

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).

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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.

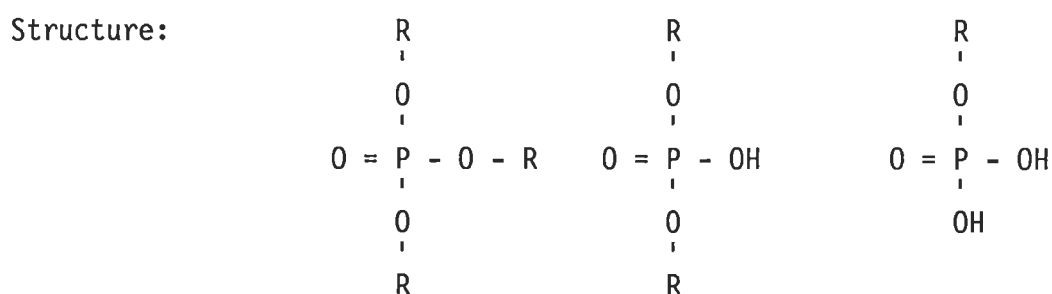
Mono (2-ethylhexyl) phosphate (MEHP) is not produced in commercial scale. Toxicological and environmental information are not available.

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 H_2O_2 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 ng/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 ng/m^3 . The source could not be identified. TEHP was not detected outdoors.

A representative mean concentration inside 7 office buildings of 5 ng/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.

5.1.4 Sediment

In Japan, TEHP was found at 2 - 70 ng/g (limit of detection 1 - 5 ng/g) in 43 out of 63 sediment samples (EAJ, 1987). In one river sediment and 5 sea sediments Ishikawa et al (1985b) could not detect TEHP (detection limit 10 ng/g).

5.1.5 Food

Total diet studies of the US Food and Drug Administration were reported by Gartrell et al (1986a, 1986b). Baskets of 120 food items representing a typical 14 day diet for infants, young children and adults were collected from October 1980 - March 1982 from retail markets throughout U.S. Foods were classified into various groups. TEHP was found in the oil and fat food group of the diet used by young children. The average concentration in this food group was 0.0385 ppm, the average daily intake was calculated to be 0.385 µg/day (Gartrell et al, 1986b).

In adult total diet samples, (Gartrell et al, 1986a), TEHP was found only in the meat, fish and poultry food group with an average concentration of 0.0067 ppm; the average daily intake was therefore calculated to be 1.73 µg/day. All the other food groups - dairy products; grain and cereal, potatoes, leafy vegetables, legume vegetables, root vegetables, fruits, oils and fats, sugar and adjuncts and beverages (including water) - were free of TEHP.

5.2 Hygiene Standards - Occupational Exposure Levels

No official values have been published and no internal standards have been adopted by industrial concerns.

6. Effects on Organisms in the Environment

This and the following chapters relate only to TEHP and BEHP. No toxicity data are available for MEHP.

6.1 Microorganisms

TEHP

A bacterial toxicity test carried out according to ISO 8192 indicates an IC_{50} for TEHP greater than 100 mg/l (Bayer, 1982b).

BEHP

For BEHP the EC_0 value of 2,500 mg/l for the growth inhibition of Pseudomonas fluorescens found by Bayer (1975) indicates that it is of negligible toxicity to bacteria (this concentration exceeded the water solubility which is <100 mg/l).

BEHP affected slightly the growth of green algae, Chlorella emersonii at a concentration of 50 mg/l. At 100 mg/l BEHP reduced growth significantly during the first 24 hrs but the EC_{50} for inhibition of growth of Chlorella emersonii was greater than 100 mg/l (Dave et al, 1979).

A mixture of BEHP/MEHP was not toxic to a mixed culture of anaerobic bacteria at 1,000 mg/l (Hoechst, 1987).

6.2 Fish

TEHP

A 96-hour exposure of zebra fish Brachydanio rerio under static conditions to concentrations of 100 mg/l TEHP produced no deaths (Bayer, 1989).

BEHP

Dave and Lidman (1978) reported a LC_{50} (96h) to rainbow trout Salmo gairdneri of 48-54 mg/l.

The acute toxicity of BEHP to rainbow trout Salmo gairdneri at exposure times up to 120 hrs at different temperatures was studied by Dave et al (1979). The following LC_{50} values were determined (nominal concentrations in mg/l):

	5°C	10°C	15°C	20°C
48h	43	40	34	22
96h	34	36	30	20
120h	34	34	29	20

The 48 h LC_0 and LC_{100} of BEHP to Golden Orfe Leuciscus idus were 20 mg/l and 40 mg/l respectively (Bayer, 1975).

Berglind and Dave (1981) made replicate determinations of the acute lethal concentration of BEHP to Daphnia magna. The mean values and (standard deviations) were:

72 hr LC_{50} = 36.5 (10.0) mg/l,

96 hr LC_{50} = 16.5 (9.8) mg/l.

6.3 Terrestrial Organisms

No data are available.

7. Kinetics and Metabolism

Limited studies suggest that TEHP and BEHP are metabolised by rats.

7.1 Experimental

TEHP

In a radiotracer inhalation study nine male rats received a single, head only, exposure of 20 minutes to an aerosol of p^{32} -TEHP. The animals were killed after the following intervals post exposure: 5 minutes, 30 minutes, 1, 4, 17, 18, 24, 48 and 70 hours. Exposure concentrations ranged between 0.72 and 0.91 mg/l. TEHP was rapidly distributed into the lungs, stomach contents, brain and liver, and lower amounts were found in other organs and depot tissues. Faecal excretion was high but urinary excretion was relatively low. Chromatographic analysis of urine and faeces showed TEHP underwent some biotransformation but the nature of the metabolites was not mentioned (MacFarland and Punte, 1966).

Kluwe et al (1985) assumed, although no confirmatory data are available, that TEHP is hydrolysed to 2-ethylhexanol and BEHP. This would be analogous to di(2-ethylhexyl)-phthalate and to di(2-ethylhexyl)-adipate which both contain the ethylhexyl moiety and are readily hydrolysed to the corresponding monoester and 2-ethylhexanol, (NTP, 1981, 1982).

BEHP

In male Sprague-Dawley rats (number not specified) exposed to a diet containing 0.25%, 1% or 3% BEHP for five days a twofold increase of liver cytosolic epoxide hydrolase activity was found together with an increase of microsomal cytochrome P-450 activity with the 1% and 3% diets. While no increase was observed in cytochrome P-450c, cytochromes P-450b and e were induced 20 to 35 fold. Considerably smaller effects were observed on NADPH-cytochrome c reductase, microsomal epoxide hydrolase and microsomal cytochrome b5 and there was no effect on cytosolic glutathione transferase

activity under the same conditions. A 28 fold increase in cyanide-insensitive palmitoyl-CoA oxidation and a 4 fold increase of the total mitochondrial protein, with smaller increases in total catalase and cytochrome oxidase activities, were observed after treatment with BEHP, indicating that this compound causes proliferation chiefly of peroxisomes but also mitochondria in rat liver. The authors postulated that it is not BEHP but a metabolite (2-ethylhexanol) which is directly responsible for the induction of the xenobiotic-metabolising enzymes and/or the proliferation of peroxisomes and/or mitochondria (Lundgren and De Pierre, 1987).

Lundgren et al (1988) investigated the relationship between peroxisome proliferation and induction of cytosolic and microsomal epoxide hydrolases in male 20 - 22 g C57BL/6 mice. BEHP was administered at 1% (w/w) in the diet, subcellular fractionation of liver homogenates was performed and the specific activity of hepatic cytosolic and microsomal epoxide hydrolase activity was measured. BEHP caused an approximately threefold induction of cytosolic epoxide hydrolase and a twofold induction of microsomal epoxide hydrolase. The increase in specific activity of hepatic cytosolic epoxide hydrolase reflected a corresponding increase in enzyme protein, as determined immunochemically.

7.2 Human

No data are available.

8. Effects of Experimental Animals and In Vitro Test Systems

8.1 Acute Toxicity

The results of the acute toxicity studies for TEHP and BEHP are summarised in Table 3.

TEHP has a low acute toxicity. In rats the acute oral LD₅₀ is greater than 10,000 mg/kgbw (Bayer, 1958). No mortality was observed in rats after inhalation of TEHP at concentration of 447 mg/m³ for 3.5 h (MacFarland and Punte, 1966). The dermal LD₅₀ in rabbits was greater than 20,000 mg/kgbw (Marhold, 1966).

The acute toxicity for BEHP is also relatively low: in rats the acute oral LD₅₀ was 4,940 mg/kgbw and the dermal LD₅₀ in rabbits was 1,250 mg/kgbw (Union Carbide, 1972).

Single exposures to TEHP aerosol having a mean median diameter of 1.5 μ produced no mortality in rats for exposures up to 447 mg/m³ for 210 minutes and in guinea pigs for exposures up to 448 mg/m³ for 90 minutes or 283 mg/m³ for 180 minutes (MacFarland and Punte, 1966).

8.2 Skin and Eye Effects

A single dose of 250 mg pure TEHP applied to the clipped skin of rabbits produced moderate erythema which persisted for a week (MacFarland and Punte, 1966). Repeated applications of 0.1 ml on 5 days a week (10 or 20 applications) produced moderate erythema after the first application. With further applications a spreading zone of erythema developed with desquamation, leatheriness and some fissuring with haemorrhage. At the end of the observation period thickening and severe hyperkeratosis of the skin was apparent. The purity of the material was not reported.

TEHP was not irritant to the rabbit eye; doses up to 0.5 ml pure TEHP produced moderate conjunctivitis which subsided within 24 hours (MacFarland and Punte, 1966). Nevertheless BEHP is reported to be corrosive to skin and eyes in rabbits (Bayer, 1978).

8.3 Subacute and Subchronic Toxicity

8.3.1 Oral Administration

TEHP

Daily feeding of 110 mg to 1,550 mg TEHP/kgbw in the diet of rats for 30 days revealed a no-effect level of 430 mg/kgbw, whereas at 1,550 mg/kgbw/day some weight loss occurred (Smyth and Carpenter, 1948). Two cats were administered 1.0 ml TEHP/kgbw daily by gavage on 5 days a week for four weeks. During the treatment and the recovery periods there were no signs of intoxication. Measurements of erythrocyte cholinesterase activity during the test-period revealed no inhibitory effect (Bayer, 1958).

Groups of five male and five female F 344/N rats and five male and five female B6C3F1 mice were administered 0, 375, 750, 1,500, 3,000 or 6,000 mg TEHP/kgbw in corn oil by gavage for 14 consecutive days. No animal died. There were no bodyweight changes in mice. The final mean bodyweight of male rats that received 1,500 - 6,000 mg/kgbw and of female rats that received 3,000 or 6,000 mg/kgbw were lower than those of the vehicle controls. No compound-related effects were observed at necropsy (NTP, 1984).

Groups of 10 rats of each sex received 0, 250, 500, 1,000, 2,000 or 4,000 mg TEHP/kgbw by gavage on 5 days a week for 13 weeks. Groups of 10 mice of each sex were administered 0, 500, 1,000, 2,000, 4,000 or 8,000 mg/kgbw. Animals were examined twice daily and body weights were recorded weekly. At the end of the 13 weeks survivors were killed. Post-mortem and histopathological examinations were performed on all animals except those excessively autolysed or cannibalised. No deaths attributed to TEHP administration occurred in any of these studies and toxic effects other than slight to moderate depression in bodyweight gain were not observed (NTP, 1984; Kluwe et al, 1985).

BEHP

Administration of diet containing 0.25%, 1% and 3% w/w of BEHP for 5 days to male Sprague-Dawley rats (number not specified) resulted in no obvious signs of toxicity and the same increase in bodyweight as in controls (Lundgren and De Pierre, 1987).

8.3.2 Dermal Administration

A daily dose of 0.1 ml undiluted TEHP was applied five days a week to the clipped, intact skin of six male rabbits. Four animals received ten applications and the remaining two 20 applications. No evidence of systematic intoxication was seen (MacFarland and Punte, 1966).

8.3.3 Inhalation

TEHP

In a three-month inhalation study three test groups and a control group, each consisting of equal numbers of males and females and comprising 20 guinea pigs, two dogs and two monkeys were exposed for 6 hours a day, 5 days a week, for a total of 60 exposures (MacFarland and Punte, 1966). Four 500 litre inhalation chambers were employed operating at an air-flow of 500 l/min. Three concentrations of TEHP aerosol were tested; controls received the same air-flow but without TEHP. The mean concentrations and standard deviations received by the three test groups over the 12-week period were:

low dose	10.8 +/- 6.0 mg/m ³ ,
medium dose	24.4 +/- 16.8 mg/m ³ ,
high dose	85.0 +/- 33.3 mg/m ³ .

The median particle size was 4.4 μ with a geometric standard deviation of 3.0.

No mortality and a normal increase in body weight was observed in dogs and monkeys. The guinea pig study was invalidated due to high mortality from intercurrent respiratory infections in all groups but survivors increased weight normally. There were no treatment-related alterations in any biochemical or haematological measurement. While the lungs of monkeys were normal, the lungs of dogs showed mild, chronic, parenchymal inflammatory changes. In an evaluation of effects on trained behaviour, no effects were detected in the performance of monkeys in a visual discrimination test; the performance of dogs trained in conditional avoidance deteriorated as the exposure concentration increased.

The three-month inhalation study was repeated with guinea pigs. Two groups of 20 male guinea pigs were exposed to two concentrations of TEHP. A third group acted as controls and inhaled uncontaminated air in the exposure chamber. Tetracycline was administered prophylactically in the drinking water throughout the study. The mean concentrations and standard deviations for the two test groups were:

low dose	$1.6 \pm 0.8 \text{ mg/m}^3$,
high dose	$9.6 \pm 1.5 \text{ mg/m}^3$.

Exposures were for 6 hours a day, 5 days a week for a total of 60 exposures. The mean particle size was 3.8μ with a geometric standard deviation of 1.7.

The high dose animals showed a significantly increased bodyweight in comparison with controls. Both test groups exhibited a lower kidney weight to body weight ratio than the control group. Microscopic examination of the tissues showed inconsistent and apparently reversible changes in the renal parenchyma in the animals of the high dose group. Histopathological alterations in the lung and liver were solely those of coincidental disease. Sections of the spinal cord and sciatic nerve stained to demonstrate the myelin sheaths showed no pathological changes (MacFarland and Punte, 1966).

8.4 Chronic Toxicity and Carcinogenicity

In a NTP (1984) study TEHP was administered 5 days/week by gavage for 2 years to groups of 50 male and 50 female rats and mice. The doses administered were:

Dose	Fischer 344 rats		B6C3F1 mice	
	Male	Female	Male	Female
Control	Vehicle	Vehicle	Vehicle	Vehicle
Low	2,000 mg/kg	1,000 mg/kg	500 mg/kg	500 mg/kg
High	4,000 mg/kg	2,000 mg/kg	1,000 mg/kg	1,000 mg/kg

The animals were observed twice per day and body weight was measured weekly for the first 13 weeks and once every 4 weeks thereafter. Clinical examinations were performed once every 4 weeks. Necropsies and histopathological examinations were performed on all animals, but organ weight changes were not reported.

No compound-related clinical toxicity was observed in either sex or either species. Significant depression in body weights was limited to male rats, the low dose producing an 11.5% and the high dose a 15.8% depression compared with controls. The decreased bodyweight did not effect survival. The incidence of pheochromocytoma of adrenal glands was increased with dose in male rats and there were, in addition, two (4%) malignant pheochromocytomas in the high dose group. The incidence of adrenal pheochromocytoma in male rats was as follows:

Vehicle Control	2,000 mg/kg	4,000 mg/kg
2/50 (4%)	9/50 (18%)	12/50 (24%)

Although the incidence was dose related, the NTP considered the findings represented equivocal evidence of carcinogenicity. Comparison with historical controls showed that the 4% incidence of pheochromocytomas in male vehicle control rats equalled the lowest ever reported and was significantly below the incidences of 24% and 26% observed in vehicle control animals of two previous gavage studies at the same laboratory. The incidence of pheochromocytomas in dosed groups was similar to that of

historical controls; the apparent increase was not regarded as being clearly related to the administration of TEHP.

Although there was a trend to an increased incidence of thyroid follicular cell tumours in male rats, the incidences in the dosed groups were not statistically significantly higher than that in the vehicle controls. The incidence of thyroid tumours in male rats was as follows:

	Vehicle Control	2,000 mg/kg	4,000 mg/kg
Follicular cell carcinoma	1/46 (2%)	1/49 (2%)	3/49 (6%)
Follicular cell adenoma or cystadenoma	0/46 (0%)	1/49 (2%)	3/49 (6%)

TEHP was associated with a dose related increase in the incidence of follicular cell hyperplasia of the thyroid gland in male and female B6C3F1 mice as follows:

	Vehicle control	500 mg/kg	1,000 mg/kg
male	0/49 (0%)	12/48 (25%)	24/47 (51%)
female	1/44 (2%)	13/47 (28%)	12/46 (26%)

However, no dose-related increase in thyroid neoplasias occurred in male or female mice.

The incidence liver tumours in female mice was:

	Vehicle control	500 mg/kg	1,000 mg/kg
Adenoma	2/48 (4%)	4/50 (8%)	3/50 (6%)
Carcinoma	0/48 (0%)	4/50 (8%)	7/50 (14%)

The incidence of hepatocellular carcinoma showed a dose related positive trend and the incidence in the high dose group was statistically significantly higher than that in the vehicle controls.

The incidences of carcinomas and total hepatic tumours were not statistically significant at the lower dose. In male mice, hepatocellular carcinomas occurred in 9/50 vehicle controls, 12/50 low dose and 12/49 high

dose animals; no statistically significant, treatment related trend was observed.

The results of the studies on TEHP were interpreted by NTP as indicating some evidence of carcinogenicity in female mice, equivocal evidence of carcinogenicity in male rats and no evidence of carcinogenicity in female rats and male mice.

However, the probability is high that the adrenal phaeochromocytoma effect was spurious. The only other statistically significant neoplastic finding was hepatocellular carcinoma in female mice and, on its own, this is insufficient evidence of carcinogenicity. Considering the high doses used the low incidence rate of the tumours, the lack of genotoxic activity (see chapter 8.5) and the inconsistency of tumour development between sexes and species, a carcinogenic action in man would be highly improbable at exposure levels which do not produce other toxic effects.

Discussion

Neither subacute nor chronic studies have been made with BEHP. Nevertheless metabolic studies with BEHP (Lundgren and De Pierre, 1987; see section 7) indicate that this material exhibits liver changes consistent with other compounds (di(2-ethylhexyl)-phtalate or -adipate) that are considered to be peroxisomes proliferators. As it is likely that TEHP and BEHP share similar catabolic routes it may be speculated that TEHP would show the same metabolic pattern as BEHP. Consequently BEHP may behave in a similar manner to TEHP in long-term studies.

8.5 Genotoxicity

TEHP and BEHP were not mutagenic in Salmonella typhimurium strains TA 98, TA 100, TA 1535, or TA 1537 in the presence or absence of fractions from Arochlor 1254-induced rat or hamster liver (Bayer, 1982c; Kluwe et al, 1985; Zeiger et al, 1985; Zeiger, 1987; Hoel et al, 1988). In a NTP (1984) project to develop a database that would permit evaluation of the ability of four of the most commonly used in vitro short-term tests to

predict rodent carcinogenicity, the Ames Salmonella/microsome mutagenesis assay, the assays for chromosome aberration and sister chromatid exchange induction in Chinese hamster ovary cells and the mouse lymphoma L5178Y cell mutagenesis assay were carried out on TEHP. In all tests TEHP showed no genotoxic activity (Tennant et al, 1987; Ashby and Tennant, 1988; Piegorsch and Hoel, 1988; Benigni, 1989; Ivett et al, 1989).

8.6 Cytotoxicity

The cytotoxicity of TEHP was examined in vitro on HeLa cells by the Metabolic Inhibition Test, supplemented by microscopy of cells after 24 h incubation (the MIT-24 test system). TEHP had no acute toxicity to the cells, possibly due to its low solubility in water (Ekwall et al, 1982).

8.7 Neurotoxicity

MacFarland and Punte (1966) tested TEHP for its neurotoxic potential. Four groups of female chickens, each weighing 1.5-2.3 kg, received a single dose of test material into the crops as follows:

Group	Number of chickens (1.5 - 2.0 kg/bw)	Material	Dose
1	4	Saline	1.5 ml/kg
2	8	TOCP (a)	500 mg/kg
3	8	TEHP	500 mg/kg
4	8	TEHP	2,500 mg/kg

(a) tris (orthocresyl) phosphate - positive control

After receiving a single dose of the test material the animals were kept under observation for four weeks and then killed. Body weights were recorded weekly and changes in appearance and behaviour noted daily. Gross necropsy was performed on all chickens. Sections of brain, three levels of the spinal cord and the sciatic nerve were examined microscopically.

In the TOCP group, weight loss become apparent by the end of the first week and signs of ataxia and muscular weakness were evident by the 12th day.

These signs increased in intensity so the chickens were prostrate by the end of the study. The microscopic examination of nerve tissue sections confirmed that TOCP was producing demyelination. The chickens in the saline and TEHP groups appeared normal and maintained or gained weight throughout the study. There were no macroscopic signs of neurotoxicity and microscopically no demyelination could be detected in groups 1, 3 or 4.

No evidence of systemic intoxication or, in particular, neurotoxicity was seen on chickens receiving a single dose up to 2,500 mg/kgbw of TEHP (MacFarland and Punte, 1966)

Single hens were administered a single dose of 0.25, 0.5 or 1.0 g TEHP/kgbw by gavage. They were kept under observation for two months and examined for neurotoxicity twice weekly. No abnormalities of behaviour were detected. A single i.m. injection of 0.25, 0.5 or 1.0 g TEHP/kgbw to single chicken again induced no signs of intoxication (Bayer, 1958).

In a three-month inhalation study (see 8.3.3) with guinea pigs, dogs and monkeys, determination of plasma and erythrocyte cholinesterase activity and histological evaluation of sections of the spinal cord and sciatic nerve detected no abnormalities (MacFarland and Punte, 1966).

In two cats receiving 28 doses of 1.0 ml TEHP/kgbw by gavage (see 8.3.1) no signs of neurotoxicity and no inhibition in the red blood cell cholinesterase activity were found (Bayer, 1958).

8.8 Reproductive Toxicity

No data are available.

9. Effects on Man

No irritant effects were seen after 24 hr exposure to a TEHP saturated cotton swab placed on the skin of the forearm of six volunteers (Bayer, 1958).

10. Regulations, First Aid and Handling Advice

10.1 Regulations

For TEHP, BEHP and MEHP neither TLV value (USA) nor a MAK value (Germany) has been established.

Acute skin and eye initiation data for TEHP were obtained by protocols which do not conform to modern standards. Though these indicate some initiation potential, it is unlikely that this would be sufficient in tests under EC protocols to warrant labelling as irritating either to eyes or skin. (Nevertheless some manufacturers have labelled their product Xi, R36/38).

BEHP and mixtures of BEHP and MEHP are irritant to the skin and eyes and should be labelled according to the EEC directives for dangerous substances with symbol C and R34, S24, S25.

10.2 First Aid and Medical Treatment

In the case of contact with skin, wash with soap and water.

In the case of contact with eye, flush eyes with water for 10 minutes and seek medical advice if redness or irritation develop.

If swallowed send to a hospital for treatment.

Clothes soiled with TEHP, BEHP or BEHP/MEHP should be changed.

10.3 Safe Handling

Technical:

Keep the products in tightly closed containers and store in a cool, dry place.

Where the products are used at higher temperatures, enclosure or local exhaust ventilation is recommended.

Personal:

When handling the products wear chemical safety goggles and rubber gloves. Wash thoroughly after handling.

10.4 Fire and Explosure

No special measures are required.

10.5 Handling Spillage and Waste

There are no special regulations. The products should be incinerated in a suitable location according to local regulations.

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Table 1. Physical properties of Tris(2-ethylhexyl)phosphate

Molecular weight	434.64	(Lawrence and Douglas, 1987)
boiling point		
at 6.67 hPa (°C)	220	(Lawrence and Douglas, 1987)
at 5 hPa (°C)	210	(Bayer, 1988)
Melting point (°C)	-74	(Lawrence and Douglas, 1987)
Pour point (°C)	-70	(Bayer, 1988)
Relative density		
at 20°C	0.926	(Bayer, 1988)
Refractive index		
at 20°C	1.4426	(Lawrence and Douglas, 1987)
Vapour pressure		
at 20°C (hPa)	<0.01	(Bayer, 1988)
at 25°C (hPa)	1.1×10^{-5}	(Hinckley <u>et al</u> , 1990)
Stability	some decomposition occurs between 190°C and 233°C without change in appearance	(Lawrence and Douglas, 1987)
Flash point (°C)	207	(Lawrence and Douglas, 1987)
(°C)	195 (DIN 51376)	(Bayer, 1988)
Pog Pow	4.22	(Saeger <u>et al</u> , 1979)
Solubility in: Acetone	Soluble	
DMSO	1.0 mg/ml at 18°C	
Ether	Soluble	
Ethanol	Soluble	(Lawrence and Douglas, 1987)
Solubility in		
water at 20°C (g/l)	less than 0.1	(Bayer, 1988)

Table 2. Physical properties of Bis(2-ethylexyl)phosphate

Molecular weight	322.43	(Mellan, 1977)
Boiling point (1000 hPa)	decomposes above 240°C (DIN 51758)	(Bayer, 1990a)
Melting point (°C)	-50	(Bayer, 1990a)
Relative density at 20°C	0.96	(Bayer, 1990a)
Solubility in water (g/l)	<1	(Bayer, 1990a)
Vapour pressure at 20 (°C) (hPa)	<0.1	(Bayer, 1990a)
Flash point (°C)	198	(Bayer, 1990a)

Table 3. Acute toxicities of TEHP and BEHP

<u>Compound</u>	<u>Route</u>	<u>Species</u>	<u>LD₅₀/LC₅₀ value</u>	<u>Ref</u>
TEHP	oral	rat	37,080 mg/kgbw	(1)
	oral	rat	>10,000 mg/kgbw	(2)
	oral	rat	>36,800 mg/kgbw	(3)
	oral	rabbit	46,000 mg/kgbw	(3)
	inhalation	rat	>447 mg/m ³ /3.5h	(3)
	inhalation	guinea pig	>460 mg/m ³ /1h	(4)
	inhalation	guinea pig	<287 mg/m ³ /2h	(4)
	inhalation	guinea pig	<283 mg/m ³ /3h	(4)
	intratracheal	rabbit	>1,811 mg/kgbw	(3)
	intravenous	rabbit	> 358 mg/kgbw	(3)
	dermal	rabbit approx.	20,000 mg/kgbw	(5)
BEHP	oral	rat	4,940 mg/kgbw	(6)
	dermal	rabbit	1,250 mg/kgbw	(6)
	intraperitoneal	mouse LDLo	63 mg/kgbw	(7)
	intraperitoneal	rat	50-100 mg/kgbw	(8)

These values indicate relatively low acute toxicity.

(1) Smyth and Carpenter (1948)

(2) Bayer (1958)

(3) MacFarland and Punte (1966)

(4) Estimation based on data from MacFarland and Punte (1966)

(5) Marhold (1966)

(6) Union Carbide (1972)

(7) NRC (1957)

(8) Dave and Lidman (1978)

APPENDIX I

MEMBERS OF THE ECETOC TF

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LIST OF ECETOC PUBLICATIONS

MONOGRAPHS

<u>No.</u>	<u>Title</u>
No.1	Good Laboratory Practice
No.2	Contribution to Strategy for Identification and Control of Occupational Carcinogens
No.2	Definition of a Mutagen, for 6th Amendment
No.3	Risk Assessment of Occupational Chemical Carcinogens
No.4	Hepatocarcinogenesis in Laboratory Rodents : Relevance for Man
No.5	Identification and Assessment of the Effects of Chemicals on Reproduction and Development (Reproductive Toxicology)
No.6	Acute Toxicity Tests, LD ₅₀ (LC ₅₀) Determinations and Alternatives
No.7	Recommendations for the Harmonisation of International Guidelines for Toxicity Studies
No.8	Structure-Activity Relationships in Toxicology and Ecotoxicology: An Assessment
No.9	Assessment of Mutagenicity of Industrial and Plant Protection Chemicals
No.10	Identification of Immunotoxic Effects of Chemicals and Assessment of their Relevance to Man
No.11	Eye Irritation Testing
No.12	Alternative Approaches for the Assessment of Reproductive Toxicity (with emphasis on embryotoxicity/teratogenicity)
No.13	DNA and Protein Adducts: Evaluation of their Use in exposure Monitoring and Risk Assessment
No.14	Skin Sensitisation Testing
No.15	Skin Irritation
No.16	Mutation Research, Special Issue: Early Indicators of Non-Genotoxic Carcinogenesis

TECHNICAL REPORTS

<u>No.</u>	<u>Title</u>
No.1	Assessment of Data on the Effects of Formaldehyde on Humans
No.2	The Mutagenic and Carcinogenic Potential of Formaldehyde
No.3	Assessment of Test Methods for Photodegradation of Chemicals in the Environment
No.4	The Toxicology of Ethylene Glycol Monoalkyl Ethers and its Relevance to Man
No.5	Toxicity of Ethylene Oxide and its Relevance to Man
No.6	Formaldehyde Toxicology : an Up-Dating of the ECETOC Technical reports 1 and 2
No.7	Experimental Assessment of the Phototransformation of Chemicals in the Atmosphere
No.8	Biodegradation Testing: An Assessment of the Present Status
No.9	Assessment of Reverse-Phase Chromatographic Methods for Determining Partition Coefficients
No.10	Considerations Regarding the Extrapolation of Biological Data in Deriving Occupational Exposure Limits
No.11	Ethylene Oxide Toxicology and its Relevance to Man : An Up-Dating of ECETOC Technical Report n°5
No.12	The Phototransformation of Chemicals in Water : Results of a Ring-Test
No.13	The EEC 6th Amendment : A Guide to Risk Evaluation for Effects on the Environment
No.14	The EEC 6th Amendment : A Guide to Risk Evaluation for Effects on Human Health
No.15	The Use of Physical-Chemical Properties in the 6th Amendment and their Required Precision, Accuracy and Limiting Values
No.16	A review of Recent Literature on the Toxicology of Benzene
No.17	The Toxicology of Glycol Ethers and its Relevance to Man : An Up-Dating of ECETOC Technical Report n°4
No.18	Harmonisation of Ready Biodegradability Tests
No.19	An Assessment of Occurrence and Effects of Dialkyl-o-Phthalates in the Environment
No.20	Biodegradation Tests for Poorly-Soluble Compounds
No.21	Guide to the Classification of Carcinogens, Mutagens and Teratogens Under the 6th Amendment

- No.22 Classification of Dangerous Substances and Pesticides in the EEC Directives. A Proposed Revision of Criteria for Inhalational Toxicity
- No.23 Evaluation of the Toxicity of Substances to be Assessed for Biodegradability
- No.24 The EEC 6th Amendment : Prolonged Fish Toxicity Tests
- No.25 Evaluation of Fish Tainting
- No.26 The Assessment of Carcinogenic Hazard for Human Beings Exposed to Methylene Chloride
- No.27 Nitrate and Drinking Water
- No.28 Evaluation of Anaerobic Biodegradation
- No.29 Concentrations of Industrial Organic Chemicals Measured in the Environment : The Influence of Physico-Chemical Properties, Tonnage and Use Pattern
- No.30(4) Existing Chemicals : Literature Reviews and Evaluations
- No.31 The Mutagenicity and Carcinogenicity of Vinyl Chloride : A Historical Review and Assessment
- No.32 Methylene Chloride (Dichloromethane) : Human Risk Assessment Using Experimental Animal Data
- No.33 Nickel and Nickel Compounds : Review of Toxicology and Epidemiology with Special Reference to Carcinogenesis
- No.34 Methylene Chloride (Dichloromethane) : An Overview of Experimental Work Investigating Species, Differences in Carcinogenicity and their Relevance to Man
- No.35 Fate, Behaviour and Toxicity of Organic Chemicals Associated with Sediments
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- No.37 Tetrachloroethylene : Assessment of Human Carcinogenic Hazard
- No.38 A Guide to the Classification of Preparations Containing Carcinogens, Mutagens and Teratogens
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- No.40 Hazard Assessment of Chemical Contaminants in Soil
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- No.43 Emergency Exposure Indices for Industrial Chemicals
- No.44 Biodegradation Kinetics
- No.45 Nickel, Cobalt and Chromium in Consumer Products: Allergic Contact Dermatitis

JACC REPORTS

<u>No.</u>	<u>Title</u>
No.1	Joint Assessment of Commodity Chemicals, Melamine
No.2	Joint Assessment of Commodity Chemicals, 1,4-Dioxane
No.3	Joint Assessment of Commodity Chemicals, Methyl Ethyl Ketone
No.4	Joint Assessment of Commodity Chemicals, Methylene Chloride
No.5	Joint Assessment of Commodity Chemicals, Vinylidene Chloride
No.6	Joint Assessment of Commodity Chemicals, Xylenes
No.7	Joint Assessment of Commodity Chemicals, Ethylbenzene
No.8	Joint Assessment of Commodity Chemicals, Methyl Isobutyl Ketone
No.9	Joint Assessment of Commodity Chemicals, Chlorodifluoromethane
No.10	Joint Assessment of Commodity Chemicals, Isophorone
No.11	Joint Assessment of Commodity Chemicals, (HFA-132b) 1,2-Dichloro-1,1-Difluoroethane
No.12	Joint Assessment of Commodity Chemicals, (HFA-124) 1-Chloro-1,2,2,2-Tetrafluoroethane
No.13	Joint Assessment of Commodity Chemicals, (HFA-123) 1,1-Dichloro-2,2,2-Trifluoroethane
No.14	Joint Assessment of Commodity Chemicals, (HFA-133a) 1-Chloro-2,2,2-Trifluoroethane
No.15	Joint Assessment of Commodity Chemicals, (HFA-141B) 1-Fluoro 1,1-Dichloroethane
No.16	Joint Assessment of Commodity Chemicals, (HCFC-21) Dichlorofluoromethane
No.17	Joint Assessment of Commodity Chemicals, (HFA-142b) 1-Chloro-1,1-Difluoroethane
No.18	Joint Assessment of Commodity Chemicals, Vinylacetate
No.19	Joint Assessment of Commodity Chemicals, Dicyclopentadiene
No.20	Joint Assessment of Commodity Chemicals, Tris-/Bis-/Mono-(2-ethylhexyl)phosphate
No.21	Joint Assessment of Commodity Chemicals, Tris-(2-butoxyethyl)-phosphate