

THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD PRODUCTS
INTENDED FOR CONSUMERS

OPINION

CONCERNING

DIETHYL PHTHALATE

adopted by the SCCNFP during the 26th Plenary meeting
of 9 December 2003

1. Terms of Reference

1.1 Context of the question

The Scientific Committee on Cosmetics and Non Food Products intended for Consumer adopted an opinion on Diethyl Phthalate, doc. n° SCCNFP/0411/01, during its 20th plenary meeting of 4 June 2002. In its opinion, the SCCNFP stated that the safety profile of diethyl phthalate supports its use in cosmetic products at current levels.

Recently, the European Commission received two publications on phthalates :

- * Duty SM et al. (2003) "The Relationship between Environmental Exposures to Phthalates and DNA Damage in Human Sperm Using the Neutral Comet Assay", *Environm. Health Persp.* 111, 1164-1169.
- * Barr DB et al. (2003) "Assessing Human Exposure to Phthalates using Monoesters and their Oxidised Metabolites as Biomarkers", *Environm. Health Persp.* 111, 1148-1151.

1.2 Requests to the SCCNFP

The SCCNFP has been requested to review the publications cited above and to answer the following questions :

- * *Does the data provided in the attached publications change the overall assessment of diethyl phthalate as stated in the opinion of SCCNFP SCCNFP/0411/01 ?*
- * *If yes, what does the SCCNFP recommend on the basis of the new data provided ?*

1.3 Statement on the toxicological evaluation

The SCCNFP is the scientific advisory body to the European Commission in matters of consumer protection with respect to cosmetics and non-food products intended for consumers.

The Commission's general policy regarding research on animals supports the development of alternative methods to replace or to reduce animal testing when possible. In this context, the SCCNFP has a specific working group on alternatives to animal testing which, in co-operation with other Commission services such as ECVAM (European Centre for Validation of Alternative Methods), evaluates these methods.

The extent to which these validated methods are applicable to cosmetic products and its ingredients is a matter of the SCCNFP.

SCCNFP opinions include evaluations of experiments using laboratory animals; such tests are conducted in accordance with all legal provisions and preferably under chemical law regulations. Only in cases where no alternative method is available will such tests be evaluated and the resulting data accepted, in order to meet the fundamental requirements of the protection of consumer health.

2. Toxicological Evaluation and Characterisation

2.1. General

2.1.1. Primary name

Diethyl phthalate (INCI name)

2.1.2. Chemical names

1,2-benzenedicarboxylic acid, diethyl ester ; diethyl *o*-phthalate ; ethyl phthalate ; *o*-benzene dicarboxylic acid diethyl ester ; diethyl ester phthalic acid ; diethyl-*o*-phenylenediacetate.

2.1.3. Trade names and abbreviations

Anozol, DPX-F5384, Estol 1550, Neantine, Palatinol A, Phthalol, Placidol E, Solvanol, Unimoll DA.

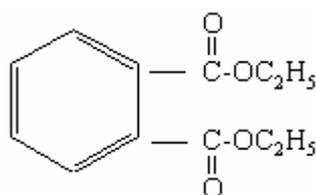
Abbreviations: DEP

2.1.4. CAS no. / EINECS n°

CAS n° : 84-66-2

EINECS n°: 201-550-6

2.1.5. Structural formula



2.1.6. Empirical formula

Emp. Formula : C₁₂H₁₄O₄

Mol. weight : 222.26

2.1.7. Purity, composition and substance codes

The purity of manufactured phthalate ester is reported between 99.70% and 99.97%, with the main impurities being isophthalic acid, terephthalic acid, and maleic anhydride.

2.1.8. Physical properties

Appearance : clear, colourless, practically odourless liquid

Melting point : - 40.5°C

Boiling point : 298°C (295-302°C)

Flash point	:	161°C
Density	:	1.120 g/ml at 25°C
Vapour Pressure	:	< 0.001 torr at 20°C
Log P _{ow}	:	2.47 (1.4 – 3.3)
Henry's law constant	:	7.8 x 10 ⁻⁷ atm m ³ /mol

2.1.9. Solubility

Fairly soluble in water (1.08 g/l), miscible in all quantities in alcohol, ether, acetone, ketones, benzene, esters, aromatic hydrocarbons, aliphatic solvents and vegetable oils.

2.2. Function and uses

Diethylphthalate is used as solvent and vehicle for fragrance and cosmetic ingredients, as well as alcohol denaturant. DEP was reported in 1995 as an ingredient in 67 formulations in the USA at concentrations ranging from less than 0.1% to 50%.

They include bath preparations (oils, tablets, salts), eye-shadows, toilet waters, perfumes and other fragrance preparations, hair sprays, wave sets, nail polish, and enamel removers, nail extenders, nail polish, bath soaps, detergents, after-shave lotions, and skin care preparations.

TOXICOLOGICAL CHARACTERISATION

2.3. Toxicity

2.3.1. Acute oral toxicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.3.2. Acute dermal toxicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.3.3. Acute inhalation toxicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.3.4. Repeated dose oral toxicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.3.5. Repeated dose dermal toxicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.3.6. Sub-chronic oral toxicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.3.7. Sub-chronic dermal toxicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.3.8. Chronic toxicity (see paragraph 2.9)

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.4. Irritation & corrosivity**2.4.1. Irritation (skin)**

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.4.2. Irritation (mucous membranes)

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.5. Sensitisation

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.6. Reproduction Toxicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.7. Toxicokinetics (incl. Percutaneous Absorption)

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.8. Mutagenicity/Genotoxicity**Review of the publications**

* The Relationship between Environmental Exposures to Phthalates and DNA Damage in Human Sperm Using the Neutral Comet Assay

This paper describes an effort to study the possible effect of exposure to phthalates on the DNA integrity in human sperm by the COMET assay. Using this assay it was measured DNA integrity on human sperm and investigated whether DNA integrity was associated with urinary concentrations of five phthalate monoesters.

It was found that urinary levels of MEP (monoethyl-phthalate), at levels found in the general population is significantly associated with increased DNA migration in sperm using the COMET assay, whereas the other four of these metabolites, MMP (monomethyl), MBP (monobutyl), MBzP (monobenzyl) and MEHP were not significantly associated with COMET assay parameters.

The authors are cautious about the representativity of these results (small number of selected people), pointing out that they need to be duplicated in a larger study. They also speculate that the lack of significant associations between the other 4 phthalate metabolites may indicate a true difference in genotoxicity between monoesters.

The results have to be considered with caution because of confoundings that belong to the representativity of the population exposed, the small number of selected people extracted from an andrology clinic and also, to limitations in term of interpretation regarding health effects.

This study should therefore be considered as a “pilot study” that needs to be confirmed.

Ref. : 1

* Assessing Human Exposure to Phthalates using Monoesters and their Oxidised Metabolites as Biomarkers

The paper is a short review related to the general human exposure to phthalates and the suitability of the currently used biomarkers of exposure to Di-Ethyl-Hexyl Phthalate (DEHP), i.e. mainly its monoester (MEHP). Since the urinary levels of MEHP in 2,541 persons in the U.S.A. have been found lower than anticipated, especially when compared with urinary metabolite levels of other commonly used phthalates, they suggest another two biomarkers, MEOHP (2-ethyl-5-oxo-hexyl-phthalate), MEHHP (2-ethyl-5-Hydroxy-hexyl-phthalate). These metabolites are formed by oxidative metabolism, of MEHP, and according to their findings in 62 individuals, the urinary levels of MEHHP and MEOHP were found 8.2 and 5.9 higher than MEHP respectively. It is speculated that an oxidative step is involved in the metabolism of all high molecular-weight phthalates, in contrast to the lower molecular weight homologues, that are hydrolysed to their monoester and excreted. However, it is stated that to date there is no information on the biological activity of the oxidative metabolites.

Ref. : 2

2.9. Chronic Toxicity and Carcinogenicity

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.10. Special investigations

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.11. Safety evaluation

See SCCNFP opinion on diethyl phthalate of 4 June 2002, doc. n° SCCNFP/0411/01

2.12. Opinion

The SCCNFP is of the opinion that the data provided in the above-mentioned publications do not change the overall assessment of diethyl phthalate as stated in its opinion on diethyl phthalate of 4 June 2002 (doc. n° SCCNFP/0411/01).

2.13. References

1. Duty SM et al. (2003) "The Relationship between Environmental Exposures to Phthalates and DNA Damage in Human Sperm Using the Neutral Comet Assay", *Environm. Health Persp.* 111, 1164-1169
2. Barr DB et al. (2003) "Assessing Human Exposure to Phthalates using Monoesters and their Oxidised Metabolites as Biomarkers", *Environm. Health Persp.* 111, 1148-1151.