Chemosphere 313 (2023) 137549

Contents lists available at ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere

Assessment of the per- and polyfluoroalkyl substances analysis under the Stockholm Convention – 2018/2019

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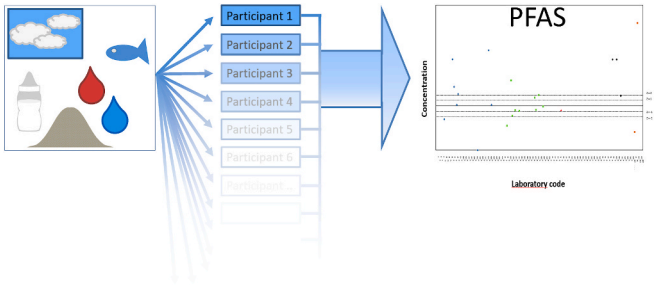
HIGHLIGHTS

- Worldwide Interlaboratory assessment on per- and polyfluorinated alkyl substances.
- Increasing number of participants compared to previous rounds.
- Performance of individual participants vary.
- Mean coefficients of variation were above 25% except for the human plasma material.
- Lack of participation from Africa, and low participation degree in GRULAC region.

GRAPHICAL ABSTRACT



ARTICLE INFO

Handling Editor: Derek Muir

Keywords:
Interlaboratory assessment
Perfluorinated alkyl substance
United Nations
Variation
Water
Plasma

ABSTRACT

The comparability of laboratories for the analysis of per- and polyfluoroalkyl substances (PFAS) was assessed in the fourth round (2018/2019) of a series of interlaboratory assessments coordinated by the United Nations Environment Programme (UNEP) in support of the Stockholm Convention quality assurance activities as to persistent organic pollutants (POPs) laboratories reporting data under this Convention. The participating laboratories were asked to analyse PFAS concentrations in a test solution of the target compounds, in the four core matrices of the global monitoring plan (GMP), human milk, human plasma, an air extract, and water, and in a sediment and a fish matrix. 39 participating laboratories submitted PFAS data for one or more test materials. The majority of the participating laboratories originated from the Asia-Pacific region, and from the 'Western European and other groups' (WEOG). Only one laboratory from the group 'Latin America and Caribbean' (GRULAC), and two from the Central and Eastern Europe (CEE) region submitted results. None of the African laboratories submitted data. The coefficients of variation (CVs) varied from 7% to 24% (mean 14%) for the test solution. Mean CVs for all matrices, except for the human plasma test material (18%), were above the satisfactory limit of 25%. The highest mean CV was found for human milk (61%). In total 1457 z-scores were assigned of which 64% were satisfactory ($|z| < 2$). Instrumentation used was mainly high-performance liquid chromatography (HPLC), in combination with various mass spectrometric (MS) techniques, in most cases tandem MS (MS/MS). Additional PFAS beyond perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA), which are listed at the Stockholm Convention POPs list, as well as water as a matrix for PFAS only and human plasma were added as a service for the laboratories.

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https://doi.org/10.1016/j.chemosphere.2022.137549
Received 15 July 2022; Received in revised form 1 December 2022; Accepted 11 December 2022
Available online 16 December 2022

1. Introduction

Per- and polyfluoroalkyl substances (PFAS) are gaining attention from a human health as well as from an environmental perspective. Legislation for these compounds started in 2006 with perfluorooctane sulfonic acid (PFOS) as the first PFAS regulated by the European Commission (Regulation Directive, 2006/122/EC) (EU, 2006). In 2009, PFOS was listed under the Stockholm Convention on Persistent Organic Pollutants (POPs) with perfluorooctanoic acid (PFOA) following in 2019 (UNEP, 2009, 2019a, b). Perfluorohexane sulfonic acid (PFHxS) will be listed under Annex An under the Convention (UNEP, 2022). Further regulations of PFAS are expected. The Stockholm Convention plans to include long-chain perfluorocarboxylic acids (C9–C20), their salts and related compounds (UNEP, 2021). The advisory value of the European Food Safety Authority (EFSA) with a maximum uptake of 4.4 ng/kg bodyweight (bw) per week (EFSA, 2020) for the sum of four compounds (PFOS, PFOA, PFHxS and perfluorononanoic acid (PFNA)), and the drinking water health advisory of Environmental Protection Agency (EPA) for four PFAS (EPA, 2022) further emphasizes the high toxicity of PFAS and the need for reliable analytical methods for PFAS.

Since 2005, as part of the United Nations Environment Programme's (UNEP) capacity building projects for laboratories, worldwide interlaboratory assessments for analysing POPs were held (UNEP, 2010;van Bavel et al., 2011; Fiedler et al., 2021). In the second round of the UNEP-coordinated biennial interlaboratory assessments (IL2) (2012/2013) (Nilsson et al., 2014), PFAS were included for the first time (Nilsson et al., 2014). In that IL2, and in the following two rounds, IL3 (2016/2017) (Fiedler et al., 2017; Fiedler et al., 2020), and the present study IL4 (2018/2019) (Fiedler et al., 2021b; Fiedler et al., 2022), participating laboratories were offered reporting PFAS concentrations in a test solution of the target compounds, and in the four core matrices of the global monitoring plan (GMP) (human milk, human plasma, air extract, water). In addition, reporting PFAS concentrations in sediment and fish samples was also offered. The list of PFAS was extended in IL4, because of interest of participants, and in case z-scores might be needed in the future for multiple PFAS because of new regulations. In this paper we present the PFAS results in IL4. Results were compared with those of previous rounds (Nilsson et al., 2014; Fiedler et al., 2017; Fiedler et al., 2020) and with other PFAS proficiency tests to assess progress.

2. Material and methods

2.1. Design of the assessment

This IL4 followed the structure of IL3 (Fiedler et al., 2017; Fiedler et al., 2020). In April 2018, POPs laboratories were invited to register. In September 2018, test materials and a mixture of PFAS substances in an inert test solution (TS) (described in Chapter S1 of the Supplementary Information (SI)) were dispatched by the Vrije Universiteit Amsterdam (VU), the Netherlands (sediment, fish and water test materials), and by the University of Örebro, Sweden (human milk, human plasma, and air extract test materials, and TS). Detailed instructions, including information on the nature of the test matrices, the storage conditions, and the requested reporting units, and an MS Excel reporting form were sent to the participants by e-mail. Participants were requested to report the concentrations of PFAS using their in-house methods. In addition, participants were asked to provide information on the method of extraction, clean-up and instrumental analyses used. The deadline for reporting was January 15, 2019.

Data evaluation was performed by using Cofino statistics (Cofino et al., 2000, 2017) as earlier described (de Boer et al., 2022). Submitted results with $|z| < 2$ were classified as satisfactory (S), with $2 < |z| < 3$ as questionable performance (Q), with $|z| > 3$ as unsatisfactory (U), and with $|z| > 6$ as extreme. For left censored values (LCVs, values below the detection limit) the results were either classified as consistent (C, LCV/2 < concentration corresponding to $|z| = 3$), or inconsistent (I, LCV/2 > concentration corresponding to $|z| = 3$).

2.2. Target compounds for analysis

The protocol allowed reporting of 22 PFAS for the test solution, and for the core matrices human plasma, and the air extract, and 17 PFAS for fish and sediment and for the core matrices human milk and water. The PFAS to report on were: perfluorobutanoic acid (PFBA), perfluoropentanoic acid (PFPeA), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), PFOA, PFNA, perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), perfluorododecanoic acid (PFDoDA), perfluorotridecanoic acid (PFTrDA), and perfluorotetradecanoic acid (PFTeDA), linear-perfluorobutane sulfonic acid (L-PFBS), L-PFHxS, L-PFOS, branched-PFOS (br-PFOS), L-perfluorodecane sulfonic acid (L-PFDS), and 6:2 fluorotelomer sulfonic acid (6:2 FTSA) in all test materials. The PFOS precursors perfluorooctane sulphonamides (FOSAs) and perfluorooctane sulfonamidoethanols (FOSEs) (including FOSA, N-methyl perfluorooctane sulfonamide (MeFOSA), N-ethyl perfluorooctane sulfonamide (EtFOSA), N-methyl perfluorooctane sulfonamidoethanol (MeFOSE), N-ethyl perfluorooctane sulfonamidoethanol (EtFOSE)) were to be reported for human plasma, the air extract and the test solution.

Of all PFAS only the concentration of the linear isomer could be reported, except for PFOS. Total-PFOS (tot-PFOS) concentrations were either submitted by the participants or were calculated as the sum of L-PFOS and br-PFOS, with a lower-bound value (LB) calculated as < Limit of detection (LOD) = 0, and an upper-bound value (UB) calculated as n < LOD = LOD.

3. Results

3.1. Participation

In total, 148 laboratories from 62 countries representing all five UN regions, Africa, Asia-Pacific, Central and Eastern Europe (CEE), 'group of Latin America and Caribbean countries' (GRULAC), and 'Western European and other groups' (WEOG) registered for this interlaboratory assessment. Among these laboratories, 53 registered for the analyses of PFAS in one or more test materials. Finally, 39 laboratories submitted results. None of the three registered laboratories from Africa submitted results. Only one of the five laboratories in the GRULAC region submitted results, and only for three test materials, while 25 of the 28 (89%) laboratories from the WEOG submitted data (Table 1).

Of the 39 laboratories that submitted results, 38 provided information on instrumentation and methods used for the PFAS analysis. All laboratories reported the use of liquid chromatography (LC). The vast majority reported tandem mass spectrometric (MS/MS) detection. Three laboratories used an Orbitrap instrument, and one laboratory used a time-of-flight mass spectrometer (ToF-MS) for detection.

3.2. Statistical evaluation

Detailed results as submitted by the 39 laboratories are given in the SI (Table S 3.1-S 3.7) and are summarized in Table S 4.1-S 4.7. The laboratory performances of all compounds in all test matrices are given in Table S 5.1-S 5.7 and are summarized in Table 2. In Table S 6.1 a summary is given of all submitted results for PFOS, and the laboratory performance for PFOS in all test matrices.

In total 1457 z-scores were assigned (tot-PFOS UB, and LB are not included) (Table 3). Of these, 939 were satisfactory, corresponding to 64% of all z-scores assigned for the PFAS. 232 (16%) were unsatisfactory, and 147 (10%) were questionable. For 9% of the data no z-score could be calculated since those results were either C or I. One laboratory, which only submitted results for the human plasma test material, had 100% satisfactory z-scores. Three laboratories had only unsatisfactory results (L259, L279 and L287). Those laboratories analysed one (L259),

two (L287) or three (L279) test materials. For the test solution, seven participants (L027, L117, L124, L224, L242, L276, and L293) out of 29, obtained 100% satisfactory results, although only two of those laboratories (L027 and L276) reported on all PFAS (z-scores obtained by individual laboratories can be found in the report on the fourth round of the UNEP IL (Fiedler et al., 2021b).

22 determinants were reported for the test solution. The assigned values (AVs) are shown in Table S 4.1; there were no LCVs. The coefficients of variation (CVs) were between 7% and 32% (mean 14%) (Fig. 1, Table 2 and Table S 4.1). The differences between the theoretical values and the AVs for the PFAS in the test solution were less than 7% except for br-PFOS (22%), and 6:2 FTSA (16%) (Table S 4.1).

Only a small percentage of the participants reported all requested PFAS (test solution, 31%; human plasma, 6%; air extract, 17%; human milk, 6%; water 23%; sediment, 31%; fish, 20%). PFOS (either L-PFOS, total-PFOS or both) was reported by all participants but one in all matrices. This participant did not report PFOS in water, although it was reported in fish (Table S 3.3). PFOA concentrations were reported by the majority of the participants for the core matrices (human plasma 16 of 16 participants; air extract 16 of 18; human milk, 14 of 18; water 19 of 22). For the relevant compounds in air, the PFOS precursors (FOSAs, and FOSEs), ten out of 18 participants reported concentrations.

4. Discussion

4.1. Evaluation of the number of participants

Since the introduction of PFAS in the UNEP IL the number of participants for PFAS analyses has increased from 25 in IL2 to 39 in the present study. This is partly due to the participation of food labs, for which no other ILs were organized for PFAS. This shows the rising interest in PFAS analysis. However, striking is the entire lack of participation by laboratories from Africa, and the low participation degree in the GRULAC region (Table 1). This is in line with IL2 (Africa: 0, GRULAC: 0) and IL3 (Africa: 2, GRULAC: 1) (Fiedler et al., 2020). The main reason is the lack of proper LC/MS instruments in many laboratories. These are either absent or not working because service by MS companies takes a very long time. The initial registration of 53 laboratories shows that the ambition of the laboratories is often high, but then hindered by practical conditions. Three labs did not receive the test materials. In the past few years, sending and receiving packages with biota or environmental samples has become more difficult. In various countries, regulations for the import and export of environmental and biological materials are becoming increasingly strict, and for some countries it is even impossible to receive certain types of matrices like e.g., fish in Japan or Cameroon. For other countries import permits are required. Laboratories participating in the UNEP ILs had to arrange their own import permits on time, which they did not always manage. Then test materials stay too long in customs. Other reasons for not submitting data could be lack of facilities, lack of consumables, difficulties with ordering analytical standards abroad, or others.

According to Directive (2020)/2184 (EU, 2020) from January 12, 2024, the European Commission will deliver guidelines for the monitoring of the sum of 20 PFAS in water for human consumption. Fourteen of those PFAS were requested in our study, but only 50% of the participants (n = 11) which reported PFAS concentrations in the water material managed to deliver results on all 14 PF AS, showing first that half of the laboratories of this study are not ready yet to report on the sum of PFAS for water, and second that making a comparison between the performance of the participants on the sum of PFAS does not give an accurate reflection of the performance.

4.2. Laboratory performance

The mean CVs for all PFAS for which an AV could be calculated in other matrices, except the human plasma test material (18%), were above the desired maximum of 25% (UNEP, 2019c) (Fig. 1). Since the inclusion of PFAS in the second round of the UNEP IL, L-PFOS could be reported for all test materials. For the analyses of L-PFOS in the present round, the CV values fulfilled the criteria of 25% for all matrices except for the water (33%), and the human milk (40%) (Table S 6.1). The concentration of L-PFOS in the water test material was more than 3 times higher than in the previous rounds, but the performance was equal to the performance on L-PFOS in IL3, although a higher percentages of satisfactory z-scores was assigned in this fourth round (IL3: 45%, IL4: 53%) (Fig. 2). In IL2 the performance was better (CV: 21%) and 70% of the participants received a satisfactory z-score.

Fig. 3 shows that WEOG laboratories performed better than Asian laboratories on L-PFOS in the water test material, which is one of the core matrices of the GMP. Of the WEOG laboratories only two participants received unsatisfactory z-scores (−3.4 and 4.4), while of the Asian laboratories only two participants managed to receive satisfactory z-scores, two laboratories obtained very extreme positive z-scores (822 and 7215) and one laboratory received an extreme negative z-score (−7.7). The same figure also shows the low participation of laboratories from the other three regions.

Laboratory code on the x-axis, concentration in ng/g on the y-axis. The assigned value is given by the straight line, z = ± 1 (12.5%) and z = ± 2 (25%) are given by the dotted lines. The blue ◆ symbols represent Asia, the green ■ symbols represent WEOG, the red ▲ symbols represent GRULAC. Note: None of the laboratories from Africa and CEE submitted results.

Not only L-PFOS, but also the analyses of the other PFAS in the human milk test material posed some problems to the laboratories; possibly due to the low concentrations (20 pg/g wet weight for L-PFOS) (Table 2). Sensitivity is always a difficulty for laboratories, especially when matrix such as fat is relatively high. For most of the analytes, it was not possible to calculate an AV. For the PFAS for which an AV could be assigned, the variation was quite high (CV values from 38% for PFOA to more than 100 for br-PFOS, and PFHxS). Even higher CV values were obtained for PFNA (CV: 611%) and PFUnDA (CV: 231%) (Table S 4.4).

Although the PFAS concentrations in the sediment test material were

Table 1
Number of participants that registered for the analyses of PFAS in IL4 per matrix and the number of participants which submitted results for PFAS per matrix.

	Number of participants											
	Registered						Submitted results					
Matrix	Total	Africa	Asia-Pacific	CEE	GRULAC	WEOG	Total	Africa	Asia-Pacific	CEE	GRULAC	WEOG
Total	**53**	**3**	**15**	**2**	**5**	**28**	**39**	**0**	**11**	**2**	**1**	**25**
Test solution	40	1	10	2	4	23	29	0	7	2	1	19
Sediment	22	1	10	1	1	9	13	0	5	1	0	7
Fish	34	1	12	1	1	19	25	0	7	1	0	17
Human milk	27	0	8	1	1	17	18	0	6	1	0	11
Human plasma	23	1	8	2	0	12	16	0	5	2	0	9
Air extract	23	1	10	1	1	10	18	0	7	1	1	9
Water	33	3	13	1	2	14	22	0	8	1	1	12

CEE = Central and Eastern Europe; GRULAC = Group of Latin America and Caribbean; WEOG = Western European and other groups.

on the low side for most of the compounds, only for three compounds (PFBA, PFPeA, L-PFDS) no AV could be calculated. For the other compounds the CV values ranged from 2% (6:2 FTSA) to 53% (PFDA), with a mean of 30%.

AVs could be calculated for nine of the 17 compounds in the fish test material (Table S 4.3). The other PFAS, except L-PFDS, all contained a maximum of eight carbon atoms. Short-chain PFAS are more water soluble, and hence less present in fish. As a result, the low concentrations of those PFAS caused the majority of participants reporting an LCV for short-chain PFAS.

In the fish material the sum of the concentrations of PFOA (NAV: median: 0.06 ng/g), PFNA (AV: 0.04 ng/g), L-PFOS (AV: 8.5 ng/g), and PFHxS (AV: 0.05 ng/g) was 8.65 ng/g (Table S 4.3). With an average fish consumption of 22 kg/y (EUData News Hub,) per person in the Netherlands, and an average bodyweight of an adult of approx. 80 kg, this would be a weekly intake of the sum of four PFAS of 45 ng/kg bw/w, which is about 10 times higher than the TWI (4.4 ng/kg bw/w) set by EFSA (EFSA, 2020). This high concentration was mainly due to the high concentration of L-PFOS (AV: 8.5 ng/g). The CV for L-PFOS in this material was excellent (11%) (Table S 4.3), with 90% of the participants receiving a satisfactory z-score (Table S 5.3). Analyzing samples with higher concentrations results mostly in a better performance since the matric is much more diluted, and the analysis is less disturbed by fat. However, the concentrations of PFOA, PFNA and L-PFHxS were much lower (0.15 ng/g) and together responsible for approx. 0.79 ng/kg bw/w (Table S 4 3). Those low concentration resulted for PFOA in 16 of 22 participants reporting a LCV, and hence that no AV could be calculated, and a laboratory performance which was extreme high (CV: 174%). Also, the performance on L-PFHxS was high (CV: 81%) with 20% of the participants receiving a satisfactory z-score (Table S 4.3, and S 5.3). The performance on PFNA in the fish was slightly better (CV: 38%), with 29% of the participants obtaining a satisfactory z-score.

The performance for PFDA (CV: 13%), and PFDoA (CV: 16%) was also very good. The CVs of the other six compounds for which an AV could be calculated was a bit higher (32–81%, mean 46%). Of those compounds, only for br-PFOS the majority (69%) of the participants was able to receive a satisfactory z-score. The better performance of the laboratories in fish is due to a combination of higher PFOS concentration and a lower fat percentage of the fish species (pike perch) used.

Except for the fish, and the human milk test materials, an AV could be calculated for all matrices for PFOA (CV: 9–25%), PFNA (CV: 12–34%), PFDA (CV: 10–53%), L-PFHxS (CV: 7–20%), L-PFOS (CV: 9–33%) and also for br-PFOS (CV: 32–99%).

The relatively poor performance of a number of labs for the standard solution is most likely due to the lack of experience of laboratories in analyzing such solutions. Laboratories analyse samples – fish, sediment, food, etc., but normally not standard solutions. Therefore, mistakes are more easily made. The phenomenon has been observed in many other interlaboratory studies (de Boer and Wells, 2006; Su and Hung, 2010). This emphasizes again the essence of experience in this type of complex analysis.

The performance of PFOA, which is listed as POP at the Stockholm Convention met the criterion (max CV: 25% (UNEP, 2019c)) set in the GMP for the core matrices human plasma (CV: 9%), air extract (CV: 25%), and water (CV: 23%), with 75%, 63%, and 58% respectively of the participants obtaining a satisfactory z-score. For the human milk, which is also one of the core matrices, this criteria was not met (CV: 38%), with 36% receiving a satisfactory z-score (Table S 4.4 – S 4.7, and Table S 5.4- S 5.7).

For PFHxS which will be listed in Annex A of the Convention (UNEP, 2022), the performance was very good for four of the test matrices (sediment CV: 20%, plasma CV: 7%, air extract CV: 19%, and water CV: 16%), and for the test solution (CV: 12%). However, extreme high CVs were calculated for the fish (81%) and human milk (113%), which is most likely cost by the low contamination of those materials, resulting the majority of participant reporting an LCV (65% for fish, and 67% for human milk).

FOSAs and FOSEs could only be reported for the test solution, the

Table 2
Summary of statistical results.

	Between lab CV (%)							Percentage of satisfactory z-scores |z|<2						
Analyte	Test Solution	Sediment	Fish	Human milk	Human plasma	Air extract	Water	Test Solution	Sediment	Fish	Human milk	Human plasma	Air extract	Water
L-PFOS anion	16	23	11	40	9	21	33	75	67	90	40	71	65	53
br-PFOS anion	32	45	32	105	38	NAV	40	58	57	69	42	50		43
tot-PFOS LB	*18*	*32*	*14*	*59*	*22*	*21*	*42*	*79*	*77*	*84*	*39*	*88*	*67*	*48*
tot-PFOS UB	*18*	*30*	*16*	*103*	*9*	*26*	*33*	*80*	*67*	*88*	*47*	*92*	*73*	*56*
FOSA	17				NAV	23		80					60	
MeFOSA	8				NAV	6		86					78	
EtFOSA	16				NAV	10		79					67	
MeFOSE	7				NAV	28		77					50	
EtFOSE	11				NAV	4		85					70	
PFBA	11	NAV	NAV	NAV	NAV	41	34	83					38	63
PFPeA	12	NAV	NAV	NAV	NAV	34	36	80					46	38
PFHxA	15	26	NAV	NAV	NAV	22	17	93	45				60	78
PFHpA	15	17	NAV	NAV	NAV	27	19	86	36				57	67
PFOA	12	23	NAV	38	9	25	23	83	50		36	75	63	58
PFNA	15	34	38	NAV	12	21	16	89	55	29		67	64	44
PFDA	10	53	13	NAV	10	21	14	93	36	62		64	67	41
PFUnDA	16	41	34	NAV	16	30	224	86	36	48		60	57	0
PFDoDA	13	17	16	NAV	47	30	115	75	64	71		36	62	0
PFTrDA	19	21	41	NAV	NAV	55	NAV	74	45	50			43	
PFTeDA	12	45	52	NAV	NAV	56	NAV	89	36	33			31	
L-PFBS	17	51	NAV	NAV	NAV	26	24	89	36				60	67
L-PFHxS	12	20	81	NAV	7	19	16	79	55	20		73	60	61
L-PFDS	15	NAV	NAV	NAV	NAV	35	NAV	81					64	
6:2 FTSA	22	2	NAV	NAV	NAV	51	31	79	50				44	56

CV = Coefficient of variation; NAV: No assigned value; LB = Lower-bound value; UB = Upper-bound value.

human plasma test material, and the air extract. The performance for those compounds in the test solution (CV: 7–17%) and the air extract (CV: 4–28%) was extremely good, with more than 77% (77–86%, mean 81%) of the participant receiving a satisfactory z-score for the test solution, and more than 50% (50–78%, mean 65%) receiving it for the air extract. This was a clear improvement in comparison with IL3. In that IL the concentrations in the test solution were up to 5 times higher and de CVs for the test solution were 27–51% (mean 33%), while no AV could be calculated for any of the FOSAs in the air extract.

For eight PFAS in human plasma an AV could be calculated. The performance on six of those compounds was very good (CV: 7–16%) with more than 60% (60–75%) of the results being satisfactory (Table 2). For br-PFOS (CV: 38%) and PFDoDA (CV: 47%) the performance was less good, which might for PFDoDA have been caused by the very low concentration in the plasma (AV: 0.07 ng/g).

4.3. Analytical methods

All laboratories, which reported on their analytical methods (n = 38) used LC for the separation of PFAS, and only one laboratory reported to have use gas chromatography (GC) for the separation of PFOS precursors. For the separation of traditional POPs, like polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) mostly GC is used. This is why traditional POP laboratories do own a GC, but not always possess an HPLC, which is needed for the PFAS analyses. This might explain, the low participation degree in the GRULAC region and Africa. Also, the extraction solvents needed for PFAS are different than those for traditional POPs. The majority of the participants used methanol (70%), and acetonitrile was used in 8.8% of the samples. An additional column was used by 43.6% of the laboratories between the pump and the injector of the HPLC, in order to retain PFAS which leach out of the HPLC system. 56.4% of the participants did not use such a column. It was not reported by those laboratories if their systems contained polytetrafluoroethylene (PTFE) parts.

For all test materials results on the analyses of br-PFOS were worse than results obtained for L-PFOS (Table S 6.1). It was not investigated in this study how participants performed the calculations for the br-PFOS and the L-PFOS. However, quantification of L-PFOS is often based on calibration standards consisting of 100% of the linear isomer. The quantification of the br-PFOS is often based on calibration standards of a technical mixture of PFOS isomers. Since all isomers have a different fragmentation ratio for the *m/z* 80 and the *m/z* 99 fragments, and the ration is also depended on the analytical instrument, which is used, this can result in a higher CV. The laboratory performance on tot-PFOS was worse than the performance on L-PFOS for all matrices, except for tot-PFOS UB in the human plasma, and water, and tot-PFOS LB in the air extract, for which all less satisfactory z-scores were obtained than for L-PFOS (Table S 6.1). These results can partly be explained by the performance on br-PFOS. However, the assessment of the laboratory performance on tot-PFOS was not reliable, since some laboratories reported the concentration of tot-PFOS, while for other participants the LB and UB of tot-PFOS was calculated as the sum of L-PFOS and br-PFOS, while not all participant reported on both compounds.

4.4. Comparison with other ILs

In comparison with previous interlaboratory assessments (Nilsson et al., 2014; Fiedler et al., 2017; Fiedler et al., 2020), more PFAS laboratories participated in this IL4 and more determinants were included; both resulting in a larger number of z-scores that could be calculated (sums of PFAS not included) (Fiedler et al., 2020, Table 3). It must be noted that the performance decreased from 86% satisfactory results in IL2 to 64% in IL4.

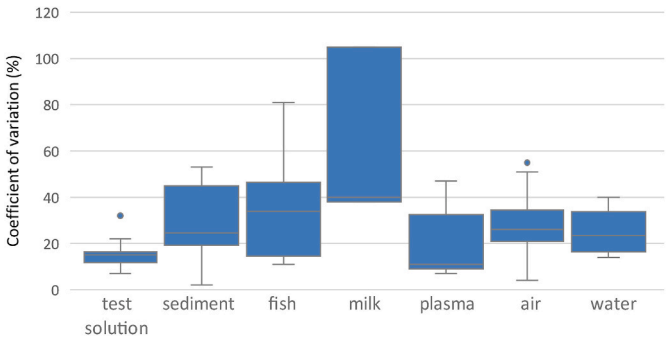

Fig. 1. Coefficients of variation (CVs) (%) in IL4 for PFAS analyses per matrix for compounds for which an assigned value (AV) could be calculated.

The same sediment test material of our study was also analysed in a small intercomparison study organized by Wageningen Evaluating Programmes for Analytical Laboratories (WEPAL, Wageningen, The Netherlands) in commission of the Dutch National Institute for Public Health and the Environment (RIVM) in 2019. (Van Vark, 2019). In that exercise nine laboratories participated. All compounds which could be reported in our study could also be reported in the study of WEPAL. For four compounds (PFHpA, PFNA, PFDoDA, PFHxS) no AV could be calculated in the WEPAL study, while it could in our study. The number of participants analyzing those compounds was almost similar, but in the WEPAL study more reported an LCV value. For PFOS, and PFOA the performance was similar, but for all other compounds (except 6:2 FTSA) the performance was better in the WEPAL study (4–30%, mean 16%) compared to our study (21–53%, mean 39%). Most likely this can be explained by the fact that in our study a number of participants were less experienced in the analyses of PFAS, other than PFOA and PFOS, while in the WEPAL study only experienced labs were invited to participate. In 2006 the first IL was organized on the analyses of PFAS in environmental and human samples (van Leeuwen et al., 2006). This IL was followed by four other ILs on PFAS of which the last was organized in 2011 on PFAS in food and environmental samples (Weiss et al., 2013). The performance over the ILs increased, for the analyses of PFAS in water and fish, mainly due to the availability of labeled internal standards in the later study (Weiss et al., 2013). In the study of Weiss et al. (2013), besides other matrices, two fish test materials, and a drinking water test material were analysed,. The performance on the water test material was a little better in the current study (mean CV 25% vs 28% for all PFAS with an AV in both studies). For the fish material the performance in the current study was equal to the performance on the low contaminated fish of the study of Weiss et al. (2013). Over the last years more is known on the analyses of PFAS, more labeled standards have come available, and more sensitive mass spectrometers are on the marked, so it would be expected that the performance would have improved compared to 2011.

Although results of individually, laboratories have improved in various cases, the results of the UNEP ILSs show a varying performance

Table 3
Summary of performance of all laboratories submitting results for PFAS (all individual PFAS and all matrices included).

	Number of z-scores						Percentages of z-scores				
Interlab assessment	#S	#Q	#U	#C	#I	**Total**	% S	% Q	% U	% C	% I
IL4	939	147	232	63	76	**1457**	64	10	16	4	5

S = satisfactory: $|z| < 2$; Q = Questionable: $2 < |z| < 3$; U= Unsatisfactory: $|z| > 3$; C= Consistent: LCV/2 < concentration corresponding to $|z| = 3$; I= Inconsistent: LCV/2 > concentration corresponding to $|z| = 3$.

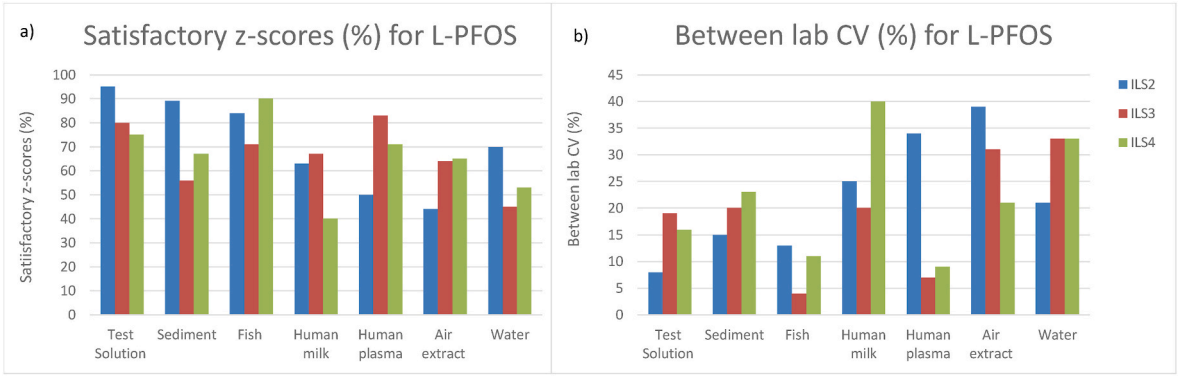

Fig. 2. Statistical evaluation of L-PFOS results in all matrices in the last three rounds of the UNEP IL. a) Percentage of satisfactory z-scores, b) percentage of between lab CV.

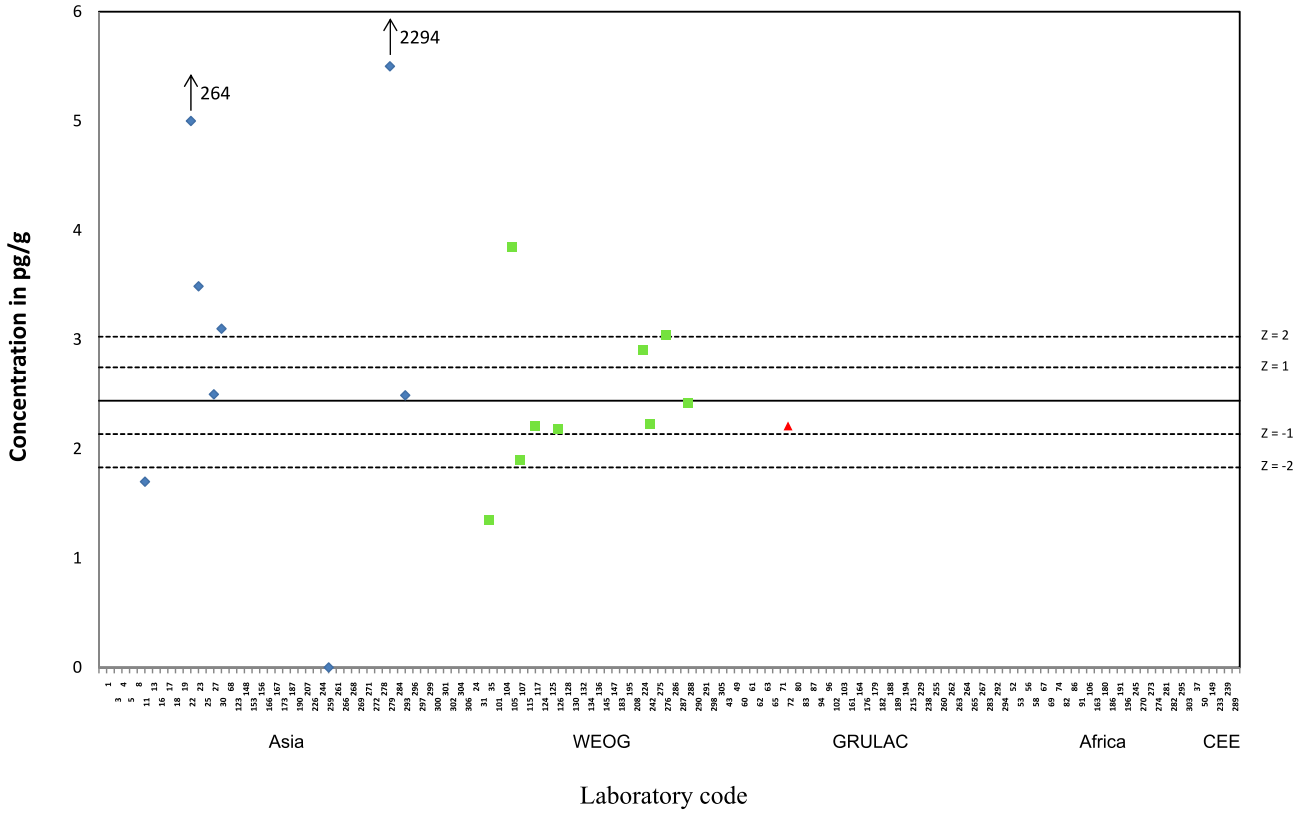

Fig. 3. Results for L-PFOS anion in the water test material in IL4.

of individual participants. 24 laboratory participated, and received z-scores in two or three of the UNEP ILs (IL2, IL3, and IL4) for the same compounds in the same matrix types. Those z-scores are given per laboratory in Table S 7.1 of the SI. Two of those laboratories (L124 and L224) received only satisfactory z-scores for the compounds for which z-scores were assigned in both ILs they participated in. Some other laboratories performed equal or almost equal in two (L002, L027, L130, L195) or three of the ILs (L001, L030, L117). For some laboratories the performance was worse in the later ILs (L023, L035, L107, L129), while the performance of some other laboratories (slightly) improved (L022, L221, L128).

To the best of our knowledge no more recent IL were organized on the analyses of PFAS, except IL2 and IL3 of the UNEP IL, although it would be recommended to laboratories to regularly test their performance in an intercomparison exercise to validate their method.

5. Conclusions

The percentage of assigned satisfactory z-scores decreased compared to previous rounds of the UNEP ILs. The overall performance in this IL showed that most of the participating laboratories are not yet able to deliver good quality data (CV<25%) for the GMP for human milk, air extract, and water. However, the results on human plasma (CV: 18%), fulfilled the criterion.

Naturally contaminated test materials, which contain target compounds above LOD, are required for an IL, but not always available. In case in future ILs such materials would be unavailable, it should be considered to fortify materials with the target compounds, on a realistic level above LOD, in order to enable participants to report on all requested compounds. For future ILs it should also be considered to encourage participants on forehand to make arrangements for import permits on time in case needed, in order to avoid packages to be left in

customs for weeks. In future ILs it is recommended to request participants to report on the concentration of L-PFOS, br-PFOS, and tot-PFOS separately, in order to make a reliable assessment on the laboratory performance of either reported tot-PFOS, or the calculated sum of L-PFOS and br-PFOS.

Although the performance of individual participants in the UNEP ILs varies, it is recommended that laboratories carry out PFAS analyses on a regular basis in order not to lose the built-up knowledge. Governments should support their laboratories herein, as only participation in this interlaboratory study will not be enough to guarantee reliable analytical results for POPs. The recently introduced new safety limits of EFSA for PFAS (TWI of 4.4 ng/kg bw/w for the sum of four PFAS) also include PFNA (EFSA, 2020). At this moment PFNA is not yet listed as a POP by the European Commission. However, it is encouraging to see that the PFNA results belonged to the better ones in terms of CV values. Assuring the quality of PFAS analysis by regularly carrying out analyses, including the use of quality control (QC) charts, the analyses of certified reference materials, and the regular participation in ILs will help to produce reliable results.

Credit author statement

Ike van der Veen: Data curation; Formal analysis, Visualization, Writing – original draft. Heidelore Fiedler: Conceptualization; Data curation; Writing – review & editing. Jacob de Boer: Project administration, Supervision; Writing – review & editing

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgments

The work presented in this paper was developed under agreement with UN Environment, Economy Division, Chemicals and Waste Branch with funds from the Global Environment Facility (GEF) through four regional projects “(Continuing) Support for the implementation of the GMP under the Stockholm Convention in the African/Asian/GRULAC/Pacific Islands Region” to UN Environment. The authors thank Prof. W. P. Cofino for assistance with the statistics.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2022.137549.

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