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Stepping-up accurate quantification of chlorinated paraffins: Successful certification of the first matrix reference material

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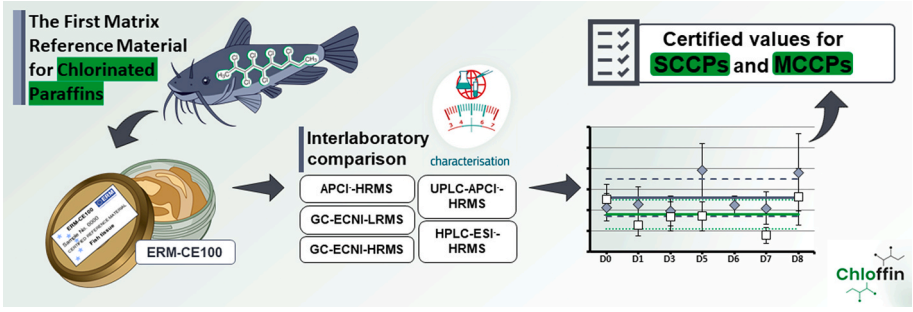
HIGHLIGHTS

- Successful interlaboratory comparison for chlorinated paraffins (CPs) in fish.
- First certification of a matrix reference material for short- and medium-chain CPs.
- Certified values assigned combining LC and GC-based analytical results.
- Fish CRM produced as a wet paste to enhance similarity to routine biota samples.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Chlorinated paraffins (CPs) are industrial chemicals categorised as persistent organic pollutants because of their toxicity, persistency and tendency to long-range transport, bioaccumulation and biomagnification. Despite having been the subject of environmental attention for decades, analytical methods for CPs still struggle reaching a sufficient degree of accuracy. Among the issues negatively impacting the quantification of CPs, the unavailability of well-characterised standards, both as pure substances and as matrix (certified) reference materials (CRMs), has played a major role. The focus of this study was to provide a matrix CRM as quality control tool to improve the comparability of CPs measurement results.

Results: We present the process of certification of ERM®-CE100, the first fish reference material assigned with certified values for the mass fraction of short-chain and medium-chain chlorinated paraffins (SCCPs and MCCPs, respectively). The certification was performed in accordance with ISO 17034:2016 and ISO Guide 35:2017, with the value assignment step carried out via an intercomparison of laboratories of demonstrated competence in CPs analysis and applying procedures based on different analytical principles. After confirmation of the homogeneity and stability of the CRM, two certified values were assigned for SCCPs, depending on the calibrants used: 31 ± 9 μg kg^{-1} and 23 ± 7 μg kg^{-1}. The MCCPs certified value was established as 44 ± 17 μg kg^{-1}. All assigned values are relative to wet weight in the CRM that was produced as a fish paste to enhance similarity to routine biota samples.

Significance and novelty: The fish tissue ERM-CE100 is the first matrix CRM commercially available for the analysis of CPs, enabling analytical laboratories to improve the accuracy and the metrological traceability of their measurements. The certified CPs values are based on results obtained by both gas and liquid chromatography coupled with various mass spectrometric techniques, offering thus a broad validity to laboratories employing different analytical methods and equipment.

Abbreviations

ANOVA	Analysis of variance
CC	Common calibrant
CP	Chlorinated paraffins
CQC	Calibration quality control
CRM	Certified reference material
JRC	Joint Research Centre of the European Commission
ECNI	Electron capture negative ionisation
EU	European Union
HRMS	High resolution mass spectrometry
ISO	International Organization for Standardisation
LCCPs	Long-chain chlorinated paraffins
LRMS	Low resolution mass spectrometry
MCCPs	Medium-chain chlorinated paraffins
MQC	Method quality control
POP	Persistent organic pollutant
RM	Reference material
SCCPs	Short-chain chlorinated paraffins
SI	International System of Units
WFD	Water Framework Directive

1. Introduction

Chlorinated Paraffins (CPs), also referred to as polychlorinated *n*-alkanes (PCAs), are complex technical mixtures of *n*-alkanes with variable chain length where several hydrogen atoms are substituted by chlorine atoms, giving rise to different chlorination degrees. They are high-production volume industrial chemicals (estimated volumes of ca. 33 million tonnes in total [1]) used in a wide range of applications because of their valuable features, from metal working fluids to flame retardants, from plasticizers to additives in paints and surface coatings [2,3].

They are commonly categorised according to the carbon number of the *n*-alkane chain: short-chain chlorinated paraffins (SCCPs) having between 10 and 13 carbon atoms, medium-chain chlorinated paraffins (MCCPs) having 14 to 17 carbon atoms and long-chain chlorinated paraffins (LCCPs) with ≥18 carbon atoms.

SCCPs were the first regulated CPs in the environment and several national/regional restrictions on their production and use have been enforced since the early 90s [3]. The European Union (EU) Water Framework Directive (WFD), enforced in 2000, included them in the list of priority substances to be mandatorily monitored by the Member States [4]. Their use is restricted in the EU under the Persistent Organic Pollutants (POPs) regulation (enforced in 2004, amended in 2015 and recast in 2019 [5]).

SCCPs were included in the POPs list of the Stockholm Convention in 2017 [6], with recognised characteristics of toxicity [7], persistency [8], long-range transport [9], bioaccumulation [10–12] and biomagnification [13]. They eventually end up in the human body [14–18] via the food we eat [19,20] and/or via exposure to different environmental media such as water [21,22], air [23–25] and soil/sediment [26,27]. The International Agency for Research on Cancer (IARC) have classified SCCPs of average carbon chain length C12 and average degree of chlorination approximately 60 % as possibly carcinogenic to humans (Group 2B) [28].

The SCCPs global restrictions induced “regrettable substitutions” by their longer chain homologues MCCPs (and LCCPs), which started recently to rise environmental concerns as they are often detected at higher levels compared to the SCCPs, and sharing similar characteristics of persistency and toxicity to the aquatic organisms [29]. In 2021, the European Chemicals Agency (ECHA) inserted MCCPs in the Candidate List of substances of very high concern for Authorisation under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation. MCCPs are currently under review by the Stockholm convention on POPs.

Despite having been the subject of environmental attention for decades, the monitoring of CPs remains challenging: they are among the most difficult organic compounds for the analysts to obtain comparable and accurate measurement results [30–33]. This difficulty arises from their intrinsic nature: they can be composed of tens – hundreds of thousands isomers, which are hardly (if not impossibly) separable and distinguishable, even with the most advanced analytical techniques. The measurand definition for the CPs is a complex issue and a nightmare from the metrological point of view. Additionally, they show instrument responses that depend on the chlorine content and pattern and isobaric self-interferences, especially when using low resolution mass spectrometry (MS) [34].

Since the pioneering work carried out by Tomy et al. [35], there have

been several reports in the literature highlighting the analytical challenges and suggesting ways to improve their quantification and achieve a better data comparability. The efforts of the research community in this respect targeted all the different steps of the analytical procedure, from the sample preparation to the detection, to the final quantification [34,36–49]. Nonetheless, the interlaboratory comparison studies and proficiency testing schemes organised so far highlight that inter-method and inter-laboratory variability is still high [31,32,50,51]. Reference materials are, together with standard methods and proficiency testing schemes, the tools that laboratories have to support quality assurance and quality control of their measurements.

Among the main hurdles to overcome for improving the quantification of CPs in the various matrices there is the availability of standard methods and well-characterised standards, both as pure substances for calibration [52–62], as well as matrix certified reference materials (CRMs) for method validation [63].

The Eurostars project CHLOFFIN (Development of reference standards for the analysis of chlorinated paraffins, 2019–2022) [64–66] aimed at addressing some of the shortcomings in CPs quantification by enlarging the range of available calibration standards, improving their characterisation (i.e. assessment of purity) and providing the first matrix CRM to quality-assure the whole process of the sample extraction and analysis. The optimisation and validation of methods of analysis to be applied in the purity assessment of calibration standards and in the characterisation study of the matrix CRM were also pursued.

This contribution presents the certification process of the fish tissue ERM®-CE100 for CPs, the first ever-available matrix CRM for these compounds, with particular emphasis on the characterisation (i.e., value assignment) step. The certified values were assigned via an intercomparison of qualified laboratories employing analytical methods based on both liquid chromatography (LC) and gas chromatography (GC) coupled with various MS techniques. The data evaluation of the characterisation campaign and the comparison of measurement results obtained by different quantification principles and approaches provided useful insights in the analysis of CPs. The introduction of a purity-assessed common calibrant in the interlaboratory study further enabled the assignment of a certified value for the mass fraction of SCCPs traceable to the International System of Units (SI).

2. Materials and methods

2.1. Standards and certified reference materials

CRM ERM-CE100, the fish tissue used as study sample (40 g of fish paste in a vacuum-sealed glass jar), was previously certified for the mass fractions of hexachlorobenzene and hexachlorobutadiene and released in 2016 [67]. It is available from the European Commission Joint Research Centre (JRC, Geel, BE and its authorised distributors [68]). ERM-CE100 was chosen as candidate reference material (RM) for certification of SCCPs after an extensive screening study described elsewhere [63]. In addition to having endogenous appropriate and relevant levels of CPs, this biota material was deemed best suited to possibly address the needs of both the environmental monitoring as well as the food control laboratories. The non-spiked contamination and the wet texture (similar to baby food, Fig. 1) are characteristics that improve its commutability, i.e., similarity in analytical behaviour to routinely analysed fresh fish samples. For example, the biota Environmental Quality Standards (EQS) for WFD priority substances are set in μg kg^{-1} wet weight [4]. The laboratories had therefore to analyse the material as such, with the explicit request of not freeze-drying it, and to submit the measurement results on wet weight basis.

CRM SRM 1946 Lake Superior Fish Tissue (8 gr of frozen fish homogenate in a glass jar), used as blinded method quality control (MQC) sample in the characterisation study, is available from the National Institute of Standards and Technology (NIST, Gaithersburg, MD, USA) [69].

Fig. 1. Fish tissue ERM-CE100. Study sample used in the certification campaign of CPs.

CRM solutions of five SCCP single congeners CLF-5248-100-IO (*iso*-octane) and CLF-5248-100-AN (acetonitrile), 97 ± 5 μg mL^{-1}, used as common calibrants (CC) and CRM solutions of five SCCPs single chain mixtures CLF-5371-10-IO (*iso*-octane) and CLF-5371-10-AN (acetonitrile), 10.0 ± 0.5 μg mL^{-1} used as calibration quality control (CQC) samples are available from Chiron AS (Trondheim, NO). They were custom made in the frame of the Eurostars project CHLOFFIN and their compositions are reported in detail in Table S1 and Table S2, respectively.

Chloroparaffin C10–C13 with chlorine contents (m/m) of 51.5 %, 55.5 % and 63 % and chloroparaffin C14–C17 with chlorine contents (m/m) 42 %, 52 % and 57 %, all 100 μg mL^{-1} in cyclohexane (99.9 %); chloroparaffin C10, C11, C12 and C13, with varying chlorine contents (m/m), 10 μg mL^{-1} in cyclohexane (99.9 %) and chloroparaffin C14, C15, C16 and C17, with varying chlorine contents (m/m), 100 μg mL^{-1} in cyclohexane (99.9 %) by LGC/Dr. Ehrenstorfer (Augsburg, DE) were used as calibrants.

Single-chain CP mixtures from University of Hohenheim (Stuttgart, DE) [34] with the following chlorine contents (m/m): C13: 43.07 % and 52.44 %; C14: 40.36 %, 53 %, 55.09 %; C15: 39.49 %, 51 %, 55.03 %; C16: 51.62 %, 53 %, 70.55 %; C17: 43.05 %, 49.96 %, 61 % were used as calibrants for datasets D8 (C13) and D9 (C14–C17).

2.2. Certification studies and analytical methods

The certification of ERM-CE100 was carried out in accordance with ISO Guide 35:2017 [70] and all relevant data and information are available in the certification report [71].

A large range of diverse extraction and clean-up methods were used in the interlaboratory study. All details of the analytical procedures are reported in Table S3. The analytical separation and detection steps as well as the quantification approaches applied in the characterisation study also varied among the laboratories (Table 1).

Table 1
Analytical methodologies employed in the characterisation study of ERM-CE100 for the determination of SCCPs and MCCPs.

Dataset	Instrumental analytical method	Quantification/calibration approach
D0	GC-ECNI-QTOF-HRMS	Reth et al. [41]
D1	UPLC-ESI$^-$-Orbitrap-HRMS	Bogdal et al. [37]
D2	GC-ECNI-Orbitrap-HRMS	ISO 12010:2019 [72]
D3	GC-ECNI-QTOF-HRMS	Bogdal et al. [37]
D4	GC-ECNI-LRMS (triple quadrupole)	Reth et al. [41]
D5	GC-ECNI-Orbitrap-HRMS	Bogdal et al. [37]
D6	UPLC-APCI$^-$-QTOF-HRMS (Cl enhanced)	Yuan et al. [38]
D7	APCI$^-$-QTOF-HRMS (Cl enhanced)	Bogdal et al. [37]
D8	GC-ECNI-LRMS (single quadrupole)	Reth et al. [41]
D9	HPLC-ESI$^-$-FT-ICR-HRMS	Reth et al. [41]

2.3. Homogeneity and stability measurements

The CPs measurements for the homogeneity and stability studies of ERM-CE100 were conducted at A-LIFE, Vrije Universiteit Amsterdam (Amsterdam, NL) by chlorine enhanced-APCI$^-$-QTOF-HRMS. The applied analytical procedure is described in detail in the Supplementary data.

2.4. Interlaboratory comparison study set-up

Eight laboratories (for a total of nine datasets) participated in the intercomparison aiming at value assigning the candidate CRM for CPs mass fractions. Each participant was requested to operate a quality system meeting the requirements of ISO/IEC 17025:2017 [73] (formal accreditation was not mandatory). Additionally, the participating laboratories had to deliver documented evidence of proficiency in the analysis of CPs in relevant matrices (primarily biota, but experience with sediment, soil or particulate matter was considered sufficient) by submitting results of interlaboratory comparisons or method validation reports. There was no prescription on the methods to be used, but only validated methods were admitted.

The items received by the laboratories participating in the intercomparison are shown in Table 2. The candidate CRM to be characterised (ERM-CE100) was re-labelled as ERM-SCCPs, in order to prevent that participants could link the material to previously published SCCPs results [63]. The method quality control (MQC) sample, alias NIST SRM 1946 Lake Superior Fish Tissue, was also made anonymous. The concentration of the calibration quality control (CQC) sample (mixture of five SCCPs single carbon chain mixtures in *iso*-octane or acetonitrile) was not disclosed to the participants, as its purpose was to serve as a control sample for the calibration step. The common calibrant (CC) concentration was on the contrary declared because it had to be used as "alternative" calibrant for quantifying the SCCPs besides the calibrants routinely employed by the laboratory.

The technical specifications of the study contained instructions for the correct handling and storage of the samples and the analysis protocol, including the minimum sample size to be used for analysis. An important requirement was that the ERM-CE100 and MQC samples had to be analysed as such, without freeze-drying them and measurements had to be reported on wet weight basis. Sample preparations had to be split over two different days (to allow for inter-day variability conditions) with one matrix blank inserted on each day of analysis.

The participants were asked to submit the following datasets: 1) SCCPs content quantified with standards of laboratory's choice; 2) SCCPs content quantified with the common calibrant (CC); 3) sum of SCCPs Cl_6 congeners quantified with the CC; and 4) MCCPs content (optional). Each dataset consisted of ten independent results: six for the ERM-CE100 and two for the method quality control (MQC) SRM 1946 expressed in μg kg^{-1} wet weight, and two for the calibration quality control (CQC) sample expressed in μg mL^{-1}. Laboratories were asked to provide estimations of the measurement uncertainty.

The laboratories were requested to report the "sum of SCCPs" due to the legislative relevance of this parameter (regulatory limits are given so far as such e.g., SCCPs are regulated as group of substances C10-13 chloroalkanes in the WFD). Additionally, it was known that the quantification of single CP homologue groups is less reliable because of large inter-laboratory and/or inter-method data variability (by virtue of the instrument response dependency among other factors) [32].

All laboratories used single-chain and/or CPs mixtures from LGC/Dr. Ehrenstorfer as calibrants of own choice (except one laboratory that partially employed calibrants from another source, see 2.1 "Standards and certified reference materials"). Therefore, in the rest of the manuscript the datasets quantified with standards of laboratory's own choice will also be referred to as quantified by Dr. Ehrenstorfer standards.

2.5. Technical evaluation and statistical analysis

Analysis of variance (ANOVA) was applied for the evaluation of the homogeneity and stability of the candidate CRM. Histograms and normal probability plots helped in evaluating the statistical distribution of the data. Regression analyses were used to detect trends (at a 95 % confidence level) and single and double Grubbs tests were used to detect outliers (at a 99 % confidence level). A Cochran test (at a 99 % confidence level) was additionally applied for detecting outlying standard deviations in the characterisation study.

The characterisation datasets were first evaluated for their validity on a technical level. This included the compliance with the prescribed analysis protocol, the critical screening of values reported below the limit of quantification and the agreement of the reported measurement results with the assigned values of the CQC and MQC (only for the SCCPs).

The decision of including the MCCPs as optional study measurand came only at a later stage. Therefore, there was no calibration quality control (CQC) sample for the MCCPs. Additionally, the method quality control (MQC) sample contained very high levels of MCCPs that for most of the laboratories exceeded the established calibration range. For this reason, the technical evaluation for MCCPs could not include the quality control samples results.

The evaluation of the CQC followed the approach described in ERM Application Note 1 [74] to check for compliance with the assigned gravimetric value for SCCPs. The evaluation of the MQC was alternatively carried out adhering to principles used for the evaluation proficiency testing scheme results [75]. Due to the absence of an assigned value for CPs in the MQC (NIST SRM 1946), the low numbers of datasets and the presence of outliers, the median and $2*MADe/\sqrt{p}$ (MADe = median absolute deviation*1.483, p = number of datasets) were selected as the best choice for robust statistical estimators of the assigned value and expanded uncertainty, respectively. Laboratories having an E_n score $> |1|$ [75] were flagged as not compliant, and excluded from the following step of statistical evaluation.

The measurement uncertainty was an essential parameter for these evaluations. For the few participants that did not submit an estimate of measurement uncertainty, the average measurement uncertainty as calculated from all other participants was applied (this concerned D3 and D7 for the CQC and only D3 for the MQC). These assigned uncertainty budgets were nonetheless checked for coherence e.g., larger than repeatability values of the relevant dataset and compared to reported values in literature [31].

The datasets passing these stages of technical evaluation were admitted to further statistical analysis by one-way ANOVA leading to the

Table 2
Samples sent to the interlaboratory comparison participants.

Study item	Identity	Composition/content	Purpose
ERM-SCCPs	ERM-CE100 (blinded)	40 g of fish tissue paste in a vacuum-sealed glass jar	Candidate CRM
MQC	SRM 1946 (blinded)	8 g of frozen fish tissue homogenate in a glass jar	Method quality control sample
CC	CRM CLF-5248-100-IO or CRM CLF-5248-100-AN	97 ± 5 μg mL^{-1} SCCPs: solution of five SCCPs single congeners in *iso*-octane or acetonitrile	Common calibrant
CQC	CRM CLF-5371-10-IO or CRM CLF-5371-10-AN (blinded)	10.0 ± 0.5 μg mL^{-1} SCCPs: solution of five SCCPs single chain mixtures in *iso*-octane or acetonitrile	Calibration quality control sample

assignment of the certified values. The mean of means of the technically accepted laboratory datasets was used as estimate of the true value to be assigned to the candidate CRM. The uncertainty related to the characterisation was estimated as the standard error of the mean of laboratory means (SD/$\sqrt{p}$ where SD = standard deviation).

The uncertainties of the assigned values included contributions relating to characterisation u_{char}, potential between-unit inhomogeneity u_{bb}, potential degradation during transport u_{sts}, and long-term storage u_{lts} [76,77] and common calibrant purity assessment u_{CC} (where applicable i.e., for the values obtained using the CC). A coverage factor $k = 2$ was used to obtain the expanded uncertainties.

3. Results and discussion

3.1. Homogeneity and stability studies

The homogeneity of the study material for SCCPs and MCCPs was confirmed by satisfactory values of the between-unit inhomogeneity ($u_{bb,rel}$), resulting in acceptable contributions to the final certified uncertainties. The transport (short-term) stability ($u_{sts,rel}$) and storage (long-term) stability ($u_{lts,rel}$) uncertainty contributions were estimated for the CPs at 18 °C and 4 °C, respectively, conditions already established during the previous certification of ERM-CE100. These data are reported in Table S4 (CPs quantified with Dr. Ehrenstorfer calibrants) and available in the certification report [71].

3.2. Common calibrant preparation and purpose

The interlaboratory comparison included the use of a purity-assessed common calibrant (custom-made for the purpose) for the determination of SCCPs with the aim to address some of the recognised issues in CPs quantification. One of the main reasons for the unsatisfactory quality level of the state-of-the-art in the quantification of CPs and the low agreement of results among different analytical methodologies and laboratories is the inappropriateness of CPs standards routinely used for calibration both in terms of purity characterisation as well as sample pattern matching (% Cl and homologue groups profile) [34,52]. For CPs, well-characterised calibrants are largely unavailable and usually mixtures such as those from Dr. Ehrenstorfer are used. The authors focused on producing a well-characterised calibrant (i.e. the common calibrant CC), that could provide an anchor point of the metrological traceability for the assigned value to the SI, chaining the result to a common reference point, impermeable to time and space changes.

To obtain accurate CPs quantification results, it is important that the used calibrants match the sample in terms of degree of chlorination and carbon chain length/homologue groups pattern as close as possible. The lack of matching can be compensated mathematically by applying the deconvolution approach described by Bogdal et al. [37] or by linear regression of Cl content to response factors as proposed by Reth et al. [41]. However, there is no single method that can address all pitfalls in the CPs quantification.

The composition of the CC (Table S1) was carefully considered to mimic as much as possible the SCCPs pattern present in ERM-CE100, in regards to chain length distribution and chlorine content and pattern, as investigated during the homogeneity and stability studies (Fig. 2). It is important to note that this investigation was carried out in one laboratory by a single analytical method (chlorine enhanced-APCI$^-$-QTOF-HRMS), while it is known that relative abundancies of the congener groups can significantly differ among instruments [32]. Hence, the SCCPs pattern of the ERM-CE100 as shown in Fig. 2 should not be understood as absolute, even though a very similar pattern was obtained during the characterisation study by other methods, in specific by Cl enhanced UPLC-APCI$^-$-QTOF-HRMS (cfr. Section 3.4).

The Cl content of the SCCPs in ERM-CE100 was estimated as 56.5 % (m/m). The relative abundances of the respective homologue groups were derived from the base-peak areas of $[M+Cl]^-$ ions, after normalisation to the area of the internal standard. The SCCPs pattern in the ERM-CE100 sample showed a clear dominance of Cl_6 congeners in each carbon chain group and Cl_6 was overall the most dominant SCCPs congener homologues group (42 % of all targeted Cl_x groups where x = 3–13), followed by Cl_7 (30 %). C_{13} was the most dominant carbon chain length group (75 %) followed by C_{12} and C_{11} (both about 11 %) and finally C_{10} (about 3 %). For the preparation of the best matching common calibrant, we assessed mixtures made of different single Cl_6 congeners as well as made of single carbon chain mixtures of Cl_6 congeners. Because of the obvious cost in time and resources to produce purity-characterised standards, the common calibrant (CC) was finally conceived as a mixture of five SCCP Cl_6 single congeners (one $C_{10}Cl_6$, one $C_{11}Cl_6$, one $C_{12}Cl_6$ and two $C_{13}Cl_6$). The Cl_6 single congeners were deliberately designed and synthesised with the aim of being closer in structure to CPs most probably present in real samples, in regards to the chlorine distribution pattern. Therefore, in contrast to previous generations of CPs standards developed in early 2000, all the CP single congeners (except one) in the CC do not contain any geminal (adjacent) or terminal (at both ends) chlorine atoms [65,78,79]. Evidences gained during the characterisation study by the chlorine enhanced UPLC-APCI$^-$-QTOF-HRMS method confirmed retrospectively this assumption: the retention times of the single congeners contained in the CC ($C_{10}Cl_6$ with a bit less certainty) fit with the ones present in the ERM (and method quality control MQC) sample extracts (data shown in Fig. S1). The relative presence of the different carbon chain groups in the common calibrant (CC) was set in a ratio similar to the abundance in ERM-CE100 as follows: C_{10}: C_{11}: C_{12}: C_{13} = 3.7 : 13.2: 14.6 : 68.5. The Cl content of the SCCPs in the final formulation of the CC was estimated 55.4 % (m/m).

The similarity of the SCCPs pattern between the CC and the ERM-CE100 was tested according to the deconvolution method by Bogdal et al. A correlation $R^2 = 0.56$ was calculated, indicating that the pattern

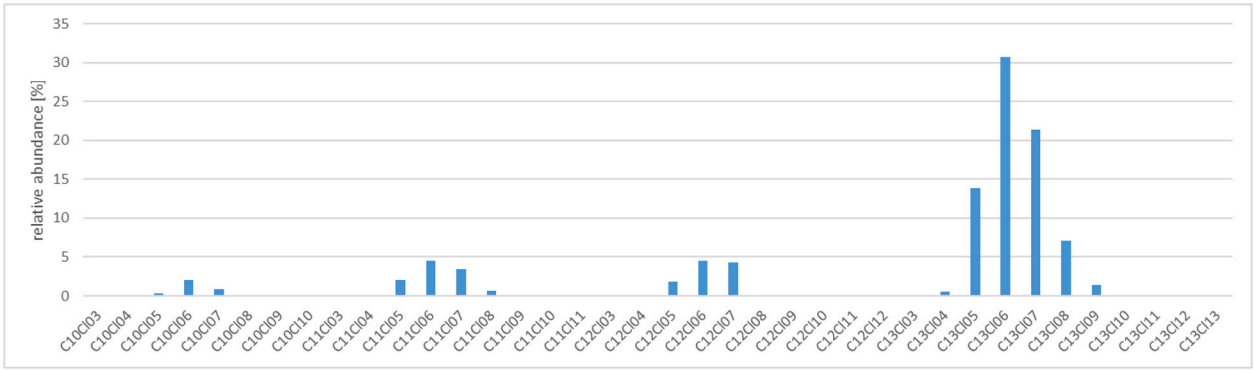

Fig. 2. SCCPs homologue pattern in ERM-CE100 (by Cl enhanced-APCI$^-$-QTOF-HRMS): relative abundances of the congener groups.

matched sufficiently well ($R^2 > 0.50$) to allow a meaningful quantification [36,37].

The common calibrant (CC) can be considered as a "proxy" to the SCCPs calibrant formulation that the laboratories would normally use for quantification and the best compromise between suitability and providing an appropriate anchoring to a sound metrological traceability of the assigned value. The request of additionally reporting the sum of SCCPs $C_{10–13}Cl_6$ congeners raised from the fact that the CC was exclusively composed of Cl_6 single congeners. During the planning phase of the study, the authors were not sure to what extent the quantification with the CC of congeners other than Cl_6 would be reliable (knowing that response factors might change among congener groups or even from single congener to congener). Here, the authors were charting on an unknown territory, acknowledging the risk that the quantification of the SCCPs content with the CC could be significantly biased and/or not fit for the assignment of a value to the candidate CRM.

The expanded uncertainty ($k = 2$) of the concentration values of the common calibrant solutions (U_{CC}), was estimated 5 %, by combining the standard uncertainties coming from the mass balance approach used for the purity assignment of the individual SCCPs congeners, the weighing steps for the preparation of the multicomponent solution and homogeneity and stability contributions. This approach conformed to the state-of-art recommendations for the purity assessment of organic compounds [80] and ensured that the common calibrant value and uncertainty were SI-traceable. The common calibrant solutions are released as CRMs and are available from Chiron AS (http://www.chiron.no/en/) under the part number CLF-5248.

Other results from the investigations carried out to ensure the suitability of the common calibrant (CC) for SCCPs quantification and the details on the purity assessment of the single Cl_6 congeners constituting the CC are reported in the certification report of ERM-CE100 [71].

3.3. Interlaboratory comparison study (certification campaign)

The certified values were assigned via an intercomparison of qualified laboratories gathering as many methods based on different analytical principles as possible to reduce bias in the analytical result. This is the usual approach employed by the JRC for the certification of its reference materials.

Two meetings were organised with the participating laboratories (one before and one after the characterisation campaign) for clarifying doubts, for explaining the set-up of the study (different from a "normal" certification exercise), and finally for data review. These were beneficial steps in the process of the certification, giving the opportunity for an open discussion and comparison of the diverse analytical methodologies employed, characterised by very different calibration functions and quantification approaches. Unfortunately, there was no laboratory employing a validated comprehensive two-dimensional gas chromatography (GC x GC) method that was able to participate in the interlaboratory comparison.

One of the aims of the study was also to compare the results obtained by employing the common calibrant *vs.* the results obtained with the CPs standards routinely used by the laboratories, allowing an evaluation of the impact of the calibration standards on the SCCPs determination.

3.3.1. Quality control samples results

Together with the study material ERM-CE100, the participants had to analyse the calibration quality control (CQC) solution (for which no sample preparation other than possible dilution was required) and the fish method quality control (MQC) SRM 1946. The results on the CQC solution served as a check for the accuracy of the calibration step and quantification approach adopted by the laboratories. On the other hand, the evaluation of the results for the matrix material SRM 1946 helped in evaluating the accuracy of the overall analysis (including the sample preparation step). SRM 1946 was previously analysed to assess the level and pattern of SCCPs, to ensure that they were sufficiently comparable with the ones in the ERM-CE100, so that the laboratories could apply the same calibration range and approach.

The evaluation of the laboratories' performance for the determination of SCCPs based on the quality control samples followed a step-wise approach: the CQC results of the laboratories were compared to the gravimetrically assigned value, and only the datasets successfully passing this stage, were "admitted" to the second stage of evaluation involving the MQC. This first step of compliance against the CQC was only applied to the datasets of SCCPs quantified with Dr. Ehrenstorfer calibrants. The common calibrant SCCPs pattern did not match sufficiently well the homologues profile of the CQC. Therefore, it was deemed not appropriate to use it for determining the SCCPs concentration in the CQC. For the datasets quantified by the common calibrant (CC), the compliance check only included the second stage i.e. against the MQC (the flowcharts depicting the evaluation of the quality control samples are included as Fig. S2 and Fig. S3 in the Supplementary data).

Looking at the evaluation of the CQC results, two datasets, namely D2 and D4, were found not compliant as depicted in Fig. 3. D2 reported a very low result of 0.401 μg mL^{-1}, while D4 reported a result almost 50 % higher than the assigned value of 10 μg mL^{-1}.

These results were somewhat surprising, considering the relatively easy task of quantifying a SCCPs standard i.e., a solution of purified single-chain SCCPs mixtures in solvent. Another important element to flag is that the average expanded uncertainty for this measurement (calculated using the uncertainties declared by the laboratories) was equal to 20.6 % (NB this value was also applied in the evaluation of the performance of D3 and D7 that did not report an uncertainty budget for their measurement). These data confirm that challenges still exist in estimating the measurement uncertainty for the "simple" quantification step of a solution of SCCPs.

Regarding the MQC sample evaluation, the results for SCCPs and sum of SCCPs Cl_6 congeners are reported in Fig. 4. The D2 dataset could not be included in the evaluation of MQC results quantified with the common calibrant (CC), because the quantification approach of the method applied in this laboratory i.e., ISO 12010:2019 [72] could not be exclusively based on the CC.

For what concerns the SCCPs values, the datasets D4 (results quantified with the CC) and D9 (results quantified with both the CC and the calibrants of laboratory's own choice) were flagged as not compliant (red markers in Fig. 4A). In the case of the sum of SCCPs Cl_6 congeners, the three datasets D4, D5 and D9 (red markers in Fig. 4B) had to be discarded from further consideration for the value-assignment step to ERM-CE100.

The estimated mass fractions for SCCPs and $\Sigma C_{10\text{-}13}Cl_6$ SCCPs in the method quality control (MQC, alias SRM 1946) following this evaluation have to be considered with caution and should definitely never to be regarded as reference or certified values. The only purpose of the quality

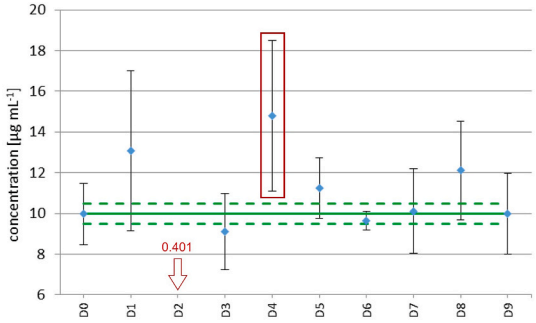

Fig. 3. SCCPs certified value (solid line) and expanded uncertainty ($k = 2$) (dotted lines) of the calibration quality control (CQC) sample. Laboratories' means for SCCPs quantified with calibrants of laboratory's own choice (Dr. Ehrenstorfer). The bars correspond to the expanded uncertainty of the means (n = 2, n = number of independent results).

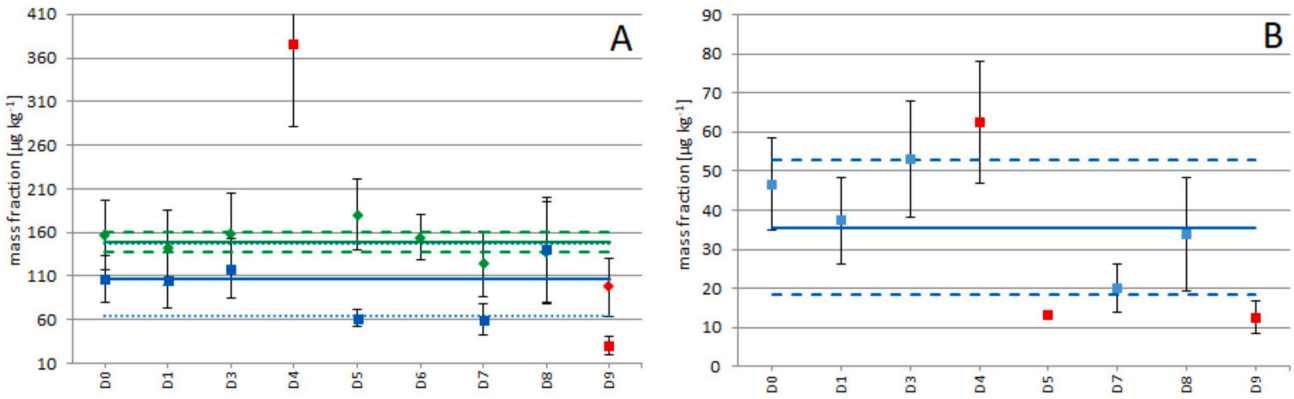

Fig. 4. SCCPs and SCCPs $C_{10–13}Cl_6$ medians (solid lines) and expanded uncertainty (dotted lines) of the method quality control (MQC) sample SRM 1946 (mass fraction wet weight). A) superimposed laboratories' means for SCCPs quantified with calibrants of own choice (Dr. Ehrenstorfer, green colour and diamond-shape marker) and SCCPs quantified with the common calibrant (CC) (blue colour and squared marker); B) laboratories' means for the sum of SCCPs $C_{10–13}Cl_6$ congeners quantified with the CC. In red the datasets flagged as not compliant. The bars correspond to the expanded uncertainty of the means ($n = 2$). NB: D4 appears in the results quantified with the CC (squared marker) because its non-compliance for the calibration quality control (CQC) (Fig. 3) is limited to results obtained with Dr. Ehrenstorfer standards.

control samples was to insert an additional checkpoint to support the technical validity of the data submitted for the value assignment of ERM-CE100.

Fig. 4A shows that the difference between the assigned values for the mass fraction of SCCPs quantified by the laboratories' own selected calibrants *vs.* the common calibrant (CC) is not statistically significant when taking into account the uncertainties. However, in the analysis of the SRM 1946 a better agreement of the results was observed (i.e., less spread around the median) when the laboratories employed calibrants of own choice (Dr. Ehrenstorfer), with a median absolute deviation of about 11 % vs. 37 % in the case of the CC. This could be due to the "rigidity" induced by the mandatory use of the CC for the calibration in the specific laboratory's practice. The laboratories analysing CPs have to optimise with extreme care the quantification step in validating the method, in terms of refining the calibration function and approach (i.e. number and composition of calibration points, *m/z* values used for the MS detection, response factors determination, etc.). Therefore, despite that the SCCPs' pattern of the CC was found to match satisfactorily the method quality control (MQC) by goodness of fit correlation ($R^2 = 0.70$), the use of the CC for SCCPs quantification is obviously showing some limitations.

The laboratories reported, as expected, higher uncertainties for the measurement results of the MQC SRM 1946 compared to the calibration quality control (CQC): the average expanded uncertainties were 29 % for the SCCPs and 28 % for the sum of SCCPs Cl_6 congeners, respectively.

Based on the evaluation of the CQC and MQC results, between three to five datasets dropped off from the further statistical analysis leading to the assignment of certified values to ERM-CE100.

3.3.2. *ERM-CE100 characterisation results and value assignment*

The number of datasets "validated" as described in Section 3.3.1 were seven for the SCCPs content (quantified with Dr. Ehrenstorfer calibrants), six for the SCCPs content quantified with the common calibrant (CC) and five for the sum of SCCPs Cl_6 congeners (quantified with the CC).

The certification study contemplated the optional reporting of the MCCPs content. Six datasets were received and were evaluated similarly to the SCCPs datasets, except for the check based on the quality control samples for the reasons explained in Section 2.5. The satisfactory agreement of the MCCPs datasets permitted the assignment of a certified value also for this measurand, respecting the JRC requirements. A retroactive evaluation of the homogeneity and stability data for MCCPs was possible thanks to the inclusion of MCCPs calibrants during the homogeneity and stability measurements for SCCPs.

Three certified values were assigned to ERM-CE100: SCCPs content quantified by Dr. Ehrenstorfer calibrants, SCCPs content quantified by the CC and MCCPs content quantified by Dr. Ehrenstorfer calibrants, Figs. 5 and 6.

An indicative value was assigned for the sum of SCCPs Cl_6 congeners because only five datasets contributed to its assignment and the uncertainty was deemed too large, Fig. 7. Indicative values are less reliable than certified values.

The certified values assigned to ERM-CE100 for the content of SCCPs quantified by Dr. Ehrenstorfer calibrants (31 ± 9 µg kg^{-1}) and by the common calibrant (23 ± 7 µg kg^{-1}) are not significantly different i.e., the uncertainties overlap, similarly to what was already observed for the method quality control (MQC) SRM 1946. This consideration corroborates the validity of the CC as "proxy" of the routinely used calibrants, with due consideration of the magnitude of the certified uncertainties.

A look at the intralaboratory performance flags a significant difference between the SCCPs content quantified with the two calibrants for the two laboratories D5 and D7, Fig. 5. This intralaboratory difference does not seem to be linked to the instrumental technique used (D5 employed GC-ECNI-Orbitrap HRMS while D7 employed direct injection chlorine enhanced APCI$^-$-QTOF-HRMS), neither to an underestimation of the measurement uncertainty that for both laboratories is close to the average of all laboratories (about 30 %).

The average measurement uncertainty (calculated based on the

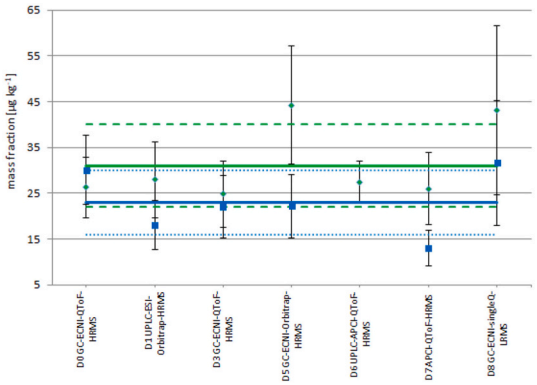

Fig. 5. SCCPs certified values (solid lines) and expanded uncertainty ($k = 2$) (dotted lines) (31 ± 9 µg kg^{-1} and 23 ± 7 µg kg^{-1} wet weight) in ERM-CE100. Laboratories' means quantified by Dr. Ehrenstorfer standards (green colour, diamond-shape marker) and by the common calibrant (blue colour, squared marker). The bars correspond to the expanded uncertainty of the means ($n = 6$).

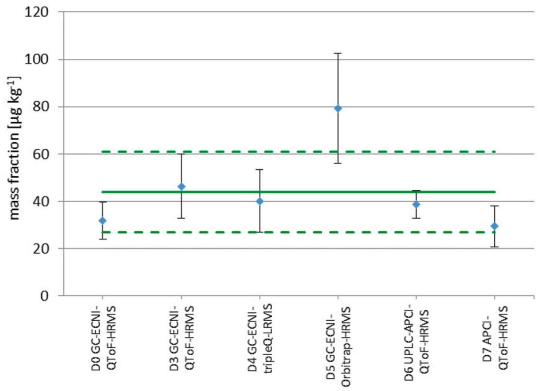

Fig. 6. MCCPs certified value (solid line) and expanded uncertainty ($k = 2$) (dotted lines) (44 ± 17 µg kg^{-1} wet weight) in ERM-CE100. Laboratories' means quantified by Dr. Ehrenstorfer standards. The bars correspond to the expanded uncertainty of the means (n = 6).

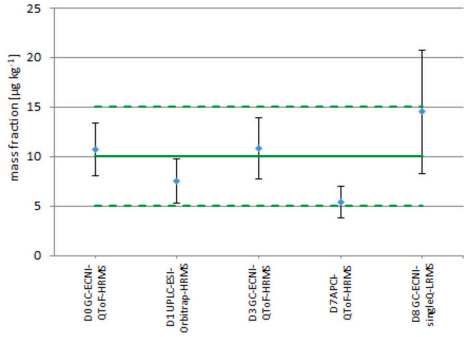

Fig. 7. Indicative value (solid line) and expanded uncertainty ($k = 2.447$) (dotted lines) for the mass fraction of the sum of SCCPs Cl_6 congeners (10 ± 5 µg kg^{-1} wet weight) in ERM-CE100. Laboratories' means quantified by the common calibrant. The bars correspond to the expanded uncertainty of the means ($n = 6$).

laboratories' reports) for the SCCPs and MCCPs results in ERM-CE100 retraces the one observed for SRM 1946, being between 27 and 30 %. These uncertainty values represent what is the state-of-the-art in the determination of CPs in fish matrices, still marked by unresolved uncertainty sources.

The laboratories had to report six independent results for ERM-CE100. Therefore, it was possible to apply one-way ANOVA to calculate the standard deviation within and among laboratories, as further insight into the analytical performance. The reader should be reminded that all selected laboratories demonstrated to be expert laboratories in CPs determination, and that there was the additional performance-refining step based on the quality control samples.

The use of the common calibrant (CC) was supposed to help mitigating the large variability that the authors expected in the characterisation study. However, looking at the relative standard deviation (RSD) among laboratories when analysing the ERM-CE100, it does not seem the case. Applying ANOVA, the RSD inter-laboratories resulted in 25.8 % when the laboratories used the Dr. Ehrenstorfer standards while it was 30.5 % in the case of the CC (Table 3).

While the RSD among laboratories shows values between 25 and 30 % for the SCCPs, it reaches a higher value of 40.7 % for MCCPs. The values include a large inter-method variability, not only in the sample preparation/clean-up and analytical instrumentation applied (both GC- and LC-based), but also for what concerns the calibration functions and quantification approaches. Therefore, the outcome of the study is quite satisfactory, particularly in comparison to previous interlaboratory studies on quantification of CPs in a fish matrix [31,32].

Table 3
Within and among laboratory relative standard deviation (RSD) in the ERM-CE100 characterisation campaign (p = number of datasets).

Measurand	*p*	Within laboratory RSD [%]	Among laboratories RSD [%]
SCCPs (by Dr. Ehrenstorfer calibrants)	7	18.8	25.8
SCCPs (by common calibrant)	6	14.6	30.5
Sum of SCCPs Cl_6 congeners (by common calibrant)	5	16.3	35.1
MCCPs (by Dr. Ehrenstorfer calibrants)	6	13.6	40.7

The certified uncertainties of the SCCPs values assigned to ERM-CE100 are about 30 % (Fig. 5). Again, the certified uncertainty of the MCCPs shows a higher value of almost 39 % (Fig. 6): this is mainly due to a higher uncertainty contribution relative to the characterisation study (u_{char}), highlighting a poorer agreement among the datasets compared to SCCPs. The magnitude of these uncertainties might seem large for values assigned as certified. However, they are perfectly reasonable when acknowledging the status of method performance in the quantification of CPs.

The visual inspection of the characterisation data for ERM-CE100 might indicate that the GC-based datasets deliver higher values compared to the LC-based datasets. Keeping in mind the low robustness of the statistics (four valid GC-based datasets against two/three LC-based datasets), a one-way ANOVA was carried out to check for statistically significant differences. No significant difference between GC-based and LC-based values was detected, apart from the dataset of the sum of SCCPs Cl_6 congeners. This evaluation should be taken with caution because of the low number of datasets involved and the large uncertainties of the values.

3.4. SCCPs homologue group profiles in ERM-CE100

The SCCPs chain length congener groups, homologue pattern and chlorine content in the candidate CRM ERM-CE100 were investigated at A-LIFE (Vrije Universiteit Amsterdam, NL) by chlorine enhanced-$APCI^-$-QTOF-HRMS before the characterisation campaign (Fig. 2), with the purpose to establish a matching composition of the common calibrant to be provided to the participating laboratories.

As previously mentioned, the measured SCCPs pattern can change depending on the instrument used. This is confirmed by observing the SCCPs homologue group profiles reported as additional information by the laboratories participating to the ERM-CE100 characterisation exercise, Fig. 8. While acknowledging that the laboratories analysed different ranges of Cl groups, from the widest range $Cl_{4\text{-}12}$ to the narrowest range $Cl_{6\text{-}9}$, some conclusions can nonetheless be drawn.

The C_{13} chain length congener group confirms as the most abundant (in relative terms) regardless of the instrument used [average of all datasets and standard deviation (SD) = 59 ± 11 %]. The C_{11} is the second most abundant group for the majority of the submitted datasets (average and SD of 19 ± 5 %), while C_{12} results as second most abundant group for a couple of them (average and SD of 16 ± 4 %). These data are in line with the preliminary investigation conducted at A-LIFE on ERM-CE100 (Section 3.2).

Regarding the Cl_x homologue groups, the SCCPs Cl_6 group appears as the most abundant in five datasets while for the other four Cl_7 is the most abundant (Fig. 9).

It is not possible to discern a connection between this observation and the analytical equipment used, e.g., GC vs LC-based. Calculating an average composition for the Cl_x homologue groups provides little insight, due to the high variation of the reported data (at least for the $Cl_{4\text{-}5}$ and $Cl_{9\text{-}11}$ groups that have the lowest relative abundances, between 1 % and 8 %). Even for the most abundant Cl_6, Cl_7 and Cl_8 groups (calculated average abundance of 31.7, 34.4 and 15.6 % respectively),

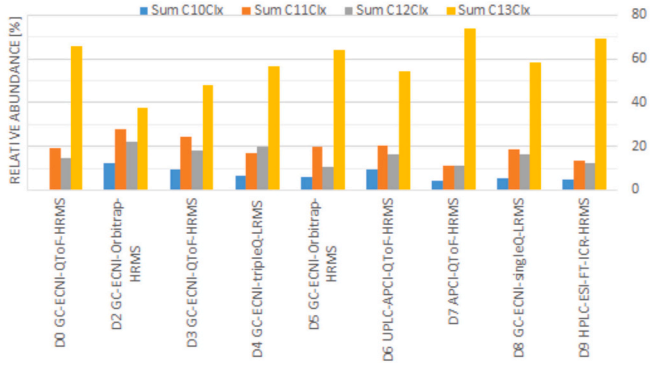

Fig. 8. Relative abundances of SCCPs carbon chain length groups in ERM-CE100. Values as reported during the characterisation study (x = from 6-9 to 4–12).

the relative standard deviation of the datasets' average lies between 31 and 39 %. These observations confirm the findings published by Krätschmer et al. [32] about the high inter-laboratory variation (up to 40 %) in the quantification of CPs homologue groups. The CPs pattern does not only depend on the choice of the equipment employed but it is also significantly influenced by the instrumental parameters and quantitation approach within the same analytical instrumental technique. As an example of the latter, Fig. 10 shows a superimposition of the SCCPs homologue patterns reported by laboratories D2 and D5, applying the same analytical equipment, i.e. GC-ECNI-Orbitrap-MS but different quantification approaches (Table 1). In C_{11} and C_{12} chain length congener groups, the Cl_6, Cl_7 and Cl_8 homologue groups do not show the same relative abundances.

3.5. Metrological traceability of the assigned values

The certified and indicative values assigned to ERM-CE100 are reported on the certificate publicly accessible [68].

A separate discussion is necessary for what concerns the definition of the measurands and metrological traceability of the assigned values.

For the purpose of this study, the measurand SCCPs is to be intended as the sum of SCCPs $C_{10–13}Cl_{4-12}$, the measurand MCCPs as the sum of MCCPs $C_{14–17}Cl_{4-10}$ and the measurand "sum of SCCPs Cl_6 congeners" as the sum of all congeners $C_{10–13}Cl_6$. The span of congener groups reported by the participants varied depending on the measurement technique employed but eventually there was always at least one dataset included in the assigned values covering the chlorine range Cl_{4-12} and Cl_{4-10} for SCCPs and MCCPs, respectively.

The common calibrant (CC) is a well-characterised mixture of five purity assessed SCCPs Cl_6 single congeners and it was designed to match the distribution of the Cl_6 chain length congener groups and the % Cl of the ERM-CE100 for an appropriate quantification. The match is clearly limited, i.e., a 5-isomers mixture for quantification of a mixture of thousands of isomers. This was nevertheless the best available option ensuring that the calibrant could be one of the anchor points of the metrological traceability of the assigned value to the SI.

The choice of using a CC linked also to the possible expectation of reducing the variability among the characterisation datasets. This approach seemed to work in previous examples [81], but unfortunately did not work for the CPs' case, once again reaffirming the undisputable difficulty in the analytical determination of these analytes and confirming the dependence of the measurement accuracy on multiple factors.

The SCCPs and MCCPs values based on Dr. Ehrenstorfer standards cannot claim the SI traceability because these standards miss a thorough purity assessment and are thus much less characterised compared to the CC from Chiron AS.

The traceability to the SI for the values quantified by the CC (including thus the sum of SCCPs Cl_6 congeners) is further assured by the agreement of measurements obtained by the different analytical methods employed in the characterisation study. Both GC- and LC-based separation techniques were coupled with different HRMS detectors. The datasets D4 and D8 were even acquired with a GC coupled to a low resolution mass spectrometer. While it is known that lower chlorinated CPs (i.e., with less than five chlorine atoms), show low sensitivity using ECNI (most common applied ionisation technique for routine analysis of CPs), in the present study the ECNI-based methods performed equally well. This is likely to be attributed to the very low relative abundance of Cl_4 congeners in ERM-CE100, accounting only for the 0.83 % of the total (as estimated by chlorine enhanced-APCI$^-$-QTOF-HRMS). This enhances the usefulness of ERM-CE100, i.e., also laboratories employing ECNI-MS can use this CRM as a valid quality control tool in the validation and/or

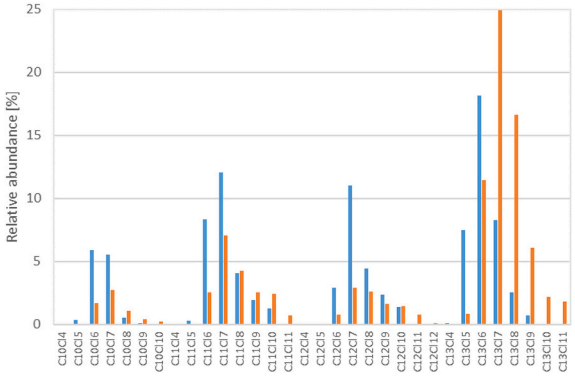

Fig. 10. SCCPs homologue pattern in ERM-CE100: relative abundances of the congener groups. Results of laboratory D2 (blue) and D5 (orange) by GC-ECNI-Orbitrap-HRMS in the characterisation study.

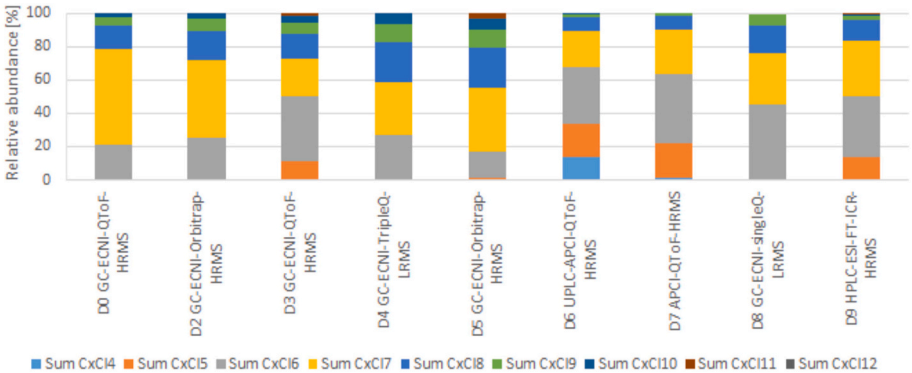

Fig. 9. Relative abundances of SCCPs homologue congener groups in ERM-CE100. Values as reported during the characterisation study (x = 10–13).

trueness check of their method.

Having two certified values assigned for the same SCCPs measurand should not be interpreted in a negative way. Rather it opens the choice of being traceable to different points (also in terms of quality) via the use of the two calibrants.

There are still open questions in the metrological traceability in CPs quantification, but the results of this study have provided useful insights.

4. Conclusions

The fish tissue ERM-CE100 is the first commercially available matrix CRM for the analysis of chlorinated paraffins enabling analytical laboratories to ensure better control on the performance of their determination method.

This matrix CRM together with the suite of pure standard CRMs produced under the frame of the CHLOFFIN project can be considered a tool-box that can help analytical laboratories in quality-assuring their CPs measurements in the analysis of environmental and food samples. The use of ERM-CE100 together with the purity-assessed common calibrant provides the laboratories with a way to establish metrological traceability of their SCCPs measurement results to the SI. Certified values assigned for SCCPs and MCCPs based on measurements carried out using Dr. Ehrenstorfer standards "stop" their traceability to these calibrants.

A significant outcome of this study is that the two certified SCCPs values obtained using the common calibrant and the Dr. Ehrenstorfer standards are not significantly different. This is certainly facilitated by the high uncertainty associated with these values, but it also indicates that using Cl_6 single congeners as a "proxy" for quantification of the other congeners in ERM-CE100 did not result in a significantly biased result.

The usefulness of the CRM is magnified by the fact that the certified values are comprehensively based on results obtained by GC and LC-based analytical methodologies coupled with different MS detectors, providing the laboratories with a quality control tool characterised by a general validity (while acknowledging the relatively large certified uncertainty).

Despite the successful outcome of the certification campaign, the interlaboratory comparison shows that the comparability of CPs measurements among laboratories/methods has still room for improvement. The relative standard deviation among laboratories is about 25–30 % for SCCPs, and peaks over to 40 % for the MCCPs. The average expanded uncertainty for CPs measurements of about 30 % calculated in this study is indicative of the laboratories' struggle to obtain accurate results. The outcome of the intercomparison exercise re-confirm as well that data comparability of CPs homologue groups is still an issue. Therefore, future regulations of CPs should still be based on "sum parameters".

Thanks to the joint efforts within the Eurostars Project CHLOFFIN, we are few steps further in an improved quantification of CPs, both regarding data comparability and metrological traceability. The way ahead to an ideal measurement accuracy for these analytes is nonetheless still full of hurdles.

CRediT authorship contribution statement

Marina Ricci: Writing – original draft, Visualization, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jacob de Boer:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Jon Eigill Johansen:** Writing – review & editing, Resources, Methodology, Funding acquisition. **Huiling Liu:** Writing – review & editing, Supervision, Methodology, Investigation. **Pierre Dumas:** Writing – review & editing, Investigation. **Nicholas Alexander Warner:** Writing – review & editing, Investigation. **Ingus Pērkons:** Writing – review & editing, Investigation. **Thomas Jacob McGrath:** Writing – review & editing, Investigation. **Anders Røsrud Borgen:** Writing – review & editing, Investigation. **Stine Marie Bjørneby:** Writing – review & editing, Investigation. **Jakub Tomasko:** Writing – review & editing, Investigation. **Helena Steer:** Writing – review & editing, Investigation. **Anouk Lentjes:** Writing – review & editing, Investigation. **Martin van Velzen:** Writing – review & editing, Investigation. **Louise van Mourik:** Writing – review & editing, Methodology, Investigation.

Declaration of competing interest

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

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aca.2024.342757.

References

[1] C. Chen, A. Chen, F. Zhan, F. Wania, S. Zhang, L. Li, J. Liu, Global Historical production, Use, in-use stocks, and emissions of short-, medium-, and long-chain chlorinated paraffins, Environ. Sci. Technol. 56 (2022) 7895–7904.
[2] G.T. Tomy, A.T. Fisk, J.B. Westmore, D.C.G. Muir, Environmental chemistry and toxicology of polychlorinated n-alkane, Rev. Environ. Contam. Toxicol. 158 (1998) 53–128.
[3] J. Glüge, Z. Wang, C. Bogdal, M. Scheringer, K. Hungerbühler, Global production, use, and emission volumes of short-chain chlorinated paraffins – a minimum scenario, Sci. Total Environ. 573 (2016) 1132–1146.
[4] Directive 2013/39/EU of the European Parliament and of the Council of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy [2013] L226/1.
[5] Regulation (EU) 2019/1021 of the European Parliament and of the Council of 20 June 2019 on Persistent organic pollutants (recast) [2019] OJ L 169/45.
[6] UNEP, UNEP/POPS/COP, 8. SC-8/11 listing of short-chain chlorinated paraffins, Available at: http://chm.pops.int/Portals/0/download.aspx?d=UNEP-POPS-COP.8-SC-8-11.English.pdf, 2017. (Accessed 25 August 2023).
[7] N. Geng, X. Ren, Y. Gong, H. Zhang, F. Wang, L. Xing, R. Cao, J. Xu, Y. Gao, J. P. Giesy, J. Chen, Integration of metabolomics and transcriptomics reveals short-chain chlorinated paraffin-induced hepatotoxicity in male Sprague-Dawley rat, Environ. Int. 133 (2019) 105231–105241.
[8] S. Iozza, C.E. Muller, P. Schmid, C. Bogdal, M. Oehme, Historical profiles of chlorinated paraffins and polychlorinated biphenyls in a dated sediment core from Lake Thun (Switzerland), Environ. Sci. Technol. 42 (2008) 1045–1050.
[9] K. Vorkamp, J. Balmer, H. Hung, R.J. Letcher, F.F. Riget, A review of chlorinated paraffin contamination in Arctic ecosystems, Emerg. Contam. 5 (2019) 219–231.
[10] R. Sun, J. Chen, H. Shao, L. Tang, X. Zheng, Q.X. Li, Y. Wang, X. Luo, B. Mai, Bioaccumulation of short-chain chlorinated paraffins in chicken (Gallus domesticus): comparison to fish, J. Hazard Mater. 396 (2020) 122590–122598.
[11] P. Labadie, C. Blasi, K. Le Menach, E. Geneste, M. Babut, O. Perceval, H. Budzinski, Evidence for the widespread occurrence of short- and medium-chain chlorinated paraffins in fish collected from the Rhone River basin (France), Chemosphere 223 (2019) 232–239.
[12] L. Zeng, J.C.W. Lam, Y. Wang, G. Jiang, P.K.S. Lam, Temporal trends and pattern changes of short- and medium-chain chlorinated paraffins in marine mammals

from the South China sea over the past decade, Environ. Sci. Technol. 49 (2015) 11348–11355.
[13] W. Wang, J. Wanga, H. Niea, R. Fana, Y. Huang, Occurrence, trophic magnification and potential risk of short-chain chlorinated paraffins in coral reef fish from the Nansha Islands, South China Sea, Sci. Total Environ. 739 (2020) 140084–140091.
[14] D. Xia, L. Gao, M. Zheng, J. Li, L. Zhang, Y. Wu, Q. Tian, H. Huang, L. Qiao, Human exposure to short- and medium-chain chlorinated paraffins via mothers' milk in Chinese urban population, Environ. Sci. Technol. 51 (2017) 608–615.
[15] Y.X. Liu, M. Aamir, M.Y. Li, K. Liu, Y.H. Hu, N. Liu, Y.F. Xu, J.Y. Du, J.R. Xu, W. P. Liu, Prenatal and postnatal exposure risk assessment of chlorinated paraffins in mothers and neonates: occurrence, congener profile, and transfer behaviour, J. Hazard Mater. 395 (2020) 122660–122667.
[16] T. Li, Y. Wan, S. Gao, B. Wang, J. Hu, High-throughput determination and characterization of short-, medium-, and long-chain chlorinated paraffins in human blood, Environ. Sci. Technol. 51 (2017) 3346–3354.
[17] K. Krätschmer, R. Malisch, W. Vetter, Chlorinated paraffin levels in relation to other persistent organic pollutants found in pooled human milk samples from primiparous mothers in 53 countries, Environ. Health Perspect. 129 (2021) 870041–8700412.
[18] S. Xu, S. Hansen, A. Rautio, M.R. Järvelin, K. Abass, J. Rysä, S. Palaniswamy, S. Huber, J.O. Grimalt, P. Dumas, J.Ø. Odland, Monitoring temporal trends of dioxins, organochlorine pesticides and chlorinated paraffins in pooled serum samples collected from Northern Norwegian women: the MISA cohort study, Env, Res. 204 (2022) 111980–111989.
[19] Y. Huang, X. Qing, G. Jiang, L. Chen, Q. He, X.Z. Meng, B. Gao, Short-chain chlorinated paraffins in fish from two developed regions of China: occurrence, influencing factors and implication for human exposure via consumption, Chemosphere 236 (2019) 124317–124323.
[20] Y. Cao, K.H. Harada, W. Liu, J. Yan, C. Zhao, T. Niisoe, A. Adachi, Y. Fujii, C. Nouda, T. Takasuga, A. Koizumi, Short-chain chlorinated paraffins in cooking oil and related products from China, Chemosphere 138 (2015) 104–111.
[21] X.T. Wang, H.H. Jia, B.P. Hu, H.X. Cheng, Y. Zhou, R. Fu, Occurrence, sources, partitioning and ecological risk of short- and medium-chain chlorinated paraffins in river water and sediments in Shanghai, Sci. Total Environ. 653 (2019) 475–484.
[22] A. Rubirola, F.J. Santos, M.R. Boleda, M.T. Galceran, Routine method for the analysis of short-chain chlorinated paraffins in surface water and wastewater,, Clean – Soil, Air, Water 46 (2018) 1600151–1600160.
[23] A.K. Sakhi, E. Cequier, R. Becher, A. Kocbach Bølling, A.R. Borgen, M. Schlabach, N. Schmidbauer, G. Becher, P. Schwarze, C. Thomsen, Concentrations of selected chemicals in indoor air from Norwegian homes and schools, Sci. Total Environ. 674 (2019) 1–8.
[24] P.S. Diefenbacher, C. Bogdal, A.C. Gerecke, J. Glüge, P. Schmid, M. Scheringer, K. Hungerbühler, Short-chain chlorinated paraffins in Zurich, Switzerland - atmospheric concentrations and emissions, Environ. Sci. Technol. 49 (2015) 9778–9786.
[25] L.M. van Mourik, X. Wang, C. Paxma, P.E.G. Leonards, F. Wania, J. de Boer, J. F. Mueller, Spatial variation of short- and medium-chain chlorinated paraffins in ambient air across Australia, Environ. Pollut. 261 (2020) 114141–114151.
[26] Y. Wu, J. Wu, H. Tan, Q. Song, J. Zang, X. Zong, J. Zhou, W. Wu, X. Cai, W. Zhang, X. Liu, Distributions of chlorinated paraffins and the effects on soil microbial community structure in a production plant brownfield site, Environ. Pollut. 262 (2020) 114328–114338.
[27] A.M. Muscalu, D. Morse, E.J. Reiner, T. Górecki, The quantification of short-chain chlorinated paraffins in sediment samples using comprehensive two-dimensional gas chromatography with μECD detection, Anal. Bioanal. Chem. 409 (2017) 2065–2074.
[28] International Agency for Research on Cancer, IARC monographs on the identification of carcinogenic hazards to humans. https://monographs.iarc.who.int/list-of-classifications/. (Accessed 9 November 2023).
[29] J. Glüge, L. Schinkel, K. Hungerbuehler, R. Cariou, C. Bogdal, Environmental risks of medium-chain chlorinated paraffins (MCCPs) - a review, Environ. Sci. Technol. 52 (2018) 6743–6760.
[30] G.T. Tomy, Analysis of chlorinated paraffins in environmental matrices: the ultimate challenge for the analytical chemist, in: J.d. Boer (Ed.), Chlorinated Paraffins, the Handbook of Environmental Chemistry, Springer, Berlin Heidelberg, 2010, pp. 83–106.
[31] L.M. van Mourik, I. van der Veen, S. Crum, J. de Boer, Developments and interlaboratory study of the analysis of short-chain chlorinated paraffins, Trends Anal. Chem. 102 (2018) 32–40.
[32] K. Krätschmer, A. Schächtele, Interlaboratory studies on chlorinated paraffins: evaluation of different methods for food matrices, Chemosphere 234 (2019) 252–259.
[33] L.M. van Mourik, P.E.G. Leonards, C. Gaus, J. de Boer, Recent developments in capabilities for analysing chlorinated paraffins in environmental matrices: a review, Chemosphere 136 (2015) 259–272.
[34] M. Mézière, K. Krätschmer, I. Pērkons, D. Zacs, P. Marchand, G. Dervilly, B. Le Bizec, A. Schächtele, R. Cariou, W. Vetter, Addressing main challenges regarding short- and medium-chain chlorinated paraffin analysis using GC/ECNI-MS and LC/ESI-MS methods, J. Am. Soc. Mass Spectrom. 31 (2020) 1885–1895.
[35] G.T. Tomy, G.A. Stern, D.C.G. Muir, A.T. Fisk, C.D. Cymbalisty, J.B. Westmore, Quantifying C10-C13 polychloroalkanes in environmental samples by high-resolution gas chromatography/electron capture negative ion high-resolution mass spectrometry, Anal. Chem. 69 (1997) 2762–2771.
[36] B. Yuan, D. Muir, M. MacLeod, Methods for trace analysis of short-, medium-, and long-chain chlorinated paraffins: critical review and recommendations, Anal. Chim. Acta 1074 (2019) 16–32.
[37] C. Bogdal, T. Alsberg, P.S. Diefenbacher, M. MacLeod, U. Berger, Fast quantification of chlorinated paraffins in environmental samples by direct injection high-resolution mass spectrometry with pattern deconvolution, Anal. Chem. 87 (2015) 2852–2860.
[38] B. Yuan, C. Bogdal, U. Berger, M. MacLeod, W.A. Gebbink, T. Alsberg, C.A. de Wit, Quantifying short-chain chlorinated paraffin congener groups, Environ. Sci. Technol. 51 (2017) 10633–10641.
[39] M. Coelhan, M. Saraci, H. Parlar, A comparative study of polychlorinated alkanes as standards for the determination of C10-C13 polychlorinated paraffines in fish samples, Chemosphere 40 (2000) 685–689.
[40] P. Castells, F.J. Santos, M.T. Galceran, Evaluation of three ionisation modes for the analysis of chlorinated paraffins by gas chromatography/ion-trap mass spectrometry, Rapid Commun. Mass Spectrom. 18 (2004) 529–536.
[41] M. Reth, Z. Zencak, M. Oehme, New quantification procedure for the analysis of chlorinated paraffins using electron capture negative ionization mass spectrometry, J. Chromatogr. A 1081 (2005) 225–231.
[42] Y. Gao, H. Zhang, L. Zou, P. Wu, Z. Yu, X. Lu, J. Chen, Quantification of short-chain chlorinated paraffins by deuterodechlorination combined with gas Chromatography−Mass spectrometry, Environ. Sci. Technol. 50 (2016) 3746–3753.
[43] S. Geiß, D. Löffler, B. Körner, M. Engelke, G. Sawal, P. Bachhausen, Determination of the sum of short chain chlorinated n-alkanes with a chlorine content between 50% and 67% in sediment samples by GC–ECNI-MS and quantification by multiple linear regression, Microchem. J. 119 (2015) 30–39.
[44] B. Yuan, T. Alsberg, C. Bogdal, M. MacLeod, U. Berger, W. Gao, Y. Wang, C.A. de Wit, Deconvolution of soft ionization mass spectra of chlorinated paraffins to resolve congener groups, Anal. Chem. 88 (2016) 8980–8988.
[45] L. Schinkel, S. Lehner, N.V. Heeb, P. Marchand, R. Cariou, K. McNeill, C. Bogdal, Dealing with strong mass interferences of chlorinated paraffins and their transformation products: an analytical guide, Trends Anal. Chem. 106 (2018) 116–124.
[46] L. Chen, Y. Huang, S. Han, Y. Feng, G. Jiang, C. Tang, Z. Ye, W. Zhan, M. Liu, S. Zhang, Sample pretreatment optimization for the analysis of short chain chlorinated paraffins in soil with gas chromatography–electron capture negative ion-mass spectrometry, J. Chrom. A 1274 (2013) 36–43.
[47] F. Pellizzato, M. Ricci, A. Held, H. Emons, Validation of a method for the determination of short-chain chlorinated paraffins in soil and sediments, Accred Qual. Assur. 14 (2009) 529–540.
[48] D. Xia, L. Gao, M. Zheng, Q. Tian, H. Huang, L. Qiao, A novel method for profiling and quantifying short- and medium-chain chlorinated paraffins in environmental samples using comprehensive two-dimensional gas chromatography-electron capture negative ionization high-resolution time-of-flight mass spectrometry, Environ. Sci. Technol. 50 (2016) 7601–7609.
[49] J.F. Ayala-Cabrera, M.T. Galceran, E. Moyano, F.J. Santos, Chloride-attachment atmospheric pressure photoionisation for the determination of short-chain chlorinated paraffins by gas chromatography-high-resolution mass spectrometry, Anal. Chim. Acta 1172 (2021) 338673–338683.
[50] G.T. Tomy, J.B. Westmore, G.A. Stern, D.C.G. Muir, A.T. Fisk, Interlaboratory study on quantitative methods of analysis of C10-C13 polychloro-n-alkanes, Anal. Chem. 71 (1999) 446–451.
[51] F. Pellizzato, M. Ricci, A. Held, H. Emons, W. Boehmer, S. Geiss, S. Iozza, S. Mais, M. Petersen, P. Lepom, Laboratory intercomparison study on the analysis of short-chain chlorinated paraffins in an extract of industrial soil, Trends Anal. Chem. 28 (2009) 1029–1035.
[52] A.R. Fernandes, W. Vetter, C. Dirks, L. van Mourik, R. Cariou, J. Sprengel, N. Heeb, A. Lentjes, K. Krätschmer, Determination of chlorinated paraffins (CPs): analytical conundrums and the pressing need for reliable and relevant standards, Chemosphere 286 (2022) 131878–131889.
[53] N.V. Heeb, S. Iten, L. Schinkel, M. Knobloch, J. Sprengel, P. Lienemann, D. Bleiner, W. Vetter, Characterization of synthetic single-chain CP standard materials - removal of interfering side products, Chemosphere 255 (2020) 126959–126966.
[54] J. Sprengel, W. Vetter, Synthesis and characterization of eight single chain length chlorinated paraffin standards and their use for quantification, Rapid Commun. Mass Spectrom. 33 (2019) 49–56.
[55] J. Sprengel, N. Wiedmaier-Czerny, W. Vetter, Characterization of single chain length chlorinated paraffin mixtures with nuclear magnetic resonance spectroscopy (NMR), Chemosphere 228 (2019) 762–768.
[56] J. Sprengel, W. Vetter, NMR and GC/MS analysis of industrial chloroparaffin mixtures, Anal. Bioanal. Chem. 412 (2020) 4669–4679.
[57] G.T. Tomy, B. Billeck, G.A. Stern, Synthesis, isolation and purification of C10-C13 polychloro-n-alkanes for use as standards in environmental analysis, Chemosphere 40 (2000) 679–683.
[58] B. Yuan, D.H. Lysak, R. Soong, A. Haddad, A. Hisatsune, A. Moser, S. Golotvin, D. Argyropoulos, A.J. Simpson, D.C.G. Muir, Chlorines are not evenly substituted in chlorinated paraffins: a predicted nmr pattern matching Framework for isomeric discrimination in complex contaminant mixtures, Environ. Sci. Technol. Lett. 7 (2020) 496–503.
[59] L. Schinkel, C. Bogdal, E. Canonica, R. Cariou, D. Bleiner, K. McNeill, N.V. Heeb, Analysis of medium-chain and long-chain chlorinated paraffins: the urgent need for more specific analytical standards, Environ. Sci. Technol. Lett. 5 (2018) 708–717.
[60] J. Sprengel, K. Krätschmer, W. Vetter, A new synthesis approach for the generation of single chain CP mixtures composed of a few major compounds, Chemosphere 287 (2022) 132372–132378.
[61] K. Krätschmer, A. Schächtele, R. Malisch, W. Vetter, Quantification standards - the Achilles heel of chlorinated paraffin determination? Organohalogen Compd. 81 (2019) 344–347.

[62] N. Hanari, T. Nakano, Comparison of short-chain chlorinated paraffin concentrations and homolog profiles by interlaboratory trial using a candidate reference material, Chemosphere 291 (2022) 132783–132789.
[63] L.M. van Mourik, R. Lava, J. O'Brien, P.E.G. Leonards, J. de Boer, M. Ricci, The underlying challenges that arise when analysing short-chain chlorinated paraffins in environmental matrices, J. Chromatogr. A 1610 (2020) 460550–460559.
[64] L.M. van Mourik, M. Ricci, S. Valderhaug, A. Gorovoi, S. Brandsma, J. Button, H. Liu, J. de Boer, J.E. Johansen, Chloffin – answering the urgent call for chlorinated paraffins standards, 3.07P.3, in: SETAC Europe 30th Annual Meeting, 2020, 3-7 May 2020, Dublin.
[65] S. Valderhaug, A. Gorovoi, L.M. van Mourik, M. Ricci, S. Brandsma, J. Button, J. de Boer, H. Liu, J.E. Johansen, New standards for chlorinated paraffins – Eurostars CHLOFFIN project, 3.07P.6, in: SETAC Europe 30th Annual Meeting, 2020, 3-7 May 2020, Dublin.
[66] http://chloffin.eu/. (Accessed 25 August 2023).
[67] I. Dosis, M. Ricci, L. Majoros, R. Lava, H. Emteborg, A. Held, H. Emons, Addressing analytical challenges of the environmental monitoring for the water Framework directive: ERM-CE100, a new biota certified reference material, Anal. Chem. 89 (2017) 2514–2521.
[68] European Commission, Joint Research Centre (JRC), Certified reference materials catalogue. https://crm.jrc.ec.europa.eu/. (Accessed 8 February 2023).
[69] National Institute of Standards and Technology, Standard Reference Materials, NIST store, https://shop.nist.gov/ (Accessed 9 November 2023).
[70] International Organization for Standardization, ISO Guide 35:2017, Reference Materials – Guidance for Characterization and Assessment of Homogeneity and Stability, Geneva, Switzerland, 2017.
[71] M. Ricci, L. van Mourik, J.E Johansen, J de Boer. The Certification of the Mass Fraction of Short-Chain Chlorinated Paraffins (SCCPs) and Medium-Chain Chlorinated Paraffins (MCCPs) in Fish Tissue: ERM®-CE100, Publications Office of the European Union, Luxembourg, 2022, 10.2760/430109, JRC131533.
[72] International Organization of Standardization, ISO 12010, Water Quality - Determination of Short-Chain Polychlorinated Alkanes (SCCP) in Water - Method Using Gas Chromatography-Mass Spectrometry (GC-MS) and Negative-Ion Chemical Ionization (NCI), Geneva, Switzerland, 2019.
[73] International Organization for Standardization, ISO/IEC 17025:2017, General Requirements for the Competence of Testing and Calibration Laboratories, Geneva, Switzerland, 2017.
[74] ERM Application Note 1, Comparison of a measurement result with the certified value. https://crm.jrc.ec.europa.eu/e/132/User-support-Application-Notes. (Accessed 25 August 2023).
[75] International Organization of Standardization, ISO 13528, Statistical Methods for Use in Proficiency Testing by Interlaboratory Comparison, Geneva, Switzerland, 2015.
[76] T.P.J. Linsinger, J. Pauwels, A.M.H. van der Veen, H. Schimmel, A. Lamberty, Homogeneity and stability of reference materials, Accred Qual. Assur. 6 (2001) 20–25.
[77] T.P.J. Linsinger, J. Pauwels, A. Lamberty, H. Schimmel, A.M.H. van der Veen, L. Siekmann, Estimating the uncertainty of stability for matrix CRMs, Fres. J. Anal. Chem. 370 (2001) 183–188.
[78] J.E. Johansen, A. Gorovoi, L.M. van Mourik, M. Ricci, S. Brandsma, J. Button, J. de Boer, S. Valderhaug, J. Tuma, O. Gautun, H. Liu, Synthesis and certification of chlorinated paraffins – the Eurostars CHLOFFIN project, 3.05.P-Tu124, in: SETAC Europe 32th Annual Meeting, 2022. Copenhagen.
[79] H. Liu, S. Valderhaug, A. Gorovoi, J. Tuma, O.R. Gautun, J. Nygren, J. Button, C. McKenzie, L.M. van Mourik, M. Ricci, S. Brandsma, J. de Boer, J.E. Johansen, New generation of reference standards for chlorinated paraffins – The Eurostars CHLOFFIN, the EU GreenREF and REVAMP projects, O-5, in: 10th International Symposium on Flame Retardants, BFR, 4-7 September 2022, Athens, 2022.
[80] S. Westwood, K. Lippa, Y. Shimuzu, B. Lalerle, T. Saito, D. Duewer, X. Dai, S. Davies, M. Ricci, A. Baldan, B. Lang, S. Sarge, H. Wang, K. Pratt, R. Josephs, M. Mariassy, D. Pfeifer, J. Warren, W. Bremser, S. Ellison, B. Toman, M. Nelson, T. Huang, A. Fajgelj, A. Gören, L. Mackay, R. Wielgosz, Methods for the SI-traceable value assignment of the purity of organic compounds (IUPAC Technical Report), Pure Appl. Chem. 95 (2023) 1–77.
[81] R. Zeleny, H. Schimmel, Influence of the approach to calibration on the accuracy and the traceability of certified values in certified reference materials, Trends Anal. Chem. 33 (2012) 107–116.