

# Diethyl Phthalate

## 1 Nonproprietary Names

BP: Diethyl phthalate  
PhEur: Diethylis phthalas  
USPNF: Diethyl phthalate

## 2 Synonyms

DEP; ethyl benzene-1,2-dicarboxylate; ethyl phthalate; *Kodaflex DEP*; phthalic acid ethyl ester.

## 3 Chemical Name and CAS Registry Number

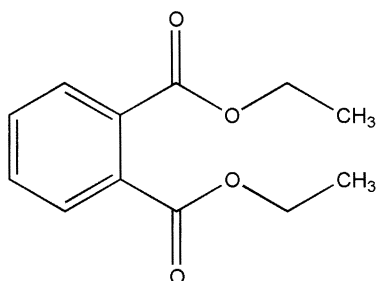
1,2-Benzenedicarboxylic acid, diethyl ester [84-66-2]

## 4 Empirical Formula Molecular Weight

C<sub>12</sub>H<sub>14</sub>O<sub>4</sub>

222.24

## 5 Structural Formula



## 6 Functional Category

Film-former; plasticizer; solvent.

## 7 Applications in Pharmaceutical Formulation or Technology

Diethyl phthalate is used as a plasticizer for film coatings on tablets, beads, and granules at concentrations of 10–30% by weight of polymer.

Diethyl phthalate is also used as an alcohol denaturant and as a solvent for cellulose acetate in the manufacture of varnishes and dopes. In perfumery, diethyl phthalate is used as a perfume fixative at a concentration of 0.1–0.5% of the weight of the perfume used.

## 8 Description

Diethyl phthalate is a clear, colorless, oily liquid. It is practically odorless, or with a very slight aromatic odor and a bitter, disagreeable taste.

## 9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for diethyl phthalate.

Test	PhEur 2002	USPNF 20
Identification	+	+
Characters	+	—
Specific gravity	1.117–1.121	1.118–1.122
Refractive index	1.500–1.505	1.500–1.505
Acidity	+	+
Related substances	+	—
Water	≤0.2%	≤0.2%
Residue on ignition	—	≤0.02%
Sulfated ash	≤0.1%	—
Assay (anhydrous basis)	99.0–101.0%	98.0–102.0%

## 10 Typical Properties

Boiling point: 295°C

Flash point: 160°C (open cup)

Melting point: –40°C

Refractive index:  $n_D^{25} = 1.501$

Solubility: miscible with ethanol (95%), ether, and many other organic solvents; practically insoluble in water.

Specific gravity: 1.120 at 25°C

Vapor density (relative): 7.66 (air = 1)

Vapor pressure: 1.87 kPa (14 mmHg) at 163°C

## 11 Stability and Storage Conditions

Diethyl phthalate is stable when stored in a well-closed container in a cool, dry place.

## 12 Incompatibilities

Incompatible with strong oxidizing materials.

## 13 Method of Manufacture

Diethyl phthalate is produced by the reaction of ethanol with phthalic acid.

## 14 Safety

Diethyl phthalate is used in oral pharmaceutical formulations and is generally regarded as a nontoxic and nonirritant material at the levels employed as an excipient. However, if consumed in large quantities it can act as a narcotic and cause paralysis of the central nervous system.

Although some animal studies have suggested that high concentrations of diethyl phthalate may be teratogenic, other studies have shown no adverse effects.<sup>(1)</sup>

LD<sub>50</sub> (guinea pig, oral): 8.6 g/kg<sup>(2)</sup>

LD<sub>50</sub> (mouse, IP): 2.7 g/kg

LD<sub>50</sub> (mouse, oral): 6.2 g/kg

LD<sub>50</sub> (rat, IP): 5.1 g/kg

LD<sub>50</sub> (rat, oral): 8.6 g/kg

**15 Handling Precautions**

Observe normal precautions appropriate to the circumstances and quantity of material handled. Diethyl phthalate is irritant to the skin, eyes, and mucous membranes. Protective clothing, eye protection, and nitrile gloves are recommended. Diethyl phthalate should be handled in a fume-cupboard or a well-ventilated environment; a respirator is recommended. In the UK, the long-term (8-hour TWA) exposure limit for diethyl phthalate is  $5 \text{ mg/m}^3$ . The short-term (15-minute) exposure limit is  $10 \text{ mg/m}^3$ .<sup>(3)</sup>

**16 Regulatory Status**

Included in the FDA Inactive Ingredients Guide (oral capsules and tablets). Included in nonparenteral medicines licensed in the UK.

**17 Related Substances**

Dibutyl phthalate; dimethyl phthalate.

**18 Comments**

The EINECS number for diethyl phthalate is 201-550-6.

**19 Specific References**

- 1 Field EA, Price CJ, Sleet RB, *et al.* Developmental toxicity evaluation of diethyl and dimethyl phthalate in rats. *Teratology* 1993; 48(1): 33–44.
- 2 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 1292.
- 3 Health and Safety Executive. *EH40/2002: Occupational Exposure Limits 2002*. Sudbury: Health and Safety Executive, 2002.

**20 General References**

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**21 Authors**

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**22 Date of Revision**

22 April 2002.