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HBM4EU chromates study – PFAS exposure in electroplaters and bystanders

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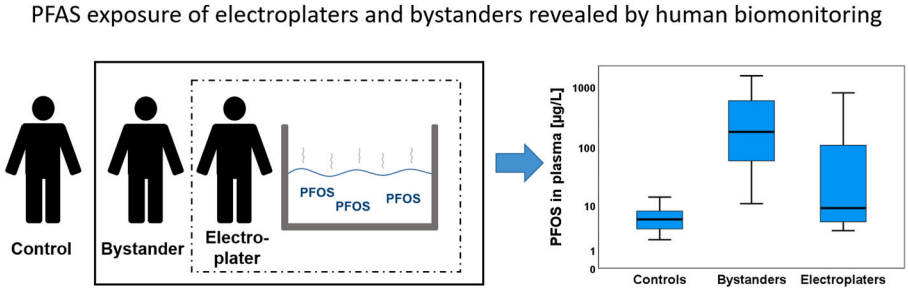
HIGHLIGHTS

- HBM of chromium workers and controls from 4 European countries to 12 PFAS
- HBM revealed significant exposure of bystanders beside PFAS handling workers
- Bystanders may own special risk of exposure due to missing awareness and protection

GRAPHICAL ABSTRACT



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ABSTRACT

The study aims to reveal the exposure to perfluoroalkyl substances (PFAS) in workers in different industry sectors with exposures to hexavalent chromium (Cr(VI)). The PFAS exposure of in total 172 individuals from 4 countries was assessed by the determination of 8 perfluoroalkyl carboxylic acids and 4 perfluoroalkyl sulfonic acids in plasma samples. The participants were 52 chrome plating workers, 43 welders, 3 surface treating workers and 74 workers without any occupational Cr exposure as controls. Significant differences between workers with Cr exposure and controls were found for the perfluoroalkyl sulfonic acids, particularly for perfluorooctane sulfonic acid (PFOS). The median and maximum levels were, respectively, 4.83 and 789 µg/l for chrome plating workers, 4.97 and 1513 µg/l for welders, and 3.65 and 13.9 µg/l for controls. The considerably high PFOS exposure in Cr platers and welders can be explained by the former application of PFOS as mist suppressants in electroplating baths, which resulted in an exposure of the directly involved operators, but also of welders performing maintenance and repair service at these workplaces.

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1. Introduction

Per- and polyfluoroalkyl substances (PFAS) are a group of synthetic substances, not originally occurring in the environment (Buck et al., 2011). Due to their physical and chemical properties, e.g. nonflammable, water- and grease-repellent, stain-resistant, impairing of surface tension and dielectric, they are used in many industrial processes and in consumer products (Glüge et al., 2020; Kotthoff et al., 2015). Prominent applications of PFAS are their use as dielectrics, extinguishing foam ingredients, water-repellents for any surface (including metals, clothes, paper and cardboard) and surface tension modulators (Glüge et al., 2020). Most PFAS are extremely stable and persistent in the environment, can bioaccumulate in the food chain and persist and accumulate in the human body (Domingo and Nadal, 2017; Olsen et al., 2007; Brede et al., 2010; Seals et al., 2011). Several health outcomes, e.g., immunological and endocrine alterations, hepatoxicity, nephrotoxicity, reproductive and developmental effects, and positive associations for cancer of testis and kidney have been associated with the exposure to PFAS (Fenton et al., 2021; Panieri et al., 2022; Steenland and Winquist, 2021). Their toxicological properties and persistent behavior cause a high concern for occupational and public health and demand for exposure evaluation and management. Due to the accumulative behavior and the different routes of exposure, human biomonitoring (HBM) is the most effective option for exposure assessment of many PFAS (Houde et al., 2006). Consequently, PFAS were approved for the first priority substance list of the pan-European project HBM4EU (European Human Biomonitoring Initiative) (Louro et al., 2019), which aimed to harmonize and advance HBM in Europe and support policy making with regard to chemical risk management (Ganzleben et al., 2017). Within HBM4EU a multicenter study on the occupational exposure to chromium (Cr) was implemented, which targeted mainly the concerns related to the occupational exposure to hexavalent chromium (Cr(VI)) (Santonen et al., 2019; Santonen et al., 2022), but also included the assessment of accompanying compounds.

Perfluorooctane sulfonic acid (PFOS) has earlier been the most important PFAS used as mist suppressant in plating activities in Europe, but since June 27, 2008, the use of PFOS and its salts has been largely restricted in the EU (EEC, 2006). The current regulation (EC, 2010) provides that the uses of PFOS will be phased out as soon as the use of safer alternatives is technically and economically feasible and releases of PFOS into the environment have been minimized by applying best available techniques. Hence, the necessity of exemptions is intended to be reviewed at regular intervals. After expiration of the derogation for wetting agents for use in controlled electroplating systems on August 26, 2015, the only specific exemption on the use of PFOS in electroplating has applied to mist suppressants for non-decorative hard Cr(VI) plating in closed loop systems (EC, 2019). The use of PFOS as mist suppressant for non-decorative hard Cr(VI) plating in closed loop systems is allowed until September 7, 2025 (EC, 2019). As mentioned before, further restrictions for other PFAS are in place or planned (EC, 2017; EC, 2021; ECHA, 2020; ECHA, 2021; ECHA, 2023). Further restrictions are in place or planned also for other PFAS. Perfluorooctanoic acid (PFOA), its salts and PFOA-related substances have been banned under the Persistent Organic Pollutants Regulation since July 4, 2020 (EC, 2017) and $C_{9\text{-}14}$-perfluorinated carboxylic acids, their salts and precursors have been restricted in the EU/European Economic Area (EEA) from February 2023 onwards (EC, 2021). Also, restrictions of perfluorohexane-1-sulphonic acid (PFHxS) and perfluorohexanoic acid (PFHxA), their salts and related substances are under consideration in EU (ECHA, 2020; ECHA, 2021). In addition to these restrictions, there is an initiative for a wide-range PFAS ban in EU covering entire group of PFAS and wide-range of uses (ECHA, 2023). Since PFAS, including PFOS may have been used in plating activities, we designed a sub-study within the HBM4EU chromates study, which assessed the exposure of these workers to PFAS, particularly to PFOS.

2. Materials and methods

The HBM4EU chromates study was designed as a multi-center cross-sectional survey, carried out originally in nine countries (Santonen et al., 2019; Galea et al., 2021). For the side aspect on the PFAS exposure, a sub-study was conducted in workers from four countries, i.e. Belgium, Finland, France and Italy. Detailed Standard Operating Procedures (SOPs), providing information on the collection, handling, storage and transfer of the biological samples, were designed to allow the study team to perform data collection in a harmonized way, resulting in comparable data for the nine participating countries (Santonen et al., 2019). All the samplings were performed between October 2018 and December 2019.

2.1. Study population

Exposed workers were recruited from companies with activities that are known to be associated with occupational exposure to Cr(VI), more specifically (i) chrome plating, (ii) surface treatment by sanding, spraying or painting, and (iii) stainless-steel welding. Unexposed workers were recruited either within the same company, but from activities that are known not be associated with Cr(VI) exposure (for example office staff), or from other companies with no activities associated with Cr(VI) exposure. Recruitment of the companies and workers followed the dedicated SOP for the selection of participants, recruitment, informing participants and obtaining informed consent. Common information leaflets and informed consent forms were developed and translated into the national languages. Study protocols were submitted for approval by ethics review boards in each of the participating countries with the approvals being granted before recruiting the study participants (Santonen et al., 2019).

2.2. Sample processing

All countries of the sub-study collected blood samples for plasma analysis. Blood samplings were preferentially performed on the 3rd - 5th day of the working week. The blood sample was collected in a tube with potassium ethylenediamine tetra acetic acid (K-EDTA) from each participant. To avoid haemolysis, separation of red blood cells and plasma was conducted, preferably within 8 h (and maximum 24 h) from the specimen collection. Samples were centrifuged (10 min at 1000–2000×*g* or 5 min at 2700×*g*) and the supernatant containing the plasma and white blood cells was used for PFAS analyses (storage at +4 °C up to 7 days or −20 °C for longer periods).

2.3. Analytical procedures

PFAS analyses were performed in the Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine of the University of Erlangen-Nürnberg (IPASUM) for samples from Belgium, Finland and France and the Istituto Superiore di Sanità (ISS) for samples from Italy. The plasma samples were analyzed for perfluoropentanoic acid (PFPeA), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), PFOA, perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), PFUnDA, perfluorododecanoic acid (PFDoDA), perfluorobutane sulfonic acid (PFBS), PFHxS, perfluoroheptane sulfonic acid (PFHpS) and PFOS. Both laboratories had successfully passed the ICI (Interlaboratory Comparison Investigations)/EQUAS (External Quality Assessment Scheme) program organized by the HBM4EU Quality Assurance Unit (Nübler et al., 2022). In IPASUM, PFAS biomarkers were quantified according to a published method (Gledhill et al., 2006). The ^{13}C-labeled analogues of PFHxA, PFOA, PFNA and PFOS served as internal standards (IS, i.e. $^{13}C_2$-PFHxA, $^{13}C_2$-PFOA, $^{13}C_4$-PFNA and $^{13}C_4$-PFOS). 500 µL of serum were doped with 50 µL of IS solution in acetonitrile. To precipitate the proteins, 2 mL of formic acid (50% aqueous solution) were added, and the samples were placed in the ultrasonic bath for 15 min. After centrifugation, the supernatant was placed on Oasis WAX columns

conditioned with 2 mL methanol and 2 mL water. The columns were then washed with 2 mL of a 40% aqueous methanol solution. Elution was conducted with 1.25 mL of 2% NH_4OH in methanol. The eluates were concentrated to 100 μL in a stream of nitrogen and then 75 μL of 20 mM ammonium acetate solution in methanol (25/75, v/v) were added. The chromatographic separation took place on a Phenomenex Kinetex C18 2.6 μm column (150 × 4 mm) with ammonium acetate (20 mM)/methanol as eluents (LC system: Agilent HP 1100 quaternary pump and HP1200 autosampler). Triple quadrupole mass spectrometry (API, 2000; Applied Biosystems) was used for detection and operated in negative ESI and multiple reaction monitoring (MRM) mode. The calibration was performed by standard solution in plasma which was processed in the same manner as the real samples. The limits of quantification, which were calculated based on the calibration graph procedure, were 0.4 μg/l for PFPeA, 0.3 μg/l for PFHxA, 0.2 μg/l for PFHpA, PFDA, PFUnDA, PFDoDA and PFHpS and 0.1 μg/l for the others PFAS.

Sample analysis in ISS was performed according to a previously published method (Marra et al., 2020). About 250 μL of serum were spiked with ^{13}C- and $^{18}O2$-labeled internal standards of PFBA, PFHxA, PFOA, PFHxS, PFOS, PFNA, PFDA, PFUnDA, PFDoDA (Wellington Laboratories Inc., Ontario, Canada). Protein precipitation was performed with 2 mL of acetonitrile (Sigma–Aldrich Corp, Saint Louis, MO, USA). After centrifugation and separation, the acetonitrile phase was reduced in volume, transferred to an autosampler vial, evaporated to dryness and added with 300 μL of the injection standard solution ($^{13}C_4$-PFHpA 50 ng/mL in acetonitrile) to undergo instrumental analysis. Analysis was carried out by HPLC (Waters Alliance 2695, Waters Corporation, Milford, MA, USA) interfaced with a triple quadrupole mass spectrometer (Micromass QuattromicroTM API, Waters Corporation, Milford, MA, USA) operated in electrospray negative ionization mode. Chromatographic separation was achieved using a Kinetex C18 column (5 μm, 100 mm × 2.1 mm ID, 100 Å) supplied by Phenomenex (Torrance, CA, USA) operated at 45 °C. The mobile phases were an acetic acid/ammonium acetate solution in water and acetonitrile. Analytes were detected by MRM. According to the quality system for each batch of test samples (20 test samples in one batch) at least one procedural blank and one quality control sample were analyzed. The LOQ of ISS procedure, which were calculated by a signal-to-noise ratio of 3 to 1, were 0.06 μg/l for PFBS and PFHxS, 0.04 μg/l for PFHpS, 0.03 μg/l for PFOS and 0.02 μg/l for the other PFAS.

2.4. Calculations and statistics

For harmonization of the data set, we applied the higher LOQ values of the IPASUM procedure not only to the samples of Belgium, Finland and France but also to the Italian samples which were analyzed by a more sensitive procedure. For statistical analysis we set all samples below the IPASUM LOQ to LOQ/2. Within a descriptive analysis of the data, we calculated median, range and the portion of samples greater than or equal to the LOQ. We applied the Mann-Whitney (asymptotic) test for comparing groups. Moreover, we performed Spearman regression analyses to reveal associations between the different PFAS. We excluded the analysis for parameters which data showed less than 10% results above the LOQ. Results with probability of error below 5 percent ($p < 0.05$) were considered as significant difference. Statistical analyses were conducted using SPSS Statistics software, version 29 (IBM Corporation, NY, United States).

3. Results and discussion

Fifty-two electroplating workers, 43 welders, 3 workers employed in other surface treatment activities and 74 individuals without potential occupational exposure to chromium and PFAS provided a total of 172 samples to be analyzed (Table 1). Contextual data on the study populations, including age, sex and duration of employment, are presented in the Supplemental Material (Table S1). A special setting resulted from the Belgium recruitment, which included electroplaters and welders working from the same small plant. In fact, in this plant, welding and electroplating working areas were not strictly separated. In addition, the hand washing facility for all workers was provided in the electroplating area.

Table 1
Distribution of samples according to working tasks and countries.

	Controls (BE, FI, IT)	Electroplating (BE, FI, FR)	Welders (BE, IT)	Surface treatment (IT)
total	74	52	43	3
BE	17	9	6	–
FI	25	17	–	–
FR	–	19	–	–
IT	32	7	37	3

Our control data shows levels which can be considered comparable to levels reported in earlier studies in Europe. For example, PFOS levels in our control population showed median of 3.65 μg/l (P95 and maximum levels being 11.8 and 13.9, respectively). PFOS levels of the adult general population in Europe has been summarized in EFSA risk assessment report of PFOS and PFOA (EFSA, 2018). Median levels reported have been generally <10 μg/l with maximum levels below 30 μg/l. The levels of PFOS and PFOA in general population have been decreasing during the past 20 years in Europe. The fact that the data reported in EFSA (2018) is more than 10 years old may explain higher maximum values reported in those studies.

The more recent EFSA risk assessment of PFAS summarizes the levels of other PFAS in the general population in Europe (EFSA, 2020). When compared to these data, the median PFAS concentration determined in our control population resulted in the same order of magnitude or at the most one order of magnitude greater with respect to those reported in the general population. Maximum levels measured, on the other side, were almost in the same order of magnitude as those reported in the general population with few exceptions (EFSA, 2020).

3.1. PFAS levels observed in exposed workers

Quantifiable plasma levels were found for each of the 12 PFAS parameters, however with different frequency and extent (Table 2). The most pronounced parameters were PFOA, PFNA, PFHxS and PFOS, which were detected in the four categories of workers in each or almost every sample. Non-parametric group comparison showed some significant differences between the subgroups, most consistently for the perfluoroalkylsufonic acids i.e. PFOS, PFBS, PFHxS and PFHpS (Table 2). Further analysis revealed significant higher perfluoroalkylsulfonic acid levels in electroplaters and welders from the Belgian cohort compared to the samples of the other countries (Table S2; Fig. 1a and b). Moreover, perfluoroalkylsulfonic acid levels of several Belgian workers clearly exceeded the background levels generally reported in Europe, (EFSA, 2018, 2020). Although the workers from other countries showed lower exposure to PFOS when compared to Belgian workers, also six out of 17 Finnish platers exceeded the control range observed in this study and showed levels ranging 27–66 μg/l. These levels are also higher than the levels generally reported in other studies for the adult population without known occupational (or other specific) exposure in Europe. This finding suggests occupational exposure to PFOS in plating applications, which might reflect the past use of PFOS as none of the companies reported to use PFOS based mist suppressants at the time of study. From the questionnaire to the management of the company it was disclosed that PFOS was used as suppressor agent in the Belgian plant until two years before the start of the sampling campaign.

Table 2
PFAS plasma concentrations in μg/L (Median (%>LOQ); Min-Max; P95); all countries.

	Controls (C)	Electroplating (E)	Welders (W)	Mann-Whitney test (p-value)		
	N = 74	N = 52	N = 43	E vs. C	W vs C	E vs W
PFPeA	<0.4 (3% ≥ LOQ) <0.4–0.57; <0.4	<0.4 (6% ≥ LOQ) <0.4–0.60; 0.50	<0.4 (0% ≥ LOQ) <0.4; <0.4	NA	NA	NA
PFHxA	<0.3 (12% ≥ LOQ) <0.3–0.86; 0.45	<0.3 (2% ≥ LOQ) <0.3–0.30; -	<0.3 (26% ≥ LOQ) <0.3–1.12; 0.71	NA	0.094	NA
PFHpA	<0.2 (1% ≥ LOQ) <0.2–0.2; <0.2	<0.2 (8% ≥ LOQ) <0.2–1.22; 0.75	<0.2 (9% ≥ LOQ) <0.2–2.56; 0.40	NA	NA	0.798
PFOA	1.42 (99% ≥ LOQ) <0.1–9.58; 3.43	1.45 (98% ≥ LOQ) <0.1–3.38; 3.07	1.29 (100 % ≥ LOQ) 0.34–5.36; 4.72	0.400	0.769	0.382
PFNA	0.51 (100% ≥ LOQ) 0.14–3.22; 1.86	0.51 (100% ≥ LOQ) 0.19–2.42; 1.27	0.49 (100% ≥ LOQ) 0.10–1.79; 1.21	0.469	0081	0.282
PFDA	0.27 (82% ≥ LOQ) <0.2–1.47; 0.71	0.24 (63% ≥ LOQ) <0.2–0.56; 0.53	0.26 (65% ≥ LOQ) <0.2–0.88; 0.51	0.095	0.270	0.719
PFUnDA	<0.2 (42% ≥ LOQ) <0.2–0.61; 0.30	<0.2 (13% ≥ LOQ) <0.2–0.80; 0.30	<0.2 (23% ≥ LOQ) <0.2–0.27; 0.25	**<0.001**	**0.029**	0.225
PFDoDA	<0.2 (0% ≥ LOQ) <0.2; <0.2	<0.2 (0% ≥ LOQ) <0.2; <0.2	<0.2 (2% ≥ LOQ) <0.2–0.20; <0.2	NA	NA	NA
PFBS	<0.1 (4% ≥ LOQ) <0.1–0.16; <0.1	<0.1 (8% ≥ LOQ) <0.1–8.07; 1.60	<0.1 (44% ≥ LOQ) <0.1–9.94; 3.12	NA	NA	**<0.001**
PFHxS	0.55 (97 % ≥ LOQ) <0.1–4.36; 1.97	1.29 (98% ≥ LOQ) <0.1–28.7; 10.2	0.55 (100 % ≥ LOQ) 0.15–34.4; 22.3	**<0.001**	0.217	**<0.001**
PFHpS	<0.2 (39% ≥ LOQ) <0.2–0.79; 0.40	0.26 (69% ≥ LOQ) <0.2–22.4; 5.20	<0.2 (49% ≥ LOQ) <0.2–34.7; 16.1	**<0.001**	0.181	**0.011**
PFOS	3.65 (100 % ≥ LOQ) 0.52–13.9; 11.8	4.83 (100% ≥ LOQ) 0.89–789; 192	4.97 (100% ≥ LOQ) 1.01–1513; 560	0.136	**0.031**	0.593

NA, not applicable, statistical comparison not done due to the low number of measurements ≥ LOQ.

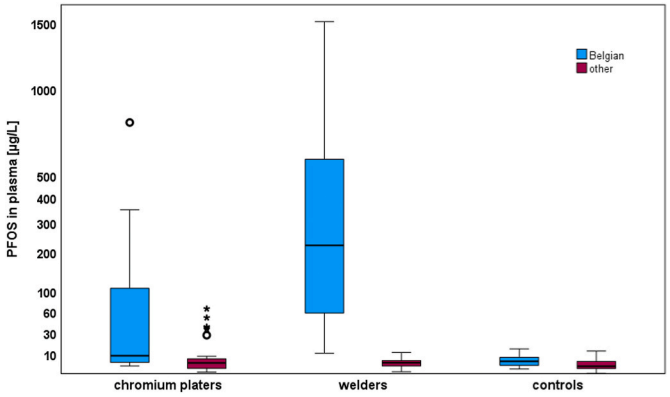

Fig. 1a. Box-Plot of PFOS exposure of chromium platers (n = 9), welders (n = 6) and controls (n = 17) in the Belgian cohort and the remaining countries (IT, FI, FR). (The lower and higher border of the boxes show the 25th and 75th percentile, respectively, the line within the box the median; a circle indicates an outlier, which is value which is higher than the 3rd quartile plus 1.5 times the interquartile range; an asterisks indicates and extreme outlier, which is higher than the 3rd quartile plus 3 times the interquartile range.).

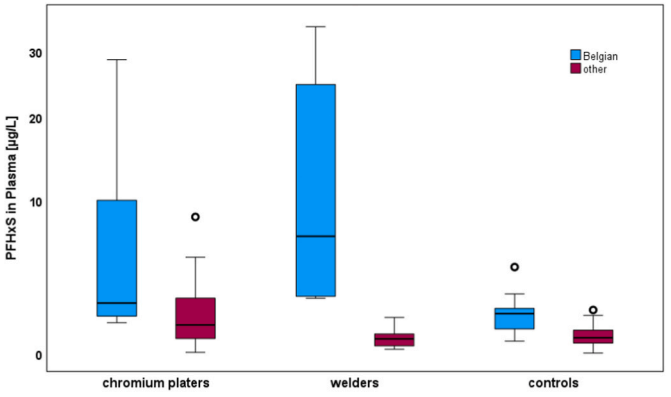

Fig. 1b. Box-Plot of PFHpS exposure of chromium platers (n = 9), welders (n = 6) and controls (n = 17) in the Belgian cohort and the remaining countries (IT, FI, FR).

3.2. Comparison with other occupational investigations

Suitable comparison between our results and those obtained in other occupational investigations is a challenging issue. This is due to the limited number of PFAS-HBM studies on occupationally exposed subjects and to the different workplace settings explored, such as fluorochemical production workers, professional ski waxers, and firefighters that do not specifically include employees engaged in Cr(VI) related job tasks. Additionally, some studies have been performed before restrictions in PFAS uses have been adopted, so that their results should be interpreted with caution.

As regards PFOS and PFOA, the exposure in electroplating (median 4.83 and 1.45 μg/l, respectively) and surface treatment workers (5.47 and 1.10 μg/l, respectively) as well as in welders (4.97 and 1.29 μg/l, respectively) were not significantly different between each other subgroup, and also in comparison to the concentrations determined in unexposed controls (3.65 and 1.42 μg/l, respectively). These levels were lower compared to those reported in fluorochemical production workers, involved in the production of perfluorinated substances or in their incorporation into final products. In workers engaged in a production plant in Trissino, Italy, Costa et al. (2009) reported serum PFOA concentrations ranging from 200 to 47,040 μg/l in exposed employees, and from 530 to 18,660 μg/l in those formerly exposed. In Olsen (2015), PFHxS have been described with geometric mean concentrations up to 700 μg/l serum, a level extremely higher compared to the median range of concentrations determined in our analysis (0.49–1.29 μg/l). In a cohort of workers in a West Virginia plant that manufactured fluoropolymers, median serum PFOA concentrations for 5 different job categories, such as: fine powder/granular PTFE (direct exposure to PFOA), fluorinated ethylene propylene and perfluoroalkoxy fluoropolymer (direct exposure to PFOA), non-PFOA use in Teflon polymer/-copolymer production (intermittent direct or plant background PFOA exposure), maintenance job category (intermittent direct or plant background PFOA exposure), non-Teflon/copolymer production

division with no PFOA use (plant background PFOA exposure) were found to be 595, 2950, 1730, 451, 513 and 164 μg/l (calculated from ppm using plasma density of 1025 g/l), respectively (Woskie et al., 2012). PFAS concentrations in Chinese workers from a fluorochemical plant and in nearby residents resulted in median levels of serum PFOA and PFOS of 284.34 μg/l and 34.16 μg/l in residents and of 1635.96 μg/l and 33.46 μg/l in occupational participants, respectively (Wang et al., 2012).

In Swedish ski waxing technicians which were exposed to perfluorinated chemicals from fluorinated wax fumes the PFAS concentrations in whole blood samples ranged between 0.3 and 27 μg/l for PFOS, 4.8–535 μg/l for PFOA, 0.8–163 μg/l for PFNA, 0.9–24 μg/l for PFDA, and 0.1–2.8 μg/l for PFUnA; the median level of PFOA was 112 μg/l (Nilsson et al., 2010). For comparing of PFAS levels in whole blood with serum or plasma samples, it must be considered that almost of all of the PFAS amount is aggregated in the plasma fraction, and thus, whole blood levels are diluted by a factor of about 2 compared to plasma levels for most PFAS (Poothong et al., 2017). In Norwegian professional ski wavers, the seasonal median levels of PFOA and PFOS in serum ranged between 50 and 57 μg/l and 24–27 μg/l, respectively (Freberg et al., 2010). A significant correlation was found between number of working years and levels of perfluorocarboxylates in both the studies, supporting evidence for a possible bioaccumulation of these compounds (Freberg et al., 2010; Nilsson et al., 2010).

Several studies have found increased blood concentrations of different PFAS from firefighters. In a study on Finnish firefighters, PFNA (range 0.43–6.69 μg/l, median 1.22 μg/l) and PFHxS (1.05–4.30 μg/l, median 2.19 μg/l) concentrations in serum increased during three consecutive training sessions, although the limited number of enrolled workers prevented the statistical analysis of such increase (Laitinen et al., 2014).

In a US pilot study, Tao et al. (2008) analyzed 458 plasma samples of New York State employees and National Guard personnel assigned to work in the vicinity of the world trade center between September 11 and December 23, 2001, to assess exposure to perfluorochemicals released in dust and smoke. PFOS, PFOA, PFHxS, and PFNA, were consistently detected in almost all samples. Median PFOS concentrations ranged from 22.1 to 31.4 μg/l among the six exposure groups. Elevated concentrations of PFOA, PFNA and PFDA compared to the general US population were observed in two subsequent studies on Californian firefighters (Dobraca et al., 2015; Shaw et al., 2013). A cross-sectional exploratory study was performed on 47 firefighters enrolled from two fire departments in Ohio to assess the possible association between the metabolic syndrome and the serum concentrations of four PFAS (Leary et al., 2020). This resulted in 18%–74% higher concentrations in firefighters than the general population, and 21%–62% higher in airport firefighters than suburban ones. Compared with US general population, an elevated risk of hypertension was noted in firefighters, but no significant association between PFAS and the metabolic syndrome was found.

Exposure to aqueous film forming foam (AFFF) was evaluated in 149 firefighters working at AFFF training facilities in Australia by analysis of PFOS and related compounds in serum (Rotander et al., 2015). Median concentrations of 66 and 25 μg/l were reported for PFOS and PFHxS, respectively. The concentrations of PFOS and PFHxS were found to be positively associated with years of jobs with AFFF contact. PFAS serum concentration trends were more recently addressed in Australia firefighters after the replacement of AFFF (Nilsson et al., 2022). A total of 799 participants provided blood samples in 2018–2019. Of these, 130 previously provided serum in 2013–2014. In 2018–2019, mean (arithmetic) serum concentrations of 27, 1.7 and 14 μg/l of PFOS, PFHpS, and PFHxS could be determined, respectively. Serum concentrations were associated with the use of PFOS/PFHxS based AFFF. In fact, participants who commenced service after the replacement of this foam had serum concentrations similar to those in the general population.

Burgess et al. (2023) compared the serum levels of nine PFAS in 290 firefighters from four municipal fire departments in US to three participants of the National Health and Nutrition Examination Survey (NHANES), a national survey exploring the exposure of the general US population, matched to each firefighter on sex, ethnicity, age, and PFAS collection year. They found that serum PFHxS, Sm-PFOS, n-PFOS, n-PFOA, and PFNA concentrations were increased in at least two of four fire departments in comparison to controls.

3.3. Detailed analysis of the Belgian cohort

Because of the higher levels among Belgian platers, a special analysis of the Belgian cohort was performed in an explorative approach (Table 3). The data showed significant higher levels of all perfluoroalkylsulfonic acids in the welders compared to the controls, whereas the plasma levels in the electroplaters tended to be higher compared to the controls but did not reach statistical significance. Nevertheless, PFOS plasma levels of several individuals in both welders and electroplaters reached extremely high values with maximum levels of 1513 and 789 μg/l, respectively. Boxplots (Fig. 1a and b) demonstrate the differences between the subgroups for PFOS and PFHpS. Moreover, a bivariate regression analysis revealed very strong associations between the perfluoroalkylsulfonic acids in the Belgian cohort (Table 4). Significant associations between these parameters were also found for the total multinational group, but they were much less pronounced (Table S3). A further linear correlation analysis of the Belgian data showed a very tight linear association between these parameters (Fig. 2a and b), indicating the same source for the elevated exposure in these workers. The special and congruent exposure to perfluoroalkylsulfonic acids in Belgian electroplaters and welders is explained by the fact that both subgroups were recruited from the same electroplating plant, in which PFOS was applied as surface tension modulator in the plating baths in the past. Interestingly, the welders, which may generally be assigned as bystander along the plating operation, showed higher internal exposure levels than the electroplaters themselves. This may be explained by the circumstance that electroplating operators were informed on and trained for the chemical exposure by their occupational tasks, whereas the welders, which occasionally performed maintenance and repair service at these workplaces were not aware of the hazards at these positions. As mentioned before, the welding and electroplating working areas were not strictly separated and the hand washing facility was provided in the electroplating are in the Belgian plant. Furthermore, inadequate working conditions, namely poor collection and sorting of Cr (VI) waste and inadequate workplace cleaning and hygiene, causes these higher exposure levels (Fig. S1). In addition, the personal protection of the welders was insufficient which also could contribute to the higher exposure levels, namely only welding masks (not air fed or ventilated) and welding gloves were available. This leads to insufficient protection during welding tasks and additional exposure to PFAS may occur. Namely, PFAS can be used to pretreat the metal parts (Gaines, 2023). The task of these welders consists mainly of the revision of engines and the repair of hydraulic cylinders. Only a few brand new automotive parts are welded. Therefore, the exact pretreatment procedures of the welded parts are mainly unknown in the specific case of the Belgian company. Nevertheless, additional exposure to PFAS may occur during these welding tasks. Due to the biological persistence of PFAS in the human body (Cakmak et al., 2022), an internal exposure to these compounds persists and can be monitored still several years after external exposure occurred (Brede et al., 2010).

4. Conclusions

The application of PFAS as surface tension modulators in the electroplating baths can result in distinct internal exposure of electroplaters but also of bystanders, who performed occasional maintenance and repair service at these workplaces. Due to the persistent behavior of PFAS the internal exposure persists for many years, which demands

Table 3
PFAS plasma concentrations in μg/L (Median (%>LOQ); Min-Max); Belgian cohort.

	Controls (C)	Electroplating (E)	Welders (W)	Mann-Whitney test (p-value)		
	N = 17	N = 9	N = 6	E vs. C	W vs C	E vs W
PFPeA	<0.4 (0% ≥ LOQ) <0.4	<0.4 (0% ≥ LOQ) <0.4	<0.4 (0% ≥ LOQ) <0.4	NA	NA	NA
PFHxA	<0.3 (0% ≥ LOQ) <0.3	<0.3 (0% ≥ LOQ) <0.3	<0.3 (0% ≥ LOQ) <0.3	NA	NA	NA
PFHpA	<0.2 (0% ≥ LOQ) <0.2	<0.2 (33% ≥ LOQ) <0.2–1.22	0.27 (67% ≥ LOQ) <0.2–2.56	NA	NA	0.529
PFOA	1.63 (100% ≥ LOQ) 1.33–3.57	2.20 (100 % ≥ LOQ) 1.05–2.96	1.10 (100% ≥ LOQ) 0.76–5.36	0.672	0.135	0.328
PFNA	0.56 (100% ≥ LOQ) 0.28–1.44	0.52 (100 % ≥ LOQ) 0.30–0.85	0.53 (100% ≥ LOQ) 0.15–1.79	0.241	0.609	1.000
PFDA	0.34 (94% ≥ LOQ) <0.2–0.79	0.28 (89% ≥ LOQ) <0.2–0.39	0.33 (67% ≥ LOQ) <0.2–0.88	0.120	0.865	0.776
PFUnDA	<0.2 (35% ≥ LOQ) <0.2–0.29	<0.2 (11% ≥ LOQ) <0.2–0.20	<0.2 (17% ≥ LOQ) <0.2–0.27	0.263	0.473	0.864
PFDoDA	<0.2 (0% ≥ LOQ) <0.2	<0.2 (0 % ≥ LOQ) <0.2	<0.2 (0% ≥ LOQ) <0.2	NA	NA	NA
PFBS	<0.1 (0% ≥ LOQ) <0.1	<0.1 (33% ≥ LOQ) <0.1–8.07	0.78 (100 % ≥ LOQ) 0.51–9.94	NA	NA	0.113
PFHxS	1.59 (100% ≥ LOQ) 0.43–4.36	2.13 (100% ≥ LOQ) 1.17–28.7	7.51 (100% ≥ LOQ) 2.39–34.4	**0.021**	**<0.001**	0.145
PFHpS	0.22 (53% ≥ LOQ) <0.2–0.79	0.40 (89% ≥ LOQ) <0.2–22.4	5.30 (100% ≥ LOQ) 0.46–34.7	**0.021**	**<0.001**	0.113
PFOS	5.40 (100% ≥ LOQ) 1.95–13.9	8.81 (100% ≥ LOQ) 3.17–789	267 (100% ≥ LOQ) 10.6–1513	0.181	**<0.001**	0.088

NA, not applicable, statistical comparison not done due to the low number of measurements ≥ LOQ.

Table 4
Spearman regression analysis between PFAS biomarkers in the Belgian cohort (regression coefficient).

	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFBS	PFHxS	PFHpS	PFOS
PFPeA	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*
PFHxA	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*
PFHpA	-*	-*	1	0.167	−0.054	−0.166	−0.299	-*	**0.883**	**0.631**	**0.703**	**0.687**
PFOA	-*	-*	0.167	1	**0.799**	**0.532**	**0.418**	-*	0.013	0.344	**0.382**	**0.413**
PFNA	-*	-*	−0.054	**0.799**	1	**0.800**	**0.614**	-*	−0.037	0.261	0.288	**0.417**
PFDA	-*	-*	−0.166	**0.532**	**0.800**	1	**0.595**	-*	−0.103	0.043	0.092	0.275
PFUnDA	-*	-*	−0.299	**0.418**	**0.614**	**0.595**	1	-*	−0.209	0.088	0.109	0.185
PFDoDA	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*	-*
PFBS	-*	-*	**0.883**	0.013	−0.037	−0.103	−0.209	-*	1	**0.726**	**0.779**	**0.764**
PFHxS	-*	-*	**0.631**	0.344	0.261	0.043	0.088	-*	**0.726**	1	**0.937**	**0.798**
PFHpS	-*	-*	**0.703**	**0.382**	0.288	0.092	0.109	-*	**0.779**	**0.937**	1	**0.915**
PFOS	-*	-*	**0.687**	**0.413**	**0.417**	0.275	0.185	-*	**0.764**	**0.798**	**0.915**	1

* regression analysis was not performed if one of the parameters showed less than 10 % results above LOQ; significant correlations ($p < 0.05$) are bold marked.

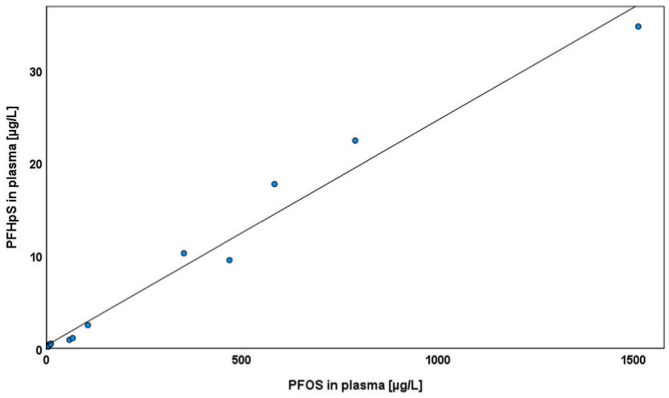

Fig. 2a. Linear regression between PFHpS and PFOS plasma concentrations in the Belgian cohort (C_{PFHpS} = 0.02 x C_{PFOS} + 0.31; Pearson R^2 = 0.979).

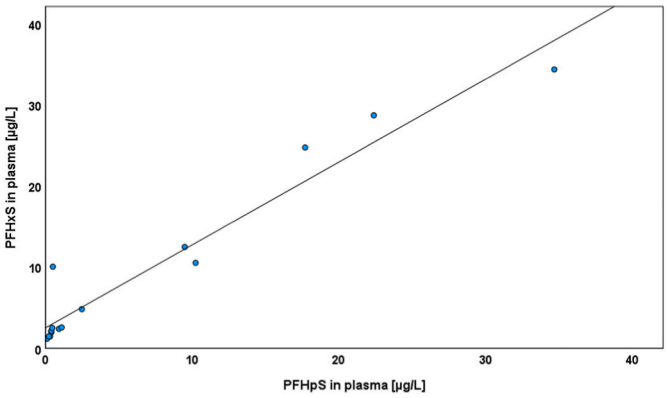

Fig. 2b. Linear regression between PFHxS and PFHpS plasma concentrations in the Belgian cohort (C_{PFHxS} = 1.02 x C_{PFHpS} + 2.52; Pearson R^2 = 0.938).

follow-up monitoring even after the cessation of the use of these compounds. In addition, health monitoring of the most highly exposed individuals needs to be considered. Increased levels of serum PFOS and PFOA have been shown to result in increased cholesterol, triglycerides, and liver enzyme ALT levels in occupational exposure (EFSA, 2018). High levels in mothers have been associated with low birth weight of

children and PFAS exposure may adversely affect the immune function of children (EFSA, 2018, 2020). These effects become relevant in case of fertile age female workers.

Considering the wide-spread use of PFAS in various applications, there is surprisingly limited information on occupational exposure to these compounds. This study is the first one to report exposure in metal sector. As pointed out recently by Moore et al. (2022) there is clearly a need for further knowledge on the sources of occupational exposure to these compounds, exposure levels, and potential health risks.

Ethics

The study involves human subjects. Consent from subjects participating in the study was received prior to conducting the study. Study protocols have been approved by ethical review boards in each of the participating countries with the approvals granted before recruiting the study participants. The ethical boards reviewing and approving the study are as follows:

- Belgium: Ethische Commissie Onderzoek UZ/KU Leuven, Belgium
- Finland: Coordinating ethics committee, HUS Joint Authority, Helsinki, Finland
- France: Comité de Protection des Personnes (CPP) Sud-Ouest
- Italy: Ethical committee in Istituto Superiore di Sanità (ISS)

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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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2023.140613.

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