Evaluation of Tris (1,3-dichloro-2-propyl)phosphate, TDCPP)

as a Possible Chemical of High Concern for MOU Listing in Connecticut

Summary:

TDCPP Toxicity: Very High Concern, Hazard Rank Score = 16 points
TDCPP Children's Exposure: High Concern, Exposure Rank Score = 40 points
Overall Assessment (tox and exposure combined): High Concern
Candidate for MOU Listing: Yes
Total Rank Score = 640 points

1) **Persistence in body and/or environment: Moderate concern (2 points)**
   - Half-life in rats is less than 5 days (Lynn et al. 1981); efficiently metabolized in liver followed by metabolite excretion. Some bioaccumulation expected because log Kow of 3.65 would suggest that any that bypasses hepatic metabolism could be retained in fat.
   - Persistence in environment is expected to be moderate as it is resistant to hydrolysis and biodegradation. Further, its relatively high Kow suggests bioconcentration in fish and terrestrial species.
   - Overall assessment – Moderate concern for human and environmental persistence and accumulation

2) **Acute Toxicity: No concern (0 points)**
   - WHO 1998 lists the TDCPP oral LD50 in rats as 2830 mg/kg giving it a low level of concern for this property. Its acute toxicity is likely based upon its organophosphate structure which can confer acetylcholinesterase inhibition properties at high dose.

3) **Repeat Dose Testing: High concern (4 points)**
   - ATSDR 2012 Tox Profile identifies Stauffer 1981 as providing intermediate (12 month) and chronic (24 month) dietary rat studies, most sensitive effect on the kidneys, **BMDL = 1.94** mg/kg/d divided by 100 fold cumulative UF to yield chronic MRL of 0.02 mg/kg/d
   - Much of tox database is missing as TDCPP has not been tested in mammalian reproductive, developmental or neurotoxicity testing. ATSDR UF did not include a database UF.

4) **Mutagenicity/Genotoxicity: High concern (4 points)**
   - Numerous tests have been run on TDCPP with mixed results; however, where results were positive they were clearly positive and not due to high dose cytotoxicity. The range of screens that were positive includes bacterial mutagenicity (Salmonella), mammalian mutagenicity (mouse lymphoma assay), in vitro chromosomal aberrations and sister chromatid exchange, and transformation of SHE cells, (Cal OEHHA 2011; ATSDR 2012). In vivo testing has generally been negative for chromosome damage although TDCPP was shown to bind covalently to DNA.
   - TDCPP is the chlorinated analogue of TDBPP, a known Tris carcinogen and mutagen. While some in vitro and in vivo testing TDCPP is a less potent genotoxicant than TDBPP, this structural analogy further supports the evidence for genotoxicity.

5) **Reproductive/Developmental Toxicity: Uncertain concern (2 points)**
   - No data

6) **Carcinogenicity: High concern (4 points) – clearly positive results in rats, both sexes, with mutagenicity evidence but only one cancer study**
   - Listed in Cal Prop 65 as known carcinogen, 2011 determination, with a cancer slope factor derivation from the 1981 rat data (see below) of 0.13/mg-kg-d. When considering young children's time of exposure compared to a full lifetime (2 yrs over 70), and with the application of age-dependent adjustment factors (ADAFs) for early life carcinogens the de minimis (1 per million) exposure level is estimated to be 0.017 ug/kg/d.
   - Positive in rat dietary study (1981) in males and females (liver and kidney, both sexes, adrenal females, interstitial cell males)

Total Toxicology Rank = 16 points

TDCPP 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 and sleep mats. Other children's products which may contain TDCPP in foam padding are children's bedding materials such as cots, playpens, and bassinets. The 2014 paper showed an association between day care centers which use padded nap mats and higher levels of TDCPP in the floor dust (Bradman et al. 2014). This suggests a key exposure pathway to young children is volatilization of TDCPP 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 TDCPP exposures from foam padding used in children's products. Other research has shown that foam mats and cushions used at gymnast schools contain this flame retardant with levels detected in both the product (mats, cushions) and in floor dust (LaGuardia and Hale 2015). Children are frequent users of such facilities.

2) Is there indirect evidence that TDCPP might be in children's products?
   - Chemical is widely used in commerce/other household products

   Yes, TDCPP 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 TDCPP in children's products has been the subject of legislative proposals in Connecticut but these have not become law. Several states including VT, MD and WA have banned TDCPP in children's products. There is no federal legislation along these lines.

   - Is the chemical found in house dust?

   Yes, numerous studies have detected TDCPP in house dust in the US. Studies reviewed by CT DPH indicate a range of TDCPP concentrations of 1.6 (median) to 101(maximum detect) ppm in the dust of US homes which were sampled recently.

   - Chemical is found in indoor air

   This is a low volatility chemical which will primarily be in dust particles rather than indoor air. However, there is likely to be some fraction present as a volatile in homes as it vaporizes from foam products to enter air and dust.

- 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 Yes. 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 degree of cancer risk from levels commonly detected in house dust. Using the CalOEHHA slope factor (0.13/mg-kg-d) and pro-rating for children's maximal time of exposure (0-2 years) with application of the USEPA ADAF for mutagenic carcinogens yields a de minimis dose of 0.017 ug/kg/d as described above. The median house dust ingestion dose is 0.01 ug/kg/d, just below the de minimis dose but the upper bound exposure estimate based upon the maximal concentration found in house dust is approximately 50 times de minimis.

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.

Summary of Exposure Assessment for HBCD

TDCPP receives a high concern for exposure (20 points) because there is direct evidence that it is present in children's products (e.g., child's padded chair, car seats). This merits an exposure rank score of 20 points. Indirect evidence is supportive of this finding. The amount of TDCPP exposure from children's ingestion of house dust appears to range above de minimis cancer risk which doubles the exposure rank score from 20 to 40 points.

Quantitative Score for Ranking

Toxicology Score: 16

Exposure Score: 40

Total Score: 640

References:

ATSDR 2012. Toxicological Profile for Phosphate Ester Flame Retardants. *(Available here)*

Bradman A et al. 2014. Flame retardant exposures in California early childhood education environments. Chemosphere. 116:61-66.

California OEHHA. 2011. tris(1,3-dichloro-2-propyl) phosphate (TDCPP) Listed Effective October 28, 2011 as Known to the State to Cause Cancer. *(Available here)*

La Guardia MJ and Hale RC. 2015. Halogenated flame-retardant concentrations in settled dust, respirable and inhalable particulates and polyurethane foam at gymnastic training facilities and residences. Environ Int. 79:106-114.

Lynn RK 1980. Diester metabolites of the flame retardant chemicals, tris(1,3-dichloro-2-propyl)phosphate and tris(2,3-dibromopropyl) phosphate in the rat: identification and quantification. Res Commun Chem Pathol Pharmacol. 28(2):351-60.

Stapleton HM et al. 2011. Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol. 45(12):5323-31.

World Health Organization 1998. Environmental Health Criteria 209: Flame Retardants, Tris(chloropropyl) phosphate and tris(2-chloroethyl) phosphate. International Program on Chemical Safety. *(Available here)*

TDCPP Ranking for MOU Prioritization