Supporting Information

Association of Aryl Organophosphate Flame Retardants Triphenyl Phosphate and 2-Ethylhexyl Diphenyl Phosphate with Human Blood Triglyceride and Total Cholesterol Levels

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Standards and reagents. Diester metabolites, dibutyl phosphate (DNBP), and di(2-ethylhexyl) phosphate (DEHP) were purchased from TCI Corp. (Tokyo, Japan). Bis(2-chloroethyl) phosphate (BCEP), bis(2-butoxyethyl) phosphate (BBOEP) and the internal standards including BCEP-d_8, DNBP-d_{18}, and DPHP-d_{10} were obtained from Toronto Research Chemicals Inc. (Toronto, Ontario, Canada).

Solvents including LC-MS grade of *n*-hexane, acetonitrile, and methanol (MeOH) and pesticide residue grade of ethyl acetate and dichloromethane were obtained from Fisher Chemicals (New Jersey, USA). Formic acid (HPLC grade) was from Dikma Technologies Inc. (California, USA). Sep-Pak® Silica (3 cm^3, 200 mg), Sep-Pak® C18 (3 cm^3, 200 mg), and Oasis WAX (3 cm^3, 60 mg) solid phase extraction (SPE) cartridges were purchased from Waters (Milford, MA, USA). β-Glucuronidase/aryl sulfatase enzyme was obtained from Merck (KGaA, Darmstadt, Germany). Ultrapure water was prepared using a Milli-Q Synthesis water purification system (Millipore, Bedford, MA, USA).

Table S1. Limits of detection (LODs), recoveries, and matrix effects of OPFR metabolites in urine samples.

Analytes	LODs (ng/mL)	Recovery ± RSD (%)			Matrix effect
		Low	Medium	High	
BCEP	0.25	74± 10	81± 5	77 ± 4	-12.3%
BCIPP	0.08	83 ± 9	79 ± 3	80 ± 8	-11.2%
BDCIPP	0.1	81 ± 5	76 ± 9	85 ± 6	-10.8%
DNBP	0.22	89± 8	91 ± 6	94 ± 7	4.3%
BBOEP	0.04	84 ± 9	90 ± 7	91 ± 5	-5.5%
DEHP	0.01	85± 11	87 ± 9	90 ± 3	-3.8%

Table S2. Pearson correlation coefficients (r) of log-transformed urinary OPFR metabolites concentrations.

OPFR metabolites		BCEP	5-OH-EHDPP	3-OH-MDTP	4-OH-TPHP	DPHP	DNBP
BCEP	r	1					
	p-value	-					
5-OH-EHDPP	r	0.128	1				
	p-value	0.040*	-				
3-OH-MDTP	r	-0.014	0.180	1			
	p-value	0.424	0.011 *	-			
4-OH-TPHP	r	0.185	0.148	0.021	1		
	p-value	0.003**	0.067	0.788	-		
DPHP	r	0.300	0.220	-0.118	0.451	1	
	p-value	<0.001**	0.003**	0.098	<0.001**	-	
DNBP	r	0.347	0.074	0.015	0.240	0.346	1
	p-value	<0.001**	0.236	0.233	<0.001**	<0.001**	-

Statistically significant (*$p < 0.05$, **$p < 0.01$).

Table S3. Percentage changes (95% CI) for total cholesterol (TC) and triglyceride (TG) levels per 0.1 ng/mL increase in urinary concentrations of OPFR metabolites.

	TC [a]	TG [a]
5-OH-EHDPP	4.8% (3.6% - 6.0%)	9.4% (6.9% - 11.9%)
4-OH-TPHP	1.5% (0.7% - 2.3%)	4.3% (3.1% - 5.5%)
DPHP	0.05% (-0.32% - 0.42%)	0.5% (0.1% - 1.0%)

[a]All models are adjusted for BMI, gender, age, household income, alcohol intake, and tobacco use.

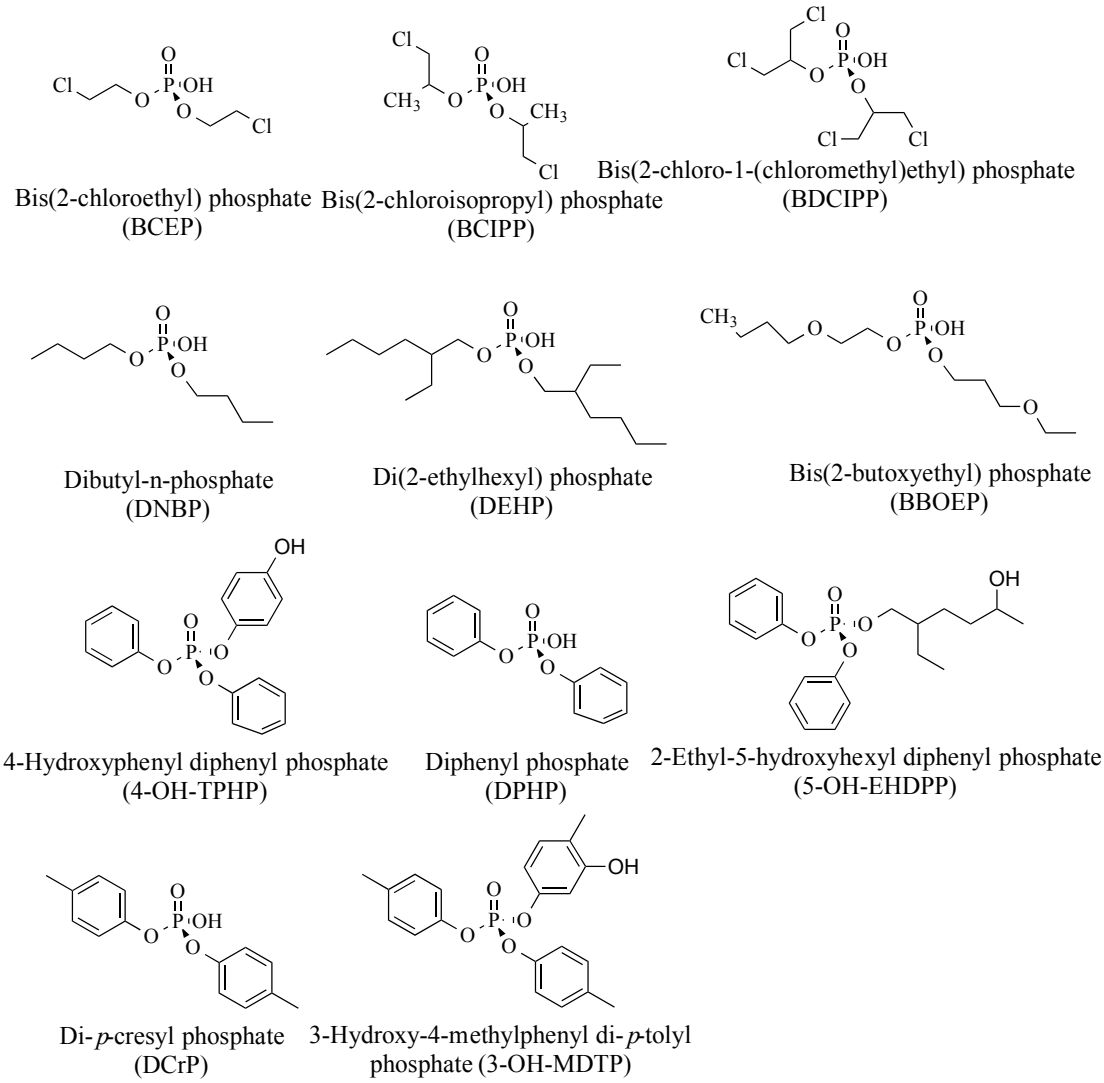

Figure S1. Structures of 11 OPFRs along with their full chemical names and abbreviations.

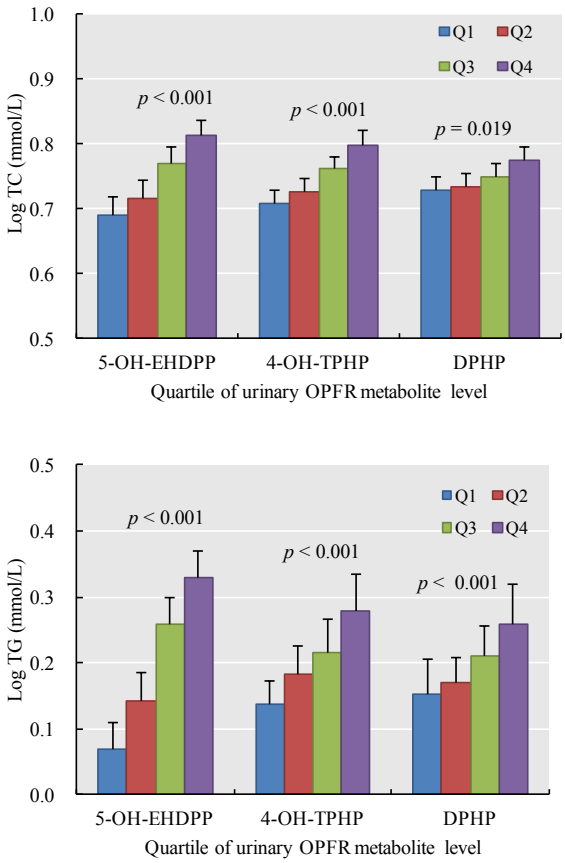

Figure S2. Changes in TC and TG with increasing creatinine-uncorrected quartiles of OPFR metabolites. Quartile 1 (Q1) is the lowest, and Q4 is the highest. All models are adjusted for BMI, gender, age, household income, alcohol intake, and tobacco use. The *p* trends for TC and TG levels across the quartiles of OPFR metabolites are presented.

Reference

1. Zhao, F. R.; Kang, Q. Y.; Zhang, X. H.; Liu, J. Y.; Hu, J. Y., Urinary biomarkers for assessment of human exposure to monomeric aryl phosphate flame retardants. *Environ. Int.* **2019,** *124*, 259-264.