



## **Evaluation of Tris(2-chloroethyl) phosphate (TCEP) as a Possible Chemical of High Concern for MOU Listing in Connecticut**

### **Summary:**

TCEP Toxicity: High Concern, Hazard Rank Score = 8 points

TCEP Children's Exposure: High Concern, Exposure Rank Score = 20 points

Overall Assessment (tox and exposure combined): High Concern

Candidate for MOU Listing: Yes

Total Rank Score = 160 points

### **1) Persistence in body and/or environment: Low concern (0 points)**

- Half-life in rats is less than 1 day as evidenced by studies showing most of an administered dose in rats is excreted in urine within 24 hrs as metabolites with the remainder in bile (ATSDR 2012). Little bioaccumulation expected given the relatively low Kow.
- Persistence in environment is expected to be low to moderate as TCEP has some volatility and mobility and relatively low Kow (1.5-2).
- Overall assessment – Low concern for human and environmental persistence and accumulation

### **2) Acute Toxicity: Moderate concern (0 points)**

- ECHA lists the TCEP oral LD50 in rats as 430-1230 mg/kg giving it a moderate level of concern for this property. Its acute toxicity may be based upon its organophosphate structure which can confer acetylcholinesterase inhibition properties at high dose.

### **3) Repeat Dose Testing: Moderate concern (2 points)**

- NTP 1991 conducted subchronic and chronic TCEP gavage dosing in rats and mice demonstrated histopathological effects to the brain (hippocampus) and kidney as sensitive endpoints. ATSDR 2012 calculated a variety of BMDL<sub>10</sub> for these endpoints, the lowest being 23 mg/kg/d (adjusted for continuous exposure) for renal tubule hyperplasia in female rats. This BMDL for a minimal toxic effect is in the moderate concern range. USEPA's PPRTV assessment found a LOAEL at a dose where ATSDR determined a NOAEL and so their benchmark dose for a mild effect (kidney weight changes) is 7 mg/kg/d rather than the 23 mg/kg/d derived by ATSDR. The PPRTV is in a moderate to high concern range but the effect is mild and so moderate concern for repeat dose testing is appropriate.

**4) Mutagenicity/Genotoxicity: No concern (0 points)**

- Numerous tests have been run on TCEP with predominantly negative results, both in mammalian and bacterial systems, mutagenicity and cytogenicity and in vivo and in vitro (ECHA 2008).

**5) Reproductive/Developmental Toxicity: Moderate concern (2 points)**

TCEP has also been tested in a rat developmental study and a mouse reproductive (fertility) study as summarized in [CalEPA 2015](#), and [WHO 1998](#). Gavage of pregnant rats during gestation at 3 relatively high doses (50 to 200 mg/kg/d) yielded minor structural variants but no malformations or other fetotoxicity or postnatal developmental abnormalities or neurotoxicity. However, fertility was adversely affected in the mouse study at all doses tested including the lowest dose (175 mg/kg/d via gavage). TCEP decreased the number of litters produced and the number of viable pups per litter, with an effect on male fertility (sperm parameters) potentially at the root of the fertility issue in dosed mice (Gulati et al. 1991 as reported by WHO and CalEPA). A NOAEL was not identified but using standard risk assessment approaches, using a 10 fold extrapolation from the LOAEL would yield a NOAEL of 17.5 mg/kg/d. A finding of a severe effect in the 100 to 1000 mg/kg/d dose range warrants a moderate level of concern for repeat dose testing.

**6) Carcinogenicity: High concern (4 points) – clearly positive results in rats, both sexes, and in mice; kidney cancer common to both species and genders; other sites also possible**

- NTP studies in rats and mice (1991) found several potential cancer endpoints with renal tubule adenomas the most consistent finding across species and genders. This effect was seen at doses as low as 44 mg/kg/d in the NTP chronic gavage studies. USEPA PPRTV 2009 derived a cancer slope factor of 0.02/mg-kg-d based upon the renal tubule adenomas+carcinomas in male mice.

**Total Toxicology Rank = 8 points**

## TCEP Exposure Ranking

1) Is the chemical currently in children's products? Yes, publications from 2011 (Stapleton et al., available [here](#)) and 2014 (Bradman et al.) document this flame retardant in children's products involving foam padding such as crib bumpers, sleep mats, changing table pads and portable mattresses. The 2014 paper showed an association between day care centers which use padded nap mats and higher levels of TCEP in the floor dust (Bradman et al. 2014). This suggests a key exposure pathway to young children is volatilization of TCEP from foam padding followed by direct inhalation as well as ingestion of floor dust. Since children would be in closest contact with such padding and since children spend more time on the floor, they are expected to receive the greatest TCEP exposures from foam padding used in children's products. Other research has shown the presence of TCEP in young children's environment as evidenced by dosimeter silicone wrist bands (Kile et al. 2016), hand wipes and indoor air (Xu et al. 2016).

2) Is there indirect evidence that TDCPP might be in children's products?

- Chemical is widely used in commerce/other household products

Yes, TCEP has been a commercially important replacement for the banned/phased out PBDE flame retardants and as such has been used in a variety of foam products such as couch cushions.

- Chemical is not banned from children's products

A ban on TCEP in children's products has been the subject of legislative proposals in Connecticut but these have not become law. There is no federal legislation along these lines.

- Is the chemical found in house dust?

Yes, numerous studies have detected TCEP in house dust in the US. Studies reviewed by CT DPH indicate a range of TDCPP concentrations of 0.83 (median) to 110(maximum detect) ppm in the dust of US homes which were sampled recently.

- Chemical is found in indoor air

Yes, with this perhaps the main exposure pathway for TCEP in the home environment (Xu et al. 2016).

- Chemical is found in children's biomonitoring studies at levels higher than adults

There is insufficient biomonitoring data for this flame retardant to compare across age groups.

- 3) Is the amount of chemical exposure in children within range of a health benchmark?

Likely No. While a formal quantitative risk assessment has not been conducted on children's exposures from products and the indoor environment, a screening level assessment suggests a small degree of cancer risk from levels commonly detected in house dust. Using the PPRTV slope factor (0.02/mg-kg-d) and pro-rating for children's maximal time of exposure (0-2 years) without application of USEPA ADAFs (TCEP unlikely to be a mutagenic carcinogen) yields a de minimis (1 in a million) dose of 0.5 ug/kg/d. The median house dust ingestion dose is 0.005 ug/kg/d, approximately 100 times below the de minimis dose.

- 4) Is the chemical currently in products children frequently contact but not designed for children?

Yes, couches, bedding, any foam-padded product around the home may contain TCEP.

### **Summary of Exposure Assessment for TCEP**

TCEP receives a high concern for exposure (20 points) because there is direct evidence that it is present in children's products (e.g., crib bumpers, sleep mats). This merits an exposure rank score of 20 points. Indirect evidence is supportive of this finding. The amount of TCEP exposure from children's ingestion of house dust appears to be well below de minimis cancer risk and so the exposure rank score is not enhanced on the basis of current estimates of exposure in house dust. However, inhalation of TCEP may substantially add to the overall exposure in a child's indoor environment.

### **Quantitative Score for Ranking**

Toxicology Score: 8

Exposure Score: 20

Total Score: 160

## References

- ATSDR 2012. Toxicological Profile for Phosphate Ester Flame Retardants. (Available [here](#))
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- ECHA (European Chemicals Bureau) 2008. Tris(2-Chloroethyl)phosphate: Risk Assessment Report. (Available [here](#))
- Gulati, D.K., et al. 1991. Final report on the reproductive toxicity of tris(2-chloroethyl)phosphate reproduction and fertility assessment in Swiss CD-1 mice when administered via gavage. PB92-129170 (as cited in USEPA 2009 and ATSDR 2012).
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- Xu F, et al. 2016. Comprehensive Study of Human External Exposure to Organophosphate Flame Retardants via Air, Dust, and Hand Wipes: The Importance of Sampling and Assessment Strategy. *Environ Sci Technol*.50(14):7752-60.

# TCEP Ranking for MOU Prioritization

