Supplementary Information for

Exposure to flame retardants in European children — Results from the HBM4EU aligned studies

Veronica van der Schyff[1], Jiri Kalina[1], Eva Govarts[2], Liese Gilles[2], Greet Schroeters[2,3], Argelia Castaño[4], Marta Esteban-López[4], Jiri Kohoutek[1], Petr Kukucka[1], Adrian Covaci[5], Gudrun Koppen[2], Lenka Andryskova[1], Pavel Piler[1], Jana Klanova[1], Tina Kold Jensen[6], Loic Rambaud[7], Margaux Riou[7], Marja Lamoree[8], Marike Kolossa-Gehring[9], Nina Vogel[9], Till Weber[9], Thomas Göen[10], Catherine Gabriel[11,12], Dimosthenis A. Sarigiannis[11,12,13], Amrit Kaur Sakhi[14], Line Småstuen Haug[14], Lubica Palkovicova Murinova[15], Lucia Fabelova[15], Janja Snoj Tratnik[16], Darja Mazej[16], Lisa Melymuk[1,*]

[1] RECETOX, Faculty of Science, Masaryk University, Kotlarska 2, Brno, Czech Republic
[2] VITO Health, Flemish Institute for Technological Research (VITO), Mol, 2400, Belgium
[3] Department of Biomedical Sciences, University of Antwerp, 2020 Antwerp, Belgium
[4] National Centre for Environmental Health, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain
[5] Toxicological Center, University of Antwerp, 2610 Wilrijk, Belgium
[6] Department of Environmental Medicine, Institute of Public Health, University of Southern Denmark, Odense, 5000, Denmark
[7] Santé Publique France, French Public Health Agency (ANSP), Saint-Maurice, 94415, France
[8] Vrije Universiteit, Amsterdam Institute for Life and Environment, Section Chemistry for Environment & Health, De Boelelaan 1108, 1081 HZ Amsterdam, Netherlands
[9] German Environment Agency (UBA), 06844 Dessau-Roßlau, Germany
[10] IPASUM - Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine; Henkestrasse 9-11, 91054, Erlangen, Germany
[11] Environmental Engineering Laboratory, Department of Chemical Engineering, Aristotle University of Thessaloniki, 54124, Thessaloniki, Greece
[12] HERACLES Research Center on the Exposome and Health, Center for Interdisciplinary Research and Innovation, Balkan Center, Bldg. B, 10th km Thessaloniki-Thermi Road, 57001, Greece
[13] Environmental Health Engineering, Institute of Advanced Study, Palazzo del Broletto - Piazza Della Vittoria 15, 27100 Pavia, Italy
[14] Department of Environmental Health, Norwegian Institute of Public Health, Oslo, Norway
[15] Faculty of Public Health, Slovak Medical University, Bratislava, 833 03, Slovakia
[16] Department of Environmental Sciences, Jožef Stefan Institute, Ljubljana, 1000, Slovenia

* Corresponding author:
Lisa Melymuk
lisa.melymuk@recetox.muni.cz
RECETOX, Faculty of Science, Masaryk University, Kotlarska 2, Brno, Czech Republic

Supplementary Text

Tables

Table S1 Details on studies and laboratories performing the analyses

Country	Study	Cohort profile	Compound	Matrix	Sample collection	Laboratory
Belgium	3xG	The 3xG study was conducted in three Flemish communities of the province Antwerp. The study was initiated as a birth cohort in 2010-2015 to follow-up health and health determinants in a regional setting. The follow-up examination included a total of 212 participants between 6-8 years, for which a subset of 133 participants contributed to the HBM4EU aligned studies.	BDCIPP BCIPP DPHP	Morning urine	New urine samples were collected between January 2019 and March 2020.	Toxicological Center, University of Antwerp
Czech Republic	CELSPAC	CELSPAC: School children study (Central European Longitudinal Studies of Parents and Children: Teenagers) was conducted in the South Moravia schools in the Czech Republic between 2019 to 2020. The main aim of this cross-sectional study was to assess the multiple factors potentially affecting the physical fitness of school children. A total sample of 195 school children was recruited to the study, completed questionnaires, underwent examinations and donated urine for the CELSPAC biobank.	BCEP BCIPP BDCIPP DPHP	Spot urine	New collection (2019/2020)	Trace Analytical Laboratory, RECETOX, Masaryk University
Germany	GerES V	The German Environmental Survey (GerES) is a representative population study carried out in order to determine the exposure to pollutants of the general population in Germany. GerES V investigated children and adolescents by determining, on a representative basis, the body burden of pollutants and the exposure to pollutants at home (European Commission, 2021a).	BCEP BCIPP BDCIPP DPHP	Morning urine	Biobanked samples of which 300 were newly analyzed for aligned studies	Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine (IPASUM), Friedrich-Alexander-Universität Erlangen-Nürnberg
Denmark	OCC	The OCC study was initiated in the Municipality of Odense in Southern Denmark. Recruitment occurred from 2010-2013. Urine was collected from children involved at 7 year timepoint.	BCIPP BDCIPP DPHP	Spot urine	New urine collection from 2018-2019	Toxicological Center, University of Antwerp

France	ESTEBAN	Cross-sectional study in the general population, representative from the French population at national level. (European Commission, 2021b)	anti-DP syn-DP PBDE-47 PBDE-153 PBDE-209 TBBPH BEH-TEBP DBDPE αHBCDD γHBCDD	Blood serum	Biobanked samples collected in 2014/2016	Department of Food Analysis and Nutrition (VSCHT), University of Chemistry and Technology, Prague
			BCIPP BDCIPP DPHP	Morning urine	Biobanked samples collected in 2014/2016	Department Environment & Health, Vrije Universiteit Amsterdam
Greece	CROME	The CROME study was initiated as a parent-children cohort in the city of Thessaloniki investigating the levels of environmental pollutants and biochemical indicators of exposure. Participants were invited through bilateral meetings and word of mouth as due to the covid-19 pandemic the initial planning, i.e. to take place through the school structures was not feasible.	anti-DP syn-DP PBDE-47 PBDE-153 PBDE-209 DBDPE αHBCDD γHBCDD	Blood serum	New serum samples were collected for OPFR metabolites in the frame of CROME cohort between July 2020 and March 2021	Trace Analytical Laboratory, RECETOX, Masaryk University
Norway	NEB II	Cross-sectional study, including children throughout Norway	anti-DP syn-DP ΣDP PBDE-47 PBDE-153	Blood plasma	Biobanked samples collected in 2016/17	Environmental Exposure and Epidemiology, Norwegian Institute of Public Health
			DPHP BDCIPP	Spot urine	Biobanked samples collected in 2016/17	
Slovenia	SLO CRP	Cross sectional study conducted in Mura region, Slovenia to assess exposure to selected chemicals in children and adolescents through their living environment. (Stajnko et al., 2020)	anti-DP syn-DP PBDE-47 PBDE-153 PBDE-209 αHBCDD γHBCDD DBDPE	Blood serum	New serum samples were collected between January and June 2018.	Trace Analytical Laboratory, RECETOX, Masaryk University

			DPHP BCEP BCIPP BDCIPP	Spot urine	New urine samples were collected between January and June 2018.	
Slovakia	PCB cohort	Longitudinal birth cohort study in region of Eastern Slovakia impacted by past manufacturing of PCBs. (Hertz-Picciotto et al., 2003)	BCEP BCIPP BDCIPP DPHP	Spot urine	Biobanked samples	Trace Analytical Laboratory, RECETOX, Masaryk University

Supplementary text. Analytical procedures of each study

3xG OPFR metabolites

Urine samples were analyzed for OPFR metabolites at the Toxicological Center, University of Antwerp, BE using the procedure described by Bastiaensen et al. (2018). Urine samples (1 mL) were spiked with mass-labelled internal standards (5 ng), adjusted to pH 6 with phosphate buffer (1 M) and deconjugated with ß-glucuronidase (2 mg/mL). Samples were extracted on Bond-Elut C18 cartridges (3 mL, 200 mg), conditioned with 3 mL of methanol and 2 mL of water. Target analytes were eluted with methanol (3 mL), concentrated and filtered in a micro-centrifuge (0.2 µm nylon, VWR). Final extracts (water:methanol 1:1) were injected on a Agilent 1290 Infinity liquid chromatography system coupled to a triple quadrupole mass spectrometer (ESI-6460, Agilent). Separation was obtained by a Kinetex Biphenyl column (2.1 mm × 100 mm, 2.6 µm; Phenomenex) and mobile phases of water with 2% methanol (A) and methanol with 2% water (5 mM ammonium acetate as additive). Target analytes were identified through dynamic multiple reaction monitoring (dMRM) in positive and negative ionization. Quantification of target analytes was performed with calibration curves in neat solvents ranging from 0.04 to 10 ng/mL, except for BCIPP and 4-HO-DPHP for which the calibration ranged from 0.2 to 50 ng/mL. Procedural blanks were analyzed to check for background contamination. DPHP, DNBP and TCEP were found at trace levels in procedural blanks (0.14, 0.08 and 0.03 ng/mL, respectively). These blank concentrations were subtracted from values in urine samples. Limits of quantification (LOQ) were determined as three times the standard deviation of procedural blank concentrations (for DPHP, DNBP and TCEP) or as the concentration corresponding to a signal-to-noise ratio of 10 in spiked urine samples. Successful participation in inter-laboratory comparison exercises (HBM4EU ICI/EQUAS and OSEQAS, 2018–2020) assured additional external quality control for several target analytes (DPHP, BDCIPP and BCIPP).

CELSPAC OPFR metabolites

Urine samples were analyzed at the RECETOX Trace Analytical Laboratories, Brno, CZ. Urine samples were brought to room temperature, homogenized by vortex and 500 µl of each urine sample was transferred to 96-well plate. Samples were spiked with 5 ng of isotopically-labelled internal standards, and 500 µL of 10 mM NH4Ac was added. Target analytes were extracted using 96-well SPE plate Oasis WAX (60mg). Conditioning was done using 2mL 5% NH4OH in MeOH and then 2 mL 10mM NH4Ac per well. Samples were washed using 1mL 30% MeOH (pH=5) and eluted using 2mL 5% NH4OH in MeOH to the 96- well plate containing 10uL DMSO/well as keeper. After evaporation to DMSO under nitrogen stream, samples were diluted by 400 ul 50% MeOH and homogenized. Final extracts were injected on an Agilent 1200 series liquid chromatography (HPLC) system coupled to a tandem mass spectrometer (AB Sciex QTrap 5500) operating in negative electrospray ionization mode. Chromatographic separation was accomplished using a Waters Acquity BEH C-18 analytical column (100 x 2.1 mm, 1.7 µm particle size) maintained at 30°C and equipped with Acquity VanGuard pre-column. The mobile phases for the gradient separation of the analytes were 1.0 mM water solution of ammonium fluoride (component A) and methanol with an addition of 1.0 mM ammonium fluoride (component B), with a flow rate was 0.3 mL·min-1, and the injection volume was 5 µL. Quantification of target analytes

was performed by isotope dilution method using 2D-labeled BCEP, BCIPP, BDCIPP and DPHP. The linear quantification range (MRM mode) was 0.1-100 µg/L urine, with limits of quantification from 0.09 to 1.0 µg/L urine (MQL, calculated as 10* the standard deviation (SD) of the blank sample). Successful participation in inter-laboratory comparison exercises (HBM4EU ICI/EQUAS and OSEQAS, 2018–2020) assured additional external quality control for DPHP, BDCIPP and BCIPP.

GerES V OPFR metabolites

Urine samples were analyzed by the Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine of the University of Erlangen-Nuremberg. Urine samples (5 mL) were acidified and spiked with an internal standard solution which included stable isotope labeled compounds structurally identical with the analytes (BDCPP-d2, BCEP-d8, DPhP-d10 and BDCPP-d10). The urinary solutions were extracted by SPE using ENV+ cartridges. After elution the extract were evaporated to dryness and the residues underwent a derivatization with pentaflurobenzyl bromide at 65 °C for 16 hours. Final extracts were injected on an Agilent 7000A gas chromatography (tandem mass spectrometer (GC-MS/MS) using electron impact ionization for DPhP, BCEP and BCPP and an Agilent 5975D gas chromatography-mass spectrometry (GC-MS) system using negative chemical ionization for BDCPP. The procedure was calibrated by standard solution prepared in pooled urine. The quality was controlled by analyzing samples of quality control materials in each series and the application of control charts. Successful participation in inter-laboratory comparison exercises (HBM4EU ICI/EQUAS 2018–2020) assured additional external quality control for DPHP, BDCIPP, BCEP and BCIPP.

OCC OPFR metabolites

Same as 3xG

ESTEBAN OPFR metabolites

Urine samples were analyzed by the Vrije Universiteit Amsterdam. Deuterated isotopically labeled internal standard (50 µl, 50 ng/ml DPHP-d10, BCIPP-d12 and BDCIPP-d10, all Toronto Research Chemicals) was added to 0.5ml urine. The conjugated metabolites were hydrolyzed by 5 µl β–glucuronidase (0.7 U per sample, Roche) under 0.5 M acetate buffered conditions at pH 6.2. The extraction and separation were done using an online SPE-LC configuration (Elute, Bruker). The extracts were trapped on a C18 cartridge (Waters Xbridge, 4.6x20mm, 5µm) and washed with 1 ml 0.2% acetic acid (v/v). The analytes were eluted from the cartridge to the analytical column (Waters Xbridge C18 100x2.1mm, 2.5µm) by a gradient of 10 mM ammonium acetate and methanol, starting at 5% methanol for 1 m, followed by a linear increase in 5 m to 95% methanol and followed by isocratic elution under these conditions for 5 m. The target compounds were detected with a mass selective detector (MS/MS, EVOQ, Bruker) using electrospray ionization operated in the negative ion mode (DPHP: 249 -> 93/155, BCIPP: 319 -> 35 & 317 -> 35, BDCIPP: 249 -> 35 & 251 -> 35).

Successful participation in inter-laboratory comparison exercises (HBM4EU ICI/EQUAS and OSEQAS, 2018–2020) assured additional external quality control for DPHP and BDCIPP. Background contaminations were checked by analyzing procedure and solvent blanks.

ESTEBAN FRs in serum

Serum samples were analyzed by the Department of Food Analysis and Nutrition from University of Chemistry and Technology, Prague (UCT Prague), following the method published in Svarcova et al., 2019. The analytical method is based on the simultaneous determination of non-polar (BDE 47, BDE 153, BDE 209, DBDPE, syn-DP, anti-DP) and less non-polar compounds (HBCDD, TBBPA, 2,4,6-TBP) in serum. To each sample (3,5 ml minimum) surrogate standards were added, specifically a mixture of 13C-HBCDD isomers, 13C-TBBPA, BDE 37, BDE 77 and 13C-BDE 209. Non-polar compounds were extracted by three-step solvent extraction using a mixture of n-hexane:diethylether (9:1, v/v), followed by purification using a solid-phase extraction (SPE) on a Florisil® column. HBCDD, TBBPA and 2,4,6-TBP were further extracted after the first step using a modified QuEChERS method. Depending on the polarity and volatility of target compounds, a different methods were used for identification and quantification of compounds. Gas chromatography coupled to (tandem) mass spectrometry (GC–MS/(MS)) was used for BDEs, DP-syn, DP-anti and DBDPE, and ultra-high performance liquid chromatography coupled to triple quadrupole tandem mass spectrometry (UHPLC–MS/MS) was used for HBCDD, TBBPA and 2,4,6-TBP. Successful participation in inter-laboratory comparison exercises (HBM4EU ICI/EQUAS and OSEQAS, 2018–2020) assured additional external quality control all serum analyses. For further details, please see the published study by Svarcova et al. (2019).

CROME FRs in serum

Serum samples were analyzed at the RECETOX Trace Analytical Laboratories, Brno, CZ. Thawed blood sera were extracted using liquid-liquid extraction (LLE). 250 µL of serum was spiked with 40 µL internal standard mix (13C labelled compounds) in isopropanol (IPA). A further 250 µL ethanol was added for protein precipitation and about 1 g of activated silica to form a slurry. Sera were extracted three times using 5 mL of dichloromethane/n-hexane (1:4, v/v) mix. The extracts were reduced in volume under stream of nitrogen. Clean-up was performed using open column (1 cm i.d.) silica chromatography. The column was filled (bottom to top) with 2 cm of activated silica, 3 cm H2SO4 modified (44%) silica and 10 cm sodium sulphate. The extracts were quantitatively loaded on the column and eluted using 30 mL dichloromethane/n-hexane (1:1 v/v). The eluates were reduced in volume under stream of nitrogen using SuperVap (FMS, USA) apparatus, then transferred into conical GC vial, volume further reduced to 15 µL (in nonane) under nitrogen stream and 20 µL syringe standards were added. Gas chromatography atmospheric chemical ionization tandem mass spectrometry (GC-APCI-MS/MS) was used for analysis. The GC was fitted with a 15 m x 0.25 mm x 0.10 µm RTX-1614 column (Restek, USA). Injection was splitless 1 µL at 280°C, with He as carrier gas at 1.5 mL min-1. The GC temperature programme was 80°C (1 min hold), then 20°C min-1 to 250°C, followed by 1.5°C min-1 to 260°C (2 min hold) and 25°C min-1 to 325°C (5 min hold). The MS was operated in MRM mode. Data were processed using Waters (UK) TargetLynx Software. Internal QA/QC was accomplished through three procedural blanks, and replicates of SRM 1957 (NIST, USA) and HBM4EU inter-laboratory study test material; blank-based LOD values were used. Successful participation in

inter-laboratory comparison exercises (HBM4EU ICI/EQUAS and OSEQAS, 2018–2020) assured additional external quality control all serum analytes.

NEB II OPFR metabolites

Urine samples were analyzed by the Environmental Exposure and Epidemiology section, Norwegian Institute for Public Health following the method of Cequier *et al* (2016). Clean up and pre-concentration with solid-phase extraction (Strata X-AW) and analysis using UPLC-QTOF Details about standards, internal standards and exact masses used are as described by *Cequier et al.* (2014).

NEB II FRs in plasma

Plasma samples were analyzed by the Environmental Exposure and Epidemiology section, Norwegian Institute for Public Health following the method of Caspersen *et al*. (2016). Solid-phase extraction (Oasis HLB) and clean-up on a sulphuric acid silica column and analysis using GC-MS/MS as described by Frederiksen *et al* (2020).

SLO CRP OPFR metabolites

Same as CELSPAC

SLO CRP FRs in serum

Serum samples were analyzed at the RECETOX Trace Analytical Laboratories, Brno, CZ (Palát et al., 2022). Samples (200 µL) were allowed to stabilize at ambient temperature (~20 °C) for 60 minutes and transferred to 2 mL amber glass vials and fortified with 13C internal standards in 40 µL IPA and vortexed for 20 s. Protein precipitation was performed by addition of 600 µL MeCN. These samples were then extracted by 96-well plate solid phase extraction (SPE; 60 mg Oasis HLB) using DCM:Hex (1:19 (v/v)), preconditioned with 1 mL DCM:Hex (1:19 (v/v)), followed by 1 mL MeOH and finally 1 mL ultrapure water. A Phree plate was prepared by the addition of 0.1 g prebaked anhydrous Na2SO4 to each well and wells prewashed with 1 mL DCM:Hex (1:19 (v/v)). The Oasis HLB plate was then stacked atop the Phree plate, and samples were eluted by addition of 1.2 mL DCM:Hex (1:19 (v/v)). The eluates were evaporated under nitrogen to ~600 µL and transferred into GC vials. After that 20 µL of nonane was added as keeper and extracts were evaporated under nitrogen to ~20 µL volume. Standards 13C-BDE 77 and 13C-BDE 138: 1000 pg, 13C-PCB 162: 500 pg were added and extracts concentrated under nitrogen to final volume of ~40 µL for analysis of FRs. Gas chromatography atmospheric chemical ionization tandem mass spectrometry (GC-APCI-MS/MS) was used for analysis. The GC was fitted with a 15 m x 0.25 mm x 0.10 µm RTX-1614 column (Restek, USA). Injection was splitless 1 µL at 280°C, with He as carrier gas at 1.5 mL min-1. The GC temperature programme was 80°C (1 min hold), then 20°C min-1 to 250°C, followed by 1.5°C min-1 to 260°C (2 min hold) and 25°C min-1 to 325°C (5 min hold). The MS was operated in MRM mode. Data were processed using Waters (UK) TargetLynx Software. Internal quality controls was accomplished through processing six solvent

blanks and ten replicates of SRM 1957 and SRM 1958 serum. Successful participation in inter-laboratory comparison exercises (HBM4EU ICI/EQUAS and OSEQAS, 2018–2020) assured additional external quality control all serum analytes.

PCB COHORT OPFR metabolites

Urine samples were analyzed for OPFR metabolites at RECETOX (Same as CELSPAC)

Table S2 Ethics committees and funding information of participating HBM4EU aligned studies

Study acronym	Country	Ethics information
3xG	BE	Approved by the ethical committee of University Hospital Antwerp and University Antwerp on 09.11.2010 (Ref N° UA A10-58), amendment for follow-up at 7 years approved on 09.01.2019. Amendment for conducting additional analysis under HBM4EU was approved on 24.08.2020 (Ref N° UA A10-58: 3xG).
CELSPAC	CZ	Approved by the Research Ethics Committee of Masaryk University, Czech Republic (Ref. No: EKV-2019-046, 27.05.2019).
GerES V	DE	Approved by the Ethics Commission of the Berlin Chamber of Physicians (Eth-14/14) and the Federal Officer for Data Protection and Freedom of Information (III-425/009#0018).
OCC	DK	Approved by the Regional Scientific Ethical Review Committee for Southern Denmark (Project ID S-0090130) and the Danish Data Protection Agency (J.No.18/33119).
CROME	EL	Approved by the Committee on Ethics and Deontology for Research of AUTH, in the assembly 1/25-10-2018, by request no. Prot. 111256 / 17-09-2018 regarding the research under the project "Cross-Mediterranean Environment and Health Network" and carried out in accordance with the Code of Ethics of Aristotle University of Thessaloniki.
ESTEBAN	FR	Approved by the Ile-de-France Protection to person committee on the 06.12.2012 (Internal number: CPP-IDF IX 12-012, EudraCT: 2012-A00459-34). The Committee has examined all provided and requested document (Informed consent, protocol, authorization form from the Ministry of Health, etc). The French Data Protection Agency gave its approval on the 14.02.2013. A Decree of the State Council establishing a processing of personal data relating to biomonitoring, health surveillance and nutrition (The Esteban study) was established after approval of the French Advisory Committee on Information Processing for Research (CCTIRS). The French National Agency for Medicines and Health Products' Safety (ANSM) gave its approval for the use of biological samples and biobanking.
NEB II	NO	Approved by The Regional Committees for Medical and Health Research Ethics in Norway, Reference: 2015/1340.
SLO CRP	SI	Approved by the National Medical Ethics Committee, Republic of Slovenia (NMEC, number of accordance: 0120-118/2017/3).
PCB cohort	SK	Approved by the ethical committee of the Slovak Medical University in Bratislava (No. 01/2018 and 02/2019).

Table S3 Limits of detection (LOD) and limits of quantification (LOQ) of compounds analyzed in serum/plasma (µg/L).

Country	PBDE-47		PBDE-153		PBDE-209		αHBCDD		γHBCDD		synDP		antiDP		TBBPA		DBDPE		BEH-TEBP	
	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ
France	0.001	0.002	0.001	0.002	0.007	0.02	0.01	0.04	0.01	0.04	0.001	0.002	0.001	0.002	0.7	2	0.013	0.04	0.7	2
Greece	0.0001	0.0002	0.00003	0.0001	0.0016	0.0052	0.0075	0.025	0.0075	0.025	0.03	0.1	0.02	0.06						
Norway	0.0003	0.0005	0.0007	0.002							0.0002	0.0005	0.0002	0.0005						
Slovenia						0.05						0.053		0.04						

Table S4 Limits of detection (LOD) and limits of quantification (LOQ) of compounds analyzed in urine (µg/L).

Country	BDCIPP		DPHP		BCEP		BCIPP	
	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ
Belgium		0.05		0.1				0.4
Czech Republic	0.09	0.3	0..3	0.09	0.03	1	0.09	0.3
Germany		0.3		0.15		0.1		0.1
Denmark		0.05		0.1				0.4
France	0.1	0.3	0.1	0.3			0.2	0.7
Norway	0.17	0.5	0.03	0.1				
Slovenia	0.09	0.3	0.03	0.09	0.3	1	0.09	0.3
Slovakia	0.09	0.3	0.03	0.09	0.3	1	0.09	0.3

Table S5 Detection frequencies of halogenated flame retardants quantified in children's serum/plasma different countries in this study. Values in green are above 40% detection frequency and were used in statistical analysis. Values in red were excluded from statistical analyses. Compounds that were not studied in a specific country is indicated by n.a.

	PBDE-47	PBDE-153	PBDE 209	anti DP	syn DP	αHBCDD	γHBCDD	DBDPE	BEH-TEBP	TBBPA
FR	45	35	65	32	11	3	0	13	0	0
EL	49	78	0	2	0	11	2	16	na	na
SI	15	80	8	41	12	27	5	18	na	na
NO	98	19	na	94	100	na	na	na	na	na

Table S6 Detection frequencies of organophosphate flame retardants quantified in children's urine different countries in this study. Values in green are above 40% detection frequency and were used in statistical analysis. Values in red were excluded from statistical analyses. Compounds that were not studied in a specific country is indicated by n.a.

	BCEP	BCIPP	BDCIPP	DPHP
FR	na	31	65	99
SI	20	18	84	97
NO	na	na	17	100
DK	na	7	97	100
SK	20	29	37	100
DE	63	53	80	99
BE	na	14	98	99
CZ	83	47	57	94

Table S7 Parameters from single-effect linear regression

country	compound	exposure determinant	estimate	standard error	t value	p value (t based)
CZ	BCEP	(Intercept)	-0.580	0.045	-12.91	<0.0001
DE	BCEP	(Intercept)	-0.798	0.025	-31.41	<0.0001
CZ	BCIPP	(Intercept)	-1.018	0.038	-27.04	<0.0001
DE	BCIPP	(Intercept)	-0.864	0.021	-41.05	<0.0001
FR	BCIPP	(Intercept)	425.310	130.366	3.26	0.001
FR	BCIPP	sampling year	-0.211	0.065	-3.26	0.001
FR	BCIPP	home built 1960-1980	0.108	0.099	1.09	0.276
FR	BCIPP	home built 1981-2000	0.061	0.107	0.57	0.569
FR	BCIPP	home built 2001-2006	0.378	0.114	3.31	0.001
FR	BCIPP	home built after 2006	0.367	0.108	3.39	0.001
FR	BCIPP	cleaning <1/month	-0.099	0.111	-0.89	0.375
FR	BCIPP	cleaning <1/week, >1/month	-0.098	0.105	-0.94	0.347
FR	BCIPP	cleaning 2-3 time/week	-0.133	0.097	-1.37	0.172
FR	BCIPP	cleaning 7 times/week	-0.498	0.150	-3.31	0.001
FR	BCIPP	Drinking tap water	-0.123	0.084	-1.48	0.141
FR	BCIPP	Drinking ground water	-0.482	0.182	-2.64	0.009
FR	BCIPP	Other drinking water source	-0.245	0.122	-2.02	0.045
BE	BDCIPP	(Intercept)	-0.307	0.042	-7.25	<0.0001
CZ	BDCIPP	(Intercept)	-0.528	0.031	-17.07	<0.0001
DE	BDCIPP	(Intercept)	-0.174	0.021	-8.44	<0.0001
DK	BDCIPP	(Intercept)	-0.283	0.028	-10.10	<0.0001
FR	BDCIPP	(Intercept)	-0.213	0.030	-7.16	<0.0001
SI	BDCIPP	(Intercept)	-0.193	0.024	-8.12	<0.0001
SK	BDCIPP	(Intercept)	-183.851	77.897	-2.36	0.019
SK	BDCIPP	sampling year	0.091	0.039	2.35	0.019
EL	BDE-47	(Intercept)	-3.367	0.342	-9.83	<0.0001
EL	BDE-47	male	0.371	0.173	2.15	0.036
EL	BDE-47	Vacuuming <1/week, >1/month	-1.066	0.321	-3.32	0.002
EL	BDE-47	Vacuuming 2-3 times/week	-1.022	0.375	-2.73	0.009
EL	BDE-47	Medium income household	-0.296	0.184	-1.61	0.114
EL	BDE-47	High income household	-0.740	0.255	-2.90	0.006
FR	BDE-47	(Intercept)	425.538	127.907	3.33	0.001
FR	BDE-47	sampling year	-0.213	0.063	-3.35	0.001
FR	BDE-47	cleaning <1/month	0.260	0.105	2.48	0.014
FR	BDE-47	cleaning <1/week, >1/month	0.162	0.103	1.57	0.118
FR	BDE-47	cleaning 2-3 time/week	0.067	0.094	0.71	0.481
FR	BDE-47	cleaning 7 times/week	0.125	0.133	0.94	0.349
NO	BDE-47	(Intercept)	-3.447	0.020	-173.26	<0.0001
EL	BDE-47	(Intercept)	-3.364	0.318	-10.58	<0.0001
EL	BDE-153	Consumes organic food daily	-0.905	0.337	-2.69	0.010
EL	BDE-153	Consumes canned food <1/month	0.653	0.311	2.10	0.041
EL	BDE-153	Consumes canned food <1/week, >1/month	-0.573	0.515	-1.11	0.271
EL	BDE-153	Consumes canned food 4-6 times/week	0.470	0.720	0.65	0.517
FR	BDE-153	(Intercept)	-3.499	0.025	-140.36	<0.0001
SI	BDE-153	(Intercept)	-3.681	0.038	-95.81	<0.0001
FR	BDE-209	(Intercept)	-2.092	0.050	-42.12	<0.0001
FR	DP	(Intercept)	209.257	69.115	3.03	0.003
FR	DP	sampling year	-0.106	0.034	-3.08	0.002
NO	DP	(Intercept)	-2.488	0.031	-79.33	<0.0001
SI	DP	(Intercept)	-1.664	0.049	-33.81	<0.0001
SI	DP	Mother employed	-0.144	0.051	-2.84	0.005
BE	DPHP	(Intercept)	0.391	0.026	14.82	<0.0001
CZ	DPHP	(Intercept)	0.284	0.023	12.50	<0.0001
DE	DPHP	(Intercept)	0.230	0.019	12.42	<0.0001
DK	DPHP	(Intercept)	0.162	0.021	7.79	<0.0001
FR	DPHP	(Intercept)	0.320	0.022	14.85	<0.0001
NO	DPHP	(Intercept)	0.268	0.020	13.31	<0.0001
SI	DPHP	(Intercept)	0.346	0.035	9.77	<0.0001
SK	DPHP	(Intercept)	0.348	0.026	13.56	<0.0001

Table S8 Flame retardant concentrations in children from previous studies. Concentrations reported in this study are indicated in bold. Studies reporting SG normalized or unadjusted urine concentrations have been converted to median creatinine-normalized units based on the following assumptions: (1) from unadjusted urine to creatinine adjusted, a median ratio of 0.7463 L/g was used (creatinine inverse concentration), determined from the creatinine levels in the CELSPAC study; (2) recalculation from SG normalized concentration to the creatinine according to the median ratio of 0.5814677 L/g (SG standardized creatinine inverse concentration) determined from CELSPAC study. Recalculated values are reported in parentheses below those in the study units.

Country	Matrix	Age group (years)	Study start	study end	Unit	Reported as	BCEP	BCIPP	BDCIPP	DPHP	BDE-47	BDE-153	BDE-209	Study
China	Urine	0-5	2016	2016	ng/ml	GM	0.67 (0.50)	0.81 (0.60)	0.08 (0.06)	0.25 (0.19)				(Zhang et al., 2018)
China	Urine	8-14	2015	2015	µg/L (SG normalised)	Mean	3.25 (1.04)	0.21 (0.07)	0.12 (0.04)	0.4 (0.13)				(Chen et al., 2018)
China	Serum	9-12	2008	2008	ng/g lipid	Median					1.01	0.61	1.73	(Zhang et al., 2011)
China	Serum	±10	2015	2015	ng/g lipid	Median					4.4	2.9	95	(Guo et al., 2016)
USA	Urine	3-6	2014	2016	ng/ml (SG corrected)	GM		0.43 (0.25)	5.63 (3.27)	2.67 (1.55)				(Phillips et al., 2018)
USA	Urine	3-5	2015	2015	ng/ml (SG normalized)	Media		0.9 (0.52)	2.6 (1.91)	3.2 (1.86)				(Gibson et al., 2019)
USA	Urine	6-11	2013	2014	µg/g (creatine normalized)	GM	0.855	0.344		2.18				(Ospina et al., 2018)
USA	Serum	<8	2008	2009	ng/g lipid	GM					61.8	16.8	2.76	(Wu et al., 2015)
Canada	Serum	6-11	2007	2009	ng/g lipid	Mean					32	14	4.3	(Rawn et al., 2014)
Canada	Serum	1-5	2006	2010	ng/g lipid	GM					34.6	10.3		
Slovakia	Serum	6	2010	2011	ng/g lipid	Median					0.18	0.176		(Drobná et al., 2019)
Norway	Urine	6-11	2012	2012	ng/ml (SG corrected)	Mean		1.4 (0.45)	0.26 (0.08)					(Cequier et al., 2015)
Norway	Serum	4-14	1998	1998	ng/g lipid	Median					2	0.86		(Thomsen et al., 2007)
Denmark	Serum	6-11	2011	2011	ng/g lipid	Mean					3.85	1.39		(Knudsen et al., 2017)
France	Serum	7-13	2014	2016	ng/g lipid	Median					**0.36**		**8.73**	This study
France	Urine	7-13	2014	2016	µg/g creatinine	Median			**0.58**	**1.92**				This study
Greece	Serum	6-11	2020	2021	ng/g lipid	Median					**0.03**	**0.09**		This study
Slovenia	Serum	7-10	2018	2018	ng/g lipid	Median						**0.29**		This study
Slovenia	Urine	7-10	2018	2018	µg/g creatinine	Median			**0.64**	**2.43**				This study
Norway	Serum	8-12	2016	2017	ng/g lipid	Median					**0.34**			This study
Norway	Urine	8-12	2016	2017	µg/g creatinine	Median				**1.78**				This study
Belgium	Urine	7-8	2019	2020	µg/g creatinine	Median			**0.38**	**2.41**				This study
Germany	Urine	6-12	2015	2016	µg/g creatinine	Median	**0.14**	**0.12**	**0.64**	**1.66**				This study
Czech Republic	Urine	11-12	2019	2019	µg/g creatinine	Median	**0.22**	**0.10**	**0.26**	**2.06**				This study
Slovakia	Urine	10-13	2014	2017	µg/g creatinine	Median				**1.43**				This study
Denmark	Urine	7	2018	2019	µg/g creatinine	Median			**0.49**	**2.21**				This study

Table S9 Lifestyle factors questionnaire and responses by country

		BE	CZ	DE	DK	EL	FR	NO	SI	SK
Sex	Female	67	106	150	130	31	194	140	82	167
	Male	66	89	150	161	24	221	160	67	133
Child age (years)	Median age	7.3	11.5	9.3	7.1	10	9.4	10	9.2	11.7

	6	0	0	15	0	4	2	0	0	0
	7	81	0	43	290	7	48	12	17	0
	8	52	0	50	1	5	100	45	36	0
	9	0	0	49	0	10	61	29	45	0
	10	0	1	59	0	10	72	112	51	4
	11	0	103	36	0	19	67	102	0	20
	12	0	91	48	0	0	54	0	0	253
	13	0	0	0	0	0	11	0	0	23
Sampling years	Start	2019	2019	2016	2019	2020	2014	2016	2018	2015
	Finish	2020	2019	2016	2019	2021	2016	2017	2018	2017
Years lived in the same house	Median years	7	11	7		9	7	8		
	1	21	0	0	0	1	122	71	14	0
	2	13	0	0	0	4	80	61	45	0
	3	8	0	0	0	14	68	55	45	0
	4	7	0	0	0	24	55	12	11	0
	5	44	0	0	0	12	60	49	31	0
	6	0	0	0	0	0	0	0	3	0
	NA	40	195	300	291	0	30	52	0	300
Cleaning frequency	Never	0	71	0	0	55	91	0	0	0
	Rarely	0	50	0	0	0	69	0	28	0
	Sometime	0	23	0	0	0	81	0	97	0
	Often	0	15	0	0	0	118	0	20	0
	Very often	0	4	0	0	0	0	0	0	0
	Every day	0	1	0	0	0	31	0	4	0
	NA	133	31	300	291	0	25	300	0	300
Vacuum frequency	Rarely	0	0	0	0	4	0	30	12	0
	Sometime	0	0	0	0	43	121	120	50	0
	Often	0	0	0	0	8	161	98	72	0
	Very often	0	0	0	0	0	39	0	0	0
	Every day	0	0	0	0	0	56	0	15	0
	NA	133	195	300	291	0	38	52	0	300
Hours indoor	Median hours indoor	NA	14.4	NA	NA	18	NA	21	23	NA
Local food consumed	Never	48	0	0	0	0	0	0	2	0
	Rarely	25	0	0	0	0	0	0	0	0
	Sometime	29	0	0	0	0	0	0	0	0
	Often	15	0	0	0	0	0	0	9	0
	Very often	0	0	0	0	0	0	0	14	0
	Every day	16	0	0	0	55	0	0	124	0
	NA	0	195	300	291	0	415	300	0	300
Organic food consumed	Rarely	0	0	0	0	0	137	114	0	0
	Sometime	0	0	0	0	0	67	74	0	0
	Often	0	0	0	0	0	42	32	0	0
	Very often	0	0	0	0	5	33	11	0	0
	Every day	0	0	0	0	50	106	11	0	0
	NA	133	195	300	291	0	30	58	149	300
Seafood consumed	Never	3	23	61	0	23	8	0	97	0
	Rarely	0	25	0	0	22	13	5	19	0
	Sometime	59	43	223	0	9	238	36	33	0
	Often	70	19	16	0	1	109	173	0	0
	Very often	1	5	0	0	0	3	22	0	0
	Every day	0	2	0	0	0	0	4	0	0
	NA	0	78	0	291	0	44	60	0	300
Fish consumption	Never	3	17	63	0	0	34	0	35	0
	Rarely	0	31	0	0	8	48	6	20	0
	Sometime	59	51	220	0	26	272	36	79	0
	Often	70	15	16	0	16	23	177	14	0
	Very often	1	3	0	0	5	0	19	1	0
	Every day	0	1	0	0	0	0	4	0	0
	NA	0	77	1	291	0	38	58	0	300

Type of drinking water consumed	Bottle water	0	0	0	0	0	101	0	25	0
	Tap water	0	0	0	0	55	235	291	120	0
	Ground water	0	0	0	0	0	16	0	4	0
	Other	0	0	0	0	0	38	0	0	0
	NA	133	195	300	291	0	25	9	0	300
Tap water source	Public	63	0	292	0	55	0	277	144	0
	Private well	0	0	0	0	0	0	23	4	0
	Both public and private well	57	0	0	0	0	0	0	1	0
	NA	13	195	8	291	0	415	0	0	300
Frequency of fast food	Never	0	5	15	0	9	146	0	9	0
	Rarely	0	36	0	0	16	0	174	29	0
	Sometime	0	106	251	0	22	221	66	110	0
	Often	0	15	32	0	7	0	0	1	0
	Very often	0	0	0	0	1	23	0	0	0
	Every day	0	1	2	0	0	0	0	0	0
	NA	133	32	0	291	0	25	60	0	300
Frequency of canned food consumed	Never	0	0	0	0	46	33	0	0	0
	Rarely	0	0	0	0	6	0	0	0	0
	Sometime	0	0	0	0	2	300	0	38	0
	Often	0	0	0	0	0	0	0	32	0
	Very often	0	0	0	0	1	57	0	0	0
	Every day	0	0	0	0	0	0	0	79	0
	NA	133	195	300	291	0	25	300	0	300
Vegetarian diet	No	80	118	283	0	55	57	0	149	0
	Yes	2	0	13	0	0	1	0	0	0
	NA	51	77	4	291	0	357	300	0	300
Number of cigarettes smoked daily	Median	0	0			0			0	
	0	125	1	272	0	50	0	0	118	0
	1	0	1	11	0	4	0	0	19	0
	2	3	0	1	0	1	0	0	3	0
	3	0	2	0	0	0	0	0	4	0
	5	2	0	16	0	0	0	0	5	0
	NA	3	191	0	291	0	415	300	0	300
Age of car (years)	Median	NA	7	NA	NA	10	NA	5	6	NA
Minutes spent in car daily	Median	20	NA	NA	NA	40	107.5	NA	20	NA
Birthplace	Europe	133	0	298	291	55	397	300	149	300
	South/Central America	0	0	0	0	0	1	0	0	0
	Africa	0	0	0	0	0	12	0	0	0
	Asia/Middle East	0	0	0	0	0	2	0	0	0
	NA	0	195	2	0	0	3	0	0	0
Parity	1	73	0	0	163	7	0	0	0	118
	2	48	0	0	100	27	0	0	0	115
	3	12	0	0	26	18	0	0	0	47
	4	0	0	0	2	3	0	0	0	16
	5	0	0	0	0	0	0	0	0	1
	NA	0	195	300	0	0	415	300	149	3
Degree of urbanization	City	0	0	65	291	46	106	86	0	0
	Town/ suburb	133	0	132	0	8	116	134	0	136
	Rural area	0	0	103	0	1	193	80	149	163
	NA	0	195	0	0	0	0	0	0	1
Highest education level of the household	Low education	1	6	15	40	0	11	0	10	16
	Medium education	19	15	116	151	4	166	14	39	222
	High education	111	25	169	100	51	237	273	100	45
	NA	2	149	0	0	0	1	13	0	17
Household income level	Low income	1	5	0	0	23	19	0	12	0
	Medium income	14	17	0	0	25	162	0	72	0
	High income	116	16	0	0	7	205	0	48	0

	Do not want to share	1	157	0	0	0	26	0	0	0
	NA	1	0	300	291	0	3	300	17	300
Occupation status of mother	employed/ working	2	0	58	0	9	0	21	12	0
	unemployed/ not working	125	0	237	0	46	0	277	135	0
	NA	6	195	5	291	0	415	2	2	300
Occupational sector of mother	Armed forces	0	0	0	0	9	0	0	0	0
	Manager	3	0	16	0	2	0	0	4	0
	Professional	60	0	55	0	36	0	0	46	0
	Technician and associated professional	7	0	52	0	0	0	0	17	0
	Clerical support	35	0	54	0	3	0	0	34	0
	Services and sales worker	13	0	41	0	3	0	0	23	0
	skilled agricultural, forestry, and fishery workers	0	0	3	0	0	0	0	3	0
	Crafts and related trade works	0	0	3	0	0	0	0	2	0
	Plant and machine operators and assemblers	0	0	3	0	0	0	0	4	0
	Elementary occupations	5	0	10	0	2	0	0	2	0
	NA	10	195	63	291	0	415	300	14	300
Occupation status of father	employed/ working	0	0	14	0	0	0	8	2	0
	unemployed/ not working	0	0	260	0	53	0	230	146	0
	NA	133	195	26	291	2	415	62	1	300
Occupational sector of father	Armed forces	0	0	0	0	0	0	0	2	0
	Manager	0	0	41	0	1	0	0	7	0
	Professional	0	0	58	0	36	0	0	25	0
	Technician and associated professional	0	0	50	0	6	0	0	42	0
	Clerical support	0	0	15	0	0	0	0	15	0
	Services and sales worker	0	0	15	0	5	0	0	30	0
	skilled agricultural, forestry, and fishery workers	0	0	9	0	0	0	0	3	0
	Crafts and related trade works	0	0	42	0	2	0	0	9	0
	Plant and machine operators and assemblers	0	0	18	0	3	0	0	13	0
	Elementary occupations	0	0	3	0	0	0	0	0	0
	NA	133	195	49	291	2	415	300	3	300
Waste incineration plant within 1 km of the home	No	0	0	0	0	55	412	0	146	0
	Yes	0	0	0	0	0	3	0	3	0
	Don't know/ NA	133	195	300	291	0	0	300	0	300
PVC wall present in residence	No	0	0	72	0	55	413	211	145	0
	Yes	0	0	0	0	0	2	18	4	0
	Don't know	0	0	0	0	0	0	18	0	0
	NA	133	195	228	291	0	0	53	0	300
PVC floors present in residence	No	119	31	68	0	52	337	171	128	181
	Yes	14	68	4	0	3	78	57	21	117
	Don't know	0	0	0	0	0	0	19	0	0

	NA	0	96	228	291	0	0	53	0	2
Carpet floors present in residence	No	119	19	20	0	32	394	0	105	247
	Yes	14	82	277	0	23	21	0	44	51
	Don't know/ NA	0	94	3	291	0	0	300	0	2
Renovations to the residence, school, or workplace in the last 2 years	No	0	13	0	0	22	180	153	61	212
	Yes	0	118	0	0	33	166	96	88	86
	Don't know	0	64	0	0	0	2	0	0	0
	NA	133	0	300	291	0	67	51	0	2
Smoking	No	133	46	300	0	55	0	0	149	292
	Yes	0	0	0	0	0	0	0	0	6
	NA	0	149	0	291	0	415	300	0	2
Exposure to passive smoking	No	128	39	272	219	49	365	298	118	154
	Yes	5	7	28	72	6	43	2	31	143
	NA	0	149	0	0	0	7	0	0	3
Alcohol consumption	No	133	0	56	0	55	0	0	0	296
	Yes	0	0	4	0	0	0	0	0	2
	NA	0	195	240	291	0	415	300	149	2
How often does the child play with plastic toys?	Never	0	0	0	0	17	0	94	81	0
	Less than once daily	0	0	0	0	11	0	98	40	0
	Daily	0	0	0	0	12	0	16	24	0
	NA	133	195	300	291	15	415	92	4	300
Chewing on plastic objects	No	0	0	213	0	39	0	0	0	0
	Yes	0	0	87	0	16	0	0	0	0
	NA	133	195	0	291	0	415	300	149	300
Time per day using handheld electronic devices weekday/schoolday	None	0	0	0	0	10	0	0	31	0
	<1 hr/day	0	0	0	0	25	0	0	74	0
	1-4 hrs/day	0	0	0	0	5	0	0	43	0
	>4 hrs/day	0	0	0	0	15	0	0	1	0
	NA	133	195	300	291	0	415	300	0	300
Time per day using handheld electronic devices weekend	None	0	0	0	0	1	0	0	30	0
	<1 hr/day	0	0	0	0	16	0	0	43	0
	1-4 hrs/day	0	0	0	0	20	0	0	70	0
	>4 hrs/day	0	0	0	0	18	0	0	6	0
	NA	133	195	300	291	0	415	300	0	300

Never; Rarely: <1 time / month; Sometimes: <= 1 time / week but >= 1 time/month; Often: 2-3 times / week; Very Often: 4-6 times / week; Everyday:> = 7 times / week; NA: Not Answered

Table S10 Lifestyle factors with significant association to flame retardant concentrations. Factors with p-values only were inserted as categorical values, and factors with both p-values and rho-values (ρ) are continuous values

	Country	Compound	Confounder	p-value	ρ value	Result
Socioeconomic factors						
1	DE	BCIPP	Father employment status	0.006		Higher concentrations where father is employed
3	NO	BDE-47	Father employment status	0.016		Higher concentrations where father is unemployed
4	DE	DPHP	Household education	0.005		Lowest in household with low levels of education
5	DE	DPHP	Father employment status	0.002		Higher concentrations where father is employed
Structural factors						
6	CZ	BCIPP	Renovations	0.012		Higher concentrations in households that were renovated in the last 2 years
7	CZ	BDCIPP	PVC floors	0.013		Higher in households without PVC floors
8	SI	BDE-153	PVC wall	0.036		Higher in houses without PVC walls
9	FR	BCIPP	Home age	0.007		Newer homes had higher concentrations
Cleaning factors						
10	CZ	BDCIPP	Cleaning	0.003		Higher concentration in “never” and “rarely” cleaned
11	FR	BDE-47	Vacuuming	0.034		Higher when vacuum frequency is “often” or “every day”
12	EL	BDE-47	Vacuuming	0.009		Higher when vacuum frequency is “never”
13	SI	BDE-153	Cleaning	0.027		Higher concentration in “never” and “rarely” cleaned
14	CZ	DPHP	Cleaning	<0.001		Higher concentration in “never” and “rarely” cleaned
Sex						
15	CZ	BCIPP	Sex	0.019		Higher concentrations in boys
16	SI	BDCIPP	Sex	0.021		Higher concentrations in boys
17	EL	BDE-47	Sex	0.024		Higher concentrations in boys
18	SI	BDE-153	Sex	0.01		Higher concentrations in boys
Age						
19	DE	BDCIPP	Age	0.002	-0.174	Concentrations decrease as age increases
20	FR	BDCIPP	Age	<0.001	-0.204	Concentrations decrease as age increases

21	DE	DPHP	Age	0.006	-0.157	Concentrations decrease as age increases
22	FR	DPHP	Age	0.005	-0.162	Concentrations decrease as age increases
Time in car						
23	BE	BDCIPP	Minutes in car	0.024	0.195	Concentrations increase as time in car increase
24	FR	BDCIPP	Minutes in car	0.001	0.189	Concentrations increase as time in car increase
Smoking and food						
25	SI	BDCIPP	Passive smoking	0.047		Higher where children are exposed to passive smoke at home
26	BE	DPHP	Fish/seafood	0.021		Concentrations increase as consumption increases

References

Bastiaensen, M., Xu, F., Been, F., van den Eede, N., Covaci, A., 2018. Simultaneous determination of 14 urinary biomarkers of exposure to organophosphate flame retardants and plasticizers by LC-MS/MS. Anal Bioanal Chem 410, 7871–7880. https://doi.org/10.1007/s00216-018-1402-2

Caspersen, I.H., Kvalem, H.E., Haugen, M., Brantsæter, A.L., Meltzer, H.M., Alexander, J., Thomsen, C., Frøshaug, M., Bremnes, N.M.B., Broadwell, S.L., Granum, B., Kogevinas, M., Knutsen, H.K., 2016. Determinants of plasma PCB, brominated flame retardants, and organochlorine pesticides in pregnant women and 3 year old children in The Norwegian Mother and Child Cohort Study. Environ Res 146, 136–144. https://doi.org/10.1016/j.envres.2015.12.020

Cequier, E., Marcé, R.M., Becher, G., Thomsen, C., 2014. A high-throughput method for determination of metabolites of organophosphate flame retardants in urine by ultra performance liquid chromatography-high resolution mass spectrometry. Anal Chim Acta 845, 98–104. https://doi.org/10.1016/j.aca.2014.06.026

Cequier, E., Sakhi, A.K., Haug, L.S., Thomsen, C., 2016. Development of an ion-pair liquid chromatography–high resolution mass spectrometry method for determination of organophosphate pesticide metabolites in large-scale biomonitoring studies. J Chromatogr A 1454, 32–41. https://doi.org/10.1016/j.chroma.2016.05.067

Cequier, E., Sakhi, A.K., Marcé, R.M., Becher, G., Thomsen, C., 2015. Human exposure pathways to organophosphate triesters - A biomonitoring study of mother-child pairs. Environ Int 75, 159–165. https://doi.org/10.1016/j.envint.2014.11.009

Chen, Y., Fang, J., Ren, L., Fan, R., Zhang, J., Liu, G., Zhou, L., Chen, D., Yu, Y., Lu, S., 2018. Urinary metabolites of organophosphate esters in children in South China: Concentrations, profiles and estimated daily intake. Environmental Pollution 235, 358–364. https://doi.org/10.1016/j.envpol.2017.12.092

Drobná, B., Fabišiková, A., Čonka, K., Gago, F., Oravcová, P., Wimmerová, S., Oktapodas Feiler, M., Šovčíková, E., 2019. PBDE serum concentration and preschool maturity of children from Slovakia. Chemosphere 233, 387–395. https://doi.org/10.1016/j.chemosphere.2019.05.284

European Commission, 2021a. GerES V - German Environmental Survey 2014-2017 [WWW Document]. https://doi.org/10.1007/S10654-019-00500-X

European Commission, 2021b. ESTEBAN - Environment, Health, Biomonitoring, physical Activity, Nutrition : Esteban [WWW Document]. URL https://ipchem.jrc.ec.europa.eu/#showmetadata/ESTEBAN (accessed 6.8.22).

Frederiksen, M., Andersen, H.V., Haug, L.S., Thomsen, C., Broadwell, S.L., Egsmose, E.L., Kolarik, B., Gunnarsen, L., Knudsen, L.E., 2020. PCB in serum and hand wipes from exposed residents living in contaminated high-rise apartment buildings and a reference group. Int J Hyg Environ Health 224. https://doi.org/10.1016/j.ijheh.2019.113430

Gibson, E.A., Stapleton, H.M., Calero, L., Holmes, D., Burke, K., Martinez, R., Cortes, B., Nematollahi, A., Evans, D., Anderson, K.A., Herbstman, J.B., 2019. Differential exposure to organophosphate flame

retardants in mother-child pairs. Chemosphere 219, 567–573. https://doi.org/10.1016/j.chemosphere.2018.12.008

Guo, W., Holden, A., Smith, S.C., Gephart, R., Petreas, M., Park, J.S., 2016. PBDE levels in breast milk are decreasing in California. Chemosphere 150, 505–513. https://doi.org/10.1016/j.chemosphere.2015.11.032

Hertz-Picciotto, I., Trnovec, T., Kočan, A., Charles, M.J., Čižnar, P., Langer, P., Sovčikova, E., James, R., 2003. PCBs and early childhood development in Slovakia: Study design and background. Fresenius Environ Bull 12, 208–214.

Knudsen, L.E., Hansen, P.W., Mizrak, S., Hansen, H.K., Mørck, T.A., Nielsen, F., Siersma, V., Mathiesen, L., 2017. Biomonitoring of Danish school children and mothers including biomarkers of PBDE and glyphosate. Rev Environ Health 32, 279–290. https://doi.org/10.1515/reveh-2016-0067

Ospina, M., Jayatilaka, N.K., Wong, L.Y., Restrepo, P., Calafat, A.M., 2018. Exposure to organophosphate flame retardant chemicals in the U.S. general population: Data from the 2013–2014 National Health and Nutrition Examination Survey. Environ Int 110, 32–41. https://doi.org/10.1016/j.envint.2017.10.001

Palát, J., Kukučka, P., Codling, G.P., Price, E.J., Janků, P., Klánová, J., 2022. Application of 96-well plate SPE method for analysis of persistent organic pollutants in low volume blood serum samples. Chemosphere 287, 132300. https://doi.org/10.1016/j.chemosphere.2021.132300

Phillips, A.L., Hammel, S.C., Hoffman, K., Lorenzo, A.M., Chen, A., Webster, T.F., Stapleton, H.M., 2018. Children's residential exposure to organophosphate ester flame retardants and plasticizers: Investigating exposure pathways in the TESIE study. Environ Int 116, 176–185. https://doi.org/10.1016/j.envint.2018.04.013

Rawn, D.F.K., Ryan, J.J., Sadler, A.R., Sun, W.F., Weber, D., Laffey, P., Haines, D., Macey, K., van Oostdam, J., 2014. Brominated flame retardant concentrations in sera from the Canadian Health Measures Survey (CHMS) from 2007 to 2009. Environ Int 63, 26–34. https://doi.org/10.1016/j.envint.2013.10.012

Stajnko, A., Snoj Tratnik, J., Kosjek, T., Mazej, D., Jagodic, M., Eržen, I., Horvat, M., 2020. Seasonal glyphosate and AMPA levels in urine of children and adolescents living in rural regions of Northeastern Slovenia. Environ Int 143. https://doi.org/10.1016/j.envint.2020.105985

Svarcova, A., Lankova, D., Gramblicka, T., Stupak, M., Hajslova, J., Pulkrabova, J., 2019. Integration of five groups of POPs into one multi-analyte method for human blood serum analysis: An innovative approach within biomonitoring studies. Science of the Total Environment 667, 701–709. https://doi.org/10.1016/j.scitotenv.2019.02.336

Thomsen, C., Liane, V.H., Becher, G., 2007. Automated solid-phase extraction for the determination of polybrominated diphenyl ethers and polychlorinated biphenyls in serum-application on archived Norwegian samples from 1977 to 2003. J Chromatogr B Analyt Technol Biomed Life Sci 846, 252–263. https://doi.org/10.1016/j.jchromb.2006.09.011

Wu, X., Bennett, D.H., Moran, R.E., Sjödin, A., Jones, R.S., Tancredi, D.J., Tulve, N.S., Clifton, M.S., Colón, M., Weathers, W., Hertz-Picciotto, I., 2015. Polybrominated diphenyl ether serum concentrations

in a Californian population of children, their parents, and older adults: An exposure assessment study. Environ Health 14. https://doi.org/10.1186/s12940-015-0002-2

Zhang, B., Lu, S., Huang, M., Zhou, M., Zhou, Z., Zheng, H., Jiang, Y., Bai, X., Zhang, T., 2018. Urinary metabolites of organophosphate flame retardants in 0–5-year-old children: Potential exposure risk for inpatients and home-stay infants. Environmental Pollution 243, 318–325. https://doi.org/10.1016/j.envpol.2018.08.051

Zhang, X., Ruan, X., Yan, M., Zhao, Y., Wei, W., Qin, Z., Yang, Y., Xu, H., Li, Y., 2011. Polybrominated diphenyl ether (PBDE) in blood from children (age 9-12) in Taizhou, China. Journal of Environmental Sciences 23, 1199–1204. https://doi.org/10.1016/S1001-0742(10)60553-0