

JACC No 20

**Tris(2-ethylhexyl)phosphate
CAS No. 78-42-2**

**Bis(2-ethylhexyl)phosphate
CAS No. 298-07-7**

**Mono(2-ethylhexyl)phosphate
CAS No. 12645-31-7**

May, 1992

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Correction

Please note that the title of the JACC Report N° 20 is:
'Tris-/Bis-/Mono-(2-ethylhexyl)phosphate'
(this has not been published yet),

and the title of the JACC Report N° 21 is:
'Tris-(2-butoxyethyl)-phosphate'

THE ECETOC SCHEME FOR THE

"JOINT ASSESSMENT OF COMMODITY CHEMICALS" (JACC)

This report has been prepared as part of the ECETOC programme for preparing critical reviews of the toxicology and ecotoxicology of selected existing industrial chemicals.

In the programme, commodity chemicals, that is those produced in large tonnage by several companies and having widespread and multiple uses, are jointly reviewed by experts from a number of companies with knowledge of the chemical. It should be noted that in a JACC review only the chemical itself is considered; products in which it appears as an impurity are not normally taken into account.

ECETOC is not alone in producing such reviews. There are a number of organisations that have produced and are continuing to write reviews with the aim of ensuring that toxicological knowledge and other information are evaluated. Thus a Producer, Government Official or Consumer can be informed on the up-to-date position with regard to safety, information and standards. Within ECETOC we do not aim to duplicate the activities of others. When it is considered that a review is needed every effort is made to discover whether an adequate review exists already; if this is the case the review is checked, its conclusions summarised and the literature published subsequent to the review assessed. To assist ourselves and others working in this field we publish annually a summary of international activities incorporating work planned, in hand, or completed on the review of safety data for commodity chemicals. Interested readers should refer to our Technical Report No 30 entitled "Existing Chemicals: Literature Reviews and Evaluations".

This document presents a critical assessment of the toxicology and ecotoxicology of Tris(2-ethylhexyl)phosphate (CAS No 78-42-2) Bis(2-ethylhexyl)phosphate (CAS No 298-07-7) and Mono(2-ethylhexyl)phosphate (CAS No 12645-31-7).

Contents

1. Summary and Conclusions	1
2. Identity, Physical and Chemical Properties, Analytical Methods	4
2.1 Identity	4
2.2 Physical and Chemical Properties	5
2.3 Analytical Methods	6
2.3.1 TEHP in Air	6
2.3.2 TEHP in Water	6
2.3.3 TEHP in Sediment	7
3 Production, Storage, Transport and Use	7
3.1 Production, Storage and Transport	7
3.2 Use	8
4. Environmental Distribution, Biotransformation and Fate	8
4.1 Environmental Distribution	8
4.2 Biotransformation and Fate	9
5. Environmental Levels and Human Exposure	11
5.1 Environmental Levels	11
5.1.1 Air	11
5.1.2 Water	12
5.1.3 Soil	12
5.1.4 Sediment	13
5.1.5 Food	13
5.2 Hygiene Standard - Occupational Exposure Levels	13

6. Effects on Organisms in the Environment	14
6.1 Microorganisms	14
6.2 Fish	14
6.3 Terrestrial Organisms	15
7. Kinetics and Metabolism	16
7.1 Experimental	16
7.2 Human	17
8. Effects on Experimental Animals and In Vitro Test Systems	17
8.1 Acute Toxicity	17
8.2 Skin and Eye Effects	18
8.3 Subacute and Subchronic Toxicity	19
8.3.1 Oral Administration	19
8.3.2 Dermal Administration	20
8.3.3 Inhalation	20
8.4 Chronic Toxicity and Carcinogenicity	22
8.5 Genotoxicity	24
8.6 Cytotoxicity	25
8.7 Neurotoxicity	25
8.8 Reproductive Toxicity	26

9. Effects on Man	26
10. Regulations, First Aid and Handling Advice	27
10.1 Regulations	27
10.2 First Aid and Medical Treatment	27
10.3 Safe Handling	27
10.4 Fire and Exposure	28
10.5 Handling Spillage and Water	28
Bibliography	29
Tables	32
Appendix I	35
Appendix II	36

1. Summary and Conclusions

Tris (2-ethylhexyl) phosphate (TEHP) is a non-flammable, colourless liquid with low water solubility and very low vapour pressure which is used as a flame retarder/plasticizer for PVC and cellulose acetate and as a solvent. It is produced from phosphorus oxychloride and 2-ethylhexanol. The worldwide production is estimated to be 1,000 - 5,000 tons a year.

Only small amounts of TEHP are expected to enter the environment during manufacturing and use. TEHP has not been detected in ambient air; it has been detected in indoor air in concentrations of less than 10 ng/m³, in polluted river water at concentrations of up to 2,000 ng/l and in sediments at 2-70 ng/g. TEHP is rapidly biodegradable in natural waters but in laboratory tests with activated sludge the results are equivocal.

The few data available indicate a low acute aquatic toxicity of TEHP. The IC₅₀ for bacteria is greater than 100 mg/l and the 96 h LC₅₀ for zebra fish Brachydanio rerio is greater than 100 mg/l.

TEHP has a low acute toxicity for mammals, the oral LD₅₀ being > 10,000 mg/kgbw and it causes only moderate skin erythema and moderate conjunctivitis in rabbits.

Thirteen week feeding studies in which rats received up to 4,000 mg/kgbw and mice 8,000 mg/kgbw revealed no toxic effects other than a slight-moderate depression in bodyweight gain.

Twenty daily doses of 0.1 ml TEHP to the skin of rabbits produced no signs of systemic intoxication.

In a 3-month inhalation study at concentrations up to 85.0 mg TEHP/m³ dogs and monkeys showed no treatment-related alterations in any biochemical or haematological measurements. The lungs of dogs showed mild inflammatory changes and the performance of dogs trained in a conditional avoidance deteriorated in relation to the concentration administered. Microscopic examination of guinea pigs exposed to 1.6 or 9.6 mg TEHP/m³ showed inconsistent and reversible changes in the renal parenchyma at the 9.6 mg/m³ TEHP concentration.

Neurotoxicity studies on TEHP revealed no alteration of cholinesterase levels nor histological evidence of demyelination.

TEHP does not induce gene mutation in bacteria, or chromosomal aberration and sister chromatid exchange induction in Chinese hamster ovarian cells and mutagenic response in the mouse lymphoma L 5178Y cell assays.

TEHP was tested for chronic toxic and carcinogenic effects in rats and mice. There was some evidence of a treatment related increase in hepatocellular carcinoma in female mice, with a significant increase in the high dose (1,000 mg/kg). In addition the incidence of carcinomas was not significant at the low dose (500 mg/kg). The findings in male rats are not regarded as being clearly related to administration of TEHP. As a consequence the validity of extrapolating the carcinogenicity data derived from female mice administered TEHP to the assessment of cancer in man is doubtful.

Bis (2-ethylhexyl) phosphate (BEHP) is a colourless liquid with a low water solubility and low vapour pressure which is used as a solvent in liquid-liquid extractions. It is produced from phosphorus oxychloride and 2-ethylhexanol. The worldwide production is estimated to be about 1,000 tons per year.

Data on environmental levels are not available. Laboratory tests demonstrate that BEHP is biodegradable.

BEHP is practically nontoxic to bacteria. The EC₅₀ for growth inhibition of Chlorella emersonii was > 100 mg/l. The 96 h LC₅₀ for Daphnia magna was 16.5 mg/l and the LC₀ (48 h) to Leusiscus idus was 20 mg/l.

The acute oral toxicity to rats is low; the rat oral LD₅₀ was 5,000 mg/kgbw and the dermal LD₅₀ in rabbits was > 1,250 mg/kgbw. BEHP is corrosive to rabbit skin and eyes. Diet containing up to 3% of BEHP when fed to rats for 5 days resulted in no obvious signs of toxicity.

BEHP does not induce gene initiation in bacteria.

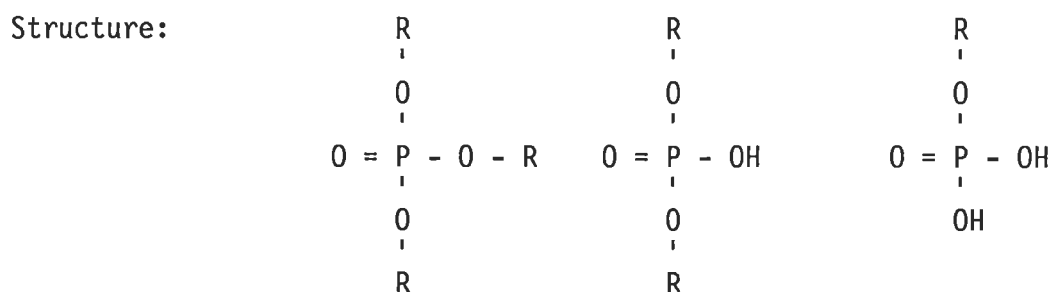
Mono (2-ethylhexyl) phosphate (MEHP) is not produced in commercial scale. Toxicological and environmental information are not available.

2. Identity, Physical and Chemical Properties, Analytical Methods

2.1 Identity

Name:	Tris(2-ethyl-hexyl)phosphate	Bis(2-ethyl-hexyl)phosphate	Mono (2-ethyl-hexyl)phosphate
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Abbreviations in this report:	TEHP	BEHP	MEHP
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where R is = - CH₂ - CH - (CH₂)₃-CH₃
|
C₂H₅

Chemical Formula:	C ₂₄ H ₅₁ O ₄ P	C ₁₆ H ₃₅ O ₄ P	C ₈ H ₁₉ O ₄ P
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CAS-No:	78-42-2	298-07-7	12645-31-7
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EINECS-No:	2011166	2060564	2357410
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RTECS-No:	MP 0770000	TB 787500
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TEHP

CAS Chemical Name : Phosphoric acid, tris(2-ethylhexyl)ester.

Synonyms: 1-Hexanol, 2-ethyl-, phosphate,
 2-Ethyl-1-hexanol phosphate,
 Triethylhexylphosphate,
 Tri(2-ethylhexyl)phosphate,
 Trioctylphosphate,
 Tris(isooctyl)phosphate.

BEHP

CAS Chemical Name: Phosphoric acid, bis (2-ethylhexyl)ester.

Synonyms: Bis(2-ethylhexyl)hydrogenphosphate,
Bis(2-ethylhexyl)orthophosphoric acid,
Bis(isooctyl)phosphate,
Bis(2-ethylhexyl)phosphoric acid,
Di(2-ethylhexyl)orthophosphoric acid,
Di(2-ethylhexyl)phosphate,
Di(2-ethylhexyl)phosphoric acid.

MEHP

CAS Chemical Name: Phosphoric acid, (2-ethylhexyl)ester.

Synonyms: 2-Ethylhexanolphosphate,
2-Ethylhexylphosphate,
Phosphated 2-ethylhexanol,
Phosphoric acid, 2-ethylhexyl ester,
Mono(isooctyl)phosphate.

2.2 Physical and Chemical Properties

The three esters are colourless or light yellow coloured liquids, nonflammable and nearly odourless. Physical and chemical data are given for TEHP in Table 1 and for BEHP in Table 2. No data are available for MEHP since this compound is not available commercially.

Conversion factors are:

TEHP: 1 ppm = 17.78 mg/m³
 1 mg/l = 56 ppm

BEHP: 1 ppm = 13.19 mg/m³
 1 mg/l = 76 ppm

2.3 Analytical Methods

Analytical methods have been reported only for TEHP. They are based on gas chromatography (GC) combined with flame ionisation detection (FID), flame photodetection (FPD), mass spectroscopy (MS) or nitrogen phosphorus detection (NPD). The detection limits are in the ng/m^3 (air) and ng/l (water) range.

Bloom (1973) applied thin-layer and gas-liquid chromatography to the qualitative and quantitative analysis of phosphoric acid esters. Lerche and March (1973) determined TEHP using GC combined with FID with a detection limit of 5-30 ng/l . The separation of various phosphoric acid esters by GC was achieved using columns filled with liquid silicone phases, e.g. the standard types QF-1, OV-210 or OV-12.

2.3.1 TEHP in Air

TEHP vapour and aerosol were collected in glass adsorber tubes packed with a plug of fine platinum mesh coated with the packing material of GC-columns (silicone OV-101) and subsequently thermally desorbed into a GC for analysis. The capacity of the adsorber was found to be 2.1 ng of pure TEHP when presented with 3×10^{-12} g TEHP/l air . Concentrations of 20 pg/l were determined with a precision of better than 10%. The aerosol concentration and its drop-size distribution were determined at a picogram level with ca. 5% precision using a cascade impactor (Krzymien, 1981). Armstrong and Yule (1978) determined TEHP deposited on foliage and twigs by extraction with toluene, drying with anhydrous sodium sulphate and using GC (OV-1 column) with FPD.

2.3.2 TEHP in Water

LeBel et al (1981) used Amberlite^R XAD-2 macroreticular resin to collect TEHP from drinking-water. The resin was extracted with an acetone/hexane mixture. TEHP was identified by GC and by GC/MS at ng/l levels.

Determination of TEHP in extracts of activated carbon by means of GC/MS is described by Frimmel et al (1987). TEHP was extracted from activated charcoal using acetone, dichloromethane and toluene. Ishikawa et al (1985a) described a procedure to extract and analyse trialkyl phosphates in water and sediment samples. Water was extracted with dichloromethane using a separating funnel. The extracts were dried with anhydrous sodium sulphate, concentrated until nearly dry, taken up in acetone and then analysed with GC combined with MS (Detection limit: 20 ng/l).

2.3.3 TEHP in Sediment

Sediment samples were extracted with acetone and then dried, concentrated and analysed by Ishikawa et al (1985a) in a similar way to water samples. The detection limit was 10 ng/g.

3. Production, Storage, Transport and Use

3.1 Production, Storage and Transport

Figures for the world production of TEHP and BEHP are not available. The present worldwide demand is estimated for ECETOC to be between 1,000 and 5,000 t/year of TEHP and about 1,000 t/year of BEHP.

The esters are stable under normal storage conditions. They are usually packed, transported and stored in steel, plastic or bulk containers.

MEHP is not produced as a single product but only in mixture with BEHP.

TEHP is produced by reaction of phosphorus oxychloride and 2-ethylhexanol. The triester is separated by vacuum distillation. Technical grade TEHP usually is 99% pure. Impurities are 2-ethylhexanol, BEHP and traces of water.

BEHP can be produced by the same reaction; its production is favoured by an excess of phosphorus oxychloride. It can also be produced by the partial hydrolysis of TEHP. Mixed mono and diesters can be produced by the reaction of 2-ethylhexanol with phosphorus pentoxide.

3.2 Use

TEHP is used as a flame retardant plasticizer, particularly for PVC in low-temperature applications. It is also used in PVC-plastisols and as a flame retardant in cellulose acetate and as a solvent for certain chemical reactions (e.g. in H₂O₂ synthesis).

BEHP is used as a solvent in liquid-liquid extractions. Various proportions of BEHP and MEHP are used for surface treatment of metals, in the textile industry as a dyeing auxiliary, and as a lubricant for films and filaments.

4. Environmental Distribution, Biotransformation and Fate

TEHP, BEHP and MEHP do not occur naturally. Releases of small quantities into the environment can be expected from fugitive losses during manufacture and use. TEHP has been detected in river and surface waters and in sediments but not in outdoor atmosphere (see section 5.1).

4.1 Environmental Distribution

Although no data on releases are available, the main sources of entry of TEHP, BEHP and MEHP into the environment are expected to be effluents from manufacturing and user industries as well as from households. Drainage from waste disposal sites is also likely to contain TEHP leached from plastics.

Since their water solubility and vapour pressure are low and octanol/water partition coefficient moderately high, TEHP and BEHP are likely to be

associated with soils and sediments where they will biodegrade (see 4.2). Saeger et al (1979) calculated the biological concentration factor (BCF) of TEHP to be 250 suggesting that some uptake by biota could occur, but the authors judged from their studies that pollution by phosphoric esters is not likely to become a widespread environmental problem because the rate of their release into the environment is low and degradation usually rapid.

4.2 Biotransformation and Fate

Hattori et al (1981) showed that abiotic hydrolysis is insignificant. Biodegradation of phosphoric-acid esters probably involves stepwise enzymatic hydrolysis to orthophosphate and alcohol moieties. The alcohol would then be expected to undergo further degradation. The nature of the alcohol moiety has a significant effect on the ultimate biodegradability of phosphate esters (Saeger et al, 1979).

TEHP

In a ready biodegradability closed bottle test (OECD Guideline 301D) no biodegradation of TEHP was observed after 28 days (Bayer, 1982a).

In semi-continuous activated sludge (SCAS) studies, which provide an indication of the inherent biodegradability with an addition rate of 3 mg/l/24 hrs of TEHP, 20% biodegradation was observed during the test period of 34 weeks (Saeger et al, 1979).

TEHP was rapidly biodegraded (50% in 48 hr) by activated sludge (Ishikawa et al, 1985a). After a 48 hr acclimation period the biodegradation increased to 60% during a further 48 hr test period.

Hattori et al (1981) studied the fate of TEHP in river and sea water, from the Osaka Bay area. After addition of 1 ppm TEHP the biodegradation was followed by analysing the increase on phosphate-ion concentration using the molybdenum blue colorimetric method. The percentage biodegradation observed is summarised as follows:

Test period (days)	Oh River	Neya River	Osaka Bay	
			Tomogashima (pure seawater)	Senboku (coastal water)
7	35.9	24.4	1.2(b)	9.9
14	65.2(a)	42.2	32.5	73.2

a) test period 15 days; b) test period 8 days.

In sterilised water TEHP did not show any degradation after 15 d. The authors consider the degradation rate depended on the microbial content of the water and this view is supported by an increase of phosphatase activity observed during the test period.

Similar results were reported by Kawai et al (1985; 1986) for river die-away tests with TEHP in water samples from rivers of the Osaka City area. Depending on the bacterial content of water, up to 80% degradation was observed. Usually the TEHP concentration decreased rapidly during the first 10 days.

BEHP

In a ready biodegradability respirometer test (OECD 301C) 75% of BEHP was biodegraded within 28 days (Bayer, 1990b).

MEHP

No data are available, but by analogy with BEHP and TEHP, MEHP presumed to biodegrade.

5. Environmental Levels and Human Exposure

5.1 Environmental Levels

No data are available on the quantities of TEHP, BEHP and MEHP released to the environment.

TEHP has not been detected in the atmosphere. In indoor air and in river water TEHP was found at concentrations of a few ng/m^3 and ng/l respectively. Human exposure from these sources can be considered insignificant.

No information are available for BEHP or MEHP. The following sections relate only to TEHP.

5.1.1 Air

In New Brunswick (Canada) forests ambient concentrations of TEHP in air were below the limit of detection ($20 \text{ ng}/\text{m}^3$ with a precision of $\pm 5\%$; Krzymien, 1981). Weschler (1980) identified TEHP in size-fractionated indoor particle samples from an office building but concentrations were not reported. TEHP was the most abundant pollutant associated with particles smaller than $1.1 \mu\text{m}$. In a second study, Weschler (1984) collected fine ($2.5 \mu\text{m}$) and coarse particles ($2.5 - 15 \mu\text{m}$) indoors and outdoors (roof) of two office buildings. Both offices had ventilation systems with a high portion of recirculated air. In one of the buildings TEHP concentration was $6 \text{ ng}/\text{m}^3$. The source could not be identified. TEHP was not detected outdoors.

A representative mean concentration inside 7 office buildings of $5 \text{ ng}/\text{m}^3$ was reported by Weschler and Shields (1986).

5.1.2 Water

As a part of the German Monitoring Programme water from the River Weser was examined for concentrations and loads of various chemicals including plasticizers. Several samples were taken at various points over 35 km of river. The average concentration of TEHP over 10 sampling points did not exceed 10 ng/l at any point. On one day in 1987 peak values of 290 ng/l were measured, indicating direct emissions. Effluents from water treatment plants into the Weser contained up to 144 ng/l TEHP (Bohlen et al, 1989).

Water samples from estuaries of the German rivers Elbe, Weser and Ems were analysed from 1977 to 1983. TEHP could be identified only in water samples from the estuary of the river Elbe where concentrations were in the range 1 - 5 ng/l (Weber and Ernst, 1983).

The concentration of TEHP in Rhine water at Duesseldorf was usually below 20 ng/l. The maximum concentration found was 50 ng/l (ARW, 1987). Ishikawa et al (1985b) could not detect TEHP at 16 river sampling sites, or 9 seawater sampling sites around Kitakyushu in Japan (detection limit 20 ng/l).

No TEHP could be detected in 63 water samples from various locations throughout Japan at a detection limit of 10 ng/l (EAJ, 1987). TEHP was found in water of the Yodo River (Osaka area) at concentrations of 80 - 2,000 ng/l with a mean value of 100 ng/l. The detection limit was 80 ng/l (Fukushima 1987). In river water of the Osaka City area Kawai et al (1985) detected 15-84 ng/l TEHP (Detection limit not reported).

In drinking water collected during October 1978 from eastern Ontario, TEHP could only be detected at a concentration of 0.3 ng/l in one sample (LeBel et al, 1981).

5.1.3 Soil

No data are available.