Batch 2 articles in green shading. Batch 1 articles in gray shading. Articles with no shading have not been shared (yet) with the Board

Batch	Added to Data Display	Substance	Year	Author	Endpoint	Title	Concentration	Test substance	Effect/ Summary
2		TPP, DPHP	2023	Australia	Environmental Hazard and risk	Triphenyl phosphate and diphenyl phosphate: Evaluation statement	N/A	many	Evaluated for environmental risks. TPP 96 h LC50 = 0.36 mg/L rainbow trout EPA 660/3-75-009; DPHP 96h LC50 = 49.98 zebrafish
2	Y	TPHP, IPP, EHDP, BPDP, TMPP, IDDP	2015	Behl et al	DT, DNT	Use of alternative assays to identify and prioritize organophosphorus flame retardants for potential developmental and neurotoxicity	1-10uM	mouse embryonic stem cells, the proliferation and growth of human neural stem cells, rat neuronal growth and network activity, and development of nematode (Caenorhabditis elegans) and zebrafish (Danio rerio)	For all of the potential adverse outcomes of concern (developmental, developmental neurotoxicity and acute neurotoxicity), it is clear based on the results in Table 3 that the OPFRs as a group have activity in these assays with potencies comparable to that of the BFRs
2		TPP	2022	Chen et al.	ecotox	Ecotoxicity assessment of triphenyl phosphate (TPhP) exposure in Hoplobatrachus rugulosus tadpoles	For acute toxicity: 20, 100, 200, and 400 mg/L; For sub-chronic toxicity: 10, 50, 100, and 200 μg/L, of which 50 μg/L was similar to the max TPP concentration reported in water	Tadpoles	In the acute toxicity analysis, the 96-h median lethal concentration (LC50) for GS35 Hoplobatrachus rugulosus tadpoles was 2.893 mg/L, and the 10% effect concen tration (EC10) was 289 μg/L. After two weeks of exposure to low TPhP concentrations, the survival and metamorphosis rates of H. rugulosus tadpoles decreased, and the metamorphosis time was prolonged as the TPhP concentration increased. The threshold concentration that affected tadpole survival and metamorphosis time was 50 μg/L and 100 μg/L, respectively. No significant differences were observed in the condition factor and hepatic somatic index of the tadpole after metamorphosis; however, tadpole body mass and TPhP concentration were negatively correlated. Further, TPhP inhibited the expressions of Cu–Zn sod and cat, thereby reducing the ac tivities of superoxide dismutase and catalase in the tadpole liver. The threshold for affecting gene expression and enzymatic activity was 100 μg/L. These findings provide significant insights on the stress ecology of aquatic organisms.
2	Y	TCP, IPP, TPHP, IDDP	2021	Hogberg	DNT	Organophosphorus flame retardants are developmental neurotoxicants in a rat primary brainsphere in vitro model	0.1-5uM	rat brain cell cultures	Employing mass spectroscopy-based metabolomics and transcriptomics, we observe at similar human-relevant non-cytotoxic concentrations (0.1–5 μM) stronger developmental neurotoxic effects by OPFR. This includes toxicity to neurons in the low μM range; all FR decrease the neurotransmitters glutamate and GABA (except BDE-47 and TPHP). Furthermore, n-acetyl aspartate (NAA), considered a neurologic diagnostic molecule, was decreased by all OPFR. At similar concentrations, the FR currently in use decreased plasma membrane dopamine active transporter expression, while BDE-47 did not. Several findings suggest astrogliosis induced by the OPFR, but not BDE-47. At the 5 μM concentrations, the OPFR more than BDE-47 interfered with myelination. An increase of cytokine gene and receptor expressions suggests that exposure to OPFR may induce an inflammatory response. Pathway/category overrepresentation shows disruption in 1) transmission of action potentials, cell–cell signaling, synaptic transmission, receptor signaling, (2) immune response, inflammation, defense response, (3) cell cycle and (4) lipids metabolism and transportation.
2	Y	TPP, EHDP	2022	Hou et al	TPP, EHDP	Penetration of Organophosphate Triesters and Diesters across the Blood–Cerebrospinal Fluid Barrier: Efficiencies, Impact Factors, and Mechanisms	0.062 to 1.62 and 0.042–1.11 ng/mL	human serum and CSF	Their penetration efficiencies across the blood–CSF barrier (BCSFB) (RCSF/serum, CCSF/Cserum) were calculated at 0.667–2.80, and these efficiencies first increased and then decreased with their log Kowvalues. The reduced penetration efficiencies of triphenyl phosphate (TPHP) and 2-ethylhexyl diphenyl phosphate (EHDPP) may be attributed to their strong binding affinities for human serum albumin and p-glycoprotein due to their high hydrophobicity and aryl structure, as indicated by molecular docking. This suggests that active efflux transport may be involved in the penetration of TPHP and EHDPP in addition to passive diffusion similar to the other four tri-OPEs. Di-OPEs were found in few serum samples and even fewer CSF samples, indicating their limited BCSFB permeability. This may be due to their high polarity, low hydrophobicity, and ionic state in blood.
2	Y	TPP	2020	Hu et. al.	metabolic immunotoxicity	Triphenyl phosphate modulated saturation of phospholipids: Induction of endoplasmic reticulum stress and inflammation	10uM, 20uM	murine macrophage cells	The expression of the gene encoding lysophosphatidylcholine acyltransferase 3 (Lpcat3) was significantly downregulated by 0.76 ± 0.03 and 0.70 ± 0.08-fold in 10 and 20 uM TPHP exposure groups, relative to the control group. This finding explains the observed decrease in lipid saturation. Correspondingly, exposure to 10 and 20 mM TPHP induced endoplasmic reticulum (ER) stress and inflammatory responses, which have been linked to metabolic dysfunction such as insulin resistance and hypertriglyceridemia. Therefore, TPHP may pose a risk to human health by promoting metabolic diseases.
2		TPP	2021	Kawashima et al	RT, ED	Summary of 17 chemicals evaluated by OECD TG229 using Japanese Medaka, Oryzias latipes in EXTEND 2016	2.13, 7.19, 17.1, 44.9 ug/L	Japanese medaka	TPP significantly reduced VTG levels in females in vivo but did not inhibit the transcriptional activity induced by competitvely spiked E2 in vitro RGAs. A statistically significant decrease in fecundity was observed for TPP. No significant effect on fertility rate was suggested for TPP in which a significant decrease of number of total eggs was found. the LOEC (repro)/MEC ratio was relatively small indicating a concern of environmental risk related to endocrine disrupting activities.
2		TPP	2019	Li et al	RT	Triphenyl Phosphate at Environmental Levels Retarded OvaryDevelopment and Reduced Egg Production in Japanese Medaka (Oryzias latipes)	1.6, 8, 40 ug/L for 100 days and 21 days	Japanese medaka	Overall, we found that TPhP can be accumulated in thelivers and ovaries of female fish, and induce ovary retardationat environmentally relevant concentrations. The mERantagonistic activity of TPhP and its metabolite 4-OH-TPhPmay initially inhibit ovary development and vtg transcription.The retardation of ovary development induced by long-termexposure of TPhP could reduce the plasma 17β-E2 level, andfurther a ffect vtg transcription, which would in turn exacerbatethe retardation of ovary development. Thus, the mERantagonistic activity of TPhP and its metabolite may play akey role in the retardation of ovary development at lowconcentrations. The impairment of the testicular developmentand reproductive behavior in male fish at environmental levelsof TPhP has been reported in our previous study.21 Thepresent study demonstrated the reproductive decline of female fish at low TPhP concentrations.
2		TPP	2018	Li et al	RT	Environmentally Relevant Concentrations of the Organophosphorus Flame Retardant Triphenyl Phosphate Impaired Testicular Development and Reproductive Behaviors in Japanese Medaka (Oryzias latipes)	134.1, 299.1, 1429.5 ng/L 0-100 dph	Japanese medaka	TPhP induced gonadal intersex in male medaka in all exposure groups, and a significant increase was observed in the 1429.5 ng/L exposure group, with an incidence of 26.2% (11 of 42; $p < 0.01$). TPhP exposure also caused abnormal chasing behavior, with a lowest observable effective concentration (LOEC) of 299.1 ng/L, and reduced the desire of males for females in the 1429.5 ng/L group, demonstrating toxicity for fish reproductive behaviors. The anti-androgenic activity of TPhP via both androgen suppression and AR blocking was proposed to be the major mechanism of the observed effects.
2	Y	TPP, mITP	2013	McGee et al	NT	Aryl Phosphate Esters Within a Major PentaBDE Replacement Product Induce Cardiotoxicity in Developing Zebrafish Embryos: Potential Role of the Aryl Hydrocarbon Receptor	TPP (4μM), mono-ITP (0.5μM) for (1) 5.25–96 hpf, (2) 10–96 hpf, (3) 24–96 hpf, and (4) 48–96 hpf	zebrafish	(1) MonoITP–induced cardiotoxicity in zebrafish embryos is mediated through an AHR-dependent pathway (albeit independent of AHR2); (2) despite high structural similarity to mono-ITP, similar cardiotoxic phenotypes resulting from TPP exposure are independent of AHR activation; and (3) mono-ITP is a potent activator of human AHR-dependent transcription.

2	Y	TPP, TCP, BPDP, DPP, EHDP, IDDP, ITPs, mITP, RDP	2015	Noyes et al	DNT	Advanced Morphological — Behavioral Test Platform Reveals Neurodevelopmental Defects in Embryonic Zebrafish Exposed to Comprehensive Suite of Halogenated and Organophosphate Flame Retardants	6.4nM-64uM from 6 to 120 hpf	embryonic zebrafish	Of the 44 FRs tested, the aryl phosphate ester (APE)-based mono-isopropylated triaryl phosphate and the brominated-bisphenol-A analog tetrabromobisphenol-A producing the greatest array of malformations (including YSEs, PEs, impaired TRs, and deformities of the trunk, body axis, snout, jaw, caudal fin, and pectoral fins). Hierarchical clustering showed that APE flame retardants with isopropyl, butyl, and cresyl substituents on phenyl rings clustered tightly and were particularly potent. All the APE- and CPE-based flame retardants altered 120 hpf larval locomotor behavior at one or more of the concentrations and light/dark epochs examined, whereas 75% of the APEs impaired spontaneous motor functioning of embryos at 24 hpf . The dominant 24 hpf PRAT response in APE-exposed embryos was hypoactivity that was also detected at baseline for some of these formulations (IPP-2, IPP-3, TCP, o-TCP, and TPP), suggesting that early development prior to 24 hpf may be an important period of heightened susceptibility to this class of flame retardants
2	Y	DPHP, TPP	2020	Selmi-Ruby	DT	In Vivo Characterization of the Toxicological Properties of DPhP, One of the Main Degradation Products of Aryl Phosphate Esters	0.1-100ug vein-tail injection, 0.1-100ug oral gavage, 0.1-10mg/L drinking water	mice	Multi-omics analysis confirmed the existence of biological effects of DPhP, even at a very low dose of 0.1mg/mL in drinking water. Chemical structural homology and pathway mapping demonstrated a clear reduction of the fatty acid catabolic processes centered on acylcarnitine and mitochondrial b-oxidation in mice exposed to DPhP in comparison with those treated with vehicle. An interesting finding was that in mice exposed to DPhP, mRNA, expression of genes involved in lipid catabolic processes and regulated by peroxisome proliferator–activated receptor alpha (PPARa) was lower than that in vehicle-treated mice. Immunohistochemistry analysis showed a specific down-regulation of HMGCS2, a kernel target gene of PPARa. Overall, DPhP absorption disrupted body weight–gain processes.
2	Y	TPP, TCP, CDP	2021	Shi et al	NT	In vitro biolayer interferometry analysis of acetylcholinesterase as a potential target of aryl-organophosphorus flame-retardants	3–1500 nM	zebrafish larvae	All three selected aryl-OPFRs, triphenyl phosphate (TPHP), tricresyl phosphate (TCP) and cresyl diphenyl phosphate (CDP), bound directly to AChE.
2		TPP	2018	Shi et al	DNT	Developmental neurotoxicity of triphenyl phosphate in zebrafish larvae	0.8, 4, 20 and 100 μg/L; 2-144 hpf	zebrafish larvae	TPhP was found to have high bioconcentrations in zebrafish larvae after exposure. Further, it significantly reduced locomotor activity as well as the heart rate at the 100 μg/L concentration. TPhP exposure significantly altered the content of the neurotransmitters γ-aminobutyric and histamine. Downregulation of the genes related to central nervous system development (e.g., α1-tubulin, mbp, syn2a, shha, and elavl3) as well as the corresponding proteins (e.g., α1-tubulin, mbp, and syn2a) was observed, but the gap-43 protein was found to upregulated. Marked inhibition of total acetylcholinesterase activity, which is considered as a biomarker of neurotoxicant exposure, was also observed in the larvae. Exposure to environmentally relevant concentrations of TPhP can affect different parameters related to center nervous system development, and thus contribute to developmental neurotoxicity in early developing zebrafish larvae.
2	Y	TPP	2024	Tachachartvanich	Metabolic dysfunction	Perinatal triphenyl phosphate exposure induces metabolic dysfunctions through the EGFR/ERK/AKT signaling pathway: Mechanistic in vitro and in vivo studies	1-25 uM for cells; 1 mg/kg/day orally to pregnant mice	mouse and human preadipocytes and mice	TPhP concentration-dependently accumulated more fat through a significant upregulation of epidermal growth factor receptor (EGFR); TPhP significantly promoted adipogenesis through the activation of EGFR/ERK/AKT signaling pathway as evident by a drastic reduction in adipogenesis of preadipocytes cotreated with inhibitors of EGFR and its major effectors; the mechanism is TPhPinduced metabolic dysfunctions in vivo; male mice perinatally exposed to TPhP had a significant increase in adiposity, hepatic triglycerides, insulin resistance, plasma insulin levels, hypotension, and phosphorylated EGFR in gonadal fat.
2	Y	TPP, TCP	2021	Walley et al.	DNT	Maternal organophosphate flame-retardant exposure alters offspring feeding, locomotor and exploratory behaviors in a sexually-dimorphic manner in mice	1 mg/kg (combination each of TDCPP, TPP and TCP) from gestation day 7 to postnatal day 14.	Wild-type C57Bl/6J mice	We observed interactions of OPFR exposure and HFD consumption on locomotor and anxiety-like behavior in males, suggesting an anxiogenic effect while reducing overall nighttime activity. We also observed an interaction of OPFR exposure and HFD on weekly food intake and feeding behaviors.
2		TPP	2022	Wiegand et al	DT	Triphenyl phosphate-induced pericardial edema is associated with elevated epidermal ionocytes within zebrafish embryos	2.5uM, 5uM, 10uM; 24-72 hpf	zebrafish embryos	Significantly decreased body length at 5 and 10 μM TPHP; no significant effects on survival (> 85%) (data not shown) nor yolk sac area at all concentrations tested; significantly increased pericardial area at all concentrations teted TPHP; anddsignificantly increased ionocyte abundance at 5 and 10 μM TPHP at 72 hpf. Data suggest that TPHP increases Na + /K + ATPase1a1 abundance when exposure is initiated at 24 hpf, leading to potential impacts on osmoregulation and secondary effects on organ development.
2	Y	TPHP, RBDPP	2023	Xie et al	ED	Emerging organophosphate ester resorcinol bis(diphenyl phosphate) exerts estrogenic effects via estrogen receptor pathways	for cell proliferation: 0.001-10uM for RDP, 0.001-20UM for TPP; for cell viability: 0.001-100uM for RDP, 0.001-1000uM for TPP for 48 h; for Luciferase reporter: 1-10uM for RDP, 1-20uM for TPP; 12, 24, 48 h; for competitive fluorescence binding 0.0001-1uM for RDP, 0.001-50uM for TPP	MCF-7 cells	RDP promoted MCF-7 cell proliferation with the lowest effect concentration of 2.5 μM, and the maximum enhancement of 1.6 folds is greater than that of TPHP (1.3 folds). The effect was inhibited completely by an estrogen receptor (ER) antagonist, suggesting that ER activation was responsible for the enhancement. In luciferase reporter gene assays both RDP and TPHP activated ER transcriptional activity at 2.5 μM, but RDP activity was higher than TPHP. RDP exerted stronger estrogenic effects than TPHP through ER-mediated pathways and may pose more health risks.
2	Y	TPP, BPDP, TMPP, IPPP	2019	Yan et.al.	DT	Effects of Organophosphate Ester Flame Retardants on Endochondral Ossification in Ex Vivo Murine Limb Bud Cultures	1uM, 3uM, 10uM	Mice embryo	Compared to tetrabromodiphenyl ether (BDE-47), which the aryl phosphate esters (APEs) are replacing, study showed that exposure to all 4 APEs tested was detrimental to endochondral ossification in mouse embryonic limb buds; furthermore, their effects occur at concentrations an order of magnitude lower than those of BDE-47. All 4 APEs significantly affected at least one of the bone formation-associated endpoints examined (COL10A1-mCherry/COL1A1-YFP fluorescence, cartilage template differentiation, and Sox9/Runx2/Sp7 mRNA expression) at concentrations as low as 1 uM. At 10 uM, their impacts were dramatic.
2	Y	TPP	2018	Yuan et al	RT, DT	Effects of triphenyl phosphate on growth, reproduction and transcription of genes of Daphnia magna	0, 5, 50 or 500 μg/L TPHP for 21 days	Daphnia magna	Results of RT-qPCR showed that the expressions of 76 genes involved in 15 pathways were significantly altered after exposure to 500 μg/L TPHP for 21 days. The significantly altered pathways related to genetic information processing, cellular process and metabolism might be responsible for the observed effects of TPHP. Overall, our results showed that chronic exposure to TPHP caused developmental and reproductive toxicities to D. magna
2	Y	TPP	2023	Zhang et al.	DNT	Neurodevelopmental toxicity of organophosphate flame retardant triphenyl phosphate (TPhP) on zebrafish (Danio rerio) at different life stages	Acute tox: 1, 1.5, 2, 2.5, 3, 5, 8, 15 mg/L; Sub-lethal exposure 20, 50, 100, 500, 1000 ug/L	zebrafish	TPhP concentration gradient exposure reduced the survival rate, hatchability, heart rate, body length and eye distance of zebrafish embryos/larvae, and caused malformations of zebrafish larvae. TPhP also leads to abnormal locomotor behaviors, such as reduced swimming distance and swimming speed, and impaired panic avoidance reflex to high light stimulation.

1	Y	TPP	2024	ECHA	ED	Support Document for Identification of TPP as an SVHC for ED (environment)	Summary of studies		The available in vitro information demonstrates the capacity of TPhP to produce agonist activity on nuclear estrogen receptors ERα and ERβ of several vertebrate species including rat, mouse, fish, chicken, frog and turtle as evidenced by ER transactivation in reporter cell lines. In addition, TPhP can induce ER-regulated gene expression, and related physiological cell responses (e.g., increased cell proliferation). Two recent studies show that TPhP can also activate GPER. The available H295R assays on human adrenal carcinoma cells show that TPhP affects steroidogenesis by increasing estrogen levels (17ß-estradiol) and by increasing expression of genes involved in this pathway like CYP19 and 3β-HSD2. In vivo fish studies indicate that CYP19A is significantly upregulated by exposure to TPhP. Significant alteration of plasmatic concentrations of E2 and E2/T ratio and E2/11-KT ratio can result from this modification in the steroidogenesis pathway. The degree of perturbation of circulating steroid concentrations depends on the fish developmental stage, species and tested concentrations. The observations of VTG concentrations, that are consistent with perturbation of E2 concentrations, suggest an EAS activity of TPhP in female and male zebrafish, with altered concentration of VTG. Therefore, TPhP exerts an effect on the endocrine balance in fish. It has EAS activity as clearly shown both in vitro and in vivo.
1	Y	TPP, EHDPP, TCrP and DPP	2022	Gao et al.	Repro and ED	Exposure assessment of aryl-organophosphate esters based on specific urinary biomarkers and their associations with reproductive hormone homeostasis disruption in women of childbearing age	n/a	urine samples from 913 women of childbearing age	Analyzed 3 ary-OPEs in urine samples from 913 women of child bearing ageand explored the association between exposure to the aryl-OPEs and reproductive hormone levels. The detection frequencies of the three metabolites were 94.6 %, 93.3 %, and 84.2 %, respectively. These results indicate that aryl-OPEs may disrupt hormone homeostasis using their specific biomarkers and may negatively affect female reproduction.
1	Y	TPP	2023	Hawkey et al.	DNT	Developmental exposure to the flame retardant, triphenyl phosphate, causes long-lasting neurobehavioral and neurochemical dysfunction	16 or 32 mg kg−1 day−1	Sprauge Dawley rats	Rats were given low doses of TPP subcutaneous osmotic minipumps, begun preconception and continued into the early postnatal period. Offspring were administered a battery of behavioral tests from adolescence into adulthood, and littermates were used to evaluate dopaminergic synaptic function. Offspring with TPP exposures showed increased latency to begin eating in the novelty -suppressed feeding test, impaired object recognition memory, impaired choice accuracy in the visual signal detection test, and sex -selective effects on locomotor activity in adolescence (males) but not adulthood. Male, but not female, offspring showed marked increases in dopamine utilization in the striatum, evidenced by an increase in the ratio of the primary dopamine metabolite (3,4-dihydroxyphenylacetic acid) relative to dopamine levels. These results indicate that TPP has adverse effects that are similar in some respects to those of organophosphate pesticides, which were restricted because of their developmental neurotoxicity.
1	Y	TPP, EHDPP, TCP, ITPs	2022	Hu et. al.	ED	Endocrine disrupting toxicity of aryl organophosphate esters and mode of action	See 21 study summary		
1	Y	TPP, EHDPP, IDPP, DPHP	2024	Jin et al	Review	Ecological and human health risk of aryl-phosphate flame retardants (APFRs): Sources, distribution, and toxicity	Review	Many	Overview of the occurrence and toxicity of triphenyl phosphate (TPHP), 2-ethylhexyl diphenyl phosphate (EHDPP), isobutyl diphenyl phosphate (IDPP), and diphenyl phosphate (DPHP). Effcts on intestinal tract, liver, heart, other organs are summarized along with DNT, RT research outcomes.
1		EHDP, TPP, IDDPP, ITP, TCP, BPDP (also non-APE's: BDE-47, 99, TBBPA, tBOEP, bBoep, TDCPP, TCIPP, TCEP)	2022	Klose et al.	DNT	Neurodevelopmental toxicity asessment of flame retardants using a human DNT in vitro testing battery	ranked from <1 µM (5 FRs), 1<10 µM (7 FRs) to the >10 µM range (3 FRs)	human cell-based DNT in vitro battery	Human cell–based developmental neurotoxicity (DNT) in vitro battery covering a large variety of neurodevelopmental endpoints. Potency according to the respective most sensitive benchmark concentration (BMC) across the battery ranked from <1 µM (5 FRs), 1<10 µM (7 FRs) to the >10 µM range (3 FRs). Evaluation of the data with the ToxPi tool revealed a distinct ranking (a) than with the BMC and (b) compared to the ToxCast data, suggesting that DNT hazard of these FRs is not well predicted by ToxCast assays. Extrapolating the DNT in vitro battery BMCs to human FR exposure via breast milk suggests low risk for individual compounds. However, it raises a potential concern for real-life mixture exposure, especially when different compounds converge through diverse modes-of-action on common endpoints, like oligodendrocyte differentiation in this study.
1	Y	TPP, IPP, EHDP, TMPP, IDDP, BPDP	2024	Kreutz et.al.	DNT and NT	Integrated Approach for Testing and Assessment form Developmental Neurotoxicity (DNT) to Prioritize Aromatic Organophosphorus Flame Retardants		22 NAMs for DNT or NT	As a class, the aromatic OPFRs were at least as active as the BFRs in the DNT battery. The integration of data from ICE (Integrated Chemical Environment) and the literature suggests that the point of departure for this class of compounds may be lower if endpoints for endocrine effects were included, likely due to endocrine effects being upstream of the key processes measured in the DNT battery.
1		TPP, ITPs	2023	Newell et al	DT	Developmental organophosphate flame retardant exposure disrupts adult hippocampal neurogenesis in Wistar rats	3.3 mg/kg bw/day	Wistar rats dams	Results indicate that developmental OPFR exposure has significant, sex specific impacts on multiple markers of AHN in the dentate gyrus of rats. In males, OPFR exposure significantly reduced the number of neural progenitors the number of new/immature neurons and reduced dentate gyrus volume. In females, exposure increased the number of neural progenitors, decreased the number of new/immature neurons, but had no significant effect on dentate gyrus volume. These results further elucidate the developmental neurotoxic properties of OPFRs, emphasize the long-term impact of early life OPFR exposure on neural processes
1	Y	TPP	2024	Schmandt	DT	Environmentally Relevant Concentrations of Triphenyl Phosphate (TPP or TPhP) Impact Development in Zebrafish	1.5–15 nM (0.5 µg/L–5 µg/L)	zebrafish larvae	Triphenyl phosphate (TPhP) is an aryl phosphate ester found in many aquatic environments at nM concentrations. Study used the model organism zebrafish (Danio rerio) to uncover the developmental impact of nM exposures to TPhP at the phenotypic and molecular levels. At concentrations of 1.5–15 nM (0.5 µg/L–5 µg/L), chronically dosed 5dpf larvae were shorter in length and had pericardial edema phenotypes that had been previously reported for exposures in the µM range. Cardiotoxicity was observed but did not present as cardiac looping defects as previously reported for µM concentrations. The RXR pathway does not seem to be involved at nM concentrations, but the tbx5a transcription factor cascade including natriuretic peptides (nppa and nppb) and bone morphogenetic protein 4 (bmp4) were dysregulated and could be contributing to the cardiac phenotypes. TPhP is a weak pro-oxidant, as it increases the oxidative stress response within hours of exposure. TPhP can affect animal development at environmentally relevant concentrations and its mode of action involves multiple pathways.
1		TPP, ITPs	2023	Witchey et. al.	DT	Reproductive and developmental toxicity following exposure to organophosphate ester flame retardants and plasticizers, triphenyl phosphate and isopropylated phenyl phosphate, in Sprague Dawley rats	0, 1000, 3000, 10 000, 15 000, or 30 000 ppm gestation day (GD) 6 through postnatal day (PND) 28; offspring were provided dosed feed at the same concentration as their dam	Sprauge Dawley rats	Body weight and organ weights were impacted with exposure in remaining dams. Reproductive performance was perturbed at 10 000 ppm TPHP and all IPP exposure groups. In offspring, both TPHP- and IPP-related toxicity was noted in pups at 10 000 ppm as well as reduction in bodyweights, delays in pubertal endpoints, and/or reduced cholinesterase enzyme activity starting at 1000 ppm TPHP or IPP. Preliminary internal dose assessment indicated gestational and lactational transfer following exposure to TPHP or IPP. These findings demonstrate that offspring development is sensitive to 1000 ppm TPHP or IPP exposure.
1	Y	TPP, ITPs	2022	Witchey et. al.	DNT	Impacts of Gestational FireMaster 550 Exposure on the Neonatal Cortex Are Sex Specific and Largely Attributable to the Organophosphate Esters	1000 ug/day, or 3.3 mg/kg bw/day orally beginning 72 hours after pairing and continuing to PND1	Wistar rats and dams	The neonatal cortex was highly sexually dimorphic in lipid and transcriptome composition, and males were more significantly impacted by FR exposure. Multiple adverse modes of action for the BFRs and OPFRs on neurodevelopment were identified, with the OPFRs being more disruptive than the BFRs via multiple mechanisms including dysregulation of mitochondrial function and disruption of cholinergic and glutamatergic systems. Disrupted mitochondrial function by environmental factors has been linked to a higher risk of autism spectrum disorders and neurodegenerative disorders. Impacted lipid classes included ceramides, sphingomyelins, and triacylglycerides. Robust ceramide upregulation in the OPFR females could suggest a heightened risk of brain metabolic disease.

1	Y	TPP	2024 (a)	Zhang et al.	DNT	Astaxanthin activates the Nrf2/Keap1/HO-1 pathway to inhibit oxidative stress and ferroptosis, reducing triphenyl phosphate (TPhP)-induced neurodevelopmental toxicity	20, 50, 100, 500, 1000 ug/L, 2-7hpf	zebrafish	Used zebrafish to explore the new mechanism of TPP inducing oxidative stress and ferroptosis to promote neurodevelopmental toxicity. The results suggested that TPP affected the embryonic development, reduced the number of new neurons, and led to abnormal neural behavior in zebrafish larvae. TPP also induced ROS accumulation, activated the antioxidant defense signal Nrf2 and Keap1, and significantly changed the activities of Acetylcholinesterase (AChE), Adenosine triphosphatase (ATPase) and glutathione S-transferase (GST).
		TTP (p-form of TCP), ITPs (tri), IDPs (di), IMPs (mono)	2004	Honkakoski	mutagenicity, mechanism	Effects of triaryl phosphates on mouse and human nuclear receptors		mice liver tissue, human cells	Human CAR and pregnane X receptor (PXR) were variably activated (2–5-fold) by triaryl phosphates while mouse PXR, peroxisome proliferator-activated receptor-a, and vitamin D receptor were refractory. Among steroid hormone receptors, the human androgen receptor was inhibited by triphenyl phosphate and di-ortho-isopropylated phenyl phosphate (40–50%) and activated by di- and tri-para-substituted phenyl phosphates (2-fold). Triaryl phosphates are efficient CAR and PXR activators and suggest steroid-dependent biological pathways that may contribute to the reproductive effects of triaryl phosphates.
	Y	TPP, DPHP	2024	Cao	Bioaccumulation	Biotransformation, Bioaccumulation, and Bioelimination of Triphenyl Phosphate and Its Dominant Metabolite Diphenyl Phosphate In Vivo	70 μg/kg body weight (bw)/day	Mice	The total concentration of DPHP in all organs was 3.55-fold greater than that of TPHP. Recovery analysis showed that the rate of TPHP elimination from mouse organs reached 38%, while only 3%–5% of DPHP was removed, suggesting that the rates of degradation and elimination of DPHP were slower than TPHP and its bioaccumulation potential was higher.
		ITPs	2020	Australia	Repro and Neuro	Isopropylated triphenyl phosphate esters: Human health tier II assessment	Looked at all exisiting studies		Repro and Neuro classifications recommended
	Y	ITPs (ti-o-creysl phosphate)	2020	Bockers et al	ED	Organophosphate ester tri-o-cresyl phosphate interacts with estrogen receptor α in MCF-7 breast cancer cells promoting cancer growth.		human cells	
		DPHP	2021	Chen et al.	DT, Mechanism	Life Cycle Exposure to Environmentally Relevant Concentrations of Diphenyl Phosphate (DPhP) Inhibits Growth and Energy Metabolism of Zebrafish in a Sex-Specific Manner	0.8, 3.9, or 35.6 μg/L	zebrafish	DPhP is being used directly as an industrial catalyst and additive
	Y	TCP	2020	Deng et al	Metabolism	The role of protein kinase C alpha in tri-ortho-cresyl phosphate-induced autophagy in human neuroblastoma SK-N-SH cells		human cells	In this study, we found that TOCP could induce autophagy by activating protein kinase C alpha (PKCα) signaling in neuroblastoma SK-N-SH cells. PKCα activators could positively regulate TOCP-induced autophagy by increasing the expression levels of neighbor BRCA1 gene protein 1 (NBR1), LC3 and P62 autophagic receptor protein. Furthermore, PKCα activation impaired the ubiquitin-proteasome system (UPS), resulting in inhibition of proteasome activity and accumulation of ubiquitinated proteins. UPS dysfunction could stimulate autophagy to serve as a compensatory pathway, which contributed to the accumulation of the abnormally hyperphosphorylated tau proteins and degradation of impaired proteins of the MAP 2 and NF-H families in neurodegenerative disorders.
	Y	mITP	2014	Gerlach et al	NT	Mono-substituted isopropylated triaryl phosphate, a major component of Firemaster 550, is an AHR agonist that exhibits AHR-independent cardiotoxicity in zebrafish	0.2 uM until 72 or 120 hpf	zebrafish	mITP is an AHR agonist, mITP causes AHR-independent cardiotoxicity through a pathway that is also antagonized by CH22319
	Y	TCP (tmCP)	2020a	Ji et al.	ED	Tricresyl phosphate isomers exert estrogenic effects via G protein-coupled estrogen receptor-mediated pathways		cell assays	Three TCP isomers were evaluated for their activities on ERα by using two-hybrid yeast assay, and action on GPER by using Boyden chamber assay, cAMP production assay, calcium mobilization assay and molecular docking analysis. The results showed that three TCP isomers were found to act as ERα antagonists. Conversely, they had agonistic activity on GPER to promote GPER-mediated cell migration of MCF7 cells and SKBR3 cells. Both ToCP and TpCP activated GPER-mediated cAMP production and calcium mobilization, whereas TmCP had different mode of action, it only triggered GPER-mediated calcium mobilization, as evidenced by using the specific GPER inhibitor (G15) and GPER overexpressing experiments.
	Y	EHDP	2024a	Jiang et al.	DNT	2-Ethylhexyl Diphenyl Phosphate Induces Autism Spectrum Disorder-Like Behaviors in Offspring Mice by Disrupting Postsynaptic Development	0.4, 2, and 10 mg/kg groups were orally dosed to pregnant ICR mice	mice	Pregnant mice were exposed to EHDPP in drinking water from gestation to lactation to investigate its effects on autism spectrum disorder-like (ASD-like) behaviors in offspring. Serum EHDPP concentrations in dams were within the concentration range in humans. At the highest dose, EHDPP exposure induced ASD-like behaviors in both female and male offspring. Significant reductions in mature dendritic spines and structural damage to the postsynaptic density zone were noted in all but the lowest exposure groups, indicating postsynaptic membrane impairment. Mechanistically, EHDPP significantly downregulated disc large MAGUK scaffold protein 4 expression by inhibiting protein kinase B and type 1 insulin-like growth factor receptor phosphorylation. In the heterologous synapse formation assay in vivo, EHDPP significantly reduced the levels of postsynaptic density protein 95 expression in neurons at 1 μM. Overall, the study utilized in vitroand in vivo experiments to confirm that EHDPP damaged postsynaptic membrane formation and might increase the incidence of ASD in offspring.
	Y	EHDP	2024	Ni et al.	DNT	Neurotoxic effects of 2-ethylhexyl diphenyl phosphate exposure on zebrafish larvae: Insight into inflammation-driven changes in early motor behavior	14 nM	zebrafish	EHDPP even at an environmentally relevant concentration of 14 nM, exhibited excitatory neurotoxicity. Potential influence of EHDPP on the release of neurotransmitters like serotonin and dopamine, which, in turn, mediated anxiety-like behavior in the zebrafish larvae. Conversely, sublethal dose EHDPP (1400 nM) exposure significantly suppressed the swimming vigor of zebrafish larvae, accompanied by morphological changes, abnormal behaviors, and alterations in intracerebral molecules.
	Y	EHDPP	2024	Shu et al	ED	Bioaccumulation and thyroid endocrine disruption of 2-ethylhexyl diphenyl phosphate at environmental concentration in zebrafish larvae	(0, 0.1, 1, 10, and 100 μg·L	zebrafish	Zebrafish development and growth were inhibited by EHDPP, as indicated by the increased malformation rate, decreased survival rate, and shortened body length. Exposure to lower concentrations of EHDPP (0.1 and 1 μg ·L− 1) significantly decreased the whole-body thyroxine (T4) and triiodothyronine (T3) levels and altered the expressions of genes and proteins involved in the hypothalamic-pituitary-thyroid axis.
	Y	ITPs	2019	Wade (in 21 study summary)	liver, adrenal, metabolic	Toxicity of Flame Retardant Isopropylated Triphenyl Phosphate: Liver, Adrenal, and Metabolic Effects	5 to 140 mg/kg/d orally for 90 days	Wistar rats	Exposure to IPTPP caused a dose-related increase in liver and adrenal gland weight in both sexes. Cells in the zona fasciculate (ZF) of the adrenal cortex were observed to be filled with droplets that stained with Nile red, suggesting they contained neutral lipid. Despite marked structural changes, there was no change in basal or stressinduced serum levels of their major secreted ZF product corticosterone (B), suggesting cell function was not altered. There were no effects on responses to glucose or insulin challenge, but serum levels of fructosamine were elevated by IPTPP exposure, suggesting a slight tendency of exposed animals to be hyperglycemic. Serum levels of total cholesterol and high-density lipoprotein cholesterol were significantly elevated in both sexes at the 2 highest doses. This study demonstrates that IPTPP exposure causes hypertrophy and neutral lipid accumulation in adrenal cortex ZF cells but does not result in impaired B production.
	Y	EHDPP	2024	Yan et al	NT	Long-Term Neurotoxic Effects and Alzheimer's Disease Risk of Early EHDPP Exposure in Zebrafish: Insights from Molecular Mechanisms to Adult Pathology	0.05, 0.5, and 5.0 μg/L EHDPP from 4 to 120 h postfertilization (hpf)	zebrafish	Exposure to EHDPP yielded hyperactive locomotor behavior, which was characterized by increased swimming speed, larger turning angles, and heightened sensitivity to light-dark stimulation. EHDPP exposure during early development (4–120 hpf) triggered early- and midstage AD-like symptoms in adulthood (180 dpf), characterized by cognitive confusion, aggression, blood–brain barrier disruption, and mitochondrial damage in brains.

	Y	EHDPP	2023	Yang et al	Bioaccumulation, ED	First insight into the sex-dependent accumulation, tissue distribution and potential toxicities of 2-ethylhexyl diphenyl phosphate and its metabolites in adult zebrafish	5, 35 and 245 μg/L of EHDPHP for 21 days	zebrafish	In this study, adult zebrafish (Danio rerio) were exposed to EHDPHP (0, 5, 35 and 245 μg/L) for 21-day, which was followed by 7-day depuration. The bioconcentration factor (BCF) of EHDPHP in female zebrafish was 26.2 ± 7.7% lower than in males due to the lower uptake rate (ku) while higher depuration rate (kd) in the females. The regular ovulation and higher metabolic efficiency promoted elimination from female zebrafish, thus leading to much less (28–44%) accumulation of ∑(M1-M16) in female zebrafish. They exhibited the highest accumulation in the liver and in testine in both sexes, which might be regulated by tissue-specific transporters and histones evidenced by mo lecular docking results. Intestine microbiota analysis further revealed that female zebrafish were more susceptible to EHDPHP exposure, with more significant changes in phenotype number and KEGG pathways in female than male fish. Disease prediction results suggested that EHDPHP exposure might cause cancers, cardiovascular diseases as well as endocrine disorders in both sexes
	Y	TCP and isomers	2024	Yi et al	Cardio	Isomer-specific cardiotoxicity induced by tricresyl phosphate in zebrafish embryos/larvae	0, 100, 300 and 600 μg/L, 2-120 hpf	zebrafish embryos	ToCP or TmCP exposure induced cardiac morphological defects and dysfunction in zebrafish, characterized by increased distance between sinus venosus and bulbus arteriosis, increased atrium and pericardial sac area, trabecular defects, and decreased heart rate and blood flow velocity, while no adverse effects of TpCP on zebrafish heart were found. Transcriptomic results revealed that extracellular matrix (ECM) and motor proteins, as well as PPAR signaling pathways, were included in the cardiac morphological defects and dysfunction induced by ToCP and TmCP. Co-exposure test with Dmannitol indicated that the inhibition of energy metabolism by ToCP and TmCP affected cardiac morphology and function by decreasing osmoregulation
	Y	TCP	2023	Yu et al.	Metabolism	Translocation and metabolism of tricresyl phosphate in rice and microbiome system: Isomer-specific processes and overlooked metabolites	observation	rice and rizosphere microbiome	TpCP and TmCP were found more liable to be translocated acropetally, compared with ToCP, although they have same molecular weight and similar Kow. Rhizosphere microbiome named microbial consortium GY could reduce the uptake of TpCP, TmCP, and ToCP in rice tissues, and promote rice growth. New metabolites were successfully identified in rice and microbiome,including hydrolysis, hydroxylated, methylated, demethylated, methoxylated, and glucuronide- products. The methylation, demethylation, methoxylation, and glycosylation pathways of TCP isomers were observed for the first time in organisms. What is more important is that the demethylation of TCPs could be an important and overlooked source of triphenyl phosphate (TPHP), which broke the traditional understanding of the only man made source of toxic TPHP in the environment. Active members of the microbial consortium GY during degradation were revealed and metagenomic analysis indicated that most of active populations contained TCPdegrading genes. It is noteworthy that the strains and function genes in microbial consortium GY that responsible for TCP isomers' transformation were different.
	Y	CDPP	2024b	Jiang et al.	RT	Cresyl Diphenyl Phosphate exposure induces reproductive functional defects in men and male mice.	(0, 4, 20, or 100 mg/kg/d) for 8 weeks	Mice	In mechanism, CDP trigger the oxidative stress and ROS production, thus partially causing DNA damage and cell apoptosis. Moreover, CDP exposure causes injury to Ledyig cells and Sertoli cells, thus disturbing the testicular microenvironment and inhibiting spermatogonia proliferation. In conclusion, this research reveals multiple adverse impacts of CDP on the male reproductive system and calls for further study of the toxicological effects of CDP on human health.
	Y	RBDPP, BPA-DP, IDDPP, CDPP, ITPs,	2021	Kubwabo et al.	Prevalence	Occurrence of aryl and alkyl-aryl phosphates in Canadian house dust	n/a	Dust	BPA-DP and RBDP detected in 69% and 78% of samples. IDDPP, CDPP, ITPs (IPPDPP, BIPPPP, TIPPP) found in 100% of samples
	Y	BEHPP, TBPP, TBPHP, CDP, 2IPPDPP	2024	Li et al	Maternal transfer, Prevelance	Exposure levels and maternal transfer of emerging organophosphate flame retardants (OPFRs) in pregnant women: Comparison with traditional OPFRs	n/a	Pregnant women	Eleven OPFRs were detected for the first time in the human early embryo. Six emerging OPFRs, especially BEHPP, underwent significant maternal transfer. Maternal transfer efficiencies of OPFRs generally depended on TTR binding activities.
	Y	ITP, TCOP	2023	Li et al.	DT	Developmental Toxicities in Zebrafish Embryos Exposed to Tri-o-cresyl Phosphate	Between 0.15 and 88.5 μg/L	Zebrafish	Diverse impairments of zebrafish embryos, such as altered morphological and physical characteristics and locomotor behaviors, were observed at different tri-o-cresyl phosphate concentrations. Furthermore, swimming behaviors were significantly inhibited at tri-o-cresyl phosphate concentrations ranging from 3.0 μg/L to 88.5 μg/L.
	Y	TPP and DPP	2020	Liu et al.	NT/Mechanism	Triphenyl phosphate permeates the blood brain barrier and induces neurotoxicity in mouse brain	0, 50, or 150 mg/kg TPP daily by oral gavage for 30 days	mice	The results showed that TPP and DPP can cross the BBB of mice. Histopathological examination of the brain revealed abnormalities in the hippocampus, cortex and thalamus and mice treated with high doses showed a potential inflammation in the thalamus and hippocampus.
	Y	BEHP, DPHP	2024	Lu et al.	DNT, ED	Trimester-specific effect of maternal co-exposure to organophosphate esters and phthalates on preschooler cognitive development: The moderating role of gestational vitamin D status.	n/a	Pregnant women	It was found in the present study that urinary DPHP concentration was associated with the significant decrease of cognitive function test scores, therefore partially corroborating previous studies.
	Y	DPP	2019	Mitchell et al	DT	Diphenyl Phosphate-Induced Toxicity During Embryonic Development	500, 250, and 125 μM DPHP; 24 to 72 hpf, 30 to 72 hpf, or 48 to 72 hpf	zebrafish embryos	DPHP significantly increased the distance between the sinus venosus and bulbus arteriosis (SV-BA) at 72 h postfertilization (hpf) following initiation of exposure before and after cardiac looping. Interestingly, pretreatment with D-mannitol mitigated DPHP-induced effects on SV-BA length despite the absence of DPHP effects on pericardial area, suggesting that DPHP-induced cardiac defects are independent of pericardial edema formation. Using mRNA-sequencing, we found that DPHP disrupts pathways related to mitochondrial function and heme biosynthesis.
	Y	TCP, CDPP	2021	Ren et al.	NT	Synthetic organic chemicals (flame retardants and pesticides) with neurotoxic potential induced behavioral impairment on zebrafish (Danio rerio): a non-invasive approach for neurotoxicology	Treatment-I 5 μL/L and Treatment-II 25 μL/L	Zebrafish	Responses of zebrafish under organophosphorus flame retardant (tri-cresyl phosphate and cresyl diphenyl phosphate) treatments were identical with pesticide (cypermethrin and methomyl) treatments.
	Y	TPP, ITPs	2020a	Rock et al	NT	Effects of Prenatal Exposure to a Mixture of Organophosphate Flame Retardants on Placental Gene Expression and Serotonergic Innervation in the Fetal Rat Brain	0, 500, 1000, or 2000 ug/day during gestation	Wistar rat dams	Relative abundance of genes responsible for the transport and synthesis of placental 5-HT were disrupted, and multiple neuroactive metabolites in the 5-HT and kynurenine metabolic pathways were upregulated. In addition, 5-HTergic projections were significantly longer in the fetal forebrains of exposed males. These findings suggest that OPFRs have the potential to impact the 5-HTergic system in the fetal forebrain by disrupting placental tryptophan metabolism.
	Y	BEHPP and EHDPP	2024	Shi et al	DT	Developmental toxicity of an emerging organophosphate ester Bis-(2-ethylhexyl)-phenyl phosphate on embryonic zebrafish: Comparison to 2-ethylhexyl diphenyl phosphate	for acute toxicity: 0.5-4.0uM; for chronic toxicity: 0.008, 0.04, 0.2 and 1.0 μM, 0-120h	zebrafish	BEHPP did not lead to mortality and malformations of embryos within the test concentration range (0.5-4.0 μM). In contrast, EHDPP had significant lethal effects, with an LC50 of 2.44 μM, and induced malformations, notably pericardial edema (PE), with an EC50 of 1.77 μM. In addition, BEHPP induced cardiac dysfunctions in embryos to a similar degree as EHDPP. Both stroke volume and cardiac output were significantly increased at BEHPP concentrations of 1.8 nM and above and at EHDPP concentrations of 4.3 nM and above.
	Y	RBDPP	2023	Shi et al	NT	Neurotoxicity of an emerging organophosphorus flame retardant, resorcinol bis(diphenyl phosphate), in zebrafish larvae	(0, 0.3, 3, 90, 300 and 900 nM) from 2 to 144 hpf	zebrafish larvae	Decreased heart rates and body lengths and the increased malformation rates were observed. RDP exposure significantly reduced the locomotor behavior under light-dark transition stimulation and the flash stimulus response of larvae. Molecular docking results showed that RDP could bind to the active site of zebrafish AChE and that RDP and AChE exhibit potent binding affinity. RDP exposure also significantly inhibited AChE activity in larvae. The content of neurotransmitters was altered after RDP exposure. Key genes and proteins related to the development of the central nervous system were downregulated.
	Y	DPHP, DCP	2022	Siddique et al.	ED	Exposure of men living in the greater Montreal area to organophosphate esters: Association with hormonal balance and semen quality	observation	Men	OPE detection rates were high and exposure to several OPEs was associated with altered hormone levels and semen parameters. DPHP and DCP were detected in over 90% of participants. Multiple linear regression analyses of the associations between OPEs and hormone concentrations suggested that DPHP concentrations may be associated with a decrease in estradiol.

	Y	EHDP, BDP, IDDP, RDP, TCP, TPP	2024	Xie et al	Bioaccumulation, ED, prevalence	Bioaccumulation and Potential Endocrine Disruption Risk of Legacy and Emerging Organophosphate Esters in Cetaceans from the Northern South China Sea	n/a	cetaceans	shows levels but not effects for the aryl
	Y	BPDP	2020	Yan et.al.	Mechanism	Exposure to tert-Butylphenyl Diphenyl Phosphate, an Organophosphate Ester Flame Retardant and Plasticizer, Alters Hedgehog Signaling in Murine Limb Bud Cultures	1 uM, 10 uM for 3 or 24 h	mouse embryos	Limb buds collected from gestation day 13 CD1 mouse embryos were cultured for 3 or 24 h in the presence of vehicle, 1 uM, or 10 uM BPDP. RNA sequencing analyses revealed that exposure to 1 uM BPDP for 24 h increased the expression of 5 transcripts, including Ihh, and decreased 14 others, including Gli1, Ptch1, Ptch2, and other targets of Hedgehog (Hh) signaling. Pathway analysis predicted the inhibition of Hh signaling
	Y	TDTBPP	2024 (b)	Zhang et al.	Cardio	Acute exposure to tris(2,4-di-tert-butylphenyl)phosphate elicits cardiotoxicity in zebrafish (Danio rerio) larvae via inducing ferroptosis	10 and 100 μg/L for 5 days	zebrafish larvae	The results in this study indicated that acute exposure to AO168 =O at 10 and 100 μg/L for 5 days obviously impaired cardiac morphology and function of zebrafish larvae, as proofed by decreased heartbeat, stroke volume, and cardiac output and the occurrence of pericardial edema and ventricular hypertrophy. Transcriptomics, polymerase chain reaction, and molecular docking revealed that the strong interaction of AO168 =O and transferrin receptor 1 activated the transportation of ferric iron into intracellular environment. The release of free ferrous ion to cytoplasmic iron pool also contributed to the iron overload in heart region, thus inducing ferroptosis in larvae via generation of excessive reactive oxygen species, glutathione peroxidase 4 inhibition, glutathione depletion and lipid peroxidation. Ferroptosis inhibitor (Fer-1) co-exposure effectively relieved the cardiac dysfunctions of zebrafish, verifying the dominant role of ferroptosis in the cardiotoxicity caused by AO168 =O. This research firstly reported the adverse impact and associated mechanisms of AO168 =O in cardiomyogenesis of vertebrates, underlining the urgency of concerning the health risks of AO168 =O.
		TPP, TMPP, CDP, EDHPHP, IPTPP	2024	Hoang et al	pericardial edema	Aryl phosphate ester-induced pericardial edema in zebrafish embryos is influenced by the ionic composition of exposure media	6.25, 3.125, 3.125, 25, and 100 μM, 24-72hpf	zebrafish embryos	We recently discovered that the severity of triphenyl phosphate (TPHP)-induced pericardial edema was dependent on the ionic strength of exposure media.
0		~~Aryl phosphate esters~~	~~2021~~	~~Liu et al.~~	~~DNT~~	~~Prenatal exposure to halogenated, aryl, and alkyl-organophosphate esters and child neurodevelopment at two years of age~~		~~urine samples~~	~~We measured urinary concentrations of OPEs collected in the first and third trimester from 184 pregnant women in Wuhan, China. Childhood neurodevelopment was assessed using the Chinese revision of Bayley Scale of Infant Development. A two-fold increase in the average of bis (1,3-dichloro-2- propyl) phosphate (BDCIPP) was associated with 3.50 decrease in Psychomotor Development Index (PDI) score (95%CI: − 5.86, − 1.14) and 5.75 decrease in Mental Development Index (MDI) score (95%CI: − 8.94, − 2.55). Average of the molar concentrations of chlorinated alkyl OPEs (ΣCl OPEs) during pregnancy was inversely associated with PDI [β = − 3.24 (95%CI: − 5.95, − 0.53)] and MDI scores [β = − 5.86 (95%CI: − 9.52, − 2.20)]. Prenatal concentrations of BDCIPP and ΣCl OPEs were inversely associated with neurodevelopment scores in boys, but not in girls.~~
0	~~¥~~	~~TPP~~	~~2015~~	~~Isales~~	~~DT~~	~~Triphenyl phosphate-induced developmental toxicity in zebrafish: Potential role of the retinoic acid receptor~~		~~zebrafish~~	~~Specific to TPP developmental toxicity in zebrafish and the possible mediation of the DT by the retinoic acid receptor. Not relevant for SAB at this time.~~
?	~~¥~~	~~TPP~~	~~2023~~	~~Wiegand et al~~	~~Mechanism, cardio~~	~~Triphenyl phosphate-induced pericardial edema in zebrafish embryos is dependent on the ionic strength of exposure media~~		~~zebrafish embryos~~	
0	~~¥~~	~~TPP, EDHP, 4IPPDPP, BPDP~~	~~2019~~	~~Phillips et.al.~~	~~mechanism~~	~~Inhibition of Human Liver Carboxylesterase (hCE1) by Organophosphate Ester Flame Retardants and Plasticizers: Implications for Pharmacotherapy~~		~~human liver carboxylesterase~~	~~This is about effect on drug treatment.....could ID some more members from their list.....~~

Batch #1 of Toxicological Studies of the aryl phosphate esters - focus on triphenyl phosphate (TPP or TPhP)

Substance	Year	Author	Endpoint	Title	Concentration	Test substance	Effect/ Summary
TPP, EHDPP, IDPP, DPHP	2024	Jin et al	Intestinal tract, liver, heart, other organs, DNT, RT	Ecological and human health risk of aryl-phosphate flame retardants (APFRs): Sources, distribution, and toxicity.			Overview of the occurrence and toxicity of triphenyl phosphate (TPP), 2-ethylhexyl diphenyl phosphate (EHDPP), isobutyl diphenyl phosphate (IDPP), and diphenyl phosphate (DPHP). Effcts on intestinal tract, liver, heart, other organs are summarized along with DNT, RT research outcomes.
TPP	2024 (a)	Zhang et al.	DNT	Astaxanthin activates the Nrf2/Keap1/HO-1 pathway to inhibit oxidative stress and ferroptosis, reducing triphenyl phosphate (TPhP)-induced neurodevelopmental toxicity	20, 50, 100, 500, 1000 ug/L, 2-7hpf	zebrafish	Used zebrafish to explore the new mechanism of TPP inducing oxidative stress and ferroptosis to promote neurodevelopmental toxicity. The results suggested that TPP affected the embryonic development, reduced the number of new neurons, and led to abnormal neural behavior in zebrafish larvae. TPP also induced ROS accumulation, activated the antioxidant defense signal Nrf2 and Keap1, and significantly changed the activities of Acetylcholinesterase (AChE), Adenosine triphosphatase (ATPase) and glutathione S-transferase (GST).
TPP	2024	Schmandt	DT	Environmentally Relevant Concentrations of Triphenyl Phosphate (TPP or TPhP) Impact Development in Zebrafish	1.5–15 nM (0.5 µg/L–5 µg/L)	zebrafish larvae	Triphenyl phosphate (TPhP) is an aryl phosphate ester found in many aquatic environments at nM concentrations. Study used the model organism zebrafish (Danio rerio) to uncover the developmental impact of nM exposures to TPhP at the phenotypic and molecular levels. At concentrations of 1.5–15 nM (0.5 µg/L–5 µg/L), chronically dosed 5dpf larvae were shorter in length and had pericardial edema phenotypes that had been previously reported for exposures in the µM range. Cardiotoxicity was observed but did not present as cardiac looping defects as previously reported for µM concentrations. The RXR pathway does not seem to be involved at nM concentrations, but the tbx5a transcription factor cascade including natriuretic peptides (nppa and nppb) and bone morphogenetic protein 4 (bmp4) were dysregulated and could be contributing to the cardiac phenotypes. TPhP is a weak pro-oxidant, as it increases the oxidative stress response within hours of exposure. TPhP can affect animal development at environmentally relevant concentrations and its mode of action involves multiple pathways.
TPP, IPP, EHDP, TMPP, IDDP, BPDP	2024	Kreutz et.al.	DNT and NT	Integrated Approach for Testing and Assessment form Developmental Neurotoxicity (DNT) to Prioritize Aromatic Organophosphorus Flame Retardants		22 NAMs for DNT or NT	As a class, the aromatic OPFRs were at least as active as the BFRs in the DNT battery. The integration of data from ICE (Integrated Chemical Environment) and the literature suggests that the point of departure for this class of compounds may be lower if endpoints for endocrine effects were included, likely due to endocrine effects being upstream of the key processes measured in the DNT battery.
TPP	2023	Hawkey et al.	DNT	Developmental exposure to the flame retardant, triphenyl phosphate, causes long-lasting neurobehavioral and neurochemical dysfunction	16 or 32 mg/kg/day	Sprauge Dawley rats	Rats were given low doses of TPP subcutaneous osmotic minipumps, begun preconception and continued into the early postnatal period. Offspring were administered a battery of behavioral tests from adolescence into adulthood, and littermates were used to evaluate dopaminergic synaptic function. Offspring with TPP exposures showed increased latency to begin eating in the novelty-suppressed feeding test, impaired object recognition memory, impaired choice accuracy in the visual signal detection test, and sex-selective effects on locomotor activity in adolescence (males) but not adulthood. Male, but not female, offspring showed marked increases in dopamine utilization in the striatum, evidenced by an increase in the ratio of the primary dopamine metabolite (3,4-dihydroxyphenylacetic acid) relative to dopamine levels. These results indicate that TPP has adverse effects that are similar in some respects to those of organophosphate pesticides, which were restricted because of their developmental neurotoxicity.
TPP, ITPs	2023	Newell et al	DT	Developmental organophosphate flame retardant exposure disrupts adult hippocampal neurogenesis in Wistar rats	3.3 mg/kg bw/day	Wistar rats dams	Results indicate that developmental OPFR exposure has significant, sex specific impacts on multiple markers of AHN in the dentate gyrus of rats. In males, OPFR exposure significantly reduced the number of neural progenitors the number of new/immature neurons and reduced dentate gyrus volume. In females, exposure increased the number of neural progenitors, decreased the number of new/immature neurons, but had no significant effect on dentate gyrus volume. These results further elucidate the developmental neurotoxic properties of OPFRs, emphasize the long-term impact of early life OPFR exposure on neural processes
TPP, ITPs	2023	Witchey et. al.	DT	Reproductive and developmental toxicity following exposure to organophosphate ester flame retardants and plasticizers, triphenyl phosphate and isopropylated phenyl phosphate, in Sprague Dawley rats	TPHP or IPP were administered via dosed feed at concentrations 0, 1000, 3000, 10 000, 15 000, or 30 000 ppm to time-mated Hsd:Sprague Dawley SD rats from gestation day (GD) 6 through postnatal day (PND) 28; offspring were provided dosed feed at the same concentration as their dam	Sprauge Dawley rats	Body weight and organ weights were impacted with exposure in remaining dams. Reproductive performance was perturbed at 10 000 ppm TPHP and all IPP exposure groups. In offspring, both TPHP- and IPP-related toxicity was noted in pups at 10 000 ppm as well as reduction in bodyweights, delays in pubertal endpoints, and/or reduced cholinesterase enzyme activity starting at 1000 ppm TPHP or IPP. Preliminary internal dose assessment indicated gestational and lactational transfer following exposure to TPHP or IPP. These findings demonstrate that offspring development is sensitive to 1000 ppm TPHP or IPP exposure.
TPP, ITPs	2022	Witchey et. al.	DNT	Impacts of Gestational FireMaster 550 Exposure on the Neonatal Cortex Are Sex Specific and Largely Attributable to the Organophosphate Esters	1000 ug/day, or 3.3 mg/kg bw/day orally beginning 72 hours after pairing and continuing to PND1	Wistar rats and dams	The neonatal cortex was highly sexually dimorphic in lipid and transcriptome composition, and males were more significantly impacted by FR exposure. Multiple adverse modes of action for the BFRs and OPFRs on neurodevelopment were identified, with the OPFRs being more disruptive than the BFRs via multiple mechanisms including dysregulation of mitochondrial function and disruption of cholinergic and glutamatergic systems. Disrupted mitochondrial function by environmental factors has been linked to a higher risk of autism spectrum disorders and neurodegenerative disorders. Impacted lipid classes included ceramides, sphingomyelins, and triacylglycerides. Robust ceramide upregulation in the OPFR females could suggest a heightened risk of brain metabolic disease.
TPP, EHDPP, TCP, ITPs	2022	Hu et. al.	ED	Endocrine disrupting toxicity of aryl organophosphate esters and mode of action			See 21 study summary

TPP, EHDPP, TCrP and DPP	2022	Gao et al.	Repro and ED	Exposure assessment of aryl-organophosphate esters based on specific urinary biomarkers and their associations with reproductive hormone homeostasis disruption in women of childbearing age		urine samples from 913 women of childbearing age	Analyzed 3 ary-OPEs in urine samples from 913 women of child bearing ageand explored the association between exposure to the aryl-OPEs and reproductive hormone levels. The detection frequencies of the three metabolites were 94.6 %, 93.3 %, and 84.2 %, respectively. These results indicate that aryl-OPEs may disrupt hormone homeostasis using their specific biomarkers and may negatively affect female reproduction.
TPP	2024	ECHA	ED	Support Document for Identification of TPP as an SVHC for ED (environment)	Summary of studies		The available in vitro information demonstrates the capacity of TPhP to produce agonist activity on nuclear estrogen receptors ERα and ERβ of several vertebrate species including rat, mouse, fish, chicken, frog and turtle as evidenced by ER transactivation in reporter cell lines. In addition, TPhP can induce ER-regulated gene expression, and related physiological cell responses (e.g., increased cell proliferation). Two recent studies show that TPhP can also activate GPER. The available H295R assays on human adrenal carcinoma cells show that TPhP affects steroidogenesis by increasing estrogen levels (17ß-estradiol) and by increasing expression of genes involved in this pathway like CYP19 and 3β-HSD2. In vivo fish studies indicate that CYP19A is significantly upregulated by exposure to TPhP. Significant alteration of plasmatic concentrations of E2 and E2/T ratio and E2/11-KT ratio can result from this modification in the steroidogenesis pathway. The degree of perturbation of circulating steroid concentrations depends on the fish developmental stage, species and tested concentrations. The observations of VTG concentrations, that are consistent with perturbation of E2 concentrations, suggest an EAS activity of TPhP in female and male zebrafish, with altered concentration of VTG. Therefore, TPhP exerts an effect on the endocrine balance in fish. It has EAS activity as clearly shown both in vitro and in vivo.
EHDP, TPP, IDDPP, ITP, TCP, BPDP (also non-APE's: BDE-47, 99, TBBPA, tBOEP, bBoep, TDCPP, TCIPP, TCEP)	2022	Klose et al.	DNT	Neurodevelopmental toxicity asessment of flame retardants using a human DNT in vitro testing battery	Potency according to the respective most sensitive benchmark concentration (BMC) across the battery ranked from <1 µM (5 FRs), 1<10 µM (7 FRs) to the >10 µM range (3 FRs)	human cell-based DNT in vitro battery	Human cell–based developmental neurotoxicity (DNT) in vitro battery covering a large variety of neurodevelopmental endpoints. Potency according to the respective most sensitive benchmark concentration (BMC) across the battery ranked from <1 µM (5 FRs), 1<10 µM (7 FRs) to the >10 µM range (3 FRs). Evaluation of the data with the ToxPi tool revealed a distinct ranking (a) than with the BMC and (b) compared to the ToxCast data, suggesting that DNT hazard of these FRs is not well predicted by ToxCast assays. Extrapolating the DNT in vitro battery BMCs to human FR exposure via breast milk suggests low risk for individual compounds. However, it raises a potential concern for real-life mixture exposure, especially when different compounds converge through diverse modes-of-action on common endpoints, like oligodendrocyte differentiation in this study.

Collected and summarized by the Massachusetts Toxics Use Reduction Institute, November 2024

Abbreviation	Chemical Name
TXP	tris(3,5-dimethylphenyl) phosphate or trixylenyl phosphate
TPP and TPHP	triphenyl phosphate
TDTBPP	tris(2,4-di-tert-butylphenyl) phosphate
TCP, TOCP, TMPP	Tricresyl phosphate, mixture of o-,m-,p-tris(4-methylphenyl) phosphate is p- AKA TTP
tbTPP	tert-butylated TPP
TBPP	Tris(4-tert-butylphenyl) phosphate
TBPHP or T4tBPPP	Tris(2-biphenylyl) phosphate
T4iPPP	Tris(4-isopropylphenyl) phosphate
T3iPPP	Tris(3-isopropylphenyl) phosphate
RBDPP, RDP	Resorcinol bis-diphenyl phosphate
TOCP	tri-o-cresyl phosphate
IPTPP	tris(2-isopropyl phenyl) phosphate
IPP-1, IPP-2, IPP-3, IPPP, IPP, ITPs	Isopropylated triphenyl phosphate
IDDP	isodecyl diphenyl phosphate
EHDPP or EHDP	2-ethylhexyl diphenyl phosphate
DPP, DPHP	Diphenyl phosphate
DBPP	Dibutyl phenyl phosphate
CDP, CDPP	Cresyl diphenyl phosphate
BPDPP	2-biphenylyl diphenyl phosphate
BPDP	t-butylphenyl diphenyl phosphate
BEHPP	Bis(2-ethylhexyl)phenyl phosphate
bDPP	Butyl diphenyl phosphate
BDP	bisphenol A bis(diphenyl phosphate)
BDMEPPP	di-tert butyl phenyl phosphate
B21PPPP	bis(2-isopropylphenyl)phenyl phosphate
4IPPDPP	4-isopropyl phenyl diphenyl phosphate
2IPPDPP, mITP	isopropylphenyl diphenyl phosphate
24DIPPDPP	2,4-diisopropylphenyl diphenyl phosphate

Abbreviation	Chemical Name	Group
24DIPPDPP	2,4-diisopropylphenyl diphenyl phosphate	IP
2IPPDPP, mITP	isopropylphenyl diphenyl phosphate	IP
4IPPDPP	4-isopropyl phenyl diphenyl phosphate	IP
B21PPPP	bis(2-isopropylphenyl)phenyl phosphate	IP
BDMEPPP	di-tert butyl phenyl phosphate	B
BDP	bisphenol A bis(diphenyl phosphate)	diphosphate
bDPP	Butyl diphenyl phosphate	B
BEHPP	Bis(2-ethylhexyl)phenyl phosphate	1 phenyl plus 2 alkyl
BPDP	t-butylphenyl diphenyl phosphate	B
BPDPP	2-biphenylyl diphenyl phosphate	Diphenyl on one
CDP, CDPP	Cresyl diphenyl phosphate	M
DBPP	Dibutyl phenyl phosphate	B
DPP, DPHP	Diphenyl phosphate	Diphenyl
EHDPP or EHDP	2-ethylhexyl diphenyl phosphate	Diphenyl plus alkyl
IDDP	isodecyl diphenyl phosphate	Diphenyl plus alkyl
IPP-1, IPP-2, IPP-3, IPPP, IPP, ITPs	Isopropylated triphenyl phosphate	IP
IPTPP	tris(2-isopropyl phenyl) phosphate	IP
None	tetrakis(2,6-dimethylphenyl)-m-phenylene biphosphate	Diphosphate
None	3-(hydroxyphenylphosphinyl)propanoic acid	?
None	tris(3-butylphenyl) phosphate	B
None	Isopropylated, tert-butylated triphenylphosphate	IP and B
None	Biphenyl-4,4'-diyl tetrakis(2,6-dimethylphenyl) bis(phosphate)	Diphosphate, M
None	Phosphoric acid, mixed esters with biphenyl-4,4'-diol and phenol	
None	(2,3-dimethylphenyl) diphenyl phosphate	M
None	Dodecyldiphenyl phosphate	
None	1,3-Isobenofurandione, 4,5,6,7-tetrabromo-, reaction products with 2-ethyl-1-hexanol	
None	1,3-Isobenofurandione, 4,5,6,7-tetrabromo-, reaction products with 2-ethyl-1-hexano	?
None	tris(2-butylphenyl) phosphate	B
RBDPP, RDP	Resorcinol bis-diphenyl phosphate	diphosphate
T3iPPP	Tris(3-isopropylphenyl) phosphate	IP
T4iPPP	Tris(4-isopropylphenyl) phosphate	IP
TBPHP or T4tBPPP	Tris(2-biphenylyl) phosphate	None, biphenyl on all
TBPP	Tris(4-tert-butylphenyl) phosphate	B
tbTPP	tert-butylated TPP	B

TCP, TOCP, TMPP	Tricresyl phosphate, mixture of o-,m-,p-	M
TDTBPP	tris(2,4-di-tert-butylphenyl) phosphate	B
TOCP	tri-o-cresyl phosphate	M
TPP and TPHP	triphenyl phosphate	base
TXP	tris(3,5-dimethylphenyl) phosphate or trixylenyl phosphate	M
	tris(4-methylphenyl) phosphate is p- AKA TTP	

m=methyl
b=butyl
i=isopropyl
di=diphosphate