

1 **Supplemental Material to:**

2 **Approaches to mixture risk assessment of PFASs in the European**
3 **population based on human hazard and biomonitoring data**

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28 **Appendix A. Information and data on the aligned studies**

29 *Population demographics*

30 Table A.1. Summary of population demographics in the nine European population studies that are part of HBM4EU and forms the basis for the
31 used exposure levels in this study

Country	Study name	European region	Year of sampling	Age (mean and P10-P90) in years	N total	N of boys	N of girls	BMI (mean and P10-P90)
Germany	GerES V-sub	West	2014-2017	14.5 (12-17)	300	150	150	21 (17-25)
Norway	NEBII	North	2016-2017	12 (12-13)	177	76	101	19 (16-22)
Slovakia	PCB cohort	East	2019-2020	15.7 (15-16)	292	125	167	22 (18-28)
Slovenia	SLO CRP	South	2018	13.8 (13-15)	94	52	42	21 (17-28)
Greece	CROME	South	2020-2021	14.4 (12-16)	52	29	23	22 (17-27)
Sweden	Riksmaten adolescents	North	2016-2017	14.8 (13-17)	300	150	150	21 (17-26)
Spain	BEA	South	2017-2018	14.8 (14-16)	299	143	156	21 (18-25)
Belgium	FLEHS IV	West	2017-2018	14.7 (14-15)	300	150	150	21 (17-26)
France	ESTEBAN	West	2014-2016	14.2 (12-16)	143	62	81	20 (16-25)

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33 *Limits of detection (LODs) and limits of quantification (LOQs) for PFAS analyses*

34 Table A.2. Summary of LODs and LOQs (ng/mL serum or plasma) for the perfluoroalkyl sulphonic acids measured in the aligned studies

	PFBS		PFHxS		PFHpS		PFOS	
	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ
Germany	NA	0.25	NA	0.25	NA	NA	NA	0.25
Norway	0.02	0.05	0.02	0.05	0.02	0.05	0.02	0.05
Slovakia	0.01	0.04	0.005	0.016	0.004	0.01	0.01	0.04
Slovenia	0.01	0.04	0.004	0.014	0.005	0.017	0.03	0.09
Greece	0.01	0.04	0.005	0.017	0.005	0.017	0.03	0.09
Sweden	NA	0.04-0.544	NA	0.022-0.464	NA	NA	NA	0.056-0.562
Spain	NA	0.1	NA	0.34	NA	0.25	NA	0.33
Belgium	NA	0.2	NA	0.2	NA	0.2	NA	0.2
France	0.05	0.19	0.05	0.19	0.05	0.19	0.03	0.1

35 NA = not available

36 Table A.2. Summary of LODs and LOQs (ng/mL serum or plasma) for the perfluoroalkyl carboxylic acids measured in the aligned studies

	PFPeA		PFHxA		PFHpA		PFOA		PFNA		PFDA		PFUnDA		PFDoDA	
	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ	LOD	LOQ
Germany	NA	0.25	NA	0.25	NA	0.25	NA	0.5	NA	0.5	NA	0.25	NA	0.25	NA	0.25
Norway	NA	NA	NA	NA	0.02	0.05	0.02	0.05	0.02	0.05	0.02	0.05	0.02	0.05	0.02	0.05
Slovakia	0.004	0.014	0.005	0.016	0.004	0.012	0.004	0.014	0.005	0.016	0.01	0.03	0.004	0.013	0.01	0.04
Slovenia	0.01	0.04	0.01	0.04	0.01	0.03	0.02	0.07	0.004	0.012	0.004	0.01	0.004	0.012	0.005	0.016
Greece	0.01	0.04	0.01	0.04	0.01	0.03	0.02	0.07	0.004	0.012	0.004	0.01	0.004	0.012	0.005	0.016
Sweden	NA	NA	NA	0.058-0.288	NA	0.058-0.288	NA	0.02-0.288	NA	0.058-0.288	NA	0.058-0.288	NA	0.058-0.288	NA	0.058-0.288
Spain	NA	0.16	NA	0.25	NA	0.2	NA	0.16	NA	0.16	NA	0.2	NA	0.2	NA	0.12
Belgium	NA	0.2	NA	0.2	NA	0.2	NA	0.2	NA	0.2	NA	0.2	NA	0.2	NA	0.2
France	0.02	0.05	0.05	0.2	0.02	0.05	0.02	0.05	0.05	0.2	0.05	0.2	0.02	0.05	0.02	0.05

37 NA = not available

38 Table A.4. Number of participants with measured values below LOD or LOQ for the perfluoroalkyl sulphonic acids measured in the aligned

39 studies

	N total	PFBS		PFHxS		PFHpS		PFOS	
		N <LOD	N <LOQ	N <LOD	N <LOQ	N <LOD	N <LOQ	N <LOD	N <LOQ
Germany	300	0	300	0	83	NA	NA	0	0
Norway	177	151	24	0	0	15	89	0	0
Slovakia	292	285	0	1	0	51	0	0	0
Slovenia	94	78	2	0	0	14	2	0	0
Greece	52	52	0	0	0	0	0	0	0
Sweden	300	0	249	0	33	NA	NA	0	0
Spain	299	0	299	0	239	0	283	0	0
Belgium	300	NA	299	NA	7	NA	291	0	0
France	143	141	2	0	1	16	121	0	0

40 NA = not available

41 Table A.5. Number of participants with measured values below LOD or LOQ for the perfluoroalkyl carboxylic acids measured in the aligned
 42 studies

	N total	PFPeA		PFHxA		PFHpA		PFOA		PFNA		PFDA		PFUnDA		PFDoDA	
		N <LOD	N <LOQ	N <LOD	N <LOQ	N <LOD	N <LOQ	N <LOD	N <LOQ	N <LOD	N <LOQ	N <LOD	N <LOQ	N <LOD	N <LOQ	N <LOD	N <LOQ
Germany	300	0	300	0	300	0	299	0	41	0	264	0	265	0	297	0	300
Norway	177	NA	NA	NA	NA	3	36	0	0	0	0	0	1	1	29	133	43
Slovakia	292	138	0	0	1	28	0	1	0	18	0	94	0	153	15	291	0
Slovenia	94	11	1	58	21	25	20	0	0	0	0	0	0	0	3	80	4
Greece	52	52	0	0	0	50	0	0	0	0	0	0	0	13	0	44	0
Sweden	300	NA	NA	0	300	0	275	0	0	0	18	0	123	0	159	0	293
Spain	299	0	299	0	299	0	296	0	0	0	32	0	252	0	274	0	294
Belgium	300	0	300	0	291	0	296	0	0	0	54	0	157	0	273	0	295
France	143	143	0	143	0	59	73	0	0	0	1	0	56	0	9	93	42

43 NA = not available

44 ***Summary of exposure from the HBM4EU aligned studies***

45 Summary statistics of exposure in ng/mL in blood serum (all except Germany and Norway) or ng/mL blood plasma (Germany and Norway) of
 46 PFAS in European teenagers as obtained from the aligned studies in HBM4EU. Please note that the difference in number of digits does not
 47 reflect the uncertainty in the measurements.

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51 Table A.6. Summary of PFBS exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	ND	ND	ND	ND
Norway	177	ND	ND	ND	ND	ND	ND	ND
Slovakia	292	ND	ND	ND	ND	ND	ND	ND
Slovenia	94	ND	ND	ND	ND	ND	0.194	0.3675
Greece	52	ND	ND	ND	ND	ND	ND	ND
Sweden	300	ND	ND	ND	ND	ND	0.121	0.2
Spain	299	ND	ND	ND	ND	ND	ND	ND
Belgium	300	ND	ND	ND	ND	ND	ND	ND
France	143	ND	ND	ND	ND	ND	ND	ND

52 NA = not available; ND = not detected

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54 Table A.7. Summary of PFHxS exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	0.39	0.53	0.763	0.9805
Norway	177	0.2288	0.2636	0.3672	0.4751	0.6211	0.9388	1.1884
Slovakia	292	0.13	0.16	0.21	0.29	0.44	0.748	0.994
Slovenia	94	0.14	0.15	0.19	0.23	0.3	0.36	0.4245
Greece	52	0.14	0.16	0.2175	0.28	0.395	0.598	0.888
Sweden	300	ND	ND	0.2597	0.39	0.5825	0.88	1.1015
Spain	299	ND	ND	ND	ND	ND	0.5054	0.7654
Belgium	300	0.25	0.29	0.37	0.49	0.66	1.1	1.4
France	143	0.3321	0.364	0.533	0.6841	1.0194	1.4861	2.3238

55 NA = not available; ND = not detected

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58 Table A.8. Summary of PFHpS exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	NA	NA	NA	NA	NA	NA	NA
Norway	177	ND	ND	ND	ND	0.0643	0.0849	0.1007
Slovakia	292	ND	ND	0.02	0.03	0.05	0.1	0.1945
Slovenia	94	ND	ND	0.02	0.03	0.05	0.08	0.1135
Greece	52	0.0255	0.03	0.04	0.05	0.07	0.11	0.1445
Sweden	300	NA	NA	NA	NA	NA	NA	NA
Spain	299	ND	ND	ND	ND	ND	ND	0.2532
Belgium	300	ND	ND	ND	ND	ND	ND	ND
France	143	ND	ND	ND	ND	ND	ND	ND

59 NA = not available; ND = not detected

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61 Table A.9. Summary of PFOS exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	1.27	1.55	1.96	2.605	3.4675	4.581	5.898
Norway	177	1.4691	1.737	2.1815	2.7923	3.6828	5.2642	7.04
Slovakia	292	0.4855	0.63	0.84	1.37	2.47	4.072	6.1455
Slovenia	94	0.8255	0.949	1.17	1.645	2.7025	3.73	5.8185
Greece	52	1.2525	1.394	1.575	2.11	3.225	4.181	5.205
Sweden	300	1.207	1.409	1.97	2.68	4.0825	6.282	8.229
Spain	299	0.5748	0.727	0.927	1.34	1.837	2.663	3.0647
Belgium	300	0.849	1	1.575	2.2	3.4	5.01	7.31
France	143	0.9762	1.132	1.5212	2.006	3.1243	5.2204	6.1553

62 NA = not available; ND = not detected

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65 Table A.10. Summary of PFPeA exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	ND	ND	ND	ND
Norway	177	NA	NA	NA	NA	NA	NA	NA
Slovakia	292	ND	ND	ND	0.02	0.07	0.11	0.17
Slovenia	94	ND	ND	0.07	0.095	0.12	0.164	0.19
Greece	52	ND	ND	ND	ND	ND	ND	ND
Sweden	300	NA	NA	NA	NA	NA	NA	NA
Spain	299	ND	ND	ND	ND	ND	ND	ND
Belgium	300	ND	ND	ND	ND	ND	ND	ND
France	143	ND	ND	ND	ND	ND	ND	ND

66 NA = not available; ND = not detected

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68 Table A.11. Summary of PFHxA exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	ND	ND	ND	ND
Norway	177	NA	NA	NA	NA	NA	NA	NA
Slovakia	292	0.03	0.04	0.06	0.07	0.1	0.12	0.14
Slovenia	94	ND	ND	ND	ND	ND	0.06	0.07
Greece	52	0.0955	0.1	0.11	0.135	0.16	0.189	0.21
Sweden	300	ND	ND	ND	ND	ND	ND	ND
Spain	299	ND	ND	ND	ND	ND	ND	ND
Belgium	300	ND	ND	ND	ND	ND	ND	ND
France	143	ND	ND	ND	ND	ND	ND	ND

69 NA = not available; ND = not detected

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72 Table A.12. Summary of PFHpA exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	ND	ND	ND	ND
Norway	177	ND	ND	0.053	0.0727	0.0965	0.1261	0.1627
Slovakia	292	ND	ND	ND	ND	ND	ND	ND
Slovenia	94	ND	ND	ND	0.04	0.06	0.08	0.0935
Greece	52	ND	ND	ND	ND	ND	ND	ND
Sweden	300	ND	ND	ND	ND	ND	ND	0.1205
Spain	299	ND	ND	ND	ND	ND	ND	ND
Belgium	300	ND	ND	ND	ND	ND	ND	ND
France	143	ND	ND	ND	ND	ND	ND	ND

73 NA = not available; ND = not detected

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75 Table A.13. Summary of PFOA exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	0.81	1.255	1.795	2.7	3.12
Norway	177	0.7665	0.8667	1.0464	1.2813	1.5685	1.9497	2.0879
Slovakia	292	0.2455	0.32	0.48	0.71	0.96	1.18	1.3945
Slovenia	94	0.5295	0.63	0.74	0.86	1.06	1.2	1.442
Greece	52	0.5655	0.621	0.7475	0.875	1.2425	1.787	2.193
Sweden	300	0.55	0.69	0.8875	1.15	1.5125	2.03	2.3615
Spain	299	0.3795	0.428	0.524	0.655	0.7975	0.9342	1.0324
Belgium	300	0.609	0.738	0.88	1.1	1.4	1.6	1.8
France	143	0.8971	0.9567	1.2231	1.4741	1.7864	2.3486	2.6201

76 NA = not available; ND = not detected

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79 Table A.14. Summary of PFNA exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	ND	ND	0.592	0.731
Norway	177	0.2209	0.2533	0.3243	0.4445	0.6248	0.8662	1.0049
Slovakia	292	ND	0.03	0.09	0.17	0.26	0.379	0.4645
Slovenia	94	0.13	0.16	0.1925	0.25	0.31	0.42	0.51
Greece	52	0.23	0.261	0.3075	0.415	0.5625	0.708	0.8405
Sweden	300	ND	0.18	0.27	0.375	0.51	0.76	0.86
Spain	299	ND	ND	0.208	0.282	0.3795	0.5094	0.5989
Belgium	300	ND	ND	0.23	0.32	ND	0.601	0.74
France	143	0.2873	0.336	0.4318	0.5414	0.7112	1.0062	1.381

80 NA = not available; ND = not detected

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82 Table A.15. Summary of PFDA exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	ND	ND	0.3	0.3705
Norway	177	0.0659	0.0741	0.0965	0.1297	0.1776	0.2578	0.3029
Slovakia	292	ND	ND	ND	0.05	0.1	0.15	0.17
Slovenia	94	0.08	0.083	0.1025	0.14	0.19	0.244	0.2805
Greece	52	0.101	0.11	0.14	0.17	0.2525	0.365	0.398
Sweden	300	ND	ND	ND	0.1483	0.24	0.33	0.43
Spain	299	ND	ND	ND	ND	ND	0.2192	0.2767
Belgium	300	ND	ND	ND	ND	0.27	0.4	0.501
France	143	ND	ND	ND	0.2167	0.3074	0.4127	0.5077

83 NA = not available; ND = not detected

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85

86 Table A.16. Summary of PFUnDA exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	ND	ND	ND	ND
Norway	177	ND	ND	0.0607	0.086	0.146	0.2217	0.2681
Slovakia	292	ND	ND	ND	ND	0.03	0.06	0.08
Slovenia	94	0.02	0.023	0.04	0.06	0.08	0.11	0.1235
Greece	52	ND	ND	ND	0.035	0.08	0.13	0.17
Sweden	300	ND	ND	ND	ND	0.17	0.2503	0.3505
Spain	299	ND	ND	ND	ND	ND	ND	0.236
Belgium	300	ND	ND	ND	ND	ND	ND	0.24
France	143	ND	0.0562	0.0741	0.1094	0.1473	0.2219	0.2873

87 NA = not available; ND = not detected

88

89 Table A.17. Summary of PFDoDA exposure in several percentiles of the study population (ng/mL serum or plasma)

Country of origin of study	N	P05	P10	P25	P50	P75	P90	P95
Germany	300	ND	ND	ND	ND	ND	ND	ND
Norway	177	ND	ND	ND	ND	ND	ND	ND
Slovakia	292	ND	ND	ND	ND	ND	ND	ND
Slovenia	94	ND	ND	ND	ND	ND	ND	0.03
Greece	52	ND	ND	ND	ND	ND	0.02	0.0245
Sweden	300	ND	ND	ND	ND	ND	ND	ND
Spain	299	ND	ND	ND	ND	ND	ND	ND
Belgium	300	ND	ND	ND	ND	ND	ND	ND
France	143	ND	ND	ND	ND	ND	ND	ND

90 NA = not available; ND = not detected

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92 *Spearman correlations*

93 Table A.18. Spearman correlations for the FLEHS IV dataset (Belgium) and their statistical significance (Prob > |r| under H0: Rho=0).¹

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDODA
PFBS	1	-0.05744	-0.01017	-0.03774	.	-0.01017	-0.00672	-0.02944	-0.04354	-0.0516	-0.01816	-0.00753
		0.3214	0.8608	0.5149	.	0.8608	0.9077	0.6115	0.4524	0.3732	0.7541	0.8967
PFHxS	-0.05744	1	0.17738	0.53008	.	0.10961	0.01163	0.58839	0.4886	0.38629	0.27013	0.11532
	0.3214		0.002	<.0001	.	0.0579	0.8411	<.0001	<.0001	<.0001	<.0001	0.046
PFHpS	-0.01017	0.17738	1	0.27241	.	-0.03092	-0.02044	0.13317	0.20326	0.23757	0.08963	0.13122
	0.8608	0.002		<.0001	.	0.5937	0.7244	0.021	0.0004	<.0001	0.1214	0.023
PFOS	-0.03774	0.53008	0.27241	1	.	0.03334	-0.02443	0.55309	0.74002	0.69693	0.3773	0.14376
	0.5149	<.0001	<.0001		.	0.5651	0.6735	<.0001	<.0001	<.0001	<.0001	0.0127
PFPeA

PFHxA	-0.01017	0.10961	-0.03092	0.03334	.	1	-0.02044	-0.00327	0.04432	0.05564	0.07507	-0.02289
	0.8608	0.0579	0.5937	0.5651	.		0.7244	0.955	0.4444	0.3368	0.1947	0.6929
PFHpA	-0.00672	0.01163	-0.02044	-0.02443	.	-0.02044	1	0.13544	0.06569	-0.02999	-0.0365	-0.01513
	0.9077	0.8411	0.7244	0.6735	.	0.7244		0.0189	0.2567	0.6049	0.5288	0.7941
PFOA	-0.02944	0.58839	0.13317	0.55309	.	-0.00327	0.13544	1	0.74019	0.49905	0.29356	0.17811
	0.6115	<.0001	0.021	<.0001	.	0.955	0.0189		<.0001	<.0001	<.0001	0.002
PFNA	-0.04354	0.4886	0.20326	0.74002	.	0.04432	0.06569	0.74019	1	0.70542	0.42664	0.19442
	0.4524	<.0001	0.0004	<.0001	.	0.4444	0.2567	<.0001		<.0001	<.0001	0.0007
PFDA	-0.0516	0.38629	0.23757	0.69693	.	0.05564	-0.02999	0.49905	0.70542	1	0.46951	0.23335
	0.3732	<.0001	<.0001	<.0001	.	0.3368	0.6049	<.0001	<.0001		<.0001	<.0001

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFUnDA	-0.01816	0.27013	0.08963	0.3773	.	0.07507	-0.0365	0.29356	0.42664	0.46951	1	0.33476
	0.7541	<.0001	0.1214	<.0001	.	0.1947	0.5288	<.0001	<.0001	<.0001		<.0001
PFDoDA	-0.00753	0.11532	0.13122	0.14376	.	-0.02289	-0.01513	0.17811	0.19442	0.23335	0.33476	1
	0.8967	0.046	0.023	0.0127	.	0.6929	0.7941	0.002	0.0007	<.0001	<.0001	

94 ¹Statistically significant effect ($p < 0.05$) indicated in bold

95 Table A.19. Spearman correlations for the GerES V-sub dataset (Germany) and their statistical significance ($\text{Prob} > |r|$ under $H_0: \text{Rho}=0$).¹

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFBS

PFHxS	.	1	.	0.49149	.	.	0.02093	0.39679	0.18938	0.2544	0.13172	.
	.		.	<.0001	.	.	0.7181	<.0001	0.001	<.0001	0.0225	.
PFHpS

PFOS	.	0.49149	.	1	.	.	-0.0798	0.44629	0.28355	0.37094	0.07604	.
	.	<.0001	.		.	.	0.168	<.0001	<.0001	<.0001	0.189	.
PFPeA

PFHxA

PFHpA	.	0.02093	.	-0.0798	.	.	1	0.0993	0.17689	0.1755	-0.00581	.
	.	0.7181	.	0.168	.	.		0.086	0.0021	0.0023	0.9201	.
PFOA	.	0.39679	.	0.44629	.	.	0.0993	1	0.35289	0.3419	0.15324	.
	.	<.0001	.	<.0001	.	.	0.086		<.0001	<.0001	0.0078	.

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFHpA	.	-0.05002	-0.02393	-0.01724	.	.	1	0.03604	0.03756	0.05427	0.09311	-0.01313
	.	0.3887	0.6803	0.7666	.	.		0.5347	0.5176	0.3497	0.1081	0.8212
PFOA	.	0.28282	0.12149	0.4943	.	.	0.03604	1	0.57825	0.30176	0.12361	0.0897
	.	<.0001	0.0357	<.0001	.	.	0.5347		<.0001	<.0001	0.0326	0.1217
PFNA	.	0.23335	0.0714	0.69547	.	.	0.03756	0.57825	1	0.50428	0.37878	0.08997
	.	<.0001	0.2183	<.0001	.	.	0.5176	<.0001		<.0001	<.0001	0.1206
PFDA	.	0.15174	0.05992	0.44995	.	.	0.05427	0.30176	0.50428	1	0.37625	0.17005
	.	0.0086	0.3017	<.0001	.	.	0.3497	<.0001	<.0001		<.0001	0.0032
PFUnDA	.	0.06653	-0.0717	0.29902	.	.	0.09311	0.12361	0.37878	0.37625	1	0.04663
	.	0.2514	0.2164	<.0001	.	.	0.1081	0.0326	<.0001	<.0001		0.4218
PFDoDA												

98 ¹Statistically significant effect ($p < 0.05$) indicated in bold

99 Table A.21. Spearman correlations for the CROME dataset (Greece) and their statistical significance ($\text{Prob} > |r|$ under $H_0: \text{Rho}=0$).¹

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFBS

PFHxS	.	1	0.77927	0.67474	.	0.41333	0.15245	0.43978	0.60672	0.27272	0.39329	-0.05439
	.		<.0001	<.0001	.	0.0023	0.2806	0.0011	<.0001	0.0505	0.0039	0.7017
PFHpS	.	0.77927	1	0.88204	.	0.2408	0.10888	0.3603	0.68824	0.41452	0.40434	-0.06864
	.	<.0001		<.0001	.	0.0855	0.4423	0.0087	<.0001	0.0022	0.0029	0.6288
PFOS	.	0.67474	0.88204	1	.	0.23227	0.16425	0.28832	0.84673	0.67432	0.69366	0.01566
	.	<.0001	<.0001		.	0.0975	0.2446	0.0382	<.0001	<.0001	<.0001	0.9123

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFPeA

PFHxA	.	0.41333	0.2408	0.23227	.	1	0.21196	0.1292	0.19839	0.13127	0.16145	-0.11049
	.	0.0023	0.0855	0.0975	.		0.1314	0.3613	0.1586	0.3536	0.2529	0.4355
PFHpA	.	0.15245	0.10888	0.16425	.	0.21196	1	0.28546	0.19722	0.24553	0.1677	-0.08497
	.	0.2806	0.4423	0.2446	.	0.1314		0.0402	0.1611	0.0794	0.2347	0.5492
PFOA	.	0.43978	0.3603	0.28832	.	0.1292	0.28546	1	0.41844	0.16392	0.15862	-0.08131
	.	0.0011	0.0087	0.0382	.	0.3613	0.0402		0.002	0.2456	0.2614	0.5666
PFNA	.	0.60672	0.68824	0.84673	.	0.19839	0.19722	0.41844	1	0.7486	0.73429	0.13283
	.	<.0001	<.0001	<.0001	.	0.1586	0.1611	0.002		<.0001	<.0001	0.3479
PFDA	.	0.27272	0.41452	0.67432	.	0.13127	0.24553	0.16392	0.7486	1	0.80702	0.24871
	.	0.0505	0.0022	<.0001	.	0.3536	0.0794	0.2456	<.0001		<.0001	0.0754
PFUnDA	.	0.39329	0.40434	0.69366	.	0.16145	0.1677	0.15862	0.73429	0.80702	1	0.28937
	.	0.0039	0.0029	<.0001	.	0.2529	0.2347	0.2614	<.0001	<.0001		0.0375
PFDoDA	.	-0.05439	-0.06864	0.01566	.	-0.11049	-0.08497	-0.08131	0.13283	0.24871	0.28937	1
	.	0.7017	0.6288	0.9123	.	0.4355	0.5492	0.5666	0.3479	0.0754	0.0375	

100 ¹Statistically significant effect (p < 0.05) indicated in bold

101 Table A.22. Spearman correlations for the NEBII dataset (Norway) and their statistical significance (Prob > |r| under H0: Rho=0).¹

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFBS	1	0.02919	0.01753	0.10076	.	.	0.19316	0.10486	0.1221	0.07783	0.13331	-0.1156
		0.6997	0.8169	0.1821	.	.	0.01	0.1648	0.1054	0.3031	0.0769	0.1255
PFHxS	0.02919	1	0.53058	0.60031	.	.	0.15142	0.42842	0.46611	0.37533	0.3186	-0.16358
	0.6997		<.0001	<.0001	.	.	0.0442	<.0001	<.0001	<.0001	<.0001	0.0296

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFHpS	0.01753	0.53058	1	0.60161	.	.	0.09318	0.39233	0.4298	0.39906	0.33781	-0.20174
	0.8169	<.0001		<.0001	.	.	0.2174	<.0001	<.0001	<.0001	<.0001	0.0071
PFOS	0.10076	0.60031	0.60161	1	.	.	0.13394	0.4655	0.58209	0.65846	0.63822	-0.36229
	0.1821	<.0001	<.0001		.	.	0.0755	<.0001	<.0001	<.0001	<.0001	<.0001
PFPeA

PFHxA

PFHpA	0.19316	0.15142	0.09318	0.13394	.	.	1	0.39418	0.13946	0.14443	0.02407	-0.23262
	0.01	0.0442	0.2174	0.0755	.	.		<.0001	0.0641	0.0551	0.7505	0.0018
PFOA	0.10486	0.42842	0.39233	0.4655	.	.	0.39418	1	0.58166	0.51657	0.28602	-0.29941
	0.1648	<.0001	<.0001	<.0001	.	.	<.0001		<.0001	<.0001	0.0001	<.0001
PFNA	0.1221	0.46611	0.4298	0.58209	.	.	0.13946	0.58166	1	0.65186	0.58709	-0.27559
	0.1054	<.0001	<.0001	<.0001	.	.	0.0641	<.0001		<.0001	<.0001	0.0002
PFDA	0.07783	0.37533	0.39906	0.65846	.	.	0.14443	0.51657	0.65186	1	0.80947	-0.51225
	0.3031	<.0001	<.0001	<.0001	.	.	0.0551	<.0001	<.0001		<.0001	<.0001
PFUnDA	0.13331	0.3186	0.33781	0.63822	.	.	0.02407	0.28602	0.58709	0.80947	1	-0.49653
	0.0769	<.0001	<.0001	<.0001	.	.	0.7505	0.0001	<.0001	<.0001		<.0001
PFDoDA	-0.1156	-0.16358	-0.20174	-0.36229	.	.	-0.23262	-0.29941	-0.27559	-0.51225	-0.49653	1
	0.1255	0.0296	0.0071	<.0001	.	.	0.0018	<.0001	0.0002	<.0001	<.0001	

102 ¹Statistically significant effect (p < 0.05) indicated in bold

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104 Table A.24. Spearman correlations for the Riksmaten adolescents dataset (Sweden) and their statistical significance (Prob > |r| under H0:
 105 Rho=0).¹

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFBS	1	-0.0009	.	-0.06886	.	.	0.05036	-0.14681	-0.12414	0.06941	0.01358	-0.06954
		0.9876	.	0.2344	.	.	0.3847	0.0109	0.0316	0.2307	0.8147	0.2298
PFHxS	-0.0009	1	.	0.52957	.	.	0.02271	0.44687	0.33597	0.18547	0.17308	-0.03473
	0.9876		.	<.0001	.	.	0.6952	<.0001	<.0001	0.0013	0.0026	0.5491
PFHpS

PFOS	-0.06886	0.52957	.	1	.	.	0.05468	0.41646	0.53518	0.41515	0.40818	0.01923
	0.2344	<.0001	.		.	.	0.3453	<.0001	<.0001	<.0001	<.0001	0.7402
PFPeA

PFHxA

PFHpA	0.05036	0.02271	.	0.05468	.	.	1	0.14003	0.09774	0.14668	0.1492	0.21096
	0.3847	0.6952	.	0.3453	.	.		0.0152	0.0911	0.011	0.0097	0.0002
PFOA	-0.14681	0.44687	.	0.41646	.	.	0.14003	1	0.52917	0.39199	0.13749	0.14301
	0.0109	<.0001	.	<.0001	.	.	0.0152		<.0001	<.0001	0.0172	0.0132
PFNA	-0.12414	0.33597	.	0.53518	.	.	0.09774	0.52917	1	0.52422	0.33202	0.13096
	0.0316	<.0001	.	<.0001	.	.	0.0911	<.0001		<.0001	<.0001	0.0233
PFDA	0.06941	0.18547	.	0.41515	.	.	0.14668	0.39199	0.52422	1	0.50973	0.16695
	0.2307	0.0013	.	<.0001	.	.	0.011	<.0001	<.0001		<.0001	0.0037
PFUnDA	0.01358	0.17308	.	0.40818	.	.	0.1492	0.13749	0.33202	0.50973	1	0.14462

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
	0.8147	0.0026	.	<.0001	.	.	0.0097	0.0172	<.0001	<.0001		0.0122
PFDoDA	-0.06954	-0.03473	.	0.01923	.	.	0.21096	0.14301	0.13096	0.16695	0.14462	1
	0.2298	0.5491	.	0.7402	.	.	0.0002	0.0132	0.0233	0.0037	0.0122	

106 ¹Statistically significant effect (p < 0.05) indicated in bold

107 Table A.25. Spearman correlations for the SLO CRP dataset (Slovenia) and their statistical significance (Prob > |r| under H0: Rho=0).¹

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFBS	1	0.23498	0.22782	0.19157	0.31008	-0.10837	0.04565	0.12234	0.00693	0.15209	0.24474	0.04501
		0.0226	0.0272	0.0644	0.0024	0.2985	0.6622	0.2401	0.9471	0.1434	0.0174	0.6666
PFHxS	0.23498	1	0.75913	0.7376	0.15521	-0.07746	0.05019	0.48277	0.60325	0.58654	0.49612	0.21317
	0.0226		<.0001	<.0001	0.1352	0.4581	0.6309	<.0001	<.0001	<.0001	<.0001	0.0391
PFHpS	0.22782	0.75913	1	0.80897	0.26825	-0.03426	0.0711	0.47878	0.60927	0.61102	0.51157	0.31742
	0.0272	<.0001		<.0001	0.0089	0.743	0.4959	<.0001	<.0001	<.0001	<.0001	0.0018
PFOS	0.19157	0.7376	0.80897	1	0.22932	0.05149	0.07063	0.44241	0.81026	0.79852	0.69859	0.237
	0.0644	<.0001	<.0001		0.0262	0.6221	0.4988	<.0001	<.0001	<.0001	<.0001	0.0215
PFPeA	0.31008	0.15521	0.26825	0.22932	1	0.0877	0.14192	0.32801	0.14034	0.19783	0.0815	-0.08078
	0.0024	0.1352	0.0089	0.0262		0.4006	0.1724	0.0012	0.1773	0.056	0.4349	0.4389
PFHxA	-0.10837	-0.07746	-0.03426	0.05149	0.0877	1	0.15332	-0.02628	0.07246	0.11788	0.0437	-0.03693

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
	0.2985	0.4581	0.743	0.6221	0.4006		0.1401	0.8015	0.4877	0.2578	0.6758	0.7238
PFHpA	0.04565	0.05019	0.0711	0.07063	0.14192	0.15332	1	0.44318	0.2014	0.12438	-0.10261	0.01822
	0.6622	0.6309	0.4959	0.4988	0.1724	0.1401		<.0001	0.0516	0.2323	0.325	0.8617
PFOA	0.12234	0.48277	0.47878	0.44241	0.32801	-0.02628	0.44318	1	0.5975	0.44235	0.22822	0.0034
	0.2401	<.0001	<.0001	<.0001	0.0012	0.8015	<.0001		<.0001	<.0001	0.0269	0.9741
PFNA	0.00693	0.60325	0.60927	0.81026	0.14034	0.07246	0.2014	0.5975	1	0.82346	0.65414	0.16413
	0.9471	<.0001	<.0001	<.0001	0.1773	0.4877	0.0516	<.0001		<.0001	<.0001	0.1139
PFDA	0.15209	0.58654	0.61102	0.79852	0.19783	0.11788	0.12438	0.44235	0.82346	1	0.75449	0.21613
	0.1434	<.0001	<.0001	<.0001	0.056	0.2578	0.2323	<.0001	<.0001		<.0001	0.0364
PFUnDA	0.24474	0.49612	0.51157	0.69859	0.0815	0.0437	-0.10261	0.22822	0.65414	0.75449	1	0.23207
	0.0174	<.0001	<.0001	<.0001	0.4349	0.6758	0.325	0.0269	<.0001	<.0001		0.0244
PFDoDA	0.04501	0.21317	0.31742	0.237	-0.08078	-0.03693	0.01822	0.0034	0.16413	0.21613	0.23207	1
	0.6666	0.0391	0.0018	0.0215	0.4389	0.7238	0.8617	0.9741	0.1139	0.0364	0.0244	

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¹Statistically significant effect (p < 0.05) indicated in bold

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110 Table A.26. Spearman correlations for the PCB cohort dataset (Slovakia) and their statistical significance (Prob > |r| under H0: Rho=0).¹

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDODA
PFBS	1	0.06249	0.02257	0.04538	0.03128	-0.03008	0.07931	0.0419	0.05327	0.01943	0.00203	-0.00919
		0.2872	0.7009	0.4398	0.5945	0.6087	0.1765	0.4757	0.3644	0.741	0.9725	0.8758
PFHxS	0.06249	1	0.80331	0.71754	-0.04408	0.0527	0.13844	0.41071	0.44735	0.33932	0.29569	0.07305
	0.2872		<.0001	<.0001	0.4531	0.3696	0.0179	<.0001	<.0001	<.0001	<.0001	0.2133
PFHpS	0.02257	0.80331	1	0.91039	-0.06442	0.12574	0.2685	0.4962	0.63487	0.51882	0.3778	0.06774
	0.7009	<.0001		<.0001	0.2726	0.0317	<.0001	<.0001	<.0001	<.0001	<.0001	0.2485
PFOS	0.04538	0.71754	0.91039	1	0.02285	0.13723	0.293	0.45777	0.691	0.62184	0.43964	0.0539
	0.4398	<.0001	<.0001		0.6973	0.019	<.0001	<.0001	<.0001	<.0001	<.0001	0.3588
PFPeA	0.03128	-0.04408	-0.06442	0.02285	1	0.31776	0.04327	0.08122	-0.00107	0.02399	0.01851	0.02134
	0.5945	0.4531	0.2726	0.6973		<.0001	0.4614	0.1663	0.9855	0.6831	0.7528	0.7165
PFHxA	-0.03008	0.0527	0.12574	0.13723	0.31776	1	0.11871	0.54607	0.28323	0.28285	0.20699	0.06535
	0.6087	0.3696	0.0317	0.019	<.0001		0.0427	<.0001	<.0001	<.0001	0.0004	0.2657
PFHpA	0.07931	0.13844	0.2685	0.293	0.04327	0.11871	1	0.34638	0.34415	0.31786	0.24779	-0.01409
	0.1765	0.0179	<.0001	<.0001	0.4614	0.0427		<.0001	<.0001	<.0001	<.0001	0.8105

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFOA	0.0419	0.41071	0.4962	0.45777	0.08122	0.54607	0.34638	1	0.61449	0.52737	0.32114	0.06677
	0.4757	<.0001	<.0001	<.0001	0.1663	<.0001	<.0001		<.0001	<.0001	<.0001	0.2554
PFNA	0.05327	0.44735	0.63487	0.691	-0.00107	0.28323	0.34415	0.61449	1	0.83414	0.57486	-0.02122
	0.3644	<.0001	<.0001	<.0001	0.9855	<.0001	<.0001	<.0001		<.0001	<.0001	0.718
PFDA	0.01943	0.33932	0.51882	0.62184	0.02399	0.28285	0.31786	0.52737	0.83414	1	0.70965	-0.00142
	0.741	<.0001	<.0001	<.0001	0.6831	<.0001	<.0001	<.0001	<.0001		<.0001	0.9808
PFUnDA	0.00203	0.29569	0.3778	0.43964	0.01851	0.20699	0.24779	0.32114	0.57486	0.70965	1	-0.04103
	0.9725	<.0001	<.0001	<.0001	0.7528	0.0004	<.0001	<.0001	<.0001	<.0001		0.4849
PFDoDA	-0.00919	0.07305	0.06774	0.0539	0.02134	0.06535	-0.01409	0.06677	-0.02122	-0.00142	-0.04103	1
	0.8758	0.2133	0.2485	0.3588	0.7165	0.2657	0.8105	0.2554	0.718	0.9808	0.4849	

¹Statistically significant effect (p < 0.05) indicated in bold

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113 Table A.27. Spearman correlations for the ESTEBAN cohort dataset (France) and their statistical significance (Prob > |r| under H0: Rho=0).¹

	PFBS	PFHxS	PFHpS	PFOS	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
PFBS	1	0.02597	0.05064	0.03029	.	.	-0.16565	0.03606	0.04616	0.04538	0.16159	-0.05864
		0.7582	0.5481	0.7195	.	.	0.048	0.6689	0.5841	0.5904	0.0538	0.4866
PFHxS	0.02597	1	-0.19012	0.38367	.	.	-0.04271	0.48924	0.33643	0.16413	0.17286	-0.03395

	0.7582		0.0229	<.0001	.	.	0.6125	<.0001	<.0001	0.0501	0.039	0.6873
PFHpS	0.05064	-0.19012	1	-0.19582	.	.	0.0255	-0.13207	-0.13843	-0.04762	-0.0956	-0.00109
	0.5481	0.0229		0.0191	.	.	0.7624	0.1159	0.0992	0.5722	0.2561	0.9897
PFOS	0.03029	0.38367	-0.19582	1	.	.	-0.18858	0.48389	0.60524	0.67216	0.55932	-0.26925
	0.7195	<.0001	0.0191		.	.	0.0241	<.0001	<.0001	<.0001	<.0001	0.0011
PFPeA

PFHxA

PFHpA	-0.16565	-0.04271	0.0255	-0.18858	.	.	1	-0.20447	-0.18791	-0.19478	-0.14585	0.05717
	0.048	0.6125	0.7624	0.0241	.	.		0.0143	0.0246	0.0197	0.0822	0.4976
PFOA	0.03606	0.48924	-0.13207	0.48389	.	.	-0.20447	1	0.67359	0.56159	0.36061	-0.13925
	0.6689	<.0001	0.1159	<.0001	.	.	0.0143		<.0001	<.0001	<.0001	0.0972
PFNA	0.04616	0.33643	-0.13843	0.60524	.	.	-0.18791	0.67359	1	0.78348	0.68839	-0.23733
	0.5841	<.0001	0.0992	<.0001	.	.	0.0246	<.0001		<.0001	<.0001	0.0043
PFDA	0.04538	0.16413	-0.04762	0.67216	.	.	-0.19478	0.56159	0.78348	1	0.73379	-0.37777
	0.5904	0.0501	0.5722	<.0001	.	.	0.0197	<.0001	<.0001		<.0001	<.0001
PFUnDA	0.16159	0.17286	-0.0956	0.55932	.	.	-0.14585	0.36061	0.68839	0.73379	1	-0.29473
	0.0538	0.039	0.2561	<.0001	.	.	0.0822	<.0001	<.0001	<.0001		0.0004
PFDoDA	-0.05864	-0.03395	-0.00109	-0.26925	.	.	0.05717	-0.13925	-0.23733	-0.37777	-0.29473	1

114

	0.4866	0.6873	0.9897	0.0011	.	.	0.4976	0.0972	0.0043	<.0001	0.0004	
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¹Statistically significant effect ($p < 0.05$) indicated in bold

115 **Appendix B. Information on the studies selected for inclusion in the hazard index**
116 **approach**

117 *Immunotoxicity*

118 In a prospective cohort study, **Grandjean et al. (2012)** examined children's antibody
119 response before and after tetanus and diphtheria vaccination (N = 380-537) at 5 years (pre-
120 and post-booster) and at 7 years of age and the association with several PFASs (PFOS, PFOA,
121 PFHxS, PFNA, PFDA) as measured in the blood serum of the children (at 5 years old) and in
122 the blood serum of their mothers at time of birth. The relation between PFAS exposure and
123 antibody response was assessed by using multiple linear regression analysis and included
124 adjustment for potential confounders, such as PCB exposure in the mother, birth weight,
125 maternal smoking during pregnancy, and duration of breastfeeding. The statistically
126 significant association between PFOS, PFOA, PFHxS, and PFDA exposure and 20-36%
127 decreased average percentage change in antibody response at the age of 7 years (2 years after
128 vaccination) expressed as doubling of substance exposure (adjusted for age, sex, and booster
129 type), reflected by the geometric mean, was chosen as point of departure for effect level in the
130 children's population. The authors reported that a total of 18 out of 408 children (compared to
131 141 children pre-booster) still had an antibody concentration below the clinically protective
132 level of 0.1 IU/mL at the age of 7. PFASs were positively correlated, showing Pearson
133 correlation coefficients (r) between 0.22-0.78.

134 In a cross-sectional study by **Kielsen et al. (2016)**, adults' (N = 12) antibody response
135 against diphtheria vaccination was followed at seven consecutive time-points (days 0, 2, 4, 7,
136 10, 14 and 30). Blood serum concentrations were obtained for PFHxS, PFHpA, PFOS, PFOA,
137 PFNA, PFDA, PFUnDA and PFDoDA. The antibody response over time was modelled by
138 using cubic splines, and the relative increase in antibody concentration between day 4 and 10
139 was used as effect for input in a linear regression model to observe an association with PFASs

140 exposure, correcting for sex and age. Statistically significant associations between PFOS,
141 PFNA, PFDA, PFDAUnDA and PFDoDA exposure and decreased change in specific antibody
142 response (12-18%) was observed, expressed as doubling of exposure. The latter effect,
143 reflected by the median in the study population, was used as point of departure for the effect
144 level of the adult population. Positive Pearson correlation coefficients were observed among
145 PFASs, from 0.07 to 0.98.

146 *Birth weight reductions*

147 Three studies on negative association between PFAS exposure and birth weight in
148 newborns, as reviewed in the EFSA (2020) opinion, were selected for further observation
149 (Table 4). Studies, in which no or only few PFASs showed to be significantly associated with
150 an adverse effect on birth weight, were excluded.

151 In a prospective cohort study, mother-child pairs were followed during pregnancy
152 until birth to study the association between prenatal exposure to PFASs and birth weight and
153 gestational age (**Meng et al. (2018)**). PFOS and PFOA (N = 3535) and PFHxS, PFNA,
154 PFHpS, and PFDA (N = 2120) were measured in maternal plasma during the first trimester.
155 Multivariable linear regression showed, among others, an association between PFOS, PFOA,
156 PFNA and PFHpS exposure and decreased birth weight with an average magnitude of 36-45
157 grams per doubling of exposure, after adjusting for infant sex, infant birth year, gestational
158 week of blood draw, maternal age, parity, socio-occupational status, pre-pregnancy body
159 mass index (BMI), smoking and alcohol intake during pregnancy. This association, reflected
160 by the median exposure, was used as point of departure for effects on development at the
161 level of the mother (effect level of the adult population). Additional analyses were performed
162 looking at quartile classifications, showing in general less statistically significant associations

163 between exposure to PFASs and birth weight. PFASs were positively correlated, showing
164 Pearson correlation coefficients varying from 0.17 to 0.89.

165 Lastly, in a prospective cohort study with mother-child pairs (**Wang et al. 2016**), birth
166 weight, birth length, head circumference and ‘small for gestational age’ (SGA), and its
167 association with prenatal exposure to PFOA, PFNA, PFDA, PFUnDA, and PFDoDA in
168 maternal serum during the last trimester was examined. Furthermore, the children were
169 followed for several years to observe general growth (as expressed by weight and length).
170 Linear regression was used to identify statistically significantly negative associations between
171 PFOS, PFOA, PFHxS and PFDA exposure on birth weight for girls, but not for boys. An
172 average decrease of 60 to 140 grams was associated with a doubling of exposure, adjusted for
173 family annual income, maternal age at delivery, maternal education, maternal previous live
174 children, and maternal pre-pregnancy BMI. This effect, reflected by geometric mean
175 exposure, was used as point of departure at the level of the mother (effect level of the adult
176 population). Also, an association between PFDA and PFUnDA and SGA was observed in
177 girls, as well as a decreased head circumference in girls associated with PFDoDA exposure.
178 Interestingly, this study observed lower average childhood height in boys at follow-up,
179 possibly due to effects of prenatal exposure on postnatal growth. Positive Pearson correlation
180 coefficients were observed among PFASs, from 0.13 to 0.86. The authors note that due to the
181 high correlations among PFASs, it is not possible to attribute any of the observed associations
182 to a single PFAS.

183

184 Table B.1. Associations between PFASs exposure and either immunotoxic effects or reduced birth weight in newborns. The beta value represents
 185 the change of effect caused by a doubling of PFAS exposure. Statistically significant associations, of which the median or geometric mean were
 186 used as point of departure/effect level for the hazard quotient calculations, are indicated in bold.

Study	Study type	Population	N	Matrix	Period	Confounders	Statistical method	Mean exposure and range in ng/mL ¹		Association between PFAS and effects (beta +/- 95% CI) ² , per doubling of exposure			Correlations among PFASs
								PFOS	PFOS	PFOA	PFHxS	PFNA	
Meng et al. (2018)	Prospective cohort study	Mother-child pairs	3535 (PFOS and PFOA) 2120 (other PFASs)	Blood plasma of mothers	First trimester, 1996-2002	Maternal age, socio-occupational status, pre-pregnancy BMI, smoking during pregnancy, alcohol consumption, dietary intake (fish consumption and organic food)	Multivariable linear regression, quartile classifications, pairwise Pearson correlation	PFOS	30.1 (22.9–39.0)	Birth weight in boys + girls (grams)	PFOS	-45.2 (-76.8, -13.6)	PFHpS-PFOS 0.89 PFNA-PFDA 0.73 PFHpS-PFOA 0.67 PFOA-PFOS 0.66 PFNA-PFHpS 0.54 PFHpS-PFDA 0.49 PFNA-PFOS 0.48 PFDA-PFOS 0.48 PFNA-PFOA 0.47 PFHxS-PFHpS 0.39 PFOA-PFHxS 0.33 PFHxS-PFOS 0.30 PFDA-PFOA 0.28 PFHxS-PFNA 0.28 PFHxS-PFDA 0.17
								PFOA	4.6 (3.3–6.0)		PFOA	-35.6 (-66.3, -5.0)	
								PFHxS	1.0 (0.7–1.3)		PFHxS	1.2 (-28.3, 30.7)	
								PFNA	0.5 (0.4–0.6)		PFNA	-36.3 (-70.6, -2.0)	
								PFHpS	0.4 (0.3–0.5)		PFHpS	-38.9 (-72.6, -5.1)	
								PFDA	0.2 (0.1–0.2)		PFDA	-9.0 (-43.2, 25.2)	
Wang et al. (2016)	Longitudinal cohort study	Mother-child pairs	106 ³	Blood serum of mothers	Third trimester, 2000-2001	Maternal age, socio-economic status, pre-pregnancy BMI. Not adjusted for smoking or alcohol consumption because few women smoked (2%) or consumed alcohol during pregnancy (1%).	Linear regression, quartile classifications, pairwise Pearson correlation	PFOA	1.98 (1.69-2.32)	Birth weight in girls (grams)	PFOA	-80 (-180, 10)	PFUnDA-PFDoDA 0.86 PFNA-PFUnDA 0.81 PFNA-PFDoDA 0.80 PFDA-PFNA 0.62 PFDA-PFDoDA 0.57 PFNA-PFUnDA 0.56 PFOA-PFDA 0.34 PFOA-PFNA 0.32 PFOA-PFDoDA 0.14 PFOA-PFUnDA 0.13
								PFNA	1.44 (1.19-1.74)		PFNA	-80 (-160, 0)	
								PFDA	0.37 (0.32-0.42)		PFDA	-140 (-260, -20)	
								PFUnDA	2.89 (2.12-3.94)		PFUnDA	-60 (-110, -10)	
								PFDoDA	0.30 (0.25-0.35)		PFDoDA	-120 (-210, -20)	
Grandjean et al. (2012)	Prospective cohort study	Children followed from birth to year 7	408	Blood serum of mothers and children	At year 5 (children), 2002-2005	PCB exposure in the mother, birth weight, maternal smoking during pregnancy, duration of breastfeeding.	Multiple regression, pairwise Pearson correlation	PFOS	16.7 (13.5-21.1)	Percentage change in specific antibody response to tetanus vaccine at year 7	PFOS	-23.8 (-44.3, 4.2)	PFNA-PFDA 0.78 PFOS-PFHxS 0.57 PFOA-PFNA 0.54 PFOA-PFHxS 0.53 PFOS-PFOA 0.50 PFOS-PFNA 0.48 PFOS-PFDA 0.39 PFOA-PFDA 0.35 PFHxS-PFNA 0.34 PFHxS-PFDA 0.22
								PFOA	4.06 (3.33-4.96)		PFOA	-35.8 (-51.9, -14.2)	
								PFHxS	0.63 (0.45-0.88)		PFHxS	-19.7 (-31.6, -5.7)	
								PFNA	1.00 (0.76-1.24)		PFNA	-17.4 (-34.1, 3.6)	
								PFDA	0.28 (0.21-0.38)		PFDA	-22.3 (-35.8, -5.8)	
Kielsen et al. (2016)	Cross-sectional study	Adults	12	Blood serum	Adults (average age 37 years)	Sex and age	Cubic splines, linear regression	PFHxS	0.37 (0.27-0.70)	Percentage change in specific antibody response to diphtheria vaccine 4-10 days post-vaccination	PFHxS	-13.31 (-25.07, 0.29)	Log-transformed PFAS concentrations showed positive correlations with Pearson coefficients from 0.07 (PFHxS and PFDoDA) to 0.98 (PFUnDA and PFDoDA)
								PFHpA	0.12 (0.094-0.14)		PFHpA	6.52 (-28.04, 57.7)	
								PFOS	9.52 (5.38-14.3)		PFOS	-11.90 (-21.92, -0.33)	
								PFOA	1.69 (1.30-2.79)		PFOA	-8.22 (-20.85, 6.44)	
								PFNA	0.66 (0.46-0.80)		PFNA	-17.90 (-27.99, -6.39)	
								PFDA	0.30 (0.20-0.32)		PFDA	-18.18 (-29.52, -5.00)	
								PFUnDA	0.21 (0.18-0.27)		PFUnDA	-12.11 (-22.06, -0.90)	
								PFDoDA	0.039 (0.035-0.048)		PFDoDA	-15.64 (-28.14, -0.98)	

¹ For Meng et al. (2018), median exposure and interquartile range (Q1-Q3) are presented. For Wang et al. (2016), geometric mean and 95% confidence interval are presented. For Grandjean et al. (2012), geometric mean and interquartile range (Q1-Q3) are presented. For Kielsen et al. (2016), median and interquartile range (Q1-Q3) are presented.

² For Meng et al. (2018), birth weight was adjusted for infant sex, maternal age, parity, socio-occupational status, pre-pregnancy body mass index (BMI), smoking and alcohol intake during pregnancy. For Wang et al. (2016), birth weight in girls was adjusted for family annual income, maternal age at delivery, maternal education, maternal previous live children, and maternal pre-pregnancy BMI. Grandjean et al. (2012), antibody response to tetanus vaccination was adjusted for age, sex, and booster type. Kielsen et al. (2016) antibody response was adjusted for sex and age. Statistically significant effects are indicated in bold, p-value in all studies was 0.05.

³ A total of 223 mother-child couples were included in the study, but only statistically significant effects were seen for girls.

193 **Appendix C. Liver toxicity data underlying the internal RPFs**

194 Table C.1. Male rat dose-response data for nine PFASs including full chemical name, chemical
 195 name abbreviation, CAS no. and reference

PFAS (abbreviation, carbon chain length) [CAS no.] ^f	Reference	Administration route	Strain	Exposure duration (days)	External dose (mg/kg bw/day)	Relative liver weight		
						Mean (g/100 g)	SD	N
Perfluorobutanesulfonic acid (PFBS, C4) ^a [375-73-5]	(Lieder, York et al.)	Oral gavage	CrI:CD(SD)IGS BR VAF/Plus (Sprague Dawley) rats	70	0	3.4	0.3	30
					30	3.5	0.4	30
					100	3.6	0.3	30
					300	3.8	0.3	30
					1000	4.1	0.4	30
Perfluorohexanesulfonic acid (PFHxS, C6) ^a [355-46-4]	(Butenhoff, Chang et al.)	Oral gavage	CrI:CD(SD)IGS BR VAF/Plus (Sprague Dawley) rats	42	0	3.12	0.03	10
					0.3	3.20	0.23	10
					1.0	3.42	0.42	10
					3.0	3.73	0.23	10
					10.0	5.25	0.72	10
Perfluorooctanesulfonic acid (PFOS, C8) ^a [1763-23-1]	(Seacat, Thomford et al.)	Oral dietary	CrI:CD (Sprague Dawley) IGS BR rats	98	0	3.2	0.3	5
					0.03	3.2	0.2	5
					0.13	3.2	0.2	5
					0.34	3.6	0.3	5
					1.33	4.3	0.4	5
Perfluorobutanoic acid (PFBA, C4) ^a [375-22-4]	(Butenhoff, Bjork et al.)	Oral gavage	Sprague Dawley rats (CrI:CD Outbred, SPF quality)	90	0	2.1	0.23	20
					1.2	2.1	0.14	10
					6	2.2	0.27	10
					30	2.6	0.39	20
Perfluorohexanoic acid (PFHxA, C6) ^a [307-24-4]	(Loveless, Slezak et al.)	Oral gavage	CrI:CD(SD) rats	90	0	2.69	0.17	10
					20	2.70	0.26	10
					100	3.00	0.23	10
					500	4.38	0.49	10
Perfluorooctanoic acid (PFOA, C8) [335-67-1]	(Perkins, Butenhoff et al.)	Oral dietary	ChR-CD rats	91	0	3.24	0.28	15
					0.06	3.24	0.23	15
					0.64	3.69	0.32	15
					1.94	4.21	0.56	15
					6.50	5.50	0.84	15
Perfluorononanoic acid (PFNA, C9) ^b [375-95-1]	(Mertens, Sved et al.)	Oral gavage	CrI:CD (SD)IGS BR rats	91	0	2.50	0.10	15
					0.025	2.63	0.19	10
					0.125	3.12	0.31	10
					0.6	4.51	0.43	15
Perfluorododecanoic acid (PFDoDA, C12) [307-55-1] ^c	(Hirata-Koizumi, Fujii et al.)	Oral gavage	CrI:CD(SD) rats	42	0	2.51	0.14	5
					0.1	2.67	0.21	5
					0.5	3.00	0.30	5
					2.5	4.30	0.27	5
					1000	5.00	0.13	5
2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-	(Haas)	Oral gavage	CrI:CD(SD) rats	90	0	2.716	0.1319	10
					0.1	2.727	0.2125	10

PFAS (abbreviation, carbon chain length) [CAS no.] ^c	Reference	Administ ration route	Strain	Exposure duration (days)	External dose (mg/kg bw/day)	Relative liver weight		
						Mean (g/100 g)	SD	N
propanoic acid (HFPO- DA) ^a [13252-13-6]					10	3.556	0.4752	10
					100	4.535	0.5144	10

197 **Appendix D. PFAS mixture risk assessment: Outcomes of the hazard index**
 198 **approach setting non-detects at half LOD/LOQ.**

199 Table D.1. Hazard Indices (HIs) for PFAS calculated for nine European countries based
 200 on P50 values, whereby non-detects are set at half LOQ/LOD. Hazard quotients are
 201 added to calculate the HI. A HI >1 indicates a potential risk.

Immunotoxi city	EL (ng/mL)	Norway	Sweden	Slovakia	Slovenia	Greece	Spain	Belgium	France	Germany
Kielsen (2016) Adults										
PFOS	9.52	0.29	0.28	0.14	0.17	0.22	0.14	0.23	0.21	0.27
PFNA	0.66	0.67	0.57	0.26	0.38	0.63	0.43	0.48	0.82	0.38 ^a
PFDA	0.3	HQ 0.43	0.49	0.17	0.47	0.57	0.33 ^a	0.33 ^a	0.72	0.42 ^a
PFUnDA	0.21	0.41	0.69 ^a	0.01 ^b	0.29	0.17	0.48 ^a	0.48 ^a	0.52	0.60 ^a
PFDoDA	0.039	0.26 ^b	3.69 ^a	0.13 ^b	0.06 ^b	0.06 ^b	1.54 ^a	2.56 ^a	0.26	3.21 ^a
		HI 2.07	5.72	0.71	1.37	1.65	2.92	4.09	2.53	4.87

Grandjean et al. (2012) Children										
PFOA	4.06	0.32	0.28	0.17	0.21	0.22	0.16	0.27	0.36	0.31
PFHxS	0.63	HQ 0.75	0.62	0.46	0.37	0.44	0.27 ^a	0.78	1.09	0.62
PFDA	0.28	0.46	0.53	0.18	0.50	0.61	0.36 ^a	0.36 ^a	0.77	0.45 ^a
		HI 1.53	1.43	0.81	1.08	1.27	0.79	1.41	2.22	1.37

Birth weight reduction

Meng et al. (2018) Mothers										
PFOA	4.6	0.28	0.25	0.15	0.19	0.19	0.14	0.24	0.32	0.27
PFOS	30.1	0.09	0.09	0.05	0.05	0.07	0.04	0.07	0.07	0.09
PFNA	0.5	HQ 0.89	0.75	0.34	0.50	0.83	0.56	0.64	1.08	0.50 ^a
PFHpS	0.4	0.09 ^c	NA	0.08	0.08	0.13	0.31 ^a	0.25 ^a	0.30 ^c	NA
		HI 1.35	1.09	0.61	0.82	1.22	1.06	1.20	1.77	0.86

Wang et al. (2016) Mothers										
PFNA	1.44	0.31	0.26	0.12	0.17	0.29	0.20	0.22	0.38	0.17 ^a
PFDA	0.37	0.35	0.40	0.14	0.38	0.46	0.27 ^a	0.27 ^a	0.59	0.34 ^a
PFDoDA	2.89	HQ 0.00 ^b	0.05 ^a	0.00 ^b	0.00 ^b	0.00 ^b	0.02 ^a	0.03 ^a	0.00 ^b	0.04 ^a
PFUnDA	0.3	0.29	0.48 ^a	0.01 ^b	0.20	0.12	0.33 ^a	0.33 ^a	0.36	0.42 ^a
		HI 0.95	1.19	0.26	0.75	0.87	0.82	0.86	1.33	0.97

EL = effect level, NA = not available

^a LOQ/2

^b LOD/2

^c (LOD+LOQ)/2

202
203
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205
206

207 Table D.2. Hazard Indices (HIs) for PFAS calculated for nine European countries based
 208 on P95 values, whereby non-detects are set at half LOQ/LOD. Hazard quotients are
 209 added to calculate the hazard index. A HI >1 indicates a potential risk.

Immunotoxi city	EL (ng/mL)	Norway	Sweden	Slovakia	Slovenia	Greece	Spain	Belgium	France	Germany
Kielsen (2016)										
Adults										
PFOS	9.52	0.74	0.86	0.65	0.61	0.55	0.32	0.77	0.65	0.62
PFNA	0.66	1.52	1.30	0.70	0.77	1.27	0.91	1.12	2.09	1.11
PFDA	0.3	HQ	1.01	1.43	0.57	0.94	1.33	0.92	1.67	1.69
PFUnDA	0.21		1.28	1.67	0.38	0.59	0.81	1.12	1.14	1.37
PFDoDA	0.039		0.26 ^b	3.69 ^a	0.13 ^b	0.77	0.63	1.54 ^a	2.56 ^a	0.26 ^b
		HI	4.80	8.96	2.43	3.68	4.58	4.81	7.27	6.06

Grandjean et al. (2012)										
Children										
PFOA	4.06		0.51	0.58	0.34	0.36	0.54	0.25	0.44	0.65
PFHxS	0.63	HQ	1.89	1.75	1.58	0.67	1.41	1.21	2.22	3.69
PFDA	0.28		1.08	1.54	0.61	1.00	1.42	0.99	1.79	1.81
		HI	3.48	3.87	2.53	2.03	3.37	2.46	4.45	6.15

Birth weight

Meng et al. (2018)										
Mothers										
PFOA	4.6		0.45	0.51	0.30	0.31	0.48	0.22	0.39	0.57
PFOS	30.1		0.23	0.27	0.20	0.19	0.17	0.10	0.24	0.20
PFNA	0.5	HQ	2.01	1.72	0.93	1.02	1.68	1.20	1.48	2.76
PFHpS	0.4		0.25	NA	0.49	0.28	0.36	0.63	0.25 ^a	0.30 ^c
		HI	2.95	2.51	1.92	1.81	2.69	2.16	2.36	3.84

Wang et al. (2016)										
Mothers										
PFNA	1.44		0.70	0.60	0.32	0.35	0.58	0.42	0.51	0.96
PFDA	0.37		0.82	1.16	0.46	0.76	1.08	0.75	1.35	1.37
PFDoDA	2.89	HQ	0.00 ^b	0.05 ^a	0.00 ^b	0.01	0.01	0.02 ^a	0.03 ^a	0.00 ^b
PFUnDA	0.3		0.89	1.17	0.27	0.41	0.57	0.79	0.80	0.96
		HI	2.41	2.98	1.05	1.53	2.23	1.97	2.70	3.29

EL = effect level, NA = not available

^a LOQ/2

^b LOD/2

^c (LOD+LOQ)/2

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 211
 212
 213

214 **Appendix E. EFSA-4 exposure with non-detects imputed by half LOQ/LOD**
 215 **or zero.**

216 Table E1. Percentiles of the distribution for the EFSA-4 sum calculated for nine
 217 European populations, where non-detects are set at half LOQ/LOD, and the percentage
 218 of participants exceeding the HBM GVs.

	N of participants in the study	Percentiles of the sum EFSA-4 in serum or plasma (ng/mL)							Participants exceeding the HBM GV of 6.9 ng/mL		Participants exceeding the HBM GV of 17.5 ng/mL	
		P05	P10	P25	P50	P75	P90	P95	N	%	N	%
Norway	177	2.95	3.50	4.14	5.15	6.33	8.96	11.0	31	17.5	0	0
Sweden	300	2.29	2.81	3.68	4.84	6.70	9.08	12.4	69	23	5	1.7
Slovakia	292	1.10	1.31	1.86	2.59	4.12	6.19	9.24	22	7.5	4	1.4
Slovenia	94	1.62	2.04	2.49	2.99	4.43	6.13	8.15	7	7.5	0	0
Greece	52	2.29	2.7	3.06	3.83	5.49	8.07	8.91	7	13.5	0	0
Spain	299	1.32	1.53	1.96	2.55	3.20	4.30	5.18	4	1.3	1	0.3
Belgium	300	2.03	2.45	3.16	4.18	5.95	8.44	10.2	51	17	1	0.3
France	143	2.87	3.17	3.94	4.91	6.88	10.2	11.3	34	23.8	2	1.4
Germany	300	2.35	2.73	3.45	4.62	6.13	7.89	9.91	54	18	3	1

219

220 Table E2. Percentiles of the distribution for the EFSA-4 sum calculated for nine
 221 European populations, where non-detects are set at zero, and the percentage of
 222 participants exceeding the HBM GVs.

	N of participants in the study	Percentiles of the sum EFSA-4 in serum or plasma (ng/mL)							Participants exceeding the HBM GV of 6.9 ng/mL		Participants exceeding the HBM GV of 17.5 ng/mL	
		P05	P10	P25	P50	P75	P90	P95	N	%	N	%
Norway	177	2.95	3.50	4.14	5.15	6.33	8.96	11.0	31	17.5	0	0
Sweden	300	2.16	2.77	3.64	4.82	6.70	9.08	12.4	69	23.0	5	1.7
Slovakia	292	1.10	1.31	1.86	2.59	4.12	6.19	9.24	22	7.5	4	1.4
Slovenia	94	1.62	2.04	2.49	2.985	4.43	6.13	8.15	7	7.5	0	0
Greece	52	2.29	2.70	3.06	3.83	5.49	8.07	8.91	7	13.5	0	0
Spain	299	1.10	1.34	1.79	2.38	3.12	4.25	5.18	4	1.3	1	0.3
Belgium	300	1.96	2.37	3.15	4.18	5.95	8.44	10.2	51	17.0	1	0.3
France	143	2.87	3.17	3.94	4.91	6.88	10.2	11.3	34	23.8	2	1.4
Germany	300	1.80	2.28	3.14	4.35	5.93	7.72	9.78	49	16.3	3	1

223

224 **Appendix F. RPF approach with sum PEQ values imputed by half**

225 **LOQ/LOD or zero.**

226 Table F1. Percentiles of the distribution for the sum of six or seven PFASs expressed as
 227 ng PEQ/mL serum or plasma, calculated for nine European populations, where non-
 228 detects are imputed by half LOD/LOQ, and the percentage of participants exceeding the
 229 HBM GV_s.

	N of substances included in sum PEQ	N of participants in the study	Percentiles of the sum of PFASs in serum or plasma expressed as PEQ ng/mL							Participants exceeding the HBM GV of 6.9 ng/mL		Participants exceeding the HBM GV of 17.5 ng/mL	
			P05	P10	P25	P50	P75	P90	P95	N	%	N	%
Norway	6 ^b	177	7.14	8.26	10.1	12.7	16.3	23.60	28.8	170	96.1	34	19
Sweden	7 ^a	300	5.96	7.66	9.75	12.8	17.4	25.3	30.8	277	92.3	73	24
Slovenia	7 ^a	94	4.19	4.50	5.99	7.42	11.0	15.9	22.0	51	54.3	7	7.5
Slovakia	7 ^a	292	2.51	3.34	4.71	6.93	10.9	16.2	26.2	147	50.3	27	9.3
Greece	7 ^a	52	6.84	7.70	9.27	11.1	16.1	19.3	25.8	49	94.2	9	17
Spain	7 ^a	299	4.77	5.33	6.50	8.20	10.1	13.3	15.7	210	70.2	7	2.3
Belgium	7 ^a	300	6.33	6.94	9.21	11.9	16.0	22.8	29.4	273	91.0	63	21
France	7 ^a	143	6.45	7.31	9.14	11.2	16.2	24.0	27.6	133	93.0	30	21
Germany	7 ^a	300	8.55	9.20	10.9	13.4	16.5	21.0	27.0	295	98.3	62	21

230 ^a PFBS, PFHxS, PFOS, PFHxA, PFOA, PFNA, PFD_oDA

231 ^b PFBS, PFHxS, PFOS, PFOA, PFNA, PFD_oDA

232 Table F2. Percentiles of the distribution for the sum of six or seven PFASs expressed as
 233 ng PEQ/mL serum or plasma, calculated for nine European populations, where non-
 234 detects are imputed by zero, and the percentage of participants exceeding the HBM
 235 GV_s.

	N of substances included in sum PEQ	N of participants in the study	Percentiles of the sum of PFASs in serum or plasma expressed as PEQ ng/mL							Participants exceeding the HBM GV of 6.9 ng/mL		Participants exceeding the HBM GV of 17.5 ng/mL	
			P05	P10	P25	P50	P75	P90	P95	N	%	N	%
Norway	6 ^b	177	7.04	8.15	10.0	12.4	16.2	23.2	28.5	169	95.5	32	18
Sweden	7 ^a	300	5.10	6.78	8.65	11.8	16.4	23.8	29.9	266	88.7	68	23
Slovenia	7 ^a	94	4.11	4.42	5.81	7.24	10.9	15.8	21.9	51	54.3	7	7.5
Slovakia	7 ^a	292	2.45	3.29	4.66	6.88	10.8	16.1	26.2	145	49.7	27	9.3
Greece	7 ^a	52	6.81	7.68	9.24	11.1	16.1	19.3	25.8	49	94.2	9	17
Spain	7 ^a	299	2.58	3.18	4.57	6.26	8.16	11.4	13.7	123	41.1	5	1.7
Belgium	7 ^a	300	3.81	4.50	7.07	9.86	14.0	20.8	27.6	230	76.7	48	16
France	7 ^a	143	6.09	6.96	8.63	10.7	15.7	23.7	27.4	130	90.9	25	17
Germany	7 ^a	300	4.68	5.32	7.11	9.63	13.0	17.7	23.9	232	77.3	30	10

236 ^a PFBS, PFHxS, PFOS, PFHxA, PFOA, PFNA, PFD_oDA

237 ^b PFBS, PFHxS, PFOS, PFOA, PFNA, PFD_oDA