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# The underlying challenges that arise when analysing short-chain chlorinated paraffins in environmental matrices

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## ABSTRACT

As short-chain chlorinated paraffins (SCCPs) are listed on several monitoring programs, validated methods are essential. However, their complexity and the lack of commercially available certified reference materials (RMs) hinder a proper validation of methods. Instead, one method is usually 'validated' by evaluating performances and results of spiked materials with that of one other method, which could easily lead to unreliable results.

This study evaluated four analytical methods with different principles (i.e. comprehensive two dimensional GC coupled to a micro electron capture detector, developed for this study, chloride enhanced atmospheric pressure chemical ionization triple quadrupole time of flight MS (APCI-QToF-HRMS), GC coupled to an electron capture negative ion low resolution MS (GC-ECNI-LRMS) and carbon skeleton GC-MS), investigated the comparability in SCCC determination in spiked and naturally contaminated samples and determined SCCC amounts in candidate RMs for possible certification.

The results cast doubt on the use of the most commonly applied method (i.e. GC-ECNI-LRMS), as well as using spiked materials for method validation. The APCI-QToF-HRMS method was found most promising as it achieves the required MS resolution (>21,000), is relatively fast and can detect also other CPs. The suitable identified SCCC levels in the candidate RMs and the agreement in results between the methods bring the first certification of a RM for SCCC within reach.

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## 1. Introduction

Chlorinated paraffins (CPs) are multi-congener mixtures of more than 10,000 different polychlorinated *n*-alkanes with a chlorine content between 20 and 70%, weight basis [1]. Based on their carbon chain length, CPs are typically divided into short- ( $C_{10-13}$ ), medium- ( $C_{14-17}$ ) and long- ( $C_{>17}$ ) chain CPs. In some countries (e.g. China, the largest CP producer worldwide), the manufacturers categorize commercial CP mixtures based on their chlorine content rather than carbon chain length (e.g. CP-52 with  $C_{10-20}$ ), as the application is usually dependent on chlorine content [2]. CPs have many applications, including as plasticisers in polyvinyl chloride (PVC) products, coolants in metal cutting fluids and lubricants in leather liquoring [3]. Production volumes are high

(>1 million tonnes/year in China alone, [4]) and concerns are rising about their ubiquitous presence in the environment as well as their hazard potential. For example, short-chain CPs (SCCPs) have been classified as persistent organic pollutants (POPs) by the United Nations Stockholm Convention since 2017 and are included in several monitoring lists such as the European Union Water Framework Directive [5].

With their recently acquired POP status, SCCCs will be monitored in the environment by an increasing number of laboratories. This requires reliable analytical methods and agreement in results between laboratories. However, recent proficiency tests show large differences in reported SCCC levels for the same samples (naturally contaminated) between laboratories (up to 137% coefficient of variation) [6]. This is mainly due to their challenging determination, as described extensively elsewhere [7]. Briefly, their response on detection systems is relatively low, depends on the chlorine content and complete chromatographic separation is unachievable because of the continuum in their congener (i.e. CPs with the same structure, for example 2,5,6,9-tetrachlorodecane). Due to weathering effects, congener group (i.e. congeners with a fixed chain length (*n*) and number of chlorines (*m*), expressed as  $C_mCl_n$  and for

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example  $C_{10}Cl_4$ ) patterns in samples might differ from those in mixtures used for quantification, which can lead to quantification errors. Suitable individual congeners to be used as markers, are not available or cannot be separated from the bulk of the other congeners present. Different approaches have been trialed to address these challenges with varying success [7,8].

The current most commonly applied method [6], the GC coupled to negative chemical ionization low resolution mass spectrometry (GC-ECNI-LRMS), has some disadvantages. For example, lower chlorinated CPs (CPs with less than 5 chlorine atoms) are hardly detectable, the resolution (ca. 1000) is too low to separate CPs from each other and from other compounds, and the data processing is time consuming [9]. Alternative approaches have been reported including carbon skeleton GC-MS (CSk-GC-LRMS) in which CPs are catalytically hydrodechlorinated to the corresponding *n*-alkanes [10]. This reduces the complexity and simplifies the calibration step. Another alternative approach is the recently developed chloride enhanced atmospheric pressure chemical ionization triple quadrupole time of flight high resolution MS (APCI-QToF-HRMS) method [11], with a fast analysis time (<2 min) and higher resolution ( $R > 10,000$ ) compared to the LRMS. Alternative approaches that have been suggested are the use of even higher resolution MS ( $R=20,500$ ) and instead of single GC, comprehensive two-dimensional GC (GC  $\times$  GC) [7].

Validation of a method requires, besides proficiency tests, materials with a consensus value of SCCPs in preferably naturally contaminated matrices (i.e. similar to that of 'real' environmental samples), also known as certified reference materials (RMs). Because certified RMs for SCCPs are still commercially unavailable, methods are usually 'validated' by testing the accuracy with a spiked solution or spiked sample and comparing the performances with only one other method such as GC-ECNI-LRMS [11–14]. The use of spiked samples or solutions does not account for the differences found in congener group patterns between samples and standards. Using such a comparison for validation is not ideal because systematic errors can easily occur [15] and an agreement between two (similar) methods cannot guarantee accuracy.

The aims of this work were therefore to a) evaluate four different methods for SCCP analysis to point out the advantages and limitations, i.e. GC  $\times$  GC, developed for this study, APCI-QToF-HRMS, adapted for this study with a resolution of >20,500, the commonly applied GC-ECNI-LRMS and the CSk-GC-LRMS, b) investigate the comparability in SCCP determination in spiked and naturally contaminated samples with these four methods and c) determine SCCP amounts in candidate RMs.

## 2. Materials and methods

Information about the standards, chemicals, suppliers and sample preparation is provided in the supporting information (S1-2).

### 2.1. Samples

The candidate RMs analysed were existing certified RMs for other compounds: ERM-CE100, Wels catfish (*Silurus glanis*) tissue from Ebro River, Spain, certified for hexachlorobenzene and hexachlorobutadiene [16], BCR 481, industrial soil from Antwerp, Belgium, certified for polychlorobiphenyls (PCBs) [17], and CCQM-K102, a "trial" batch of ERM-CC537a, freshwater sediment from a small river in Belgium, certified for polybrominated flame retardants [18].

### 2.2. Analytical methods

The four different approaches selected for this study are summarized in Table 1. The GC  $\times$  GC- $\mu$ ECD method developed for this study used an Agilent Capillary Flow Technology Modulator. A non-polar first dimension HP-5MS column, 30 m  $\times$  0.25 mm  $\times$  0.25  $\mu$ m (J&W, Agilent), was combined with a mid-polar second dimension capillary ZB-50 column, 5 m  $\times$  0.25 mm  $\times$  0.15  $\mu$ m (Phenomenex, USA). Constant hydrogen flow rates were set at 1.3 mL/min and 22 mL/min in the first and second dimension, respectively. The modulation period was set at 4 s. The temperature programming was as follows: held at 90 °C (2 min) then ramped to 180 °C at 10 °C/min (2 min), then ramped to 280 °C at 1.5 °C/min and then ramped to 320 °C at 30 °C/min (10 min). The  $\mu$ ECD operated at 300 °C with a 50 Hz acquisition rate. The make-up gas was nitrogen with a flow rate of 115 mL/min. Two software programs were used for data acquisition and processing: ChemStation (version B.04.01, Agilent Technologies) for system control and data acquisition; and GC Image software (version R2.4b, Zoex Corp, Texas, USA) for data visualization and data processing.

GC-Image can detect congeners and present them as dots (Fig. S1, red dots). Unfortunately, identification of congeners is still impossible due to the lack of suitable commercially available standards [7]. The CP groups appear as roof tiles in the contour plots (Fig. S1, orange ellipses). By using mixtures of  $C_{10}$ ,  $C_{11}$ ,  $C_{12}$ , and  $C_{13}$  with different chlorination degrees, it is possible to confirm the composition of the structured bands of CPs [19–21], with each band containing a constant number of carbon-plus-chlorine number. In this way, CPs with the same number of carbon-plus-chlorine atoms (C+Cl) can be categorised as one class (ellipse), according to its corresponding (C+Cl) number (C+Cl)<sub>n</sub>. For example, CP class 15 contained all SCCP congener groups  $C_{11}Cl_4$ ,  $C_{12}Cl_3$  and  $C_{13}Cl_2$ . The most intense peaks (or dots) were selected for quantitation. Identification of the CPs within the CP classes was based on the comparison of retention times between the SCCP mixture standards and samples.

The APCI-QToF-HRMS method used is according to Brandsma et al. [22]. The system consisted of a Triple TOF 5600+ (Sciex, Concord, Ontario, Canada) operated in APCI mode and a Shimadzu Nexera HPLC system (Shimadzu Corp., Kyoto, Japan). Injection was performed without a column, using acetonitrile (99.99%) as eluent with an isocratic flow of 250  $\mu$ L/min. Dichloromethane was used

**Table 1**  
Overview of the four methods and type of samples analysed in this study.

	I	II	III	IV
Method	GC-ECNI-LRMS	GC $\times$ GC- $\mu$ ECD	APCI-QToF-HRMS	CSk-GC-LRMS
References	[24]	This study	[11,22]	[26]
Quantification	Chlorine content & response factor <sup>a</sup>	Chlorine content & response factor <sup>a</sup>	Chlorine content & response factor <sup>a</sup>	External calibration
References	[24,27]	[24]	[24]	[26]
Samples analysed	Spiked solution Spiked samples <sup>b</sup> Candidate CRMs	Spiked solution Spiked samples <sup>b</sup> Candidate CRMs	Spiked solution Spiked samples <sup>b</sup> Candidate CRMs	- - Candidate CRMs

<sup>a</sup> Linear relationship between calculated chlorine content (%) and response factor, adapted from Reth et al. [24] and Friden et al. [27].

<sup>b</sup> Fish and Sediment.

as a dopant at a flow rate of 40  $\mu\text{L}/\text{min}$  and mixed with the eluent just before entering the ion source. The nebulizer temperature was set to 200  $^{\circ}\text{C}$ , the declustering potential (DP) at  $-90\text{ V}$  and the collision energy (CE) at  $-10\text{ V}$ . The full scan range of  $m/z$  200 to 1,500 was monitored, with a minimal resolution of 21,100 ( $m/z$  213.0997). External mass calibration was performed with the Sciex APCI Negative Calibration solution 5,600 that consists of a mix of known molecular weight polypropylene glycols (PPGs). In total 558  $m/z$  ratios were extracted from the full scan mass spectra extracted with a  $m/z$  window extraction range of ca. 0.0025 Da ( $<18\text{ ppm}$ ) using MultiQuant 3.0 software (Sciex), which are related to the two most abundant  $m/z$  signals of the CP congener groups with chain lengths of  $\text{C}_{10}\text{Cl}_3$  to  $\text{C}_{27}\text{Cl}_{27}$  according to Bogdal et al. [11].

For the GC-ECNI-LRMS method an Agilent (Santa Clara, CA, USA) 6890 GC with an Agilent Model 7683 auto sampler and an Agilent Model 5975C inert MSD was used. Injection was pulsed-splitless at 275  $^{\circ}\text{C}$ . The column used was a DB-1 (J&W Scientific, Rancho Cordova, CA, USA), 50 m length, 0.25 mm internal diameter and 0.25  $\mu\text{m}$  film thickness. The temperature program was as follows: 90  $^{\circ}\text{C}$  for 2 min, at 30  $^{\circ}\text{C}/\text{min}$  to 290  $^{\circ}\text{C}$ , at 15  $^{\circ}\text{C}/\text{min}$  to 325  $^{\circ}\text{C}$ , and 7 min at 325  $^{\circ}\text{C}$ . The (constant) helium gas flow rate was 1.0 mL/min. Detection was performed by a mass selective detector (MSD).

CPs with the same formula, i.e. of the same congener group, were identified based on an existing method (cited accordingly below), with some modifications. The two most abundant  $m/z$  values (e.g. ions) recorded for CP congener groups with chain lengths of  $\text{C}_{10}\text{Cl}_5$  to  $\text{C}_{13}\text{Cl}_{10}$  were monitored as outlined by Reth and Oehme [9] with a  $m/z$  window extraction range of ca. 0.9 Da ( $<361\text{ ppm}$ ). In addition,  $m/z$  values of MCCPs were monitored to check for MCCP presence. To improve the instrument sensitivity and identification, the ion signals of CP congener groups were divided into four groups according to Zeng et al. [23]:  $\text{C}_{10}$  and  $\text{C}_{15}$ , and  $\text{C}_{11}$  and  $\text{C}_{16}$ ,  $\text{C}_{12}$  and  $\text{C}_{17}$ , and  $\text{C}_{13}$  and  $\text{C}_{14}$ . In total 85  $m/z$  values were selected for monitoring, requiring four injections for each sample and standard, monitoring up to 20–25  $m/z$  values per injection. PCB-26 ( $m/z$  221) was monitored per injection as internal standard. Identification of the CP congener groups was based on the comparison of signal shape and retention time on the selected ion signals between the SCCP mixture standards and samples according to Reth, et al. [24]. For data obtained by GC-ECNI-LRMS, ChemStation was used for data processing (version B.04.01, Agilent Technologies)

The GC-CSk-MS method applied is according to Pellizzato et al. [10]. In brief, this method de-chlorinates the CPs in the liner with a palladium catalyst into the corresponding linear alkanes. The palladium catalyst was prepared by dissolving 0.08 g of palladium chloride (59% palladium anhydrous for synthesis) in 10 mL of hot 5% acetic acid under stirring. Then, the solution was mixed with 19 g of sand white quartz powder and dried under stirring in a steam bath for 10 min. The residue was taken up in distilled water and dried after pH adjustment to 9 with ammonia solution. The catalyst was washed with 50 mL of cyclohexane in a sintered glass funnel and completely dried before use. Then, a new GC single tapered liner (i.d. 4 mm) was packed by insertion from the bottom to top with: 0.5 cm glass wool, 0.2 cm of calcium carbonate, 1.6 cm of palladium catalyst and 0.5 cm glass wool. Glass wool, calcium carbonate and the liner were baked at 300  $^{\circ}\text{C}$  for 4 hrs prior to the packing to remove possible organic contaminants. The liner was then activated for at least 6 h inside the GC injector at 300  $^{\circ}\text{C}$  and at 1 mL/min of helium flow.

The injector was operated in splitless mode and 1  $\mu\text{L}$  was injected at a temperature of 300  $^{\circ}\text{C}$ . The carrier gas was helium at 2 mL/min. Chromatographic separation was performed on a J&W DB-5MS, 30 m  $\times$  0.25 mm  $\times$  0.25  $\mu\text{m}$  and the temperature program started with 50  $^{\circ}\text{C}$  for 3 min, ramped by 10  $^{\circ}\text{C}/\text{min}$  to 280  $^{\circ}\text{C}$ , and held at 280  $^{\circ}\text{C}$  for 10 min. The MS was operated in electron ion-

ization (EI) mode at 70 eV, with a SIM mode detection (mass accuracy of  $\pm 0.6\text{ Da}$ ) using quantification ion 57 (41 for the internal standard) and qualification ion 71, 98, 85, 99 for the 4 alkanes ( $\text{C}_{10}$ ,  $\text{C}_{11}$ ,  $\text{C}_{12}$ ,  $\text{C}_{13}$ ) and internal standard. Quantification ion 57 was chosen as the typical quantification ion detected for linear alkanes representing the  $[\text{C}_4\text{H}_9]^+$  fragment. The other ions chosen for qualification purposes (i.e. 71, 85 and 99) correspond to fragments that differ by 14 mass units (formed by the cleavage of the bonds between the different  $-\text{CH}_2-$  units). The molecular ion of the alkanes was not chosen because of its very low intensity.

The conversion efficiency of the catalyst was tested with each batch. It was calculated as the percentage of moles of alkanes experimentally found compared to the theoretical moles of  $n$ -alkanes expected upon injection of a control sample with an approximate chlorination degree of 60% (mix at known concentration of 5 single SCCP congener groups:  $\text{C}_{10}\text{Cl}_6 + \text{C}_{11}\text{Cl}_6 + \text{C}_{12}\text{Cl}_6 + \text{C}_{12}\text{Cl}_8 + \text{C}_{13}\text{Cl}_8$ , each standard purchased from Chiron, Trondheim Norway). The conversion efficiency was used to check the performance of the catalyst and to decide when to replace the liner (either when the average conversion efficiency falls below the threshold value of 50% or when the RSD of three replicate injections raises above 5%).

The APCI-QToF-HRMS method was applied in two proficiency tests in 2017 [6,25] for which the results were in agreement with other participating laboratories (i.e. satisfactory,  $z$ -scores  $<2$ ). The GC  $\times$  GC- $\mu\text{ECD}$  and GC-ECNI-LRMS method participated in one proficiency test [6], for which the results by GC  $\times$  GC- $\mu\text{ECD}$  were satisfactory too, while the GC-ECNI-LRMS was somewhat low (questionable  $2 < z$ -scores  $<3$ ). In addition to the chlorine quantification method used in this study, the deconvolution quantification method for the APCI-QToF-HRMS [11] was also applied in one proficiency test [6]. The results using the deconvolution quantification method were similar to that using the quantification method used in this study (3.9% difference) and satisfactory. The CSk-GC-LRMS method was applied in two proficiency tests, one with satisfactory results [26], while the other one was unsatisfactory ( $3 < z$ -scores  $<6$ ) [6].

### 2.3. Quantification

SCCPs were quantified in the candidate RMs as sum of total SC-CPs ( $\Sigma\text{SCCPs}$ ) using two different quantification methods. In the first method used with CSk-GC-LRMS data, the response is independent of the chlorine content. Quantification was accomplished by external calibration according to Pellizzato et al. [10] and described in S3. The second quantification method, an adaptation of Reth et al. [24] and Friden et al. [27], was applied to the GC-ECNI-LRMS data and, for the first time, also to the APCI-QToF-HRMS and the GC  $\times$  GC- $\mu\text{ECD}$  data. The method corrects for differences in the chlorine contents found between reference CP mixtures and the CPs present in environmental samples. In brief, a linear correlation between the log total response factors of up to five SCCP standard mixtures and the chlorine content was obtained for the data of all three instruments ( $R^2 > 0.88$ ; Fig. S2). The minor modifications of the method for the data of the GC-ECNI-LRMS and APCI-QToF-HRMS can be found in the supporting information (S3). The modifications for the GC  $\times$  GC- $\mu\text{ECD}$  were as follows. Instead of congener groups, the total volume (i.e. area) of a CP class  $(\text{C}+\text{Cl})_n$  was normalized by dividing by the area of the internal standard ion in the same injection. For calculation of the relative fractions of CP classes, the sum of all normalised CP class areas of a given standard or sample was set to 1. Instead of calculating the chlorine content per congener group as in GC-ECNI-LRMS, chlorine content was calculated per class  $(\text{C}+\text{Cl})_n$ . Chlorine content of a class was derived by the sum of the molecular mass of the chlorine atoms in that class divided by the sum of total molecular mass of the congener groups represented by that class.



Relative standard errors (RSEs) for the calibration models used in this study were derived according to EPA [28] by the following equation:

$$RSE = \sqrt{\frac{\sum RE^2}{(n-2)}} \quad (1)$$

where RE is the relative error between the theoretical and the calculated concentration (i.e. by the quantification method) of each calibration point of every standard mixture (i.e. SCCP 51.5%, 55.5% and 63% chlorine content) and n is the total number of calibration points.

#### 2.4. Quality assurance and control

Instrument limit of detection (LOD<sub>i</sub>) was determined at a signal-to-noise ratio of >3:1 with the lowest standard of technical 51.5% chlorine content SCCP mixture, while the instrument limit of quantification (LOQ<sub>i</sub>) was determined at a signal to noise ratio >10:1 (Table 2). The linearity of the calibration model was sufficient for a concentration between 1 and 30 ng/μL technical SCCPs (R<sup>2</sup> > 0.99, 5 points per mixture) for all GC instruments and 0.1 to 20 ng/μL for the APCI-QToF-HRMS method (R<sup>2</sup> > 0.99, 6 points per mixture).

Glassware was rinsed before use with acetone and hexane, and a pilot trial was carried out before the procedure to screen for background levels of SCCPs (below LOD<sub>i</sub>) and estimate an appropriate sample amount for extraction. Quality controls such as blanks and performance of the extraction methods (i.e. recoveries) were implemented. Laboratory blanks, consisting of 3 g diatomaceous earth, were extracted and analysed alongside each batch (n = 3), for which values were below LOQ<sub>i</sub> (Table 2). The LOQ<sub>i</sub> was used to determine the method detection limit (MDL) by multiplying the mass of LOQ<sub>i</sub> by the final volume used in the method (i.e. 250 μL) and dividing it by the grams extracted for a sample. In addition, a set of three (triplicate) 7 g of freeze-dried sediment and 2 g of freeze-dried fish samples were analysed with and without a spiked SCCP mixture (2,000 ng, 55.5% chlorine content). The analysis of all samples was performed in triplicate. Recoveries ranged from 80 to 107% for fish and from 62 to 117% for sediment.

### 3. Results and discussion

#### 3.1. Analytical performance

An overview of the performance of the four approaches of SCCP analysis is presented in Table 2. The APCI-QToF-HRMS method achieved the lowest detection limits (Table 2), while CSK-GC-LRMS achieved the lowest quantification limits, although the latter limit is for n-alkanes. Other reported LOD<sub>i</sub>'s (1 ng/μL [24]), LOQs (2 ng/μL [24]) and MDLs (10–20 ng/g wet weight for biota and 50 ng/g dry weight for sediments) for the GC-ECNI-LRMS method [29] were similar to this study.

In addition to the SCCP analysis, detection limits for medium-chain CPs (MCCPs) and long-chain CPs (LCCPs) were also determined for the APCI-QToF-HRMS method, which were even lower than that of SCCPs (Table S1). MCCPs and LCCPs are difficult to analyze by GC (LOD<sub>i</sub> 10 and 100 ng/μL, respectively [29]), because of their low volatility, which requires high oven temperatures.

GC-ECNI-LRMS can only detect SCCPs with more than four chlorine atoms [30]. It is insensitive for molecules with less chlorine atoms, as was reported earlier for polychlorinated dibenzodioxins and PCBs [31]. Furthermore, the mass range for all SCCPs is too large to run in a single analysis and ensure high sensitivity. Therefore, the analysis is limited to SCCPs with 5 to 10 chlorine atoms, with usually four injections [23]. All SCCPs can be detected by GC × GC-μECD and CSK-GC-LRMS, although congener group

**Table 2**  
Overview of performance parameters of the methods used for SCCP determination in sediment and biota.

Method	LOD <sub>i</sub> ng/μL <sup>a</sup>	LOQ <sub>i</sub> ng/μL <sup>b</sup>	MDL ng/g dw <sup>c</sup>	Detection of Cl <sub>n</sub> -SCCPs	Resolution	Injections(n)	Acquisition time	Quantification error (RSE) <sup>d</sup>	Repeatability instrument (RSD) <sup>e</sup>
GC-ECNI-LRMS	<0.7	<1.4	16	Cl <sub>5-10</sub>	1,000	4	4 × 20 min	23%	2–9%
GC × GC-μECD	<1	<3.6	48	all	NA	1	90 min	28%	3–6%
APCI-QToF-HRMS	<0.1	<0.1	7.1	Cl <sub>3-12</sub>	21,100	1	2 min	12%	6–7%
CSK-GC-LRMS	nd	0.04	20–30	all <sup>f</sup>	1,000	1	36 min	4–8%	2–6%

Cl<sub>n</sub> SCCPs with n amount of chlorine atoms LOD<sub>i</sub> instrument limit of detection LOQ<sub>i</sub> instrument limit of quantification MDL Method detection limit nd not determined RF response factor RSE relative standard error RSD Relative standard deviation.

<sup>a</sup> Determined by the lowest standard of SCCP mixture 51.5% chlorine content (by weight) with a S/N >3.

<sup>b</sup> Determined by the lowest standard of SCCP mixture 51.5% chlorine content (by weight) with a S/N >10; equal to the lowest alkane standard used for calibration for CSK-GC-LRMS.

<sup>c</sup> Procedural blanks were <LOQ<sub>i</sub>; LOQ<sub>i</sub> value was used, see text.

<sup>d</sup> According to EPA 8000D [28].

<sup>e</sup> Determined with triplicate injections of test solutions and naturally contaminated environmental extracts provided by a proficiency test [5], and in case of CSK-GC-LRMS triplicate injections of n-alkanes mix standard solution.

<sup>f</sup> While chlorine information is lost due dechlorination step, all Cl<sub>n</sub>-SCCPs congeners are detected.

abundance information is lost. This is because only  $(C+Cl)_n$  classes can be determined with GC  $\times$  GC- $\mu$ ECD and only the carbon number due to the dechlorination by CSk-GC-LRMS. Data without information about chlorination are unlikely to be very meaningful from a fate, toxicological and hazard potential context, since the toxicity of CPs possibly depends on the chlorination [32]. The APCI-QToF-HRMS analysis is limited to SCCPs with less than three chlorine atoms.

Chromatographic separation and unambiguous identification of congeners remains unachieved. The GC  $\times$  GC- $\mu$ ECD method however, has the potential to separate congeners at least of low chlorinated CPs, which makes it promising when suitable congener standards [7] become available. For example, three stereoisomers were identified for one of the few commercially available congener standards, CP-1 (Chiron), 2,5,6,9-tetrachlorodecane (Fig. S3, three stripes), as indicated on the certificate of analysis provided. Regarding separation by mass, the APCI-QToF-HRMS method was the only method with the required resolving power of 20,500 to prevent interference between CPs [33] as well with that of unsaturated CP analogues (i.e. chlorinated olefins) [34].

The APCI-QToF-HRMS method has by far the fastest analysis time. Furthermore, data processing was also faster compared to the three other methods, but in case of the GC-ECNI-LRMS, this could also depend on the different software used.

The RSE acceptance limit for the calibration model (<30% for challenging compounds by EPA [28]) was met for all methods (Table 2). The RSE for the APCI-QToF-HRMS method and CSk-GC-LRMS method was even acceptable for 'good performing' compounds (<20%), although the RSE for the latter method is based on just *n*-alkanes standards. RSE values for SCCPs remain to our knowledge unreported. As the analysis of SCCPs is very challenging, it might be possible that the RSE criteria were unmet. To ensure the quality of the data, we suggest future studies to report RSE values.

The repeatability for the CSk-GC-LRMS method was between 2 and 6%. The repeatability during the run of the GC-ECNI-LRMS, APCI-QToF-HRMS and GC  $\times$  GC- $\mu$ ECD was tested by triplicate injections test materials (solution and extracts) of a proficiency test [6] and resulted in 2–7% RSD (Table 2).

### 3.2. Analysis of the spiked solution and samples

The RSD for the  $\Sigma$ SCCPs levels measured in the spiked solution by the different methods is satisfactory (2%, Table 3, Fig. 1A). The results for the spiked samples are somewhat variable however still with acceptable RSD values (<28%). These results are in line with other reported RSD values for spiked samples measured by different methods (<30%) [35], as well as for spiked solutions

reported in interlaboratory studies (23%) [6], while in the lower range for spiked samples in interlaboratory studies (32–202%) [36]. The relative error (RE) of the spiked solution and samples is acceptable for all instruments too (<29%), and the calculated chlorine content was the same between solution and samples per instrument (<0.6% RSD). The calculated chlorine content found with the three methods deviates from the values specified by the producer (55.5% chlorine content, Table 3) and differ from each other. GC-ECNI-LRMS overestimated the chlorine content the most (5.5%), which has been observed before [24] and is probably caused by not detecting the lower chlorinated SCCPs (with less than 5 chlorine atoms) [30]. APCI-QToF-HRMS and GC  $\times$  GC- $\mu$ ECD overestimated the chlorine content both by 2.3%, which is in line with another method (chloride enhanced GC-NICI-MS) that can detect SCCPs with less than 5 chlorine atoms (1.–2.5%) [37].

### 3.3. Analysis of the candidate certified reference materials

The repeatability between the replicates of the candidate RMs, expressed as RSD, for each method were 11–63% (CSk-GC-LRMS), 15–44% (GC-ECNI-LRMS), 10–22% (GC  $\times$  GC- $\mu$ ECD), and 10–27% (APCI-QToF-HRMS). The reported mass fractions for the candidate RMs differ substantially between methods (RSD>66%, Table 4, Fig. 1D-F), similar to other reported RSD values for naturally contaminated samples reported in interlaboratory studies (47–137%) [6]. Usually, one method reported different results compared to the other three, for which possible explanations are given below.

In the case of the industrial soil BCR 481 (Fig. 1D), mass fractions obtained by GC  $\times$  GC- $\mu$ ECD are 3.5-fold higher than the average level obtained by the other three methods and above the upper inner fence (27,350 ng/g dw), which can be explained by the overflow effect in the chromatogram when high concentrations are injected (identified as vertical blue stripes and indicated with an orange circle Fig. S3) [38]. SCCP levels in this sample are very high (average mass fraction 8700 ng/g dw, excluding GC  $\times$  GC- $\mu$ ECD analysis). While only <1 g sediment was extracted, and of that ca. 2% injected, too much overflow of the response occurred on the chromatogram. Dilution of the extract was essential but unfortunately unfeasible at that time. Because of this technical reason, the results of GC  $\times$  GC- $\mu$ ECD were excluded for the comparison, resulting in an acceptable RSD (21%) between the other three instruments.

For the freshwater sediment CCQM-K102 (Fig. 1E), GC-ECNI-LRMS reported 14-fold lower mass fractions compared to the average of the three other methods. This could be explained by the presence of higher chlorinated congener groups (Fig. 2G and K; SCCPs with more than 10 chlorine atoms) that are undetected by GC-ECNI-LRMS (Fig. 2I). According to Reth et al. [24] CPs with a

**Table 3**  
 $\Sigma$ SCCPs absolute values in spiked samples and solution by three methods.

Samples	APCI-QToF-HRMS	GC $\times$ GC- $\mu$ ECD	GC-ECNI-LRMS	RSD (%)
Spiked solution ( <i>n</i> = 1)				2
$\Sigma$ SCCPs (mean ng absolute)	1,700	1,700	1,700	
Calculated chlorine content (%)	58	58	61	
RE (%)	13	13	15	
Spiked fish <sup>a</sup> ( <i>n</i> = 3)				20
$\Sigma$ SCCPs (mean ng absolute $\pm$ SD)	1,800 $\pm$ 93	2,500 $\pm$ 290	2,400 $\pm$ 600	
Calculated chlorine content (%)	58	58	61	
RE (%)	11	24	19	
Spiked freshwater sediment ( <i>n</i> = 3)				28
$\Sigma$ SCCPs (mean ng absolute $\pm$ SD)	1,400 $\pm$ 170	2,500 $\pm$ 91	1,700 $\pm$ 450	
Calculated chlorine content (%)	58	58	61	
RE (%)	29	26	14	

RSD relative standard deviation of all reported  $\Sigma$ SCCPs levels between the instruments (*n* = 3).

RE Relative error to the expected value of 2,000 ng for a SCCP mixture of 55.5% chlorine content.

<sup>a</sup> Candidate CRM ERM-CE100.

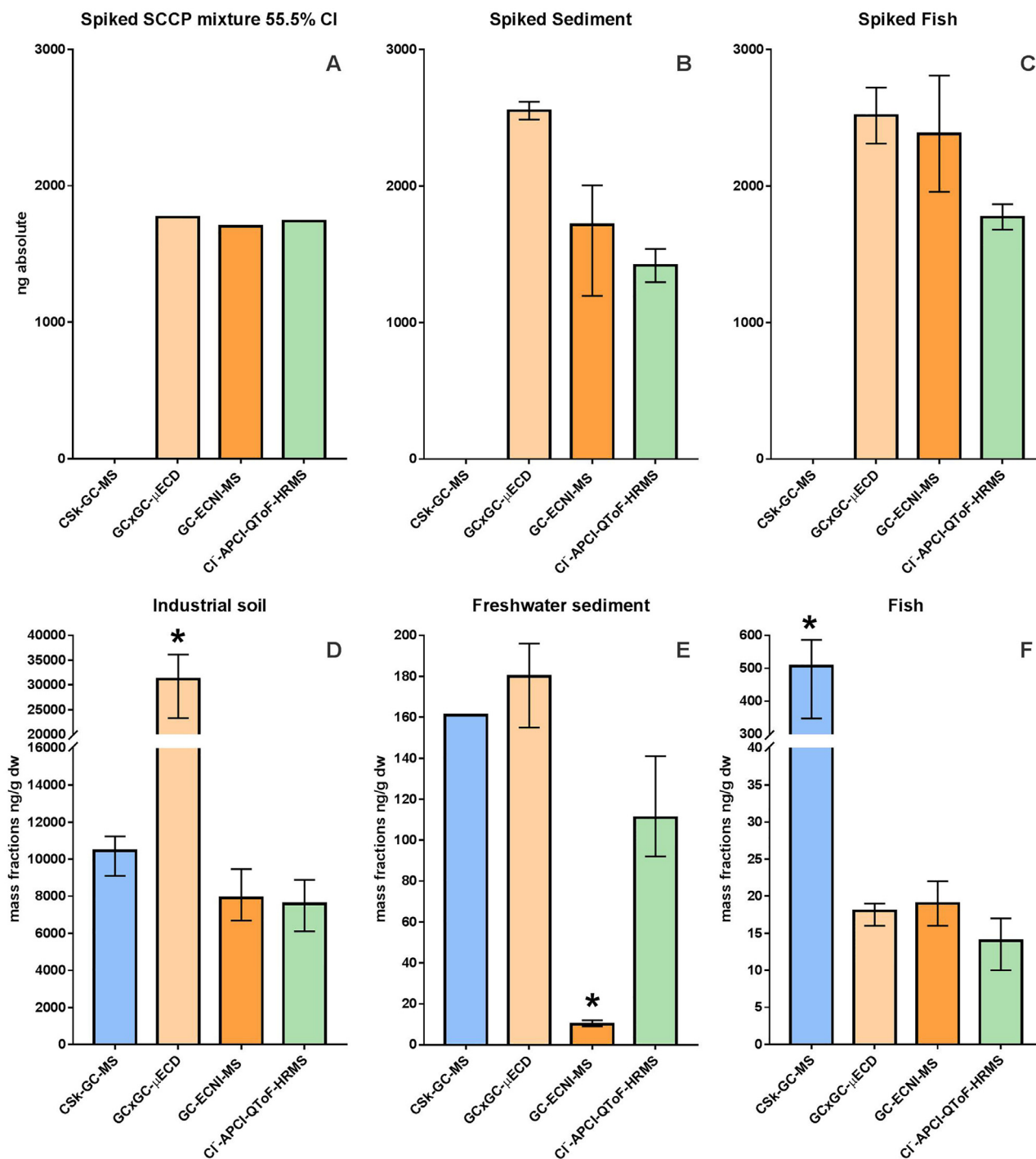


Fig. 1. Calculated average  $\Sigma$ SCCPs mass fractions with upper and lower limits in spiked solution ( $n=1$ ) (A), spiked samples ( $n=3$ ) (B-C) and (certified) reference materials ( $n=3$ ) (D-F) by four different determination methods. Identified outliers with reasons explained in the text are marked with an asterisk.

69% chlorine content or more do not occur in the environment and hence the GC-ECNI-LRMS method was limited to SCCPs less than 11 chlorine atoms. However, SCCPs with 11 or more chlorine atoms contributed for 38% of all SCCPs in this sample. Recently, Yuan et al. [39] also detected SCCPs with 11–12 chlorine atoms in sediment samples, while technical mixtures with 70 wt% chlorine content are commercially available [40]. To date, one of the major disadvantages of the GC-ECNI-LRMS method is that it cannot detect lower chlorinated CPs (SCCPs with less than 5 chlorine atoms) [7,9,14,30]. The current results show that detecting higher chlorinated SCCPs (SCCPs with more than 10 chlorine atoms) is

also important to ensure accurate results. The presence of higher chlorinated SCCPs can be verified with GC-ECNI-LRMS by the calculated chlorine content method (the higher the chlorine content, the higher the abundance of higher chlorinated congener groups). Therefore, when using GC-ECNI-LRMS, we strongly recommend to report the calculated chlorine content of samples analysed and standards to ensure the quality of the data. Reth et al. [24] reported a LOD<sub>i</sub> based on a chlorine content of 50% for SCCP analysis. While these results show that a chlorine content of 68% is apparently too high for quantification, a study is needed to investigate the exact upper limit of detection by chlorine content for

**Table 4**  
 ΣSCCPs mass fractions in candidate reference materials by four methods.

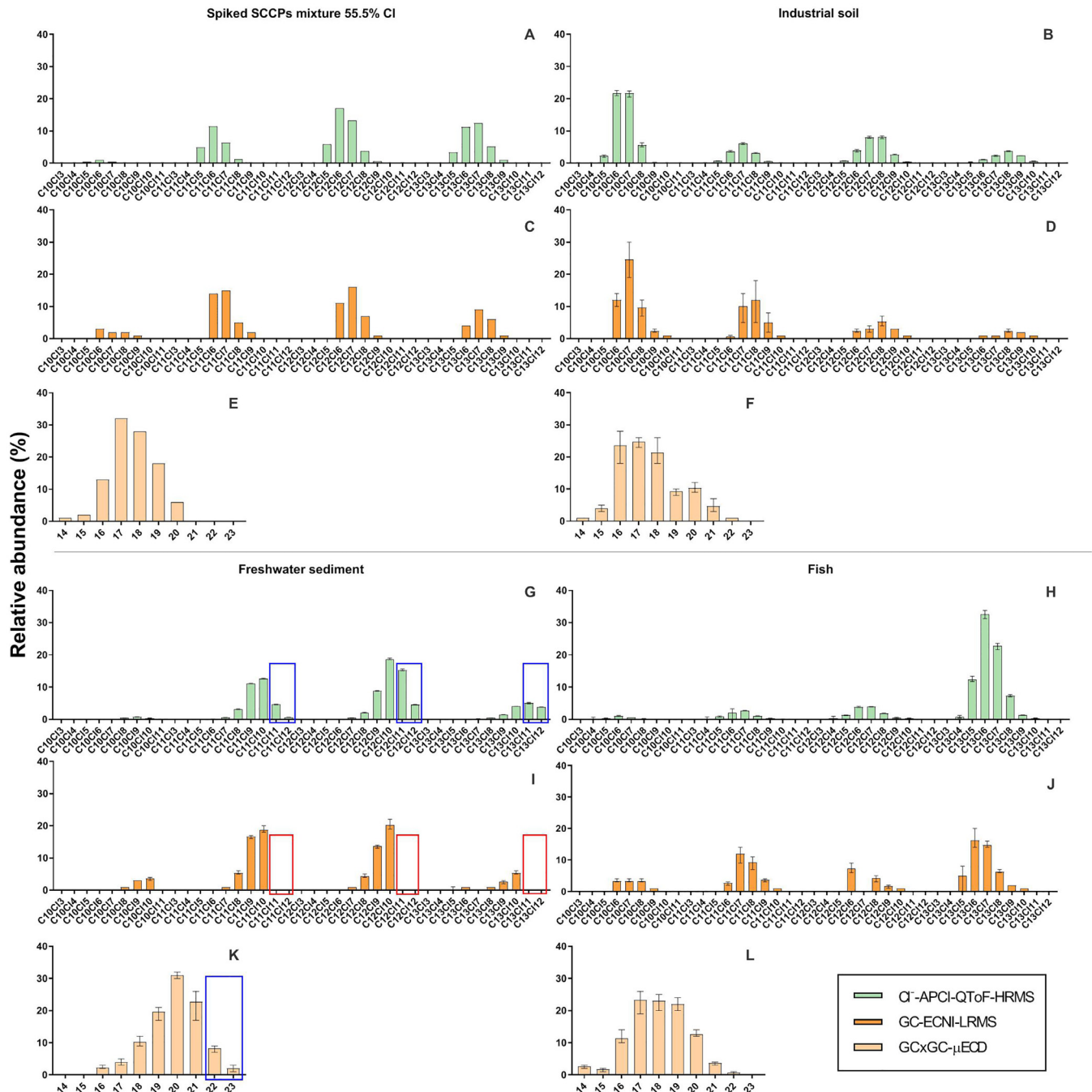
Samples	APCI-QToF-HRMS	GC × GC-μECD	GC-ECNI-LRMS	CSK-GC-LRMS	RSD (%)
Industrial soil BCR-481 ( <i>n</i> = 3)					72 (21) <sup>a</sup>
ΣSCCPs (mean ng/g dw ± SD)	7,600 ± 1,400	31,000 ± 6,900	7,900 ± 1,400	10,000 ± 1,200	
Calculated chlorine content (%)	62	57	65	nd	
Freshwater sediment CCQM-K102 ( <i>n</i> = 3)					66 (27) <sup>b</sup>
ΣSCCPs (mean ng/g dw ± SD)	110 ± 26	180 ± 22	10 ± 2	160	
Calculated chlorine content (%)	69	64	68	nd	
Fish ERM-CE100 <sup>a</sup> ( <i>n</i> = 3)					183 (21) <sup>c</sup>
ΣSCCPs (mean ng/g ww ± SD)	14 ± 4	18 ± 2	22 ± 5	500 ± 140	
Calculated chlorine content (%)	56	59	61	nd	

SD Standard Deviation RSD relative standard deviation of all reported ΣSCCPs levels between the instruments dw dry weight ww wet weight nd not determined because of dechlorination step prior analysis.

<sup>a</sup> excluding GC × GC-μECD results.

<sup>b</sup> excluding GC-ECNI-LRMS results.

<sup>c</sup> excluding CSK-GC-LRMS result.



**Fig. 2.** Relative abundance of the SCCP congener groups (A-D, G-J) and (C+Cl)<sub>n</sub> classes (E-F, K-L), measured by three different determination methods (specified in legend).



GC-ECNI-LRMS. Without the results of the GC-ECNI-LRMS, reported levels were reasonably similar between the other three methods (27% RSD).

The results obtained by CSk-GC-LRMS were inconsistent for the fish candidate RM (ERM-CE100, 30-fold higher than the average mass fraction and above the upper inner fence of 333 ng/g ww, Fig. 1F). Potential degradation of the longer chain alkanes to shorter chain alkanes and thus longer chain CPs to SCCPs could occur when using CSk-GC-LRMS resulting in an overestimation [41]. In contrast to the other RMs, MCCPs (i.e. longer chained CPs) were present in this RM (ca. 56% of the total CPs, obtained by APCI-QToF-HRMS) that were possibly degraded to SCCPs. A deeper insight in the physico-chemical behavior of the palladium catalyst towards the *n*-alkanes is probably required before using CSk-GC-LRMS. When excluding the results of the latter method, the levels differed 21% between the methods.

This study does not account for the differences caused by analyte losses during clean-up, as suitable or representative surrogate standards were unavailable. As the results of the recovery study experiments were satisfactory, and the study focused on a relative comparison of results between methods using the same sample extracts for at least APCI-QToF-HRMS, GC  $\times$  GC- $\mu$ ECD and GC-ECNI-LRMS, we believe that this is an acceptable limitation of this study. Furthermore, it is extremely difficult to account for analyte loss with just one surrogate standard during clean up as the physical-chemical properties of SCCPs and other CPs extensively differ. This is a general pitfall for SCCP analysis.

#### 3.4. Suggestions for future SCCP analysis

In addition to the GC  $\times$  GC- $\mu$ ECD, the combination of GC  $\times$  GC with HRMS could be a promising tool for SCCP analysis. However, some methods should be used with caution. For example, the GC  $\times$  GC-ECNI-ToF-HRMS [12] still only detects SCCPs with chlorine atoms between five and ten, potentially leading to underestimation of concentrations. Future research could focus on the potential of chlorine-enhanced LC  $\times$  LC-APCI-QToF-HRMS for CP analysis.

This study only corrected for the chlorine dependent response and did not investigate whether the response could also depend on other factors. Reth et al. [24] showed that response on GC-ECNI-LRMS was more influenced by chlorine content than carbon chain length. Korytar et al. [19] found that CPs with a different chlorine substitution pattern elute different over time on a GC  $\times$  GC chromatogram. While Bogdal et al. [11] discussed that the response of CPs with APCI-QToF-MS increases with increasing carbon chain length, to our knowledge the effect of chlorine content, carbon chain length and/or the chlorine substitution still remains not fully understood and needs to be investigated in future studies.

While MCCPs received little attention in the past, recent results show that MCCPs are currently found in higher levels than SCCPs [5,22,39,42,43]. When MCCPs are present in samples in higher levels than SCCPs, GC-ECNI-LRMS may cause an overestimation of SCCP levels [9]. Due to the recently acquired POP status of SCCPs, accurate analytical methods should be able to at least differentiate between SCCPs and MCCPs. That MCCPs are found in higher levels than SCCPs is a reason to analyze MCCPs as well. This makes the APCI-QToF-HRMS the most applicable method as it can determine both SCCPs and MCCPs and differentiate between them. Together with the quantification method used in this study the APCI-QToF-HRMS is suitable to quantify CPs in environmental samples with a different chlorine content. Besides the quantification method used in this study, the deconvolution quantification method [11] is also promising, especially when using single chain mixtures as quantification mixtures [40]. However at the moment, only a few single chain mixtures are commercially available and more of such mixtures are urgently needed [40]. As a result, quantification mixtures

with more than one specific chain length (e.g. C10-13, Erhrenstorfer, LGC) are used for the deconvolution method and care should be taken when using these mixtures. The reconstructed congener group pattern obtained by deconvolution should match that of the measured congener group pattern in the sample as closely as possible to prevent quantification errors. Results of the goodness of fit model between reconstructed congener group patterns and the actual congener group patterns should therefore be reported when using this method.

Other halide-enhanced methods than the one used in this study (i.e. chloride enhanced APCI) are also quite promising and several related alternatives have recently been published. For example the bromide-enhanced APCI method [44] and the chloride-enhanced ESI method [13,45]. These methods are applied in combination with either the deconvolution quantification method [11] or the method by Reth et al. [24]. Yuan et al. [46] also developed a deconvolution method to quantify SCCP congener groups with APCI-QToF-HRMS and applied that method successfully on data obtained by GC-ECNI-HRMS and GC-ECNI-Q-Orbitrap-HRMS, thereby reducing the overestimation of the chlorination degree to 0.1%. The congener group levels obtained by these three instruments agreed well with each other ( $R^2 > 0.90$ ) [46]. Further research in these candidate reference materials using these instruments is suggested.

#### 4. Conclusions

While results between the methods agreed with each other for the spiked solution and samples, substantial differences were found for the naturally contaminated samples. After critical inspection of the data, the results of some methods were excluded for technical reasons, resulting in more acceptable differences and revealing that some methods are unsuitable to analyze certain samples. These technical reasons may remain, however, unidentified when using only a single method and/or spiked samples for validation and, therefore, both interlaboratory studies and CRMs are needed. Recently, Krätschmer and Schächtele [36] recommended using naturally contaminated samples for future interlaboratory studies to facilitate comparable CP determination. The importance of the availability of naturally contaminated samples such as CRMs to ensure the reliability of method are further underlined by this study and highly recommended. Spiked materials will generally deviate too much from reality.

Of the four determination methods applied, the APCI-QToF-HRMS method was the most promising method regarding time-efficiency, resolution, repeatability and accuracy. Furthermore, it also allows determination of MCCPs and LCCPs. This is of particular advantage as MCCPs are now generally detected in higher levels than SCCPs and might become a larger problem than SCCPs as they are used as alternatives for SCCPs [5]. GC  $\times$  GC- $\mu$ ECD shows great potential in separating congeners, and when suitable congener standards become commercially available, it could be a promising tool. This study confirms that even more caution is needed when interpreting data measured by GC-ECNI-LRMS than stated five years ago [15].

By identifying potential candidate CRMs for SCCP, we have laid down the first steps in the process of producing the first certified RM for this challenging class of halogenated compounds. The availability of such a QA/QC tool will help in the validation of analytical methods for SCCPs analysis and will ensure the accuracy of the measurement results.

#### 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.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.chroma.2019.460550.

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