthalates (except diisononyl phthalate, DINP) reviewed by NICNAS revealed effects on fertility or other aspects of the male reproductive system. In this respect, DIOP may be similarly considered not to show effects on fertility. However, data are insufficient to establish definitively the potential for fertility effects.

The high molecular weight phthalates appear generally to induce slight developmental effects at high doses (NICNAS, 2008a). 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 DIOP 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
Diisooctyl phthalate (DIOP)	Oral Rat: LD50 >22000 mg/kg bw Dermal Rabbit: LD50 >3160 mg/kg bw Inhalation No data	Skin irritation: Minimal effects Eye irritation: negative Respiratory irritation: No data Skin sensitisation: No data	Insufficient data	In vitro: Negative in bacterial assay In vivo: No data	In vitro: Negative in cell transformation assay In vivo: No data	No data	No data

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# References

- Anderson WAC, Castle L, Scotter MJ, Massey RC, & Springall C (2001) A biomarker approach to measuring human dietary exposure to certain phthalate diesters. Food Addit Contam, 18:1068-74.
- BIBRA (1989) Toxicity profile of diisooctyl phthalate. Sutton, UK, British Industrial Biological Research Association.
- Biodynamics Inc (1981) Acute dermal toxicity study in rabbits (Project No. 6675-81). East Millstone, NJ, Biodynamics Inc., TSCATS Doc 878210432, microfiche 206272.
- ECB (2000) IUCLID Dataset on DIOP. European Commission, European Chemicals Bureau.
- Grasso P (1978) Unpublished report on di-2-ethylhexyl and other phthalate esters: an appraisal of the toxicological data. BP Occupational Health Memorandum No. 25-70-0015.
- ICI Chemicals & Polymers (1958) Toxicological report: Diisooctyl phthalate CTL/T/132, 11.3.58. Runcorn, Cheshire, ICI Chemicals and Polymers Limited Runcorn, ICI C&P France SA Chocques.
- ICI Chemicals & Polymers (1965) Union Carbide DataSheet 6.11.65 cited in RTECS, DataStar subfile 8.10.93.
- Ikeda GJ, Sapienza PP, Couvillion JL, Farber TM, Smith CP, Inskeep PB, Marks EM, Cerra FE, & Van Loon EJ (1978) Distribution and excretion of two phthalate esters in rats, dogs and miniature pigs. Fd Cosmet Toxicol, 16:409-13.
- Lefaux R (1972) Les matieres platiques dans l'industire alimentaire, p161.
- Litton Bionetics (1981) Evaluation of [Diisooctyl phthalate] in the in vitro transformation of BALB/C-3T3 cells assay. LBI Project no. 20992. TSCATS Doc 878210226, microfiche 206260. Maryland, Litton Bionetics Inc.
- Milkov LE, Aldyreva MV, Popova TB, Lopukhova KA, Makarenko YL, Malyar LM, & Shakhova TK (1973) Health status of workers exposed to phthalate plasticizers in the manufacture of artificial leather and films based on PVC resins. Environ Health Perspect, 3:175-8.
- NICNAS (2008a) Phthalate hazard compendium: a summary of physicochemical and human health hazard data for 24 *ortho*-phthalate chemicals. Sydney, National Industrial Chemicals Notification and Assessment Scheme.
- NICNAS (2008b) Human health hazard assessment: Di-n-octyl phthalate (DnOP) (CAS No. 117-84-0). Sydney, National Industrial Chemicals Notification and Assessment Scheme.
- Nishihara T, Nishikawa J, Kanayama T, Dakeyama F, Saito K, Imagawa M, Takatori S, Kitagawa Y, Hori S & Utsumi H (2000). Oestrogenic activities of 517 chemicals by yeast two-hybrid assay. Journal of Health Science 46 (4), 282-298.
- OECD (2004) SIDS Initial Assessment Report for SIAM 19: Category High Molecular Weight Phthalate Esters. Organisation for Economic Cooperation and Development, Berlin, Germany, 19-22 October 2004.
- Phthalate Esters Panel HPV Testing Group (2001) High production volume (HPV) chemical challenge programme test plan for the phthalate esters category. December 10, 2001. Prepared by:ExxonMobil Biomedical Sciences, Inc. for the Phthalate Esters Panel HPV Testing Group of the American Chemistry Council.

http://www.epa.gov/hpv/pubs/summaries/benzene/c13467tc.htm (Accessed 2007)

- Shibko SI & Blumenthal H (1973) Toxicology of phthalic acid esters used in food-packaging material. Environ Health Perspect, 3:131-7.
- Tatsuno T (1975) Japan Plastics Age, 13:19.
- USS Chemical (year not stated) Mutagenicity evaluation of diisooctyl phthalate. Report no 81-4-7. Goodyear Fiber and Polymer Products Research Division Laboratory, USS Chemicals. EPA doc 878210226.
- WR Grace & Co. (1948) Technical brochure: dioctyl phthalate.