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Perfluoroalkyl Substance Assessment in Turin Metropolitan Area and Correlation with Potential Sources of Pollution According to the Water Safety Plan Risk Management Approach

Rita Binetti [1,*], Paola Calza [2], Giovanni Costantino [1], Stefania Morgillo [1] and Dimitra Papagiannaki [1,*]

[1] Società Metropolitana Acque Torino S.p.A.—Centro Ricerche, Corso Unità d'Italia 235/3, 10127 Torino, Italy; giovanni.costantino@smatorino.it (G.C.); stefania.morgillo@smatorino.it (S.M.)
[2] Università di Torino, Dipartimento di Chimica, Via Pietro Giuria 5, 10125 Torino, Italy; paola.calza@unito.it
* Correspondences: rita.binetti@smatorino.it (R.B.); papagiannakidimitra@gmail.com (D.P.);
   Tel.: +39-3275642411 (D.P.)

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Abstract: Per and polyfluoroalkyl substances (PFASs) are a huge class of Contaminants of Emerging Concern, well-known to be persistent, bioaccumulative and toxic. They have been detected in different environmental matrices, in wildlife and even in humans, with drinking water being considered as the main exposure route. Therefore, the present study focused on the estimation of PFAS in the Metropolitan Area of Turin, where SMAT (Società Metropolitana Acque Torino S.p.A.) is in charge of the management of the water cycle and the development of a tool for supporting "smart" water quality monitoring programs to address emerging pollutants' assessments using multivariate spatial and statistical analysis tools. A new "green" analytical method was developed and validated in order to determine 16 different PFAS in drinking water with a direct injection to the Ultra High Performance Liquid Chromatography tandem Mass Spectrometry (UHPLC-MS/MS) system and without any pretreatment step. The validation of this analytical method resulted in really low Quantification Limits (5 ng L^{-1}), in satisfying recoveries (70%–102%) and in a good linearity (R^2 = 0.99) for every compound. Among the results, only 4 compounds and only 6% of the samples showed a pollution level higher than the limits of and Quantification (LOQ). Finally, the correlation study between the assessment findings and the industrial sites which serve as potential sources of pollution in the monitored area was carried out.

Keywords: perfluoroalkyl substances; drinking water; LC-MS/MS; direct injection; spatial and statistical analysis

1. Introduction

Per- and polyfluoroalkyl substances (PFASs) are manufactured organic chemicals that have been widely used over the past decades. They belong to the unique category of fluorosurfactants, which the carbon chain of hosts a substitution of hydrogen with fluorine that builds up the hydrophobic part of the surfactant [1,2]. The two primary commercial production processes to synthetize PFAS are the electrochemical fluorination and the telomerisation, but since 2002, only the telomerisation processes are still used. Generally, perfluorinated compounds (PFCs) like perfluoroalkyl sulfonamides and fluorotelomer alcohols can be degraded naturally under aerobic conditions to perfluoroalkyl carboxylates (PFCAs) and perfluoroalkyl sulfonates (PFSAs) [3] that have been detected in various environmental matrices, like water, soil and air as well as in food, animals and humans [4]. PFAS

(PFCAs and PFSAs) represent a huge group of different molecules with unique physicochemical properties, such as extreme hydrophilic and lipophilic character; thermal and chemical stability, making them valuable components for many industrial; and commercial applications. Their key characteristic of having one of the strongest chemical bonds (C–F) in their carbon chain makes them very stable, and they cannot degrade naturally or under heat, acids and oxidation [4,5]. PFASs are, therefore, perfect ingredients for many products with stain-resistant, waterproof or nonstick properties. Among them, there are firefighting foams, food packages, stain-resistant and waterproof fabrics for clothes and carpets, painting materials, etc.

Another way to categorize these compounds is based on their perfluorocarbon chain length. According to the nomenclature given by Buck et al. [5], they are referred to as a long chain and a short chain. The long chain substances include either perfluoroalkyl carboxylates (PFCAs) with eight atoms of carbon or more or perfluoroalkane sulfonates (PFSAs) with at least six atoms of carbon [6] (Table A1). As this category is known to be more bioaccumulative, their replacement with the shorter chained compounds has been pursued in the last couple of decades. However, both kinds are very stable and persistent in the environment as well as toxic, and due to their occurrence and fate in the environment, they have been characterized as Contaminants of Emerging Concern (CECs) [7]. Sources of PFAS in the aqueous environment are landfill leachate, industrial and municipal wastewater treatment plants, dry and wet atmospheric deposition, soil and street surface runoff [6]. Due to their stability properties, they are detected also in drinking water, which is one of the major ways of exposure that poses threats to humans [8,9]. Therefore, it is of great significance to find techniques for effectively removing them from water and of paramount importance to prevent the contamination; according to the framework of the Water Safety Plan (WSP) approach in order to protect human health, it is necessary to evaluate the risks along the drinking water supply system (from the catchment to the consumer). In line with the forthcoming National and European drinking water regulation, SMAT (Società Metropolitana Acque Torino S.p.A.)—the company in charge of the water cycle management in the Turin Metropolitan Area (Italy)—is adopting the Water Safety Plan.

The aim of this study was to assess PFAS occurrence in the Metropolitan Area of Turin in order to estimate the pollution levels and to understand the contaminants' stability properties. Pursuing the application of green analytical chemistry, a quantitative analytical method for evaluating seventeen different perfluorinated compounds in water samples, without any preconcentration step, was developed and validated. Commonly, PFASs used in consumer products are complex mixtures of many compounds that provide different specific features [10]. For this reason, in this method, we decided to target seventeen linear perfluoroalkyl substances, with a chain length ranging from four to eighteen carbon atoms in order to also investigate the variety of their properties. Among the literature, after years of research on the field of perfluoroalkyl substances, only three methods are reported using a direct injection analysis [11–13]; all of them target less than 17 compounds, and they have a longer analysis time than the one reported in this study. A book chapter by Dasu, Kempisty and Mills [3] has reported an overview of the analytical methods that occur for the determination of PFASs in environmental matrices and, more specifically, in different types of water. Even if all the listed methods report low quantitation levels, they used an extraction-pretreatment step [14–18]. Moreover, most of them focused on less number of target compounds (in comparison with those included in our method), and no great differences occurred between them. Furthermore, very few standard methods (Table A6) are reported in the literature for the determination of PFASs in water samples, and only one of them ASTM (American Society for Testing and Material) does not use any pretreatment step but does not refer to drinking water. On the other hand, both the standard ISO 25101:2029(E) method and the EPA (United States Environmental Protection Agency) 537 method, that are concerned with drinking water, use an solid phase extraction (SPE) extraction step and focus on less number of compounds than our "green" method that with direct injection achieved very low Quantitation Limits for all the 16 targets.

Moreover, an estimation study of potential pollution sources was carried out by searching the correlation between the assessment findings and the industrial sites—which represent the major source

of pollution, as well as the civilian airports and the wastewater treatment plants—using spatial analysis and multivariate statistical analysis tools. The aim was also to develop a statistical framework for investigating whether the presence of PFASs in the water is associated with the number of source points within a watershed in order to develop a tool for supporting "smart" water quality monitoring programs for emerging pollutants. Water quality monitoring programs are usually set according to the numbers of inhabitants or to the volume of water supplied.

2. Materials and Methods

2.1. Study Area and Sampling

SMAT is the company in charge of the water cycle management in the Metropolitan Area of Turin (Piedmont, Italy), supervising 293 municipalities (Figure A3, Table A5) and supplying a population of about 2.3 million inhabitants. In this study, 930 samples were collected from the 291 municipalities managed by SMAT, including 5% of surface, 19% of underground and 76% of drinking water. The sampling campaign and the analysis were carried out from March 2018 until October 2018. Due to the fact that PFASs have a wide range of applications, care needs to be taken during the sampling in order to avoid any contamination or concentration loss. For this reason, polypropylene bottles WM (wide mouth) with caps (volume 125 mL) were used as sample containers, purchased from SciLabware Limited (Stoke-on-Trent, Staffordshire, ST4 4RJ, United Kingdom). Although PFASs are very stable and not degradable at room temperature, the samples were stored at 4 °C prior the analysis (performed within 15 days), in order to prevent the biodegradation of matrix interferences that can affect the recovery of the analytes.

2.2. Reagents and Chemicals

A mix (PFAC-MXB) of seventeen PFASs was examined in this study containing compounds with various carbon chain lengths (between four to eighteen atoms of carbon): thirteen linear perfluoroalkylcarboxylic acids and four perfluoroalkylsulfonates (details in Table 1). The standard mix solution PFAC-MXB was purchased from Wellington Laboratories (Guelph, ON, Canada) with chemical purities of >98% and a concentration of 2000 ng mL^{-1} in Methanol/Water <1% for every individual perfluoroalkylcarboxylic acid and perfluoroalkylsulfonate. Another mix (MPFAC-MXA) containing seven mass-labelled (^{13}C) perfluoroalkylcarboxylic acids and two mass-labelled (^{18}O and ^{13}C) perfluoroalkylsulfonates was used as internal standards (details in Table 1). The mix solution MPFAC-MXA was purchased from Wellington Laboratories (Guelph, Ontario, Canada) with chemical impurities >98% and a concentration of 2000 ng mL^{-1} in Methanol/Water <1% for every individual mass-labelled perfluoroalkylcarboxylic acid and mass-labelled perfluoroaklylsulfonate and with isotopic impurities of 99% per ^{13}C and >94% per ^{18}O. UHPLC-grade Methanol was purchased from Sigma-Aldrich, Co (St. Louis, MO, USA), MilliQ was obtained from MilliPore (MA, USA) and Ammonium acetate for LC-MS LiChropur® was purchased from Merck KGaA (Darmstadt, Germany).

2.3. Sample Preparation

The samples were injected directly into the analytical system without any pretreatment step. A filtration step was not necessary as the samples—mostly drinking water—were not contaminated with soils or suspended organic matter. Two working standard solutions—in 50% Methanol/50% Water for the first and in 100% Water for the second—were prepared with a dilution from each of the two stock solutions and used for the calibration. The purchased solutions were stored at 4 °C in the fridge, while the other four were stored at room temperature. A volume of 700 μL of each sample was transferred into 0.7 mL Polypropylene Short Thread Micro-Vials (purchased from CPS Analitica for Chemistry, Milan, Italy), and 1 μL of the Internal Standard mix (50 ng L^{-1}) was added.

Table 1. The target compounds and related internal standards.

Target Compounds (PFAC-MXB)		Internal Standard Compounds (MPFAC-MXA)	
Full Name	**Abbreviation**	**Full Name**	**Abbreviation**
Perfluoro-n-butanoic acid	PFBA	Perfluoro-n-[13C4]butanoic acid	MPFBA
Perfluoro-n-pentanoic acid	PFPeA	Perfluoro-n-[1,2-13C2]hexanoic acid	MPFHxA
Perfluoro-n-hexanoic acid	PFHxA	Perfluoro-n-[1,2-13C2]hexanoic acid	MPFHxA
Perfluoro-n-heptanoic acid	PFHpA	Perfluoro-n-[1,2-13C2]hexanoic acid	MPFHxA
Perfluoro-n-octanoic acid	PFOA	Perfluoro-n-[1,2,3,4-13C4]octanoic acid	MPFOA
Perfluoro-n-nonanoic acid	PFNA	Perfluoro-n-[1,2,3,4,5-13C5]nonanoic acid	MPFNA
Perfluoro-n-decanoic acid	PFDA	Perfluoro-n-[1,2-13C2]decanoic acid	MPFDA
Perfluoro-n-undecanoic acid	PFUdA	Perfluoro-n-[1,2-13C2]undecanoic acid	MPFUdA
Perfluoro-n-dodecanoic acid	PFDoA	Perfluoro-n-[1,2-13C2]dodecanoic acid	MPFDoA
Perfluoro-n-tridecanoic acid	PFTrDA	Perfluoro-n-[1,2-13C2]dodecanoic acid	MPFDoA
Perfluoro-n-tetradecanoic acid	PFTeDA	Perfluoro-n-[1,2-13C2]dodecanoic acid	MPFDoA
Perfluoro-n-dexadecanoic acid	PFHxDA	Perfluoro-n-[1,2-13C2]decanoic acid	MPFDA
Perfluoro-n-octadecanoic acid	PFODA	Perfluoro-n-[1,2-13C2]decanoic acid	MPFDA
Potassium perfluoro-1-butanesulfonate	L-PFBS	Sodium perfluoro-1-hexane [$^{18}O_2$] sulfonate	MPFHxS
Sodium perfluoro-1-hexanesulfonate	L-PFHxS	Sodium perfluoro-1-hexane [$^{18}O_2$]sulfonate	MPFHxS
Sodium perfluoro-1-octanesulfonate	L-PFOS	Sodium perfluoro-1-[1,2,3,4-13C4] octanesulfonate	MPFOS
Sodium-1-decanesulfonate	L-PFDS	Sodium perfluoro-1-hexane [$^{18}O_2$]sulfonate	MPFHxS

2.4. Instrumental Analysis

Analyses were carried out using the SCIEX QTRAP® 6500 system (SCIEX, Framingham, MA, USA) with a Thermo Scientific Dionex UltiMate 3000 UHPLC system and a RS-3000 autosampler (Dionex Softron GmbH, Germering, Germany). The UHPLC instrument was equipped with a Luna® C18 (2) HPLC Column (5 μm particle size, 30 mm × 2.0 mm; Phenomenex Inc., Torrance, CA, USA) installed between the eluent mixer and the autosampler, in order to delay the potential contamination originating from the UHPLC system. The chromatographic separation was achieved using a Luna® Omega PS C18 HPLC Column (1.6 μm particle size, 50 mm × 2.1 mm; Phenomenex Inc., Torrance, CA, USA)—heated to 40 °C—by injecting a 50 μL sample volume at a mobile phase consisted of a mixture of 20 mM Ammonium Acetate in water (**A**) and Methanol (**B**), lasting a total time of 12 min. The gradient profile, with a flow rate of 0.550 mL/min, started with 98% **A** and 2% **B**, increasing to 100% **B** in 6 min, and, after keeping this ratio for 1.5 min, reversed into the initial conditions (Table A2). The QTRAP® 6500 system was operated in Negative Electrospray Ionization Mode (ESI) (parameters used: gas temperature at 350 °C, curtain gas and collision gas pressure of 30 psi and Ionspray voltage of −4500 V), using Multiple Reaction Monitoring (MRM) scan mode, where Q1 and Q3 were set to more than one single mass allowing specific fragment ions from specific parent molecular ions to be detected [19]. The parameters for the ESI source and MRM are summarized in Tables A3 and A4. The chromatograms and spectra were processed using the Analyst 1.6.2 software (SCIEX, Framingham, MA, USA).

2.5. Method Validation and Quality Assurance

A validation process was carried out in order to assure the applicability of the developed method. The validation parameters included precision, accuracy, linearity, recovery and limits of Detection (LOD) and Quantification (LOQ). The ISO/IEC 17025 accreditation requirements and, in particular the ones set by Accredia, the Italian National System for the Accreditation of Laboratories were used as guidelines of the method's validation. Six-point calibration curves were built, and for each point, fifteen replicates were analysed. The quantitation was performed using the MultiQuant™ 3.0.3 software (SCIEX, Framingham, MA, USA).

In addition, blank and quality control samples were analysed in order to ensure the best performance of the instrument during the analysis. The quality control samples were prepared by mixing the standard solution with MilliQ water at a final concentration of 50 ng L^{-1} and spiked with 50 ng L^{-1} of the internal standard mix. In the batch, their analysis was performed after the linear calibration curve (range 5–120 ng L^{-1}), used for the quantification and after every ten samples.

2.6. Spatial and Statistical Analysis

A spatial analysis was used to develop a framework for predicting the potential pollution levels in specific municipalities, based on the industrial activities and waste water treatment plants (WWTPs) that are close to the sampling points. In our study, information about 176 industrial sites (Figure A1) and 800 WWTPs present in the studied territory were taken from Arpa Piemonte [20,21], and in particular, the geographical data (coordinates in WGS 84 system and maps of the area) used were downloaded from the Diva-Gis [22] platform. The QGIS 3.4 software was used in order to find a correlation between industrial sites and WWTPs within a radius of 5 km that could be potential sources of pollution and sampling points with concentrations above the Limits of Quantification. Because of the lack of information available concerning emerging pollutants employed by the industrial sites, this led us to choose them according to their sector of activities and to products known to potentially employ PFASs. Multivariate spatial regression models [23] were developed for the areas where PFASs were detected, in order to evaluate the correlations with the potential point sources of pollution selected. We used the GeoDa 1.12 software in order to build the Ordinary Least Squares (OLS) and the Spatial Regression models. The Moran's I statistic was used to test for spatial autocorrelation between the area units, while the Akaike info criterion was used to check which of the two models is stronger in predicting the correlation between the potential point sources and the positive polluted areas [24].

3. Results and Discussion

3.1. Cross Contamination

As stated above, PFASs have many different applications, so that cross contamination at trace levels of PFAS even from laboratory equipment's which contain fluoropolymers will have a large impact on the accuracy and validity of the analytical results, especially in analytical methods performing at nanograms per liter (or parts per trillion; ppt) of sensitivity [11]. In order to minimize these effects, online SPE-LC-MS/MS methods have been developed for PFAS determination in water [12]. Although, the direct injection method, due to the absence of extraction and cleanup steps, is the best choice to avoid background contamination during all the analysis steps, a meticulous and methodical manipulation of the samples is necessary. Teflon and glass materials were avoided throughout the analysis, as well as a filtration step, even if it was not necessary for the drinking water, in order to minimize any contamination of the samples. Furthermore, a smaller HPLC column was added between the pump and the injector in order to delay any possible contamination originating from the solvents, meaning substances that can be coeluted with the target compounds [12–15].

3.2. Method Optimization

Spiked water samples analysed without any pretreatment step and by direct injection proved unsuccessful as the results showed la ow recovery for the longer chain compounds. Therefore, taking into account the different chemical properties among the seventeen target compounds, we optimized the choice of solvent added to the samples according to the reports of the EPA 537 method. Varying the solvents' percentage ratio in both the working standards (Section 2.2), we reached satisfying results by preparing the standard solutions in 50% Methanol/50% Water.

Chromatographic conditions were optimized as well. A Luna® Omega PS C18 HPLC Column was used for the analysis, but the best chromatographic separation was achieved after using another C18 column (Luna® C18 (2) HPLC Column) as an isolator to separate the target compounds in the analytical samples from those potentially present in solvents. Moreover, as stated above, a gradient elution of the mobile phase containing a Methanol and Ammonium Acetate solution was used for the analysis. Firstly, an elution starting with 40% Methanol and 60% Ammonium Acetate in water (5 mM) increasing to 100% Methanol and returning at the initial conditions within 6 min was tried. The separation of the longer chain compounds was satisfactory with these conditions, but some of the shorter chain PFASs were co-eluted at the beginning of the chromatogram (Figure A2). For this reason,

the best analyte's separation and shape of the peaks were achieved by increasing to a 20 mM the concentration of the Ammonium Acetate solution and by varying the analysis time and the gradient analysis profile.

In a PFAS analysis, the use of isotopically labelled internal standards is endorsed in order to ensure the best results. The added concentration of the internal standard was 50 ng L^{-1}. In order to calculate the PFAS concentration in the samples, the ratio between the areas of the compounds' peaks and that of the internal standards were used.

3.3. Validation Study

A calibration curve with six points of final concentrations 5, 10, 25, 50, 90 and 120 ng L^{-1} was built by mixing different amounts of the mix **B** (concentration 1 μg L^{-1}) and MilliQ water and by adding to everything 50 ng L^{-1} of the internal standard solution. The quantitative data were analysed using statistical modules in order to define the linearity, accuracy, precision and recovery as well as the Limits of Detection and Quantification.

3.3.1. Linearity

Linearity is based on the linear regression analysis of the obtained quantitative data. Six-point calibration curves were built in the 5–120 ng L^{-1} concentration range. The regression coefficients (R^2) were calculated by laying out the ratio between the target peak area, the relative Internal Standard (IS) peak area and the concentrations. A 1/x concentration-weighting factor was used in order to give more emphasis to the lower concentrations and to ensure the best assay performance [23]. Good coefficient results (R^2 0.99) (Table 2) were obtained for the short chain compounds, indicating a good linear correlation, as well as for longer chain compounds, as the coefficients for perfluoro-n-tridecanoic acid (PFTrDA), perfluoro-n-tetradecanoic acid (PFTeDA) and perfluoro-n-octadecanoic acid (PFODA) were greater than 0.98.

Table 2. The statistical analysis results.

Compounds	Spike ng L^{-1}	Accuracy %	Recovery %	Precision %	Linearity	LOQ
PFBA [1]	50	−8.6	91.38	3.132	0.997	5
PFBS	50	−4.2	95.78	2.899	0.997	5
PFPeA	50	1.3	101.28	1.673	0.999	5
PFHxA	50	−5.2	94.84	2.816	0.998	5
PFHxS [1]	50	−3.9	96.12	6.065	0.997	5
PFHpA	50	−4.7	95.28	3.632	0.999	5
PFOA [1]	50	−3.7	96.28	4.357	0.998	5
PFOS [1]	50	−8.0	92.04	1.956	0.992	5
PFNA	50	−9.6	90.38	4.819	0.999	5
PFDA	50	−14.4	85.58	7.591	0.995	5
PFUdA	50	−5.3	94.72	9.637	0.998	5
PFDoA	50	−7.2	92.78	8.715	0.999	5
PFTrDA	50	−26.8	73.22	17.526	0.989	5
PFTeDA	50	−30.0	69.98	13.758	0.987	5
PFHxDA	50	−15.1	84.88	15.971	0.995	5
PFODA	50	−13.7	86.34	5.477	0.980	5
PFDS	50	−51.3	48.68	15.776	0.997	5

[1] The compounds detected in the samples in concentrations higher than the Limit of Quantification.

3.3.2. Accuracy, Recovery and Precision

The measurement of the systematic and random errors is a crucial step of the method's validation. According to the ISO/IEC 17025, the required values for precision are RSD ≤ 20% and for a recovery within the range of 70%–120%. The variability and reproducibility of the results were calculated for each point of the calibration curve, giving results obeying the requirements; in Table 2, only those for

50 ng L^{-1} are reported. Similarly, the accuracy of the method, based on the trueness of the results, was satisfying the criterion ≤30% for every point of the calibration curve and for every analyte (Table 2). Sodium-1-decanesulfonate (PFDS) was the only compound that did not have good validation results, leading us to exclude it from our method. The recovery of the compounds was also checked in spiked real water samples, obtaining satisfying results (Table 3).

Table 3. The recovery results from spiking in real water samples.

Compounds	Spike ng L^{-1}	Real Sample 1 Recovery %	Real Sample 2 Recovery %	Real Sample 3 Recovery %	Real Sample 4 Recovery %
PFBA [1]	50	107.52	106.06	90.84	107.05
PFBS	50	106.92	107.22	90.76	103.90
PFPeA	50	108.22	105.85	90.53	109.99
PFHxA	50	104.96	106.89	91.69	107.11
PFHxS [1]	50	104.96	106.73	90.88	105.98
PFHpA	50	102.19	102.93	92.57	105.56
PFOA [1]	50	103.63	114.74	92.09	107.14
PFOS [1]	50	95.92	97.31	86.33	96.11
PFNA	50	106.18	102.78	97.41	104.91
PFDA	50	95.29	90.22	81.93	90.39
PFUdA	50	93.49	83.01	81.57	80.78
PFDoA	50	93.19	100.73	96.98	97.45
PFTrDA	50	97.89	87.62	82.73	97.13
PFTeDA	50	101.03	84.89	94.62	88.16
PFHxDA	50	100.61	101.19	84.50	101.98
PFODA	50	86.63	90.16	87.91	93.71
PFDS	50	72.26	75.31	52.28	74.51

[1] The compounds detected in the samples in concentrations higher than the Limit of Quantification.
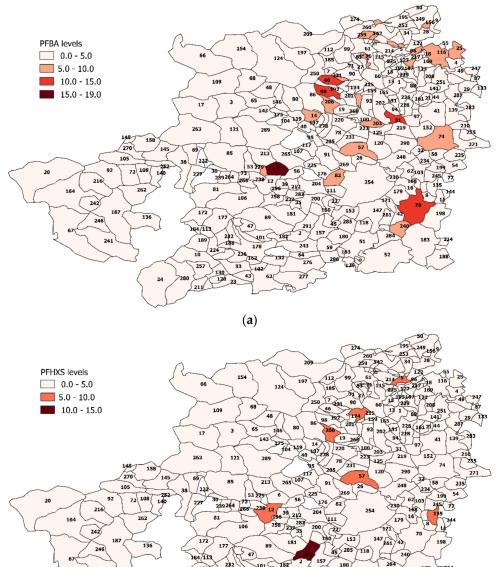
3.3.3. Limits of Detection and Quantification

The Limits of Detection and Quantification for each analyte were determined based on the results obtained from the 15 replicates of the six-point calibration curves. The LOD was calculated by multiplying 3.3 times the standard deviation of the y-intercepts and by dividing by the slope of the calibration curve, as stated in the ICH (International Conference on Harmonisation) Method. Similarly, the LOQ was 10 times the standard deviation of the y-intercepts and was divided by the slope of the calibration curve. The obtained results for the LOQs of the target PFAS varied from 3 (for shorter chain compounds) to 8 ng L^{-1} (for longer chain compounds). However, for the practical and data processing uniformity as a Limit of Quantification for every compound (as stated also in the ASTM D7979-17 method), the lowest point of the calibration curve satisfying for the accuracy and precision the criteria of less than 30% (considering the 15 replicates) was adopted In this way, for every compound, the LOQ is 5 ng L^{-1} (Table 2).

3.4. PFAS Assessment in Turin Metropolitan Area

The developed method was applied for the estimation of PFAS pollution in the Metropolitan Area of Turin. Taken from all stages of the water supply system (from the catchment till the tap) through a sampling campaign organized by SMAT were 930 samples. Among the samples, 5% of them were surface, 19% were underground and 76% were drinking water samples. As a sum of the sixteen target PFASs, the highest detected concentration was 57 ng L^{-1}. Only four out of the sixteen compounds monitored were detected in the area in concentrations above the Limit of Quantification (5 ng L^{-1}): Perfluoro-n-butanoic acid (PFBA), perfluoro-1-hexane [^{18}O$_2$] sulfonate (PFHxS), perfluoro-n-octanoic acid (PFOA) and sodium perfluoro-1-octanesulfonate (PFOS) (Figure 1). The highest detected concentration for PFBA was 19 ng L^{-1}, while for PFHxS and PFOA, it was 15 ng L^{-1} and 9 ng L^{-1}, respectively. The highest detected concentration among the four compounds

was for PFOS, 23 ng L^{-1}, and as a finding was in contrast with the results from other methods which report as a general finding that concentrations of carboxylates were higher than those of sulfonates [23]. All the results are lower than the drinking water performance values set from the Italian Ministry of Health (30 ng L^{-1} for PFOS and 500 ng L^{-1} as sum of PFAS) and are reported in the Revision of the Drinking Water European Directive (100 ng L^{-1} as single and 500 ng L^{-1} as sum of PFAS).

(a)

(b)

Figure 1. *Cont.*
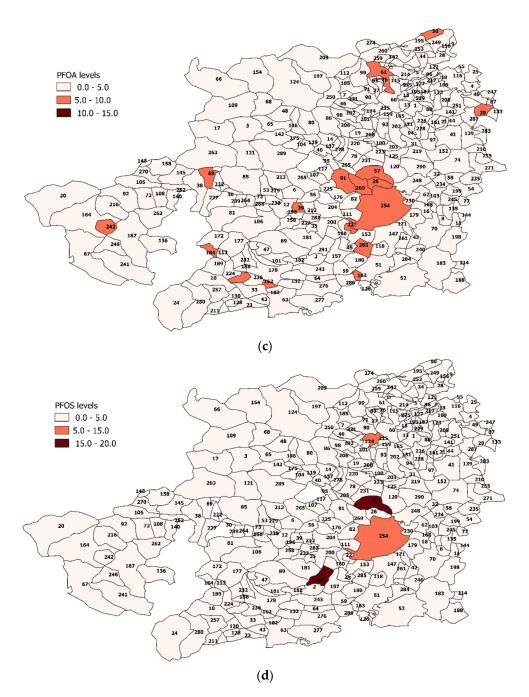
(**c**)

(**d**)

Figure 1. The pollution levels for the detected compounds in the study area: (**a**) PFBA detected levels (ng L^{-1}); (**b**) PFHxS detected levels (ng L^{-1}); (**c**) PFOA detected levels (ng L^{-1}); and (**d**) PFOS detected levels (ng L^{-1}).

Among the assessment findings, the highest pollution rates were detected near industries and Wastewater Treatment Plants (WWTPs) as could be expected. Moreover, only in one municipality were all the four compounds detected together, and that was near the airport where, as it is known from the literature, aqueous film-forming foams (AFFF)—foams with fluorinated chemicals—can be used [3].

Spatial Analysis Results

Only 54 out of the 930 samples analysed were detected with a concentration of PFAS above the quantification limit. A correlation study between the positive sampling points and the companies or the wastewater treatment plants (WWTPs) that are surrounding them within 5 km was carried out.

The results showed that around areas where PFASs were detected more industrial sites or WWTPs exist than those that showed no pollution.

The spatial regression models explain 8%–66% of the variance in the water samples for the four PFAS compounds that were detected. Increasing PFBA concentrations are positively associated with the number of industrial sites and the WWTPs that are present in the surrounding area of the sampling point, and this relationship resulted in being statistically significant ($p < 0.001$), which is the strongest statistical association across the positive sampling points and the point sources. On the contrary, the other three compounds showed a positive correlation with the industrial sites but a negative association with the waste water treatment plants, and that relationship showed also a lack of statistical significance ($p > 0.05$) (Table 4). This indicates that PFAS releases from WWTPs are important but less significant than those from industries, and it is consistent with results obtain from Hu et al. [24]. These results can be explained because of the low number of sampling points with a concentration above the quantification limit for these three compounds available (for PFHxS, only 7 out of the 930 samples were positive, whereas for PFOS, only 6 out of the 930 were positive).

Table 4. The spatial regression models for PFAS concentrations in drinking water.

Compounds	Industrial Sites	WWTPs	λ^1	R^2
PFBA				
coefficient	1.1371	0.2795	0.092	0.66
p-value	0.001	0.001	0.05	
PFHxS				
coefficient	0.1688	−0.0118	0.0329	0.30
p-value	0.002	0.523	0.07	
PFOS				
coefficient	0.2859	−0.0123	0.0822	0.08
p-value	0.001	0.527	0.07	
PFOA				
coefficient	0.6166	−0.0311	0.1586	0.24
p-value	0.001	−0.151	0.07	

[1] The spatial error term coefficient showing spatial influence.

Nevertheless, the small number of polluted samples harden the statistical analysis, as for this process, a large number of data is required. The results obtained from the spatial analysis showed that one independent variable (industrial sites) is a significant predictor for all the detected PFAS compounds and can be taken into account in order to guide the future choice of the sampling points presenting a higher risk factor. Instead, the independent variable WWTPs is a significant predictor only for the PFBA pollution (PFBA was the more frequent detected pollutant), indicating that the other three compounds are most probably released from the industries and not the WWTPs that occur in the area.

The spatial analysis performed was challenging due to the lack of information available. Geospatial data for many potentially important PFAS point sources are lacking as well as information about the companies' production processes. Moreover, there are no data about the employment of this class of substances (as PFAS are not regulated yet) or the airborne emissions, in order to value the importance of atmospheric releases. Finally, there are no information about where and if the intake of the water supply is upstream from point source of pollution, and so on.

4. Conclusions

A new "green" validated method for determining 16 different PFAS in drinking water samples is presented. The key characteristic of this method, which makes it unique, is the absence of a pretreatment or preconcentration step and a direct injection into the UHPLC system coupled to a triple quadrupole mass spectrometer. Even the numerous difficulties faced in order to achieve the

best performance, good recovery results—which were within the range reported in the standards' requirements—and really low Quantification Limits (5 ng L^{-1}) were achieved. Even if this method is oriented to be applied only for drinking water samples, it provides the analyte with a high sensitivity in determining PFASs at very low concentrations—a scale of nanograms per liter (or parts per trillion; ppt).

Another aim of this study was the PFAS assessment in the Metropolitan Area of Turin which was carried out using this method in order to estimate the pollution in the area. Among the results, only four compounds were detected above the limits of quantification and only in 6% of the analysed samples. Nevertheless, despite the low detected pollution rates, a correlation study in order to estimate the potential sources of this pollution was carried out. Instead of performing a "blind" monitoring water quality control, a spatial analysis is a useful tool in order to guide the future choice of the sampling points presenting a higher risk factor as well as the inputs to support the surveillance and water quality control activities. It has to be taken into account that PFASs include thousands of compounds, and as a result, the chemical analysis alone cannot cover the complete assessment of the potential pollution with this kind of contaminants; the same can be said for other classes of emerging pollutants. Considering the costs, the effort and the environmental impact of the chemical analysis for emerging pollutants' assessment, the "smart" monitoring program is much more better performing due to the prioritization of the site at major risks. However, the low number of data beyond the limit of quantification and the lack of information about the industrial activities which can cause pollution in the area provided us some satisfactory preliminary results. Further study is ongoing for addressing and collecting more information in order to enrich the results.

From the lessons learned in this study, it is important to highlight that the strengthening of the cooperation and active participation of the Regional Health and Environmental Protection Agencies, Water Companies and Stakeholders are crucial strategies for risk management in the watershed, as only a great number of data and information can give statistically significant results.

Author Contributions: Conceptualization, R.B. and P.C.; methodology, D.P. and S.M.; software, D.P. and S.M.; validation, D.P., S.M. and G.C.; formal analysis, D.P. and S.M.; investigation, D.P. and S.M.; data curation, D.P. and S.M.; writing—original draft preparation, D.P.; writing—review and editing, P.C. and R.B.; visualization, R.B.; supervision, R.B.; project administration, R.B.; funding acquisition, R.B. and P.C.

Appendix A

Table A1. The categorization according the chain length [3].

Perfluoroalkane Sulfonates (PFSA)		Perfluoroalkyl Carboxylates (PFCA)	
Short Chain $n \leq 5$ e.g., PFBS	Long Chain $n \geq 6$ e.g., PFHxS, PFOS and PFDS	Short Chain $n \leq 7$ e.g., PFBA, PFPeA, PFHxA and PFHpA	Long Chain $n \geq 8$ e.g., PFOA, PFNA, PFDA, PFUdA, PFDoA, PFTrDA, PFTeDA, PFHxDA and PFODA

Table A2. LC Gradient conditions.

Time (min)	Flow Rate (mL/min)	A %	B %
0.000	0.550	98	2
0.000	0.550	98	2
0.500	0.550	98	2
1.000	0.550	70	30
6.000	0.550	0	100
7.500	0.550	0	100
7.600	0.550	98	2
10.000	0.550	98	2

Table A3. Electrospray Ionization Mode (ESI) source parameters.

Parameter	Value
Polarity	Negative
Curtains Gas	30 psi
Collision Gas	30 psi
Ionspray Voltage	−4500 V
Temperature	350 °C
GS1	50 psi
GS2	55 psi

Table A4. Multiple Reaction Monitoring (MRM) transitions and the retention time (RT) for analytes and internal standards.

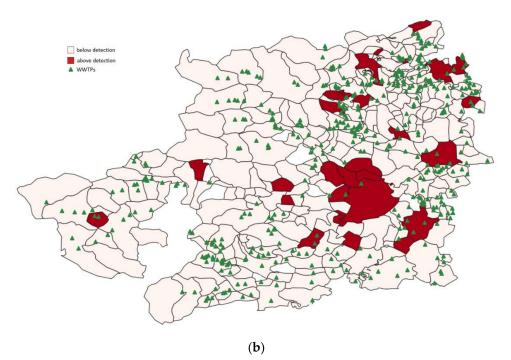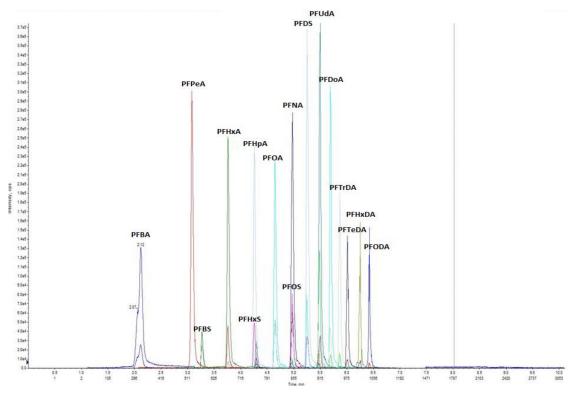| Compound	Q1 *m/z*	Q3 *m/z*	RT
PFBA	213	169	2.1
PFPeA	263	219	3.1
PFHxA	131	269	3.8
PFHpA	363	319	4.3
PFOA	413	369	4.6
PFNA	463	419	5.0
PFDA	513	469	6.9
PFUdA	563	519	5.5
PFDoA	613	569	5.7
PFTrDA	663	619	5.9
PFTeDA	713	669	6.0
PFHxDA	813	769	6.3
PFODA	913	869	6.5
L-PFBS	299	99	3.3
L-PFHxS	399	99	4.3
L-PFOS	499	99	5.0
L-PFDS	599	99	5.4
MPFHxS	403	10	4.3
MPFOS	503	99	5.0
MPFBA	217	172	2.1
MPFHxA	315	270	3.8
MPFOA	417	372	4.6
MPFNA	468	423	4.9
MPFDA	515	470	5.2
MPFUdA	565	520	5.5
MPFDoA	615	570	5.7

(**a**)

(**b**)

Figure A1. A map of the pollution levels of PFAS as a sum (limit 10 ng L^{-1}) and the selected point sources present in the studied area: (**a**) industrial sites and (**b**) waste water treatment.
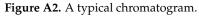
Figure A2. A typical chromatogram.

Table A5. A list of the municipalities monitored and the samples analysed.

Municipality Name ID	Number ID	Samples Analysed	Municipality Name ID	Number ID	Samples Analysed
AGLIE'	1	1	MONCALIERI	147	21
AIRASCA	2	1	MONCENISIO	148	1
ALA DI STURA	3	6	MONTALDO TORINESE	149	3
ALBIANO D'IVREA	4	3	MONTALENGHE	150	1
ALICE SUPERIORE	5	2	MONTALTO DORA	151	1
ALMESE	6	11	MONTANARO	152	2
ALPETTE	7	2	NICHELINO	153	6
ANDEZENO	8	2	NOASCA	154	4
ANDRATE	9	1	NOLE	155	3
ANGROGNA	10	2	NOMAGLIO	156	2
ARIGNANO	11	1	NONE	157	2
AVIGLIANA	12	7	NOVALESA	158	1
BAIRO	13	1	OGLIANICO	159	3
BALANGERO	14	3	ORBASSANO	160	2
BALDISSERO CANAVESE	15	1	ORIO CANAVESE	161	2
BALDISSERO TORINESE	16	3	OSASCO	162	2
BALME	17	2	OSASIO	163	2
BANCHETTE	18	1	OULX	164	2
BARBANIA	19	2	OZEGNA	165	1
BARDONECCHIA	20	1	PANCALIERI	166	1
BARONE CANAVESE	21	2	PARELLA	167	2
BEINASCO	22	9	PAVAROLO	168	2
BIBIANA	23	1	PAVONE CANAVESE	169	1
BOBBIO PELLICE	24	2	PECCO	170	1
BOLLENGO	25	3	PECETTO TORINESE	171	2
BORGARO TORINESE	26	12	PEROSA ARGENTINA	172	1
BORGIALLO	27	1	PEROSA CANAVESE	173	2
BORGOFRANCO D'IVREA	28	3	PERTUSIO	174	1
BORGOMASINO	29	1	PESSINETTO	175	2
BORGONE SUSA	30	4	PIANEZZA	176	8
BOSCONERO	31	7	PINASCA	177	1
BRANDIZZO	32	3	PINEROLO	178	1
BRICHERASIO	33	1	PINO TORINESE	179	1
BROSSO	34	1	PIOBESI TORINESE	180	1
BRUINO	35	7	PIOSSASCO	181	10

Table A5. *Cont.*

Municipality Name ID	Number ID	Samples Analysed	Municipality Name ID	Number ID	Samples Analysed
BURIASCO	36	1	PISCINA	182	1
BUSANO	37	2	POIRINO	183	5
BUSSOLENO	38	3	POMARETTO	184	2
BUTTIGLIERA ALTA	39	2	PONT CANAVESE	185	5
CAFASSE	40	2	PORTE	186	1
CALUSO	41	2	PRAGELATO	187	1
CAMBIANO	42	2	PRALORMO	188	2
CAMPIGLIONE FENILE	43	2	PRAMOLLO	189	1
CANDIA CANAVESE	44	9	PRAROSTINO	190	2
CANDIOLO	45	1	PRASCORSANO	191	2
CANISCHIO	46	2	PRATIGLIONE	192	1
CANTALUPA	47	1	QUAGLIUZZO	193	2
CANTOIRA	48	3	QUASSOLO	194	6
CAPRIE	49	4	QUINCINETTO	195	2
CARAVINO	50	3	REANO	196	2
CAREMA	51	5	RIBORDONE	197	6
CARIGNANO	52	6	RIVA PRESSO CHIERI	198	3
CARMAGNOLA	53	2	RIVALBA	199	1
CASALBORGONE	54	2	RIVALTA DI TORINO	200	2
CASCINETTE D'IVREA	55	3	RIVARA	201	1
CASELETTE	56	5	RIVAROLO CANAVESE	202	10
CASELLE TORINESE	57	5	RIVAROSSA	203	2
CASTAGNETO PO	58	2	RIVOLI	204	5
CASTAGNOLE PIEMONTE	59	2	ROBASSOMERO	205	1
CASTELLAMONTE	60	8	ROCCA CANAVESE	206	1
CASTELNUOVO NIGRA	61	5	ROLETTO	207	1
CASTIGLIONE TORINESE	62	3	ROMANO CANAVESE	208	2
CAVOUR	63	1	RONCO CANAVESE	209	9
CERCENASCO	64	1	RONDISSONE	210	1
CERES	65	5	RORA'	211	2
CERESOLE REALE	66	4	ROSTA	212	1
CESANA TORINESE	67	1	RUBIANA	213	8
CHIALAMBERTO	68	5	RUEGLIO	214	2
CHIANOCCO	69	1	SALASSA	215	2
CHIERI	70	4	SALBERTRAND	216	2
CHIESANUOVA	71	1	SALERANO CANAVESE	217	1
CHIOMONTE	72	1	SAMONE	218	2
CHIUSA DI SAN MICHELE	73	2	SAN BENIGNO CANAVESE	219	3
CHIVASSO	74	8	SAN CARLO CANAVESE	220	2
CICONIO	75	1	SAN COLOMBANO BELMONTE	221	1
CINTANO	76	1	SAN DIDERO	222	2
CINZANO	77	1	SAN FRANCESCO AL CAMPO	223	1
CIRIE'	78	8	SAN GERMANO CHISONE	224	1
CLAVIERE	79	1	SAN GILLIO	225	8
COASSOLO TORINESE	80	2	SAN GIORGIO CANAVESE	226	2
COAZZE	81	2	SAN GIORIO DI SUSA	227	3
COLLEGNO	82	13	SAN GIUSTO CANAVESE	228	1
COLLERETTO CASTELNUOVO	83	3	SAN MARTINO CANAVESE	229	2
COLLERETTO GIACOSA	84	1	SAN MAURIZIO CANAVESE	230	2
CONDOVE	85	1	SAN MAURO TORINESE	231	2
CORIO	86	2	SAN PIETRO VAL LEMINA	232	1
COSSANO CANAVESE	87	2	SAN PONSO	233	1
CUCEGLIO	88	2	SAN RAFFAELE CIMENA	234	2
CUMIANA	89	1	SAN SEBASTIANO DA PO	235	1
CUORGNE'	90	3	SAN SECONDO DI PINEROLO	236	1
DRUENTO	91	8	SANGANO	237	5
EXILLES	92	1	SANT'AMBROGIO DI TORINO	238	4
FAVRIA	93	2	SANT'ANTONINO DI SUSA	239	9
FELETTO	94	2	SANTENA	240	2
FIANO	95	1	SAUZE DI CESANA	241	1
FIORANO CANAVESE	96	2	SAUZE D'OULX	242	2
FOGLIZZO	97	2	SCALENGHE	243	2
FORNO CANAVESE	98	3	SCARMAGNO	244	6
FRASSINETTO	99	8	SCIOLZE	245	1
FRONT	100	2	SESTRIERE	246	1
FROSSASCO	101	2	SETTIMO ROTTARO	247	2
GARZIGLIANA	102	1	SETTIMO TORINESE	248	11
GASSINO TORINESE	103	6	SETTIMO VITTONE	249	1

Table A5. *Cont.*

Municipality Name ID	Number ID	Samples Analysed	Municipality Name ID	Number ID	Samples Analysed
GERMAGNANO	104	1	SPARONE	250	1
GIAGLIONE	105	2	STRAMBINO	251	1
GIAVENO	106	10	SUSA	252	9
GIVOLETTO	107	3	TAVAGNASCO	253	3
GRAVERE	108	1	TORINO	254	54
GROSCAVALLO	109	1	TORRAZZA PIEMONTE	255	1
GROSSO	110	1	TORRE CANAVESE	256	2
GRUGLIASCO	111	7	TORRE PELLICE	257	3
INGRIA	112	1	TRANA	258	1
INVERSO PINASCA	113	1	TRAUSELLA	259	2
ISOLABELLA	114	1	TRAVERSELLA	260	6
ISSIGLIO	115	2	TROFARELLO	261	1
IVREA	116	16	USSEAUX	262	1
LA CASSA	117	2	USSEGLIO	263	7
LA LOGGIA	118	8	VAIE	264	3
LANZO TORINESE	119	3	VAL DELLA TORRE	265	5
LEINI'	120	5	VALGIOIE	266	3
LEMIE	121	1	VALPERGA	267	3
LESSOLO	122	3	VAUDA CANAVESE	268	1
LEVONE	123	2	VENARIA REALE	269	30
LOCANA	124	15	VENAUS	270	1
LOMBARDORE	125	2	VEROLENGO	271	3
LOMBRIASCO	126	3	VESTIGNE'	272	2
LORANZE'	127	4	VIALFRE'	273	1
LUGNACCO	128	2	VICO CANAVESE	274	1
LUSERNA SAN GIOVANNI	129	1	VIDRACCO	275	2
LUSERNETTA	130	1	VIGONE	276	1
LUSIGLIE'	131	2	VILLAFRANCA PIEMONTE	277	1
MACELLO	132	1	VILLANOVA CANAVESE	278	1
MAGLIONE	133	1	VILLAR DORA	279	3
MAPPANO	134	1	VILLAR PELLICE	280	5
MARENTINO	135	4	VILLAR PEROSA	281	1
MASSELLO	136	1	VILLARBASSE	282	7
MATHI	137	2	VILLAREGGIA	283	2
MATTIE	138	4	VILLASTELLONE	284	3
MAZZE'	139	1	VINOVO	285	6
MEANA DI SUSA	140	2	VIRLE PIEMONTE	286	1
MERCENASCO	141	1	VISCHE	287	2
MEUGLIANO	142	2	VISTRORIO	288	1
MEZZENILE	143	4	VIU'	289	3
MOMBELLO DI TORINO	144	2	VOLPIANO	290	5
MOMPANTERO	145	1	VOLVERA	291	6
MONASTERO DI LANZO	146	2			

Figure A3. A map of the municipalities monitored in this study.

Table A6. A comparison of standard methods for PFAS analysis [3].

Standard Method	EPA 537	ISO 25101:2029(E)	ASTM D7979-16	ASTM D7868-14
Sample volume	250 mL	500 mL	5 mL	2 g
Sample matrix	Drinking water	Drinking water, groundwater, surface water and seawater	Water; wastewater sludge, influent and effluent	Solid and biosolid
Analytes	PFAS and FOSAAs 14 PFAS	PFOS and PFOA	PFAS, FOSAAs, FTSs, n:2 FTUCAs and FTCAs	PFAS, FOSAAs, FTSs, n:2 FTUCAs and FTCAs
Preservation	Trizma for buffering and removal of free chlorine	Sodium thiosulfate pentahydrate for removal of free chlorine	None	None
Holding time	Before extraction: 14 days refrigerated at $\leq$6 °C Postextraction: 28 days at room temperature	14 days at 4 $\pm$ 2 °C	28 days at 0–6 °C	28 days at 0–6 °C
Extraction Method	SPE-WAX (SPE Weak anion exchange)	SPE	Direct injection	Solvent extraction followed by filtration using polypropylene filters
Analytical instrument	LC-MS/MS (liquid chromatography tandem with mass spectrometry)	LC-MS/MS and LC/MS	LC-MS/MS	LC-MS/MS
Reporting limits	2.9–14 ng/L	2–10,000 ng/L	10–400 ng/L	25–1000 ng/L

References

1. Haukås, M.; Berger, U.; Hop, H.; Gulliksen, B.; Gabrielsen, G.W. Bioaccumulation of per- and polyfluorinated alkyl substances (PFAS) in selected species from the Barents Sea food web. *Environ. Pollut.* **2007**, *148*, 360–371. [CrossRef] [PubMed]

2. Hedlund, J. Per- and Polyfluoroalkyl Substances (PFASs) in Swedish Waters. 10 June 2016. Available online: https://stud.epsilon.slu.se/9187/ (accessed on 13 December 2018).

3. Dasu, K.; Kempisty, D.M.; Millis, M.A. Per- and polufluoroalkyl substance analysis to support site characterization, exposure, and risk management. In *Perfluoroalkyl Substances in the Environment | Theory, Practice, and Innovation*, 1st ed.; Series: Environmental and occupational health series; Kempisty, D.M., Xing, Y., Racz, L., Eds.; CRC Press Taylor & Francis: Boca Raton, FL, USA, 2018; pp. 35–66, ISBN 9781498764186.

4. Xiao, F. Emerging poly- and perfluoroalkyl substances in the aquatic environment: A review of current literature. *Water Res.* **2017**, *124*, 482–495. [CrossRef] [PubMed]

5. Buck, R.C.; Franklin, J.; Berger, U.; Conder, J.M.; Cousins, I.T.; De Voogt, P.; Jensen, A.A.; Kannan, K.; Mabury, S.A.; van Leeuwen, S.P. Perfluoroalkyl and polyfluoroalkyl substances in the environment: Terminology, classification, and origins. *Integr. Environ. Assess. Manag.* **2011**, *7*, 513–541. [CrossRef] [PubMed]

6. Ahrens, L. Polyfluoroalkyl compounds in the aquatic environment: A review of their occurrence and fate. *J. Environ. Monit.* **2011**, *13*, 20–31. [CrossRef] [PubMed]

7. Krafft, M.P.; Riess, J.G. Selected physicochemical aspects of poly- and perfluoroalkylated substances relevant to performance, environment and sustainability—Part one. *Chemosphere* **2015**, *129*, 4–19. [CrossRef] [PubMed]

8. Zhang, W.; Zhang, Y.; Taniyasu, S.; Yeung, L.W.; Lam, P.K.; Wang, J.; Li, X.; Yamashita, N.; Dai, J. Distribution and fate of perfluoroalkyl substances in municipal wastewater treatment plants in economically developed areas of China. *Environ. Pollut.* **2013**, *176*, 10–17. [CrossRef] [PubMed]

9. Paul, A.G.; Jones, K.C.; Sweetman, A.J. A first global production, emission, and environmental inventory for perfluorooctane sulfonate. *Environ. Sci. Technol.* **2009**, *43*, 386–392. [CrossRef] [PubMed]

10. Kotthoff, M.; Bücking, M. Four chemical trends will shape the next decade's directions in perfluoroalkyl and polyfluoroalkyl substances research. *Front. Chem.* **2018**, *6*, 103. [CrossRef] [PubMed]

11. Wolf, S.T.; Reagen, W.K. Method and validation for the analysis of perfluorinated compounds in water by pre-sampling isotope dilution-direct injection-LC/MS/MS. *Anal. Methods* **2013**, *5*, 2444–2454. [CrossRef]

12. Gosettia, F.; Chiuminatto, U.; Zampieri, D.; Mazzucco, E.; Robotti, E.; Calabrese, G.; Gennaro, M.C.; Marengo, E. Determination of perfluorochemicals in biological, environmental and food samples by an automated on-line solid phase extraction ultra high performance liquid chromatography tandem mass spectrometry method. *J. Chromatogr. A* **2010**, *1217*, 7864–7872. [CrossRef] [PubMed]

13. Furdui, V.I.; Crozier, P.W.; Reiner, E.J.; Mabury, S.A. Trace level determination of perfluorinated compounds in water by direct injection. *Chemosphere* **2008**, *73*, S24–S30. [CrossRef] [PubMed]

14. Ciofi, L.; Renai, L.; Rossini, D.; Ancillotti, C.; Falai, A.; Fibbi, D.; Bruzzoniti, M.C.; Santana-Rodriguez, J.J.; Orlandini, S.; Del Bubba, M. Applicability of the direct injection liquid chromatographic tandem mass spectrometric analytical approach to the sub-ng L−1 determination of perfluoro-alkyl acids in waste, surface, ground and drinking water samples. *Talanta* **2018**, *176*, 412–421. [CrossRef] [PubMed]

15. Gu, H.; Liu, G.; Wang, J.; Aubry, A.-F.; Arnold, M.E. Selecting the correct weighting factors for linear and quadratic calibration curves with least-squares regression algorithm in bioanalytical LC-MS/MS assays and impacts of using incorrect weighting factors on curve stability, data quality, and assay performance. *Anal. Chem.* **2014**, *86*, 8959–8966. [PubMed]

16. Taniyasu, S.; Kannan, K.; So, M.K.; Gulkowska, A.; Sinclair, E.; Okazawa, T.; Yamashita, N. Analysis of fluorotelomer alcohols, fluorotelomer acids, and short- and long-chain perfluorinated acids in water and biota. *J. Chromatogr. A* **2005**, *1093*, 89–97. [CrossRef] [PubMed]

17. Yamashita, N.; Kannan, K.; Taniyasu, S.; Horii, Y.; Okazawa, T.; Petrick, G.; Gamo, T. Analysis of perfluorinated acids at parts-per-quadrillion levels in seawater using liquid chromatography-tandem mass spectrometry. *Environ. Sci. Technol.* **2004**, *38*, 5522–5528. [CrossRef] [PubMed]

18. Wille, K.; Bussche, J.V.; Noppe, H.; De Wulf, E.; Van Caeter, P.; Janssen, C.R.; De Brabander, H.F.; Vanhaecke, L. A validated analytical method for the determination of perfluorinated compounds in surface-, sea- and sewagewater using liquid chromatography coupled to time-of-flight mass spectrometry. *J. Chromatogr. A* **2010**, *1217*, 6616–6622. [CrossRef] [PubMed]

19. Pasáková, I.; Klimeš, J.; Sochor, J.; Hrabálek, A. Optimization of HPLC chromatographic conditions for determination of Transkarbam 12 and its degradation products. *J. Pharm. Biomed. Anal.* **2006**, *42*, 136–142. [CrossRef] [PubMed]

20. GeoPortale ARPA Piemonte. Available online: http://webgis.arpa.piemonte.it/geoportale/ (accessed on 10 October 2018).

21. Story Map Series. Available online: http://webgis.arpa.piemonte.it/monitoraggio_qualita_acque_mapseries/monitoraggio_qualita_acque_webapp/ (accessed on 13 October 2018).

22. DIVA-GIS | Free, Simple & Effective. Available online: http://www.diva-gis.org/ (accessed on 11 November 2018).

23. Gamerman, D.; Moreira, A.R.B. Multivariate spatial regression models. *J. Multivar. Anal.* **2004**, *91*, 262–281. [CrossRef]

24. Hu, X.C.; Andrews, D.Q.; Lindstrom, A.B.; Bruton, T.A.; Schaider, L.A.; Grandjean, P.; Lohmann, R.; Carignan, C.C.; Blum, A.; Balan, S.A.; et al. Detection of poly- and perfluoroalkyl substances (PFASs) in U.S. drinking water linked to industrial sites, military fire training areas, and wastewater treatment plants. *Environ. Sci. Technol. Lett.* **2016**, *3*, 344–350. [CrossRef]