

Suggested list of biomarkers, matrices and analytical methods for the 1st prioritisation round of substances

In order to come up with a suggested list of biomarkers, matrices and analytical methods for the 1st prioritisation round of substances, partners in task 9.1 in collaboration with the chemical group leaders (CGLs) made inventories of available analytical methods as well as suitable exposure biomarkers and matrices. A template to gather information in a harmonised way and according to the criteria established in Deliverable 9.1 was agreed upon. Information in the inventories was further evaluated by partners in task 9.1 following guidelines that had been thoroughly discussed and agreed upon. The CGLs were consulted and gave their input on the final draft of the deliverable. The resulting list of suitable pairs of exposure biomarker/matrices as well as analytical methods is presented below. The substances have been categorised according to the year one scoping documents. Category C substances for which information on analytical methods in human matrices are insufficient or lacking, have been left out of the table. Information on how the inventories were compiled and the evaluations done, with specific comments and needs for methodological improvements for the individual groups of substances, are described in details in the deliverable 9.2. The inventories and evaluations will be revised and updated if new information is available in year two of HBM4EU.

Summary table listing biomarkers, matrices, analytical methods and method detection limit (MDL) suggested for the 1st prioritisation round of substances¹.

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
Phthalates and DINCH				
Category A				
Di(2-ethylhexyl) phthalate (DEHP)	Mono(2-ethylhexyl) phthalate (MEHP)	Urine (0.3 mL)	LC-MS-MS	0.2 ng/mL
	Mono(2-ethyl-5-hydroxy-hexyl) phthalate (5OH-MEHP, MEHHP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
	Mono(2-ethyl-5-oxo-hexyl) phthalate (5oxo-MEHP, MEOHP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
	Mono(2-ethyl-5-carboxy-pentyl) phthalate (5cx-MEPP, MECPP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
Butyl benzyl phthalate (BBzP)	Mono-benzyl phthalate (MBzP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
Di-n-butyl phthalate (DnBP)	Mono-n-butyl phthalate (MnBP)	Urine (0.3 mL)	LC-MS-MS	0.3 ng/mL
	3-OH-Mono-n-butyl phthalate (OH-MnBP)	Urine (0.3 mL)	LC-MS-MS	0.3 ng/mL

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
Di-isobutyl phthalate (DiBP)	Mono-isobutyl phthalate (MiBP)	Urine (0.3 mL)	LC-MS-MS	0.3 ng/mL
	2-OH-Mono-isobutylphthalate (OH-MiBP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
Diethyl phthalate (DEP)	Mono-ethyl phthalate (MEP)	Urine (0.3 mL)	LC-MS-MS	0.2 ng/mL
Category B				
Di-isononyl phthalate (DiNP)	7-OH-(Mono-methyl-octyl) phthalate (OH-MiNP, MHNP)	Urine (0.3 mL)	LC-MS-MS	0.3 ng/mL
	7-Oxo-(Mono-methyl-octyl) phthalate (oxo-MiNP, MONP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
	7-Carboxy-(mono-methyl-heptyl) phthalate (cx-MiNP, MCOP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
Di-isodecyl phthalate (DiDP) (all C10 phthalates including DPHP)	6-OH-Mono-propyl-heptyl phthalate (OH-MiDP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
	6-Oxo-Mono-propyl-heptyl phthalate (oxo-MiDP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
	Mono(2,7-methyl-7-carboxy-heptyl) phthalate (cx-MiDP, MCNP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
Di-n-octyl phthalate (DnOP)	Mono-n-octyl phthalate (MnOP, MOP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
Dimethyl phthalate (DMP)	Mono-methyl phthalate (MMP)	Urine (0.3 mL)	LC-MS-MS	0.3 ng/mL
Di-n-pentyl phthalate (DnPeP)	Mono-n-pentyl phthalate (MnPeP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
Dicyclohexyl phthalate (DCHP)	Mono-cyclo-hexyl phthalate (MCHP)	Urine (0.3 mL)	LC-MS-MS	0.1 ng/mL
Di(2-propylheptyl) phthalate (DPHP)	6-OH-Mono-propyl-heptyl phthalate (OH-MPHP)	Urine (1 mL)	GC-MS-MS	0.1 ng/mL
	6-Oxo-Mono-propyl-heptyl phthalate (oxo-MPHP)	Urine (1 mL)	GC-MS-MS	0.08 ng/mL
	Mono(2,7-methyl-7-carboxy-heptyl) phthalate (cx-MPHP)	Urine (1 mL)	GC-MS-MS	0.05 ng/mL

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
Di-isononyl cyclohexane-1,2-dicarboxylate (DINCH)	cyclohexane-1,2-dicarboxylate-mono-(7-carboxylate-4-methyl)heptyl ester (cx-MINCH, MCOCH)	Urine (0.3 mL)	LC-MS-MS	0.03 ng/mL
	cyclohexane-1,2-dicarboxylate-mono-(7-hydroxy-4-methyl)octyl ester (OH-MINCH, MHNCH)	Urine (0.3 mL)	LC-MS-MS	0.03 ng/mL
	cyclohexane-1,2-dicarboxylate-mono-(7-oxo-4-methyl)octyl ester (oxo-MINCH, MONCH)	Urine (0.3 mL)	LC-MS-MS	0.02 ng/mL
Category C				
Di-n-hexyl phthalate (DnHexP)	Mono-n-hexyl phthalate (suspected) (MnHxP)	Urine (0.1 mL)	LC-MS-MS	0.2 ng/mL
Per- and polyfluoroalkyl substances (PFAS)				
Category A				
Perfluorobutanoic acid (PFBA)	PFBA	Serum (0.15 mL)	LC-MS-MS	0.003 ng/mL
Perfluoropentanoic acid (PFPeA)	PFPeA	Serum (0.15 mL)	LC-MS-MS	0.008 ng/mL
Perfluorohexanoic acid (PFHxA)	PFHxA	Serum (0.15 mL)	LC-MS-MS	0.007 ng/mL
Perfluoroheptanoic acid (PFHpA)	PFHpA	Serum (0.15 mL)	LC-MS-MS	0.009 ng/mL
Perfluorooctanoic acid (PFOA)	PFOA	Serum (0.15 mL)	LC-MS-MS	0.006 ng/mL
Perfluorononanoic acid (PFNA)	PFNA	Serum (0.15 mL)	LC-MS-MS	0.004 ng/mL
Perfluorodecanoic acid (PFDA)	PFDA	Serum (0.15 mL)	LC-MS-MS	0.002 ng/mL
Perfluoroundecanoic acid (PFUnDA)	PFUnDA	Serum (0.15 mL)	LC-MS-MS	0.006 ng/mL
Perfluorododecanoic acid (PFDoDA)	PFDoDA	Serum (0.15 mL)	LC-MS-MS	0.007 ng/mL
Perfluorotridecanoic acid (PFTrDA)	PFTrDA	Serum (0.15 mL)	LC-MS-MS	0.004 ng/mL

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
Perfluorotetradecanoic acid (PFTeDA)	PFTeDA	Serum (0.15 mL)	LC-MS-MS	0.05 ng/mL
Perfluorobutane sulfonic acid (PFBS)	PFBS	Serum (0.15 mL)	LC-MS-MS	0.009 ng/mL
Perfluorohexane sulfonic acid (PFHxS)	PFHxS	Serum (0.15 mL)	LC-MS-MS	0.007 ng/mL
Perfluoroheptane sulfonic acid (PFHpS)	PFHpS	Serum (0.15 mL)	LC-MS-MS	0.01 ng/mL
Perfluorooctane sulfonic acid (PFOS)	PFOS	Serum (0.15 mL)	LC-MS-MS	0.003 ng/mL
Perfluorodecane sulfonic acid (PFDS)	PFDS	Serum (0.15 mL)	LC-MS-MS	0.05 ng/mL
Category B				
Perfluoro-1-octaperfluoro-1-octanesulphonamide (FOSA)	FOSA	Serum (0.15 mL)	LC-MS-MS	0.02 ng/mL
N-Ethylperfluoro-1-octanesulphonamide (N-EtFOSA)	N-EtFOSA	Serum (0.15 mL)	LC-MS-MS	0.009 ng/mL
N-Ethyl-perfluorooctane sulphonamidoethanol (EtFOSE)	EtFOSE	Serum (0.20 mL)	LC-MS-MS	0.4 ng/mL
N-Methylperfluoro-1 octanesulphonamide (N-MeFOSA)	N-MeFOSA	Serum (0.15 mL)	LC-MS-MS	0.009 ng/mL
N-ethyl-perfluorooctane sulfonamidoacetate (EtFOSAA)	EtFOSAA	Serum (1 g)	LC-MS-MS	0.002 ng/g
Category C				
6:2 polyfluoroalkyl phosphoric acid diesters (6:2 diPAP)	6:2 diPAP	Serum (0.05 mL)	LC-MS-MS	0.018 ng/mL
8:2 polyfluoroalkyl phosphoric acid diesters (8:2 diPAP)	8:2 diPAP	Serum (0.05 mL)	LC-MS-MS	0.009 ng/mL
6:2 polyfluoroalkyl phosphoric acid monoesters (6:2 monoPAP)	6:2 mono PAP	Serum (0.05 mL)	LC-MS-MS	0.09 ng/mL

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
8:2 polyfluoroalkyl phosphoric acid monoesters (8:2 monoPAP)	8:2 monoPAP	Serum (0.05 mL)	LC-MS-MS	0.045 ng/mL
Perfluorohexylphosphonic acid (PFHxPA)	PFHxPA	Serum (0.05 mL)	LC-MS-MS	0.045 ng/mL
Perfluorooctylphosphonic acid (PFOPA)	PFOPA	Serum (0.05 mL)	LC-MS-MS	0.009 ng/mL
Perfluorodecylphosphonic acid (PFDPA)	PFDPA	Serum (0.05 mL)	LC-MS-MS	0.009 ng/mL
Ammonium 4,8-dioxo-3H-perfluorononanoate (ADONA)	ADONA	Serum (0.20 mL)	LC-MS-MS	0.2 ng/mL (LOQ)
Flame retardants (FRs)				
Category A				
Polybrominated diphenylethers (PBDEs, 7 in total)	PBDEs ³	Serum (2 mL)	GC-LRMS	0.0007 - 0.002 ng/mL
Hexabromocyclododecane (HBCDs, α , β , γ isomers)	HBCDs	Serum (1 mL)	LC-MS-MS	0.002-0.005 ng/mL
Category B				
PFRs (4 in total)	Diester metabolites ⁴	Urine (1 mL)	LC-MS-MS	0.04 – 0.2 ng/mL
PFRs (4 in total)	Diester metabolites ⁵	Urine (0.01 mL)	LC-HRMS	0.1 - 0.6 ng/mL
Tetrabromobisphenol A (TBBPA)	TBBPA	Serum (1 mL)	LC-MS-MS	0.008 ng/mL
Hexabromobenzene (HBB)	HBB	Serum (2 mL)	GC-LRMS	0.0003 ng/mL
Pentabromoethylbenzene (PBEB)	PBEB	Serum (5 mL)	GC-LRMS	0.0023 ng/mL
1,2 bis(2,4,6-tribromophenoxy)ethane (BTBPE)	BTBPE	Serum (2 mL)	GC-LRMS	0.0023 ng/mL
Pentabromotoluene (PBT)	PBT	Serum (5 mL)	GC-LRMS	0.0016 ng/mL
Dechlorane Plus (DP)	DP	Serum (2 mL)	GC-LRMS	0.001 – 0.002 ng/mL

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
Decabromodiphenylethane (DBDPE)	DBDPE	Serum (2 mL)	GC-LRMS	0.02 ng/mL
Hexachlorocyclopentadienyl-dibromocyclooctane (HCDBCO)	HCDBCO	Serum (2 mL)	GC-LRMS	5.4 ng/g lw
2-ethylhexyl-2,3,4,5-tetrabromobenzoate (EH-TBB)	EH-TBB	Serum (2 mL)	GC-MS-MS	0.4 ng/g lw
bis(2-ethylhexyl)-3,4,5,6-tetrabromophthalate (BH-TEBP)	BEH-TEBP	Serum (3 mL)	GC-MS-MS	0.2 ng/g lw
Octabromotrimethylphenylindane (OBIND)	OBIND	Serum (2 mL)	GC-MS-MS	1.5 ng/g lw
2,3,5,6-tetrabromo-p-xylene (TBX)	TBX	Breast milk (8-10 mL)	GC-HRMS	0.001 ng/g lw
Tetrabromoethylcyclohexane (TBECH)	TBECH	Breast milk (8-10 mL)	GC-HRMS	1.8 ng/g lw
Category C				
2,4-Dibromophenol	Derivatised FR	Serum (2-3 mL)	GC-LRMS	5 ng/g lw
	2,4-Dibromophenol	Breast milk (15 mL)	LC-MS-MS	0.2 ng/mL
2,4,6-Tribromophenol	Derivatised FR	Serum (1 mL)	GC-MS-MS	0.05 ng/mL
	2,4,6-Tribromophenol	Breast milk (15 mL)	LC-MS-MS	0.03 ng/mL
Pentabromophenol	Derivatised FR	Serum (2-3 mL)	GC-LRMS	0.5 ng/g lw
	Pentabromophenol	Breast milk (15 mL)	LC-MS-MS	0.03 ng/mL
Dechlorane 603 (Dec603)	Dec603	Serum (2 mL)	GC-LRMS	0.00064 ng/mL
Dechlorane 602 (Dec602)	Dec602	Serum (2 mL)	GC-HRMS	0.02 ng/g lw
Dechlorane 604 (Dec604)	Dec604	Serum (2 mL)	GC-LRMS	3.6 ng/g lw
Bisphenols (BPs)				
Category A				
Bisphenol A (BPA)	BPA	Urine (0.5 mL)	LC-MS-MS	0.02 ng/mL
Category B				
Bisphenol S (BPS)	BPS	Urine (NA)	LC-MS-MS	0.03 ng/mL

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
Bisphenol F (BPF)	BPF	Urine (NA)	LC-MS-MS	0.06 ng/mL
Polyaromatic hydrocarbons (PAHs)				
Category B				
Naphthalene (NAPH)	1-, 2-hydroxynaphthalene	Urine (0.5 - 2 mL)	LC-MS-MS	0.01 – 0.04 ng/mL
Fluorene (FLUO)	2-hydroxyfluorene (2-FLUO)	Urine (0.5 - 2 mL)	LC-MS-MS	0.01 – 0.04 ng/mL
Phenanthrene (PHE)	2-, 3-, 4-, 9- hydroxyphenanthrene	Urine (0.5 - 2 mL)	LC-MS-MS	0.01 – 0.04 ng/mL
Pyrene (PYR)	1-hydroxypyrene (1-PYR)	Urine (0.5 - 2 mL)	LC-MS-MS	0.01 – 0.04 ng/mL
Chrysene (CRY)	1-, 6-hydroxychrysene (1-CRY)	Urine (0.5 - 2 mL)	LC-MS-MS	0.01 – 0.04 ng/mL
Benzo[c]-phenanthrene (BcPh)	3-hydroxybenzo[c]- phenanthrene (3-BCP)	Urine (0.5 - 2 mL)	LC-MS-MS	0.01 – 0.04 ng/mL
Benz[a]anthracene (BaA)	1- hydroxybenz[a]anthracene (1-BaA)	Urine (0.5 - 2 mL)	LC-MS-MS	0.01 – 0.04 ng/mL
Acenaphthene (ACE)	ACE	Serum (1 mL)	GC-MS-MS	0.03 ng/mL
Acenaphthylene (ACY)	ACY	Serum (1 mL)	GC-MS-MS	0.03 ng/mL
Anthracene (AN)	AN	Serum (1 mL)	GC-MS-MS	0.03 ng/mL
Benz[a]anthracene (BaA)	BaA	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Benzo[a]pyrene (BaP)	BaP	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Benzo[c]phenanthrene (BcPh)	BcPh	Serum (1 mL)	GC-MS-MS	0.05 ng/mL
Benzo[b]fluoranthene (BbFA)	BbFA	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Benzo[c]fluorene (BcFL)	BcFL	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Benzo[g,h,i]perylene (BghiP)	BghiP	Serum (1 mL)	GC-MS-MS	0.1 ng/mL
Benzo[j]fluoranthene (BjFA)	BjFA	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Benzo[k]fluoranthene (BkFA)	BkFA	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Chrysene (CRY)	CRY	Serum (1 mL)	GC-MS-MS	0.06 ng/mL

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
Cyclopenta[c,d]pyrene (CPP)	CPP	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Dibenzo[a,h]anthracene (DBahA)	DBahA	Serum (1 mL)	GC-MS-MS	0.05 ng/mL
Dibenzo[a,h]anthracene (DBahA)	DBahA	Serum (1 mL)	GC-MS-MS	0.1 ng/mL
Dibenzo[a,e]pyrene (DBaeP)	DBaeP	Serum (1 mL)	GC-MS-MS	0.3 ng/mL
Dibenzo[a,i]pyrene (DBaiP)	DBaiP	Serum (1 mL)	GC-MS-MS	0.3 ng/mL
Dibenzo[a,l]pyrene (DBalP)	DBalP	Serum (1 mL)	GC-MS-MS	0.3 ng/mL
Fluoranthene (FLA)	FLA	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Fluorene (FLUO)	FLUO	Serum (1 mL)	GC-MS-MS	0.03 ng/mL
Indeno[1,2,3-cd]pyrene (IP)	IP	Serum (1 mL)	GC-MS-MS	0.1 ng/mL
Naphtalene (NAPH)	NAPH	Serum (1 mL)	GC-MS-MS	0.03 ng/mL
Phenanthrene (PHE)	PHE	Serum (1 mL)	GC-MS-MS	0.03 ng/mL
Pyrene (PYR)	PYR	Serum (1 mL)	GC-MS-MS	0.06 ng/mL
Anilines and MOCA				
Category A				
4,4-methylenedianiline (MDA)	MDA	Urine (1 mL)	LC-MS-MS	0.01 – 0.1 ng/mL
4,4'-methylenebis(2-chloroaniline) (MOCA)	MOCA	Urine (1 mL)	LC-MS-MS	1 ng/mL
	N-acetyl 4,4'-methylenebis(2-chloroaniline) (acetyl-MOCA)	Urine (1 mL)	LC-MS-MS	0.03 ng/mL
Category B				
Aniline	Aniline / p-aminophenol	Urine (1 mL)	LC-MS-MS	0.1 ng/mL
o-, p-toluidine	o-, p-toluidine	Urine (1 mL)	LC-MS-MS	0.25 ng/mL
Category C				
o,m,p-Fluoroaniline (o,m,p-FA)	o,m,p-FA	Urine (1 mL)	GC-MS	0.6 ng/mL
3-Trifluoromethoxyaniline (3TFMA)	3TFMA	Urine (1 mL)	GC-MS	0.6 ng/mL

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
4-Trifluoromethoxyaniline (4TFMA)	4TFMA	Urine (1 mL)	GC-MS	0.6 ng/mL
4-Ethylaniline (EtA)	EtA	Urine (1 mL)	GC-MS	0.6 ng/mL
o,m,p-Chloroaniline (o,m,p-ChA)	o,m,p-ChA	Urine (1 mL)	GC-MS	1.2 ng/mL
2,4-Dichloroaniline (2,4DChA)	2,4DChA	Urine (1 mL)	GC-MS	1 ng/mL
2,5-Dichloroaniline (2,5DChA)	2,5DChA	Urine (1 mL)	GC-MS	1 ng/mL
2,3-Dichloroaniline (2,3DChA)	2,3DChA	Urine (1 mL)	GC-MS	0.7 ng/mL
3,5-Dichloroaniline (3,5DChA)	3,5DChA	Urine (1 mL)	GC-MS	0.7 ng/mL
3,4-Dichloroaniline (3,4DChA)	3,4DChA	Urine (1 mL)	GC-MS	1.6 ng/mL
4-Isopropylaniline (IPA)	IPA	Urine (1 mL)	GC-MS	0.7 ng/mL
2,6-Diisopropylaniline (DIPA)	DIPA	Urine (1 mL)	GC-MS	0.5 ng/mL
2,6-Diaminotoluene (6TDA)	6TDA	Urine (1 mL)	LC-MS-MS	0.01 – 0.1 ng/mL
2,4-Diaminotoluene (4TDA)	4TDA	Urine (1 mL)	LC-MS-MS	0.01 – 0.1 ng/mL
3-Aminobiphenyl (3ABPH)	3ABPH	Urine (1 mL)	LC-MS-MS	0.05 ng/mL
4-Aminobiphenyl (4ABPH)	4ABPH	Urine (1 mL)	LC-MS-MS	0.05 ng/mL
4-Methyl-m-phenylenediamine (PDA)	PDA	Urine (1 mL)	LC-MS-MS	0.01 – 0.1 ng/mL
Cadmium (Cd)				
Category A				
Cd	Cd	Whole blood (0.5 mL)	ICP-MS	0.05 – 0.2 ng/mL
		Urine (1 mL)	ICP-DRC-MS ⁶	0.03 – 0.09 ng/mL
Chromium (Cr)				
Category C				

Substance	Biomarker	Matrix (amount)	Analytical Method	MDL ²
Cr	Cr (VI)	Red blood cells (erythrocytes)	ICP-MS	0.01 ng/mL
	Cr (VI) and (III)	Exhaled breath condensate (EBC)	AAS	0.002 and 0.007 ng/mL

¹Sample intake, technique and MDL were extracted from the inventory and additional publications, which are mentioned in the corresponding sections. Some compounds from the scoping document (Category C) could not be included in the present Table due to lack of published analytical methods.

²These concentrations are values obtained after applying an on/off-line sample pretreatment (if needed) with acceptable QA/QC results.

³BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, BDE-183.

⁴Bis(1,3-dichloro-2-propyl) phosphate (BDCIPP), Diphenyl phosphate (DPHP), Bis(2-chloroethyl) phosphate (BCEP), bis(1-chloro-2-propyl) phosphate (BCIPP).

⁵Bis(1,3-dichloro-2-propyl) phosphate (BDCIPP), Diphenyl phosphate (DPHP), Di-n-butyl phosphate (DnBP), bis(2-butoxyethyl) phosphate (BBOEP).

⁶Inductively coupled plasma dynamic reaction cell mass spectrometry

lw lipid weight

NA not available