

Tris (2-Ethylhexyl) Phosphate *(trioctyl phosphate)*

Tris (2-ethylhexyl) phosphate (TEHP) has been widely used as a plasticizer, fire retardant and solvent. As a plasticizer, it is used as a component of vinyl stabilizers, grease additives and flame-proofing compositions for vinyl plastic and synthetic rubber compounds. As a fire retardant, it is used in consumer products, such as clothing. As a solvent, it is used as a co-solvent to produce hydrogen peroxide. The world production of TEHP was estimated to be between 1000 to 5000 tons per year (IPCS, 2000). Occupational exposure may occur through inhalation and dermal contact with TEHP at workplaces (HSDB, 2010). The general population may be exposed to TEHP via ingestion of contaminated food and drinking water (HSDB, 2010) or via dermal contact with TEHP-treated clothing.

TEHP passed the animal data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data

No cancer epidemiology studies were identified.

Animal carcinogenicity data

- Long-term gavage studies
 - 103-week studies in male and female B6C3F₁ mice: NTP (1984)
 - *Increase in hepatocellular carcinomas (by pairwise comparison and trend) in females*
 - *No treatment-related tumor findings in males*
 - 103-week studies in male and female F344/N rats: NTP (1984)
 - *Increases in adrenal pheochromocytomas (combined benign and malignant) (by pairwise comparison and trend), thyroid follicular cell adenomas, cystadenomas, or carcinomas (combined) (by trend) in males*
 - *Occurrence of a single rare, malignant, mixed salivary gland tumor in high-dose males*
 - *No treatment-related tumor findings in females*

Other relevant data

- Genotoxicity
 - Review: NTP (1984, pp. 139-140)
 - *Salmonella* reverse mutation assays in strains TA98, TA100, TA1535, or TA1537 (*negative*)
 - Review: IPCS (2000, pp. 54-55)
 - Micronucleus assay in B6C3F1 mouse bone marrow cells *in vivo* (*positive and negative*)
 - Mouse lymphoma cell mutation assay *in vitro* (*negative*)
 - Sister chromatid exchange (SCE) in Chinese hamster ovary (CHO) cells *in vitro* (*negative*)
 - Chromosomal aberrations in CHO cells *in vitro* (*negative*)
 - Chromosomal aberration assay in B6C3F1 mouse bone marrow cells *in vivo* (*negative*)
 - Liver unscheduled DNA synthesis assay in B6C3F1 mouse *in vivo* (*negative*)

- Structural activity considerations
 - Some structural similarity to organophosphate carcinogens listed under Proposition 65:
 - trimethylphosphate
 - tris(2-chloroethyl)phosphate
 - tris(2,3-dibromopropyl)phosphate

Reviews

- IPCS (2000)

References¹

Hazardous Substances Data Bank (HSDB, 2010). National Library of Medicine. Bethesda, MD.

International Programme on Chemical Safety (IPCS) (2000). Environmental Health Criteria For Flame Retardants: Tris(2-Butoxyethyl) Phosphate, Tris(2-Ethylhexyl) Phosphate, Tetrakis(Hydroxymethyl) Phosphonium Salts. Environmental Health Criteria 218, World Health Organization, Geneva.

Kluwe WM, Huff JE, Matthews HB, Irwin R, Haseman JK (1985). Comparative chronic toxicities and carcinogenesis potentials of 2-ethylhexyl-containing compounds in rats and mice. *Carcinogenesis* **6**:1577-1583.

¹ Excerpts or the complete publication have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.

National Toxicology Program (NTP, 1984). Toxicology and Carcinogenesis Studies of Tris(2-ethylhexyl)phosphate (CAS No. 78-42-2) in F344/N rats and B6C3F1 mice (Gavage studies). NTP Technical Report No. 274. NIH Publication No. 84-2530. National Toxicology Program, Research Triangle Park, NC.