



### **CAS 115-86-6 - Triphenyl phosphate (TPP)**

#### **Toxicity**

Endocrine disruption, developmental, neurological, and reproductive toxicity is observed in animals exposed to TPP.<sup>1-7</sup>

EPA classified TPP to have a moderate potential for carcinogenicity and bioaccumulation based on modeling.<sup>8</sup>

Mice fed TPP for 35 days showed oxidative liver stress, testicular tissue damage, and decreased testicular testosterone levels, testes weight, and testosterone synthesis related gene expression.<sup>9</sup> TPP has shown to be a moderate androgen-receptor binder and estrogen receptor agonist in *in vitro* testing.<sup>8</sup> *In vitro* testing has also showed TPP to be a mitochondrial activity inhibitor.<sup>10</sup> Metabolic disruption was observed in offspring of rats exposed to a commercial mixture containing TPP.<sup>11</sup>

#### **Exposure**

Triphenyl phosphate is primarily used as a plasticizer and flame retardant.<sup>12</sup> TPP has been used as a flame retardant in PVC, electronics, glues, casting resins, and hydraulic fluids, and as a plasticizer in hydraulic fluids, varnishes and lacquers including nail polish.<sup>3,12</sup> A TPP metabolite has been detected in human urine after application of nail polish.<sup>3</sup>

TPP has been detected throughout the environment in air, household dust, surface water, soil and sediment.<sup>13-21</sup>

TPP can bioaccumulate in fish.<sup>19</sup> TPP was added to the Toxic Substance Control Act work plan in 2014 due to its moderate persistence and bioaccumulation potential and acute and chronic aquatic toxicity.<sup>22</sup>

A metabolite of TPP was found through biomonitoring in human urine collected throughout North America.<sup>17,23,24</sup> DPHP, a metabolite of TBB, was detected in 100

percent of urine samples collected from pregnant women in a China.<sup>25</sup> An Indiana study detected TPP in hair and nails of young adults.<sup>26</sup> TPP was detected in breast milk in Swedish and Asian studies.<sup>27,28</sup>

## Other

TPP is a component of the commercial flame-retardant mixture Firemaster 550.<sup>12</sup>

## References

1. Boris, V., Krivoshiev, F.D., Covaci, A., Blust, R., Husson, S.J., (2016). Assessing in-vitro estrogenic effects of currently-used flame retardants. *Toxicology in Vitro*, 33, 153-162.
2. Du, Z., Zhang, Y., Wang, G., Peng, J., Wang, Z., & Gao, S. (2016). TPhP exposure disturbs carbohydrate metabolism, lipid metabolism, and the DNA damage repair system in zebrafish liver. *Scientific Reports*, 6, 21827. doi: 10.1038/srep21827.
3. Mendelsohn, E., Hagopian, A., Hoffman, K., Butt, C.M., Lorenzo, A., Congleton, J., Webster, T.F., Stapleton, H.M. (2015). Nail polish as a source of exposure to triphenyl phosphate. *Environment International*, 86, 45–51.
4. Green, A.J., Graham, J.L., Gonzalez, E.A., La Frano, M.R., Petropoulou, S.E., Park, J.S., Newman, J.W., Stanhope, K.L., Havel, P.J., La Merrill, M.A. (2016). Perinatal triphenyl phosphate exposure accelerates type 2 diabetes onset and increases adipose accumulation in UCD-type 2 diabetes mellitus rats. *Reproductive Toxicology*, 68, 119-129. doi: 10.1016/j.reprotox.2016.07.009.
5. Behl, M., Hsieh, J.H., Shafer, T.J., Mundy, W.R., Rice, J.R., Boyd, W.A., Freedman, J.H., Hunter, E.S., Jarema, K.A., Padilla, S., Tice, R.R. (2015). Use of alternative assays to identify and prioritize organophosphorus flame retardants for potential developmental and neurotoxicity. *Neurotoxicology and Teratology*, 52, 181–193.
6. Liu, X., Ji, K., Choi, K. (2012). Endocrine disruption potentials of organophosphate flame retardants and related mechanisms in *H295R* and *MVLN* cell lines and in zebrafish. *Aquatic Toxicology*, 114-115, 173-181.
7. Liu, X., Ji, K., Jo, A., Moon, H., & Choi, K. (2013). Effects of TDCPP or TPP on gene transcriptions and hormones of HPG axis, and their consequences on reproduction in adult zebrafish (*Danio rerio*). *Aquatic Toxicology*, 134-135, 104-111.
8. EPA (2015). *Flame retardants used in flexible polyurethane foam: An alternatives assessment update*. U.S. Environmental Protection Agency. Retrieved from [https://www.epa.gov/sites/production/files/2015-08/documents/ffr\\_final.pdf](https://www.epa.gov/sites/production/files/2015-08/documents/ffr_final.pdf)
9. Chen, G., Jin, Y., Wu, Y., Liu, L., Fu, Z. (2015). Exposure of male mice to two kinds of organophosphate flame retardants (OPFRs) induced oxidative stress and endocrine disruption. *Environmental Toxicology and Pharmacology*, 40(1), 310-8.

10. Behl, M. & Smith, M.V. (2016). Comparative toxicity of organophosphate flame retardants and polybrominated diphenyl ethers to *Caenorhabditis elegans*. *Toxicol Sciences*, 154(2), 241-252.
11. Patisaul, H.B., Roberts, S.C., Mabrey, N., McCaffrey, K.A., Gear, R.B, Braun, J., Belcher, S.M., Stapleton, H.M. (2013). Accumulation and endocrine disrupting effects of the flame retardant mixture Firemaster(R) 550 in rats: an exploratory assessment. *Journal of Biochemical and Molecular Toxicology*, 27(2), 124-36.
12. Toxicology Excellence for Risk Assessment (TERA) (2015). *Environmental concentrations and consumer exposure data for selected flame retardants (TDCPP, TCPP, TEP, TPP)*. June 1, 2015: Consumer Product Safety Commission contract Number CPSC-D-12-0001. Retrieved from <https://www.cpsc.gov/s3fs-public/pdfs/CPSC%2520Staff%2520Statement%2520on%2520Toxicology%2520ExcellenceRiskAssessmentsReportExposureDataSelectedFlameRetardants.pdf>
13. Meeker, J.D. & Stapleton, H.M. (2010). House dust concentrations of organophosphate flame retardants in relation to hormone levels and semen quality parameters. *Environmental Health Perspectives*, 118(3), 318-23.
14. van der Veen, I. & de Boer, J. (2012). Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis. *Chemosphere*, 88(10), 1119-53.
15. He, R., Li, Y., Xiang, P., Li, C., Zhou, C., Zhang, S., Cui, X., Ma, L.Q. (2015). Organophosphorus flame retardants and phthalate esters in indoor dust from different microenvironments: Bioaccessibility and risk assessment. *Chemosphere*, 150, 528-535. doi: 10.1016/j.chemosphere.2015.10.087.
16. Abdallah, M.A., & Covaci, A. (2014). Organophosphate flame retardants in indoor dust from Egypt: Implications for human exposure. *Environmental Science & Technology*, 48(9), 4782-4789.
17. Cequier, E., Skhi, A.K., Marce, R.M., Becher, G., Thomsen, C. (2015). Human exposure pathways to organophosphate triesters - a biomonitoring study of mother-child pairs. *Environment International*, 75, 159-65.
18. Fan, X., Kubwabo, C., Rasmussen, P.E., Wu, F. (2014). Simultaneous determination of thirteen organophosphate esters in settled indoor house dust and a comparison between two sampling techniques. *Science of the Total Environment*, 491-492, 80-6.
19. Salamova, A., Ma, Y., Venier, M., Hites, R.A. (2014). High levels of organophosphate flame retardants in the Great Lakes atmosphere. *Environmental Science & Technology Letters*, 1(1), 8-14.
20. Cao, S., Zeng, X., Song, H., Li, H., Yu, Z., Sheng, G., Fu, J. (2012). Levels and distributions of organophosphate flame retardants and plasticizers in sediment from Taihu Lake, China. *Environmental Toxicology and Chemistry*, 31(7), 1478-84.
21. Dodson, R.E., Perovich, L.J., Covaci, A., Van den Eede, N., Ionas, A.C., Dirtu, A.C., Brody, J.G., Rudel, R.A. (2012). After the PBDE phase-out: A broad suite of flame

- retardants in repeat house dust samples from California. *Environmental Science & Technology*, 46, 13056–13066.
22. EPA. (2015). *TSCA Work plan chemical problem formulation and initial assessment - chlorinated phosphate ester cluster flame retardants*. Environmental Protection Agency. Retrieved from [https://www.epa.gov/sites/production/files/2015-09/documents/cpe\\_fr\\_cluster\\_problem\\_formulation.pdf](https://www.epa.gov/sites/production/files/2015-09/documents/cpe_fr_cluster_problem_formulation.pdf)
  23. Meeker, J.D., Cooper, E.M., Stapleton, H.M., Hauser, R. (2013). Urinary metabolites of organophosphate flame retardants: temporal variability and correlations with house dust concentrations. *Environmental Health Perspectives*, 121(5), 580-5.
  24. Butt, C.M., Congleton, J., Hoffman, K., Fang, M., Stapleton, H.M. (2014). Metabolites of organophosphate flame retardants and 2-ethylhexyl tetrabromobenzoate in urine from paired mothers and toddlers. *Environmental Science & Technology*, 48(17), 10432-8.
  25. Liping F., Fengxiu O., Liangpo L., Xu, W., Xia, W., Yi-Ju, L., Amy, M., Heqing, S., Jungfeng, Z., Jun Jim, Z. (2016). Levels of urinary metabolites of organophosphate flame retardants, TDCIPP, and TPHP, in pregnant women in Shanghai. *Journal of Environmental and Public Health*, Article ID 9416054. doi:10.1155/2016/9416054.
  26. Liang-Ying Liu, K.H., Hites, R.A., & Salamova, A. (2016). Hair and nails as noninvasive biomarkers of human exposure to brominated and organophosphate flame retardants. *Environmental Science & Technology*, 50, 3065–3073.
  27. Kim, J.W., Isobe, T., Muto, M., Tue, N.M., Katsura, K., Malarvannan, G., Sudaryanto, A., Chang, K.H., Prudente, M., Viet, P.H., Takahashi, S., Tanabe, S. (2014). Organophosphorus flame retardants (PFRs) in human breast milk from several Asian countries. *Chemosphere*, 116, 91-7.
  28. Sundkvist, A.M., Olofsson, U., and Haglund, P. (2010). Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. *J Journal of Environmental Monitoring.*, 12(4), 943-51.