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TRIS- (2-BUTOXYETHYL)-PHOSPHATE

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Joint Assessment of Commodity Chemicals

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THE ECETOC SCHEME FOR THE

"JOINT ASSESSMENT OF COMMODITY CHEMICALS" (JACC)

This report has been produced 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 N°30 entitled "Existing Chemicals: Literature Reviews and Evaluations".

This document presents a critical assessment of the toxicology and ecotoxicology of tris-(2-butoxyethyl)-phosphate (CAS N° 78-51-3).

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1. SUMMARY AND CONCLUSION

Tris-(2-butoxyethyl)-phosphate (TBEP) is used as a plasticizer or flame retardant in rubber and plastics and as a component of lacquers and floor finishes. Worldwide production volumes are not high relative to other phosphate esters. In Europe the production is estimated to be less than 1000t/a.

TBEP occurs in the environment only as a result of human activity. Its distribution in the environment has been investigated in certain industrialised countries. In the few situations in which it was found in water, the concentration never exceeded 300 ng/l. None of 167 analyses detected TBEP in fish. TBEP is not a common air pollutant but it has been detected associated with fine particulates indoors and, in an isolated study, outdoors.

Sewage treatment plants and semi-continuous sludge laboratory tests indicated substantial elimination of TBEP (>80%). In river and coastal water TBEP was completely degraded. The half-life in estuarine water was about 50 days and there was little degradation in clean seawater.

There are no quantitative estimates of human exposure but there is one report that TBEP has been detected at ppb levels in human adipose tissue.

Toxicity to aquatic organisms is moderate. The 48-hour LC₅₀ in Daphnia magna was 75 mg/l and the 96-hour LC₅₀ in Pimephales promelas was 16 mg/l.

The acute toxicity and skin and eye irritation potential are low. In hens, TBEP caused no clinical or histopathological neurotoxic effects in single doses of up to 10,000 mg/kg and while brain acetylcholinesterase and plasma butyrylcholinesterase activities were slightly inhibited there was no inhibition of neurotoxicity target esterase. Neurotoxic effects in rats are inconsistent; reversible neurotoxicity has been described in animals repeatedly administered high-doses by gavage. Other effects of subchronic dosing in rats

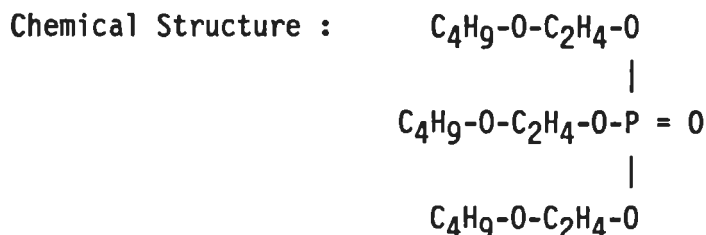
included mild changes in the liver and possibly an acceleration of the focal myocarditis to which Sprague-Dawley rats are subject. Chronic toxicity and carcinogenicity have not been studied but bacterial and mammalian cell tests for mutagenicity were negative. Teratogenicity was not observed in two studies both of which included maternally toxic doses.

A Repeat Human Insult Patch Test indicated no sensitisation and minimal skin irritation.

Toxicity data, structural considerations and human experience do not indicate a significant hazard to man. Since the toxicity to aquatic organisms is no more than moderate and persistence (based on degradation rate in natural water) is not expected to occur, TBEP is unlikely to be harmful to the environment.

2. IDENTITY, PHYSICAL CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1. Identity



Chemical Formula : $\text{C}_{18}\text{H}_{39}\text{O}_7\text{P}$

Common Name : Tris-(2-butoxyethyl)-phosphate

Synonyms : Phosphoric acid, tris-(2-butoxyethyl)-ester;
Tri-(2-butoxyethanol) phosphate;
Tris (2-n-butoxyethyl) phosphate;
Tributoxyethylphosphate;
TBEP;
TBXP (only in Japanese literature).

Other names : TBOP; 2-Butoxyethanol phosphate;
(RTECS,1989) Tri-(2-butylethylether) phosphate;
Tris (butylglycol) phosphate;
Tributyl cellosolve phosphate.

CAS Registry No. : 78-51-3

EINECS-No. : 2011229

RTECS-No. : KJ 9800000

CAS-name : Ethanol, 2 - butoxy-, phosphate (3:1).

TBEP is a technical product which contains as impurities tributylphosphate (about 3%) and traces of 2-butoxyethanol and phosphoric acid. In addition, traces of arsenic (up to 1 ppm) may be present (FMC, 1990). There is no information on the concentration of mono- or diesters or other impurities in the technical product.

2.2. Physical and Chemical Properties

TBEP is a nearly colourless, high-boiling, non-flammable liquid under normal conditions. It is more soluble in non-polar than in polar solvents. Additional physical and chemical properties of TBEP are given in Table 1.

2.3. Conversion Factors at 20°C

$$1 \text{ ppm} = 16.53 \text{ mg/m}^3$$

$$1 \text{ mg/l} = 60.5 \text{ ppm}$$

2.4. Analytical Methods

TBEP is usually analysed by gas chromatography (GC) coupled with either mass spectrometry (MS), infrared spectroscopy or nuclear magnetic resonance spectrometry. The detection limit is about 1 ng using any of these methods or a nitrogen/phosphorus-selective detector. (LeBel et al, 1981; Benoit and LeBel, 1986; Rivera et al, 1987).

2.4.1. Air

TBEP has been found in the air of offices associated with particulates. Of the methods which can be used to collect the particles, Weschler (1980) used a four stage impactor with a back-up filter and extracted with a mixture of water and methanol. Later, Weschler (1984) and Weschler and Fong (1986) collected particles on Teflon^R membranes, separating the particles according to whether the aerodynamic diameter was greater or less than 2.5 μm . The samples were analysed by GC-MS after thermal desorption of the collector membranes. Sometimes samples were desorbed or dissolved with toluene.

2.4.2 Water

TBEP has been extracted either with dichloromethane after acidification to pH 2 or by passage through a column filled with Amberlite XAD-2 resin which was subsequently extracted with acetone and hexane. After dehydration and concentration, extracts are analysed as described above (section 2.4). (LeBel et al, 1981; Benoit and LeBel, 1986; Watts and Moore, 1988).

2.4.3. Sediments

After decanting the supernatant water the sediment samples were mixed with an equal volume of pre-extracted anhydrous sodium sulphate and transferred to a Soxhlet thimble. Soxhlet extraction was carried out overnight using dichloromethane (300 ml). The solvent extract was concentrated to a volume of 5 ml using a Kuderna-Danish apparatus with a macro-Snyder column and further concentrated to 1 ml using a micro-Snyder column and a concentrator tube (Watts and Moore, 1988).

2.4.4. Soils and Foodstuffs

There are no reports of extraction or clean up methods for soils and food.

2.4.5. Biological Media

LeBel and Williams (1983) analysed human adipose tissue for TBEP by extraction with a mixture of acetone and hexane in presence of anhydrous sodium sulphate. The solution was centrifuged and the supernatant filtered and evaporated. The resulting extract was dissolved in solvent (5% methylene chloride in cyclohexane) for gel permeation chromatography (GPC) to separate residual lipids from phosphate esters.

In investigating artifacts in the measurement of plasma drug concentrations, Devine (1984) analysed blood which had been in contact with rubber stoppers for TBEP by extracting the serum with

dichloromethane, dehydrating and evaporating to dryness and dissolving in ethyl acetate (See Section 7).

3. PRODUCTION, STORAGE, TRANSPORT AND USE

TBEP is produced by reacting phosphorus oxychloride and butoxyethanol (butylglycol) and stripping hydrochloric acid and excess of butoxyethanol. Another production method uses the sodium salt of the glycol. In this case, the by-product is sodium chloride.

Production capacities and tonnages used have not been reported. Annual European production is likely to be less than 1000 tonnes. The product is normally transported in drums. TBEP is used as a plasticizer or flame retardant in rubber, plastic materials and lacquers and as a component in floor-finishes.

4. ENVIRONMENTAL DISTRIBUTION, TRANSFORMATION AND FATE

4.1. Environmental Distribution

TBEP has not been found to occur naturally in the environment. All environmental TBEP derives from human activities but the input rate to the environment cannot be estimated from available data. The input is expected to be mainly to soil, sediments and surface waters from leachates from plastics on landfills from spillages and from effluents.

The low vapour pressure, the high soil sorption coefficient KOC and water solubility of approx. 1 g/l suggests that TBEP in the environment will be found mainly in water and sediment. In actual fact, TBEP has been detected in surface water and sediments but only at low concentrations (ppb level).

In Canada, TBEP was found in sewage effluent and in river water downstream but not upstream of its point of discharge (LeBel et al, 1987). Inputs

to indoor air may derive from volatilisation or dusts from plasticized rubber and plastics and from floor coatings (Weschler, 1984).

4.2. Transformation

No data are available on mechanisms of abiotic or biotic transformation. Analogy with other phosphate esters suggests that enzymatic hydrolysis would be expected to dominate.

4.3. Fate

4.3.1. Water

In a test of primary biodegradation using the semi-continuous activated sludge procedure and an addition rate of 3 mg/l TBEP per test cycle, 88% of TBEP was eliminated. The ultimate biodegradability (using the Monsanto shake flask procedure) was 51% of the theoretical CO₂ generated after 28 days (Monsanto, 1976).

In a sewage treatment plant in Osaka, 81% TBEP was found to be eliminated. In 1 of 3 river water samples, TBEP concentrations decreased to zero between 10 and 20 days, in the other two there was no significant decrease in 30 days (Fukushima and Kawai, 1986).

Hattori et al (1981) studied the degradation of TBEP in environmental water. Using the molybdenum blue colorimetric method the increase of phosphate ions was analysed in river water and seawater from Osaka-Bay to which 1 ppm TBEP had been added. The degradation depended on the source of water, as follows:

Test time (days)	Degradation %			
	Oh-river	Neya-river	Osaka Bay Off Tomagashima (clean seawater)	Osaka Bay Off Senboku (coastal water)
7	29.1	0	1.9 ^{b)}	0
14	100 ^{a)}	100	17.6	100

a) 15 days b) 8 days

A sterilised distilled water control did not show any degradation after 15 days. TBEP was rapidly degraded in less than 14 days after an acclimatisation period of some days in water containing micro-organisms. Where degradation was rapid, the phosphatase activity increased during the test period.

TBEP was eliminated from estuarine water with a half-time of approximately 50 days (Ernst, 1988).

TBEP was considered to behave similarly to other phosphate esters in drinking water purification plants. Chlorine water treatment lead to formation of chlorinated compounds while treatment with chlorine oxides, peroxides or ozone resulted in oxidation products. (Huck et al, 1987).

4.3.2. Air

No data have been reported on the fate of TBEP in air and soil.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1. Environmental levels

5.1.1. Air

Weschler (1984) studied air pollutants inside and on the roof of air-conditioned office buildings in USA cities. TBEP was not detectable outdoors or in the vapour phase indoors but it was detectable indoors associated with small (<2.5 μm) but not larger (2.5 - 15 μm) particulates.

The mean concentrations measured in representative samples of dust from 7 offices was reported to be 15 ng/m^3 (Weschler and Shields, 1986). The significance of floor finishes - which may contain 1% TBEP - as a source

of these particulates is suggested by the fact that the highest concentration measured (25 ng/m³) was found immediately following floor polishing work.

Yasuda (1980) reported the results of a study of pesticides in 19 air samples from 7 locations in 1976. Three samples were reported to contain TBEP. Two samples from Kawauchi Town contained 149.1 and 176.8 ng/m³ and one from Ehime University 9.6 ng/m³. It is not clear whether TBEP was unmeasured or not detectable in the other 16 samples, nor whether the samples were indoor or outdoor.

TBEP was also detectable (quantities not specified) in cigarette smoke (Schumacher *et al*, 1977).

5.1.2. Drinking Water and Surface Water

Levels of TBEP have been determined in rivers, sewage, tap water, lakes and estuaries. The investigations have been carried out in the Great Lake district of Canada, USA, Japan, the Federal Republic of Germany, Spain and the United Kingdom.

TBEP was detected at a wide range of concentrations :

Surface water	:	0.2	-	125	ng/l
Drinking water	:	8	-	272	ng/l
Effluents	:	12	-	34,900	ng/l

Details are given in Table 2.

The Japanese Environmental Agency (EAJ) summarised the results of environmental monitoring programmes which included measurements of TBEP. The EAJ 1975 report summarised analyses of 100 samples of surface water from various locations throughout Japan: TBEP was identified in none (detection limits ranged from 20 to 500 ng/l). The EAJ 1978 report summarised analyses of a further 114 samples: TBEP was again not identified (detection limits ranged from 5 to 1,500 ng/l).

5.1.3. Sediment and Fish

Sediment:

TBEP was detected in 7 out of 80 samples of sediment; concentrations ranged from 0.22 - 0.54 mg/kg and the detection limits were 0.002 - 0.1 mg/kg (EAJ, 1975). The 1978 review reported that none of 114 sediment samples contained TBEP; detection limits were 0.0005 - 0.12 mg/kg sediment (EAJ, 1978). These samples were not taken systematically so that the results from the two reports can not be compared.

Watts and Moore (1988) did not detect TBEP in suspended particles or bottom sediments in a UK river even though TBEP was found in corresponding water columns.

Fish:

No TBEP could be detected in 74 samples of fish from numerous locations throughout Japan, (detection limits ranged from 0.005 to 0.1 mg/kg) (EAJ, 1975). Another report (EAJ, 1978) states that TBEP was not detected in 93 fish samples (detection limits ranged from 0.0005 to 0.15 mg/kg).

5.2. Human Exposure

No data are available. The range of environmental data available is insufficient for an estimate of total exposure to man.

6. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

6.1. Invertebrate Aquatic Species Toxicity

The LC₅₀ values in Daphnia magna were 84 mg/l (24 hours) and 75 mg/l (48 hours) (Monsanto, 1984a).