



# Traceable and accurate quantification of iron in seawater using isotope dilution calibration strategies by triple quadrupole ICP-MS/MS: Characterization measurements of iron in a candidate seawater CRM

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## ARTICLE INFO

### Keywords:

Isotope dilution mass spectrometry  
Single dilution  
Double dilution  
Triple dilution  
Seawater  
Iron  
Triethylamine  
Mg(OH)<sub>2</sub> co-precipitation

## ABSTRACT

Accurate quantification of iron is crucial for the characterization of a candidate seawater certified reference material. Isotope dilution mass spectrometry as a primary method is one of the options for this purpose. In this study, triethylamine (TEA) assisted Mg(OH)<sub>2</sub> co-precipitation is developed and combined with isotope dilution mass spectrometry for the characterization of candidate certified reference material, UME CRM 1206. The analytical protocol of co-precipitation was optimized to achieve reproducible yields of ~100% Fe with high salt rejection (residual salinity ~0.003%). Three calibration strategies, single, double and triple isotope dilution mass spectrometry (IDMS) coupled with co-precipitation were investigated in terms of metrological aspects. The determination of Fe was carried out by ICP-MS with tandem configuration (ICP-MS/MS) using NH<sub>3</sub>/He cell gas which was optimized for the minimum background equivalence concentration to be able to measure highly accurate <sup>56</sup>Fe/<sup>57</sup>Fe ratio with the highest possible sensitivity. The background corrected typical procedural blank levels and limit of detection calculated based on three times the standard deviation of blanks were found as 9 ng/kg (0.16 nM) and 11 ng/kg (0.20 nM) for single IDMS, respectively. Trueness of the developed analytical methods has been demonstrated using CASS-6 and NMIA MX014 with complete and very precise recoveries. SI-traceable values with combined uncertainty ( $k = 2$ ) were obtained for single, double and triple IDMS as (12.70 ± 0.16) ng/g, (12.728 ± 0.084) ng/g and (12.732 ± 0.062) ng/g, respectively. The relative combined uncertainty for each approach was calculated as 0.64%, 0.33% and 0.24%, respectively.

## 1. Introduction

Iron is the fourth most abundant element in Earth's crust [1] and known to be an essential trace element with an important role in oceanic carbon cycle [2] by binding the active sites of molecules which are responsible for oxygen transport and mitochondrial electron transfer [3].

In last three decades, intensive research has been performed based on the effect of iron on phytoplankton growth which is related to the global carbon cycle and have indirect consequences on world's climate [4–7]. Different species of iron are present in seawater depending on the equilibrium between inorganic particulate, organic particulate, dissolved organic complexes, inorganic iron, and also the transformation model between physical-chemical species of iron [8]. However, dissolved Fe(II) and Fe(III) which are known as bioavailable forms of iron are thought to be limiting factor for primary productivity of oceans [9].

Hence, accurate and sensitive analytical strategies are very important for the determination of iron in variety of matrices. One of the earliest analytical methods was based on spectrophotometry with tripyridyl as the selective reagent which enabled to detect Fe(II) and also total iron [10]. Ferrozine was discovered as iron selective complexing reagent in 1970 by Stookey [11], and started to be used widely in the determination of iron [3]. Although the detection limits of spectrophotometric methods with ferrozine were down to 0.1 nmol/L for Fe(II) and 0.3 nmol/L for Fe(III), major drawback of selective complexing reagents can result in interconversion of Fe(III) to Fe(II) [12]. Voltammetry having the advantage of being fast and simple, as well as capable of measuring different species of iron is also one of the most commonly used methods. Although the detection limits of voltammetric methods were quite high in the past, lower detection limits were achieved in the range of 35 nmol/L and 7.2 nmol/L (0.4 µg/L) without using complexing ligand by developing a series of modified electrodes

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<https://doi.org/10.1016/j.talanta.2019.120503>

Received 19 July 2019; Received in revised form 20 October 2019; Accepted 23 October 2019

Available online 01 November 2019

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[13–17]. Moreover, stripping voltammetry seems to be superior to those techniques offering 13pM detection limits [18].

Graphite furnace atomic absorption spectrometry coupled with preconcentration techniques have also been developed. Although detection limits were reported at pmol/L levels [19,20], either high reagent blank levels or the need of high sample intake resulted in changing the main direction of research in determination of iron in seawater [3]. Another widely preferred atomic spectrometry technique is inductively coupled plasma mass spectrometry (ICP-MS). In 1992, the detection power of ICP-MS in the determination of iron and ten other trace elements in the open ocean seawater (NASS-3) by applying separation and concentration on silica-immobilized 8-hydroxyquinoline [21] was demonstrated at the National Research Council of Canada. In that study, in order to measure  $^{56}\text{Fe}$ , the most abundant isotope, aerosol desolvation and a nitrogen-argon mixed-gas plasma were used.

In 2006, Shirasaki et al. has been introduced a novel chelating resin called as Nobias Chelate-PA1 which is a hydrophilic methacrylate polymer [22]. This innovation has been turned into a commercially available system called as seaFAST [23] which is mostly coupled by ICP-MS. As the system is a closed and consist of complete fluoropolymer flow part, it provides very low blank levels for iron (0.14 nmoL/L) [24] by using ultrapure reagents and very practical for especially routine analysis laboratories [25,26]. Beside these advantages, research laboratories may not prefer to use due to the high cost of the whole system and the resin used.

In recent years, high resolution (sector field) ICP-MS has become one of the most preferred technique with the advantage of resolving molecular isobaric interferences and powerful detection limits [27–33]. Quadrupole ICP-MS instrument equipped with reaction/collision cell technology also allows us to measure the iron isotopes by removing/reducing possible interferences [34–37]. In order to increase the accuracy and precision of the results obtained from the measurements of iron in seawater, isotope dilution mass spectrometry (IDMS) has been preferred. The method is particularly attractive as full recovery of analyte in the consecutive analytical steps is not essential as long as the conditions for isotopic equilibrium is established [38]. However, while accurate isotope ratio measurements are easier using high resolution ICP-MS (all possible molecular interferences on each isotopes of iron can be easily removed by applying medium resolution), it is a more challenging issue with quadrupole ICP-MS using reaction/collision cell gas as mentioned by Vanhaecke [34].

The aim of this work is to demonstrate an SI traceable and highly accurate analytical method for the quantification of iron in candidate seawater certified reference material, UME CRM 1206, using triple quadrupole ICP-MS/MS. This method fulfills all the requirements of ISO 17034 [39] and ISO Guide 35 [40]. Based on the guidance listed in ISO Guide 35, characterization of iron in the candidate reference material was performed by using the approach “using single reference measurement procedure in a single laboratory”. For certification of iron, single, double and triple IDMS calibration strategies were investigated in great detail in terms of accuracy and related measurement uncertainties. Isotope dilution mass spectrometry was combined with triethylamine ( $\text{N}(\text{CH}_2\text{CH}_3)_3$ , TEA) assisted  $\text{Mg}(\text{OH})_2$  co-precipitation to minimize the matrix on isotope ratio measurements.

## 2. Experimental

### 2.1. Instrumentation

An Agilent 8800 triple quadrupole ICP-MS/MS instrument (Agilent Technologies, Japan) equipped with an octopole collision/reaction cell (CRC) located in between two mass-selective quadrupoles was used in this study. The instrument was equipped with a double pass quartz spray chamber which was cooled by Peltier system to 2.0 °C and fitted with Glass Expansion Micromist nebulizer. As a relatively high

**Table 1**

Typical operating condition of triple quadrupole ICP-MS/MS.

Agilent 8800 Triple Quadrupole ICP-MS/MS	
Nebulizer	Micromist glass nebulizer
Spray chamber	Scott type-double pass
RF applied power (W)	1550
Sampling depth (mm)	8.2
Nebulizer pump (rps)	0.2
Reaction Gas	$\text{NH}_3/\text{He}$
Scan Type	SQ
Carrier gas flow rate ( $\text{L min}^{-1}$ )	0.75
Dilution gas flow rate ( $\text{L min}^{-1}$ )	0.60
Cell gas flow rate ( $\text{mL min}^{-1}$ )	35/6 ( $\text{NH}_3/\text{He}$ )
Extract 1 (V)	–65
Extract 2 (V)	–200
Omega bias (V)	–105
Omega lens (V)	4.0
Octopole bias (V)	–18
KED (V)	–7.1
Wait time offset (ms)	0
Sweeps/replicate	350
Integration time/mass (s)	1.9998
Number of replicates	8
Total analysis time/sample (min)	1.0

dissolved salt concentration was introduced to the ICP-MS during analysis of seawater, high matrix introduction system (HMI) was used to minimize oxide formation. On the other hand, a dual argon humidifier (Elegra, Glass Expansion) was also adapted to alleviate salt deposits in the nebulizer and torch injector providing long term stability of the instrument. Tune parameters were optimized using the auto-tuning tool present in the MassHunter software (Agilent). The optimum reaction/collision cell gas and operating mode of instrument was evaluated using  $^{56}\text{Fe}$  and  $^{57}\text{Fe}$  isotopes using a simulated matrix. Based on these optimization results a  $\text{NH}_3/\text{He}$  gas mixture was used as reaction/collision cell gas to provide the most accurate isotope ratio measurements in the matrix. The operational conditions are given in Table 1.

An analytical balance with a resolution of 0.01 mg (Sartorius MSA225S-100-DA) was used throughout the whole sample preparation. Its calibration was done annually and its SI traceability is maintained via TUBITAK UME where daily performance control of the balance was carried out using calibrated E' class weights. A centrifuge (Beckman Coulter, Allegra X-15R) was used for the separation of colloidal particles from the supernatant solutions.

### 2.2. Reagents, samples and reference materials

Ultrapure deionized water (18.2 M cm resistivity) was obtained from an Elga PURELAB system. Ultrapure nitric acid was obtained by Milestone subPUR sub-boiling distillation system from lower purity grade nitric acid (Merck, 65% Emsure). Iron standard solutions (NIST SRM 3126a, Lot: 140818) were prepared gravimetrically by spiking of treated seawater samples used as mass bias correction (K factor) solutions and calibration blends. NIST SRM 3109a Ca, NIST SRM 3152a Na, NIST SRM 4141a K and NIST SRM 3131a Mg were used to perform residual salinity measurements.  $\text{Mg}(\text{OH})_2$  co-precipitation used for matrix separation was performed by the addition of 99.7% extra pure TEA (Acros Organics).  $\text{MgSO}_4$  used in the experiments was taken from Fluka (purity > 98.0%). Certified reference materials used for trueness of the method were NMIA MX014 and CASS-6 from National Metrology Institute of Australia and the National Research Council of Canada, respectively.

Single, double and triple IDMS experiments were performed using  $^{57}\text{Fe}$  enriched certified reference material IRMM-620 ( $10.3684 \pm 0.0062 \text{ k} = 2 \text{ mg/kg Fe in } 4.5 \text{ M HCl}$ ). Dilution of enriched certified

reference material was performed gravimetrically using 2.0% (v/v) sub-boiled  $\text{HNO}_3$ . The standard reference material NIST SRM 3126a Fe standard solution was used as primary reference standard material (PSRM) in the application of double and triple IDMS.

Treated seawater matrix which was used for method development was stored in pre-cleaned perfluoroalkoxy (PFA) bottles; enriched certified reference material was stored in pre-cleaned high density polyethylene bottles. All sample preparation was performed using 15 mL VWR polypropylene centrifuge tubes. Only new centrifuge tubes were used, and cleaned by applying a procedure consisting of the following steps: (1) Rinse by ultrapure water, (2) filled by 5.0%  $\text{HNO}_3$  (analytical grade), (3) filled by ultrapure water, (4) filled by 2.0% sub-boiled  $\text{HNO}_3$ , (5) filled by ultrapure water, (6) dried in ISO 4 ultra-clean laminar flow cabinet.

All sample preparation for ID-ICP-MS measurements were performed gravimetrically in ISO 6 clean chemistry laboratory in TÜBİTAK ÜME.

### 2.3. Development of triethylamine assisted $\text{Mg}(\text{OH})_2$ co-precipitation method

#### 2.3.1. Preparation of treated matrix matched seawater

Method development studies were performed using treated matrix matched seawater collected from Marmara Sea ( $40^\circ 46.200' \text{ N}$ ;  $29^\circ 12.956' \text{ E}$ ). Acid cleaned 10 L high density polyethylene drums were used for sampling, and the material was adjusted to the pH of 1.6 by using sub-boiled  $\text{HNO}_3$ . Trace elements in 1.0 L of seawater was tried to be removed by applying TEA assisted co-precipitations. For the treatment process, a 40-mL aliquot of seawater sample was transferred into 50 mL pre-cleaned centrifuge tube, and mixed with 0.40 mL TEA. After centrifuging at 10000 rpm for 30 min, supernatant solutions were taken into 50 mL centrifuge tubes. In order to get rid of excess TEA, these solutions were exposed to  $110^\circ \text{C}$  heating for a period of 60 min in an ISO 4 laminar fume hood using digestion block (DigiPrep, SCP Science). All evaporated samples were collected into pre-cleaned 1.0 L PFA bottle.

For the purpose of matrix matching, Ca, K, Mg and Na as the major electrolytes of original seawater and treated seawater were determined by triple quadrupole ICP-MS/MS. Although the difference on mass fractions of Ca, K and Na were negligible after co-precipitation and evaporation step, the fraction of remaining Mg was almost 50% in the treated seawater sample compared to the original seawater matrix. As matrix separation is based on co-precipitation of  $\text{Mg}(\text{OH})_2$ , this makes the amount of Mg a critical parameter. In order to adjust concentration of Mg to approximately 700 mg/L, 1.48 g  $\text{MgSO}_4$  was added into treated seawater to obtain matrix matched treated seawater to be used in the method development studies.

#### 2.3.2. Optimization of conditions of co-precipitation based on residual matrix for ID-ICP-MS measurement

Matrix removal efficiency is a key parameter for the accurate isotope ratio measurements. In order to figure out this efficiency, treated matrix matched seawater solution was used and amount of TEA and number of co-precipitation steps were studied. To achieve the conditions for full isotopic equilibration, isotopically enriched standard was added at the beginning, prior to co-precipitation stage. Although the analyte recovery at the co-precipitation stage is not so crucial for IDMS applications, it is necessary to get the highest recovery possible in order to get enough sensitivity in ICP-MS measurements so that better repeatability on isotope ratio can be obtained based on counting statistics. Therefore, recovery of co-precipitation stage was also investigated in the optimization of the procedure. Recovery studies were performed by spiking treated matrix matched seawater by spiking subsequent amount of NIST SRM 3126a Fe standard solution gravimetrically. Recovery studies were always performed and evaluated with the non-spiked treated matrix match seawater samples. Residual salinity was assumed

to be sum of amounts of Ca, K, Mg and Na in resulting solution. All the samples were analyzed for these four elements contents using external calibration with internal standard ( $^{115}\text{In}$ ) by ICP-MS/MS. As residual salinity studies were studied volumetrically, recovery studies were performed gravimetrically.

First attempt for optimizing co-precipitation procedure was the addition of different amount TEA ranging from 50 to 150  $\mu\text{L}$  into 5.0 g of treated matrix matched seawater. For the completion of co-precipitation, samples were mixed for homogenization and centrifuged at 4700 rpm for 25 min. The supernatant solutions were discarded, pellets were rinsed by ultrapure water, and dissolved in 0.60 mL of 5.0%  $\text{HNO}_3$  (v/v). Samples were diluted to initial amount of sample by ultrapure water so that no pre-concentration was applied. Although quantitative recovery was achieved even with the minimum amount of TEA, the resulting solutions from applying single step co-precipitation were not sufficiently free of salts mainly due to presence of Mg. Residual salinity decreased as the amount of TEA decreased, and minimum salinity (0.6 g/L) was observed in the samples added by 50  $\mu\text{L}$  of TEA. Since co-precipitation could not be initiated by using smaller amount of TEA than 40  $\mu\text{L}$  in pH 1.6 samples, second co-precipitation step was evaluated to reduce the total dissolved salt content of resulting solutions. Different amounts of TEA in two steps were tested using 5.0 g of treated matrix matched seawater. The tested total amount of TEA were 90, 100 and 120  $\mu\text{L}$ . Pellets were dissolved in 0.50 mL using 5.0%  $\text{HNO}_3$  (v/v) after the first precipitation step, and diluted to 2.0 mL by adding ultrapure water. While co-precipitation was completed in a couple of minutes in the first step, it took longer time in the second one. After addition of second amount of TEA, samples were centrifuged at 4700 rpm for 45 min as performed in the first step. Pellets were dissolved by 0.50 mL using 5.0%  $\text{HNO}_3$  (v/v) and samples were diluted to 5.0 g by ultrapure water. Residual salinity was decreased from 8.9 g/L to 0.03 g/L in the resulting solution obtained by addition of 50  $\mu\text{L}$  at the first and 40  $\mu\text{L}$  at the second co-precipitation steps. Concentration of Mg, Na, K and Ca as major analytes in the resulting solution was determined as  $21 \pm 2$ ,  $1.4 \pm 0.2$ ,  $2.4 \pm 0.2$  and  $0.60 \pm 0.07 \text{ mg/L}$ , respectively. Combination of two step co-precipitation procedure provided the best removal of matrix. Although quantitative recovery of iron originally present in seawater matrix is not curial providing that isotopic equilibration reached, 15 ng/g Fe spiked treated matrix matched seawater sample and non-spiked treated matrix matched seawater were analyzed by applying two step co-precipitation procedures to establish the recovery of proposed procedure. Measurements were performed using three different optimized tune parameters in which He and  $\text{O}_2$  cell gas were used. In addition to using different cell gas, different modes of the instrument as single quad (SQ) and MS/MS were also used. Recoveries of triplicate blank corrected samples were found to be  $99\% \pm 6\%$ ,  $100\% \pm 6\%$  and  $98\% \pm 6\%$  for the analysis mode of He-SQ,  $\text{O}_2$ -SQ and  $\text{O}_2$ -MS/MS, respectively. Therefore, the procedure of TEA assisted  $\text{Mg}(\text{OH})_2$  co-precipitation in two steps (50  $\mu\text{L}$ /40  $\mu\text{L}$ ) was decided to be used in determination of Fe in seawater by ID-ICP-MS.

#### 2.3.3. Calibration strategies for isotope dilution measurements

Traceable and highly accurate quantification with the possible lowest measurement uncertainty was the aim of the method which is going to be used in characterization of a candidate certified reference material (UME CRM 1206). Although traceability does not guarantee accuracy of a measurement, based on the ISO 17034 and ISO Guide 35, well established traceability chain is a must in the characterization measurements of candidate certified reference materials. In this study, three different calibration strategies (single, double and triple IDMS) for isotope dilution technique were studied which provided three different chains of traceability. These strategies have been well described in literature [41–43], and, to the best of our knowledge, this is the first application of triple IDMS for quantification of iron and the second as applied in elemental determination [42].

The first and classical isotope dilution technique is single IDMS which is relatively more practical with respect to other two strategies and applicable as long as the concentration and isotopic composition of enriched certified reference material (iCRM) is well known [42,44]. In this approach, only the isotope ratio of sample blend and isotope ratio of mass bias correction solution is measured and all other parameters except the masses of sample and iCRM are coming from the certificate of isotopically enriched (iCRM) and/or IUPAC. The equation for single IDMS is given in Equation (1).

The second isotope dilution approach is called as double (reverse) IDMS, and used when isotopically enriched reference material needs to be characterized in terms of mass fraction [42,44]. This case is mostly applied when there is a lack of metrological control of iCRM for the concentration. In order to characterize mass fraction of iCRM, a PSRM solution which is prepared from a primary assay (purity > 99.99%) element or certified standard reference material is used. In double IDMS application,  $\Sigma R_X$ ,  $\Sigma R_Y$  and  $\Sigma R_Z$  are eliminated unless there is an isotopically variation exists between the sample and PSRM solution which is the usually case and double IDMS equation results as in Equation (2). Expected measurement uncertainty budget of double IDMS is lower than the single IDMS due to the cancellation of parameters [38,44,45].

Milton et al. introduced the third isotope dilution approach in 2002 which can be applied when there is a doubt or insufficient information on certified isotopic composition of isotopically enriched standard [43,46]. This approach is mostly preferred if there is no infrastructure available for measurement of isotopic composition of enriched material or to avoid contamination of mass spectrometer with highly isotopically enriched material. This calibration approach in isotope dilution is referred to as Triple IDMS. A third calibration blend between isotopically enriched material (iCRM) and primary standard reference material (PSRM) is used to replace  $R_Y$  in Equation (2) which finally results in Equation (3).

$$C_X = C_Y \cdot \frac{m_{Y1}}{m_X} \cdot \frac{R_Y - K_{XY} \cdot r_{XY}}{K_{XY} \cdot r_{XY} - R_X} \cdot \frac{\sum (R_i)_X}{\sum (R_i)_Y} \quad (1)$$

$$C_X = C_{Z2} \cdot \frac{m_{Z2}}{m_X} \cdot \frac{m_{Y1}}{m_{Y2}} \cdot \frac{R_Y - K_{XY1} \cdot r_{XY1}}{K_{XY1} \cdot r_{XY1} - R_X} \cdot \frac{R_Y - K_{ZY2} \cdot r_{ZY2}}{K_{ZY2} \cdot r_{ZY2} - R_Y} \quad (2)$$

$$C_X = \frac{m_{Y1}}{m_{X1}} \left( C_{Z2} \cdot \frac{m_{Z2}}{m_{Y2}} \cdot \frac{(r_{ZY2} - R_Z) \cdot (r_{ZY3} - r_{ZY1})}{(r_{ZY1} - R_X) \cdot (r_{ZY3} - r_{ZY2})} + C_{Z3} \cdot \frac{m_{Z3}}{m_{Y3}} \cdot \frac{(r_{ZY3} - R_Z) \cdot (r_{ZY1} - r_{ZY2})}{(r_{ZY1} - R_X) \cdot (r_{ZY3} - r_{ZY2})} \right) \quad (3)$$

$$K = R_{IUPAC} / r_{measured} \quad (4)$$

Parameter	Unit	Definition
X	–	Sample
Y	–	Isotopically enriched standard, iCRM
Z	–	Primary standard reference material with natural isotopic composition, PSRM
xy	–	Blend of X and Y
yz	–	Blend of Y and Z
$C_X, C_Y, C_Z$	mol/kg	Mass fraction of sample, iCRM and PSRM
$m_X$	kg	Mass of sample
$m_Y, m_{Y2}, m_{Y3}$	kg	Mass of isotopically enriched standard
$m_Y, m_{Y2}, m_{Y3}$	kg	Mass of isotopically enriched standard
$m_{Z2}, m_{Z3}$	kg	Mass of PSRM
$R_X, R_Y, R_Z$	–	Isotope ratio in sample, iCRM and PSRM
$r_{XY}, r_{ZY2}, r_{ZY3}$	–	Measured isotope ratio in sample-iCRM (sample blend), iCRM-PSRM (calibration blend)
$K_{XY}, K_{ZY}$	–	Mass bias correction factor
$\Sigma R_X, \Sigma R_Y$	–	Sum of all isotope amount ratios of the same denominator

## 2.4. Estimation of measurement uncertainty

In order to obtain combined uncertainty all individual uncertainty components were propagated based on ISO/GUM and Eurachem guides [47,48]. A dedicated software program which follows the principles given in DIN/ISO/BIPM Guidelines on the evaluation of measurement uncertainty [49] was used.

## 3. Results and discussion

### 3.1. Optimization of reaction/collision cell gas conditions for highly accurate iron isotope ratio measurements

As a potential primary method to produce analytical results with high accuracy and precision, isotope dilution mass spectrometry is one of the most suitable reference method for reference material characterization [50]. However, all the prerequisite conditions, the traceability of standards, establishment of isotopic equilibrium and uniformity of isotopes should be fulfilled in order to get the highest metrological quality. Detailed investigation of spectral interferences is one of the critical aspects for accurate isotope ratio measurements of iron especially in such a complex matrix with a low analyte concentration. The most severe polyatomic interferences are  $^{40}\text{Ar}^{16}\text{O}$  and  $^{40}\text{Ar}^{16}\text{O}^{1}\text{H}$  on  $^{56}\text{Fe}$  and  $^{57}\text{Fe}$ , respectively. Moreover, highly accurate isotope measurement gets more challenging especially at sub-ppb level of Fe as mass fraction of Ca which interferes as  $^{40}\text{Ca}^{16}\text{O}$  and K which interferes as  $^{41}\text{K}^{16}\text{O}$  and  $^{39}\text{K}^{18}\text{O}$  in co-precipitated seawater matrix is at about a few ppm level [34]. To evaluate the removal efficiency of these interferences, background equivalent concentration (BEC) was measured using  $\text{H}_2$ ,  $\text{Q}_2$ , He and  $\text{NH}_3/\text{He}$  cell gases in both single quad (SQ) and MS/MS mode of triple quadrupole ICP-MS/MS. All tune parameters for each were optimized using auto-tuning tool present in MassHunter software just before optimizing flow rate of cell gases. For the optimization of cell gases flow rates to overcome the spectral interferences resulting not only from matrix but also plasma conditions, two solutions were analyzed: A solution containing 2.0 mg/L Na, 3.0 mg/L K, 1.0 mg/L Ca and 15.0  $\mu\text{g/L}$  Fe in 1.0% (v/v)  $\text{HNO}_3$  to obtain intensity and a background solution containing 2.0 mg/L Na, 3.0 mg/L K, 1.0 mg/L Ca in 1.0% (v/v)  $\text{HNO}_3$  to obtain BEC.

Performances of cell gases in different modes of the instrument were robustly evaluated in terms of isotope ratio measurements performed by using the same solutions described above under the optimized conditions except the best repeatability condition for isotope ratio measurements like optimum run and pass cycle (Fig. 1). Ratio measurement results obtained were evaluated by dividing IUPAC value to measured ratio (K). The typical background equivalence concentration,

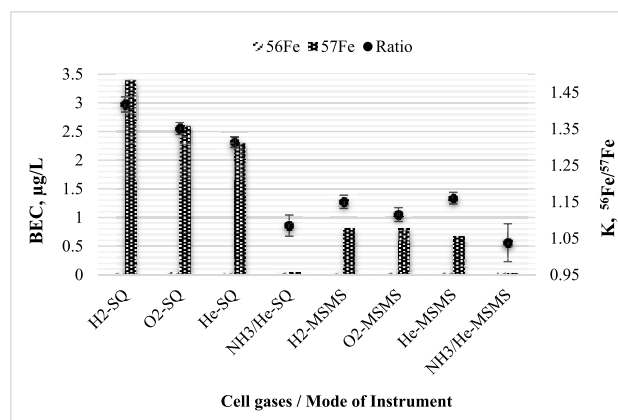
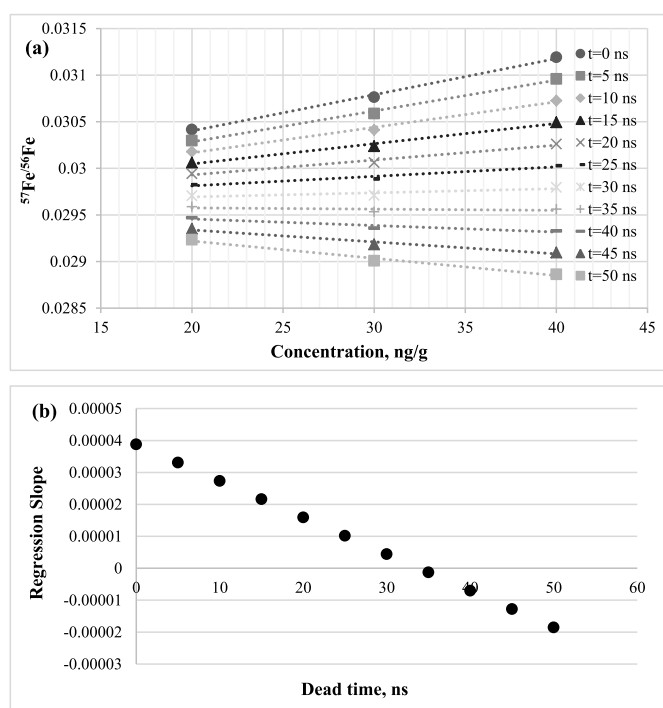


Fig. 1. Performance of reaction/collision cell gases in Single Quad and MS/MS mode of ICP-MS/MS.



**Table 2**  
Results of reaction/collision cell optimization.

Mode	Optimum gas flow rate	Isotopes	BEC, $\mu\text{g/L}$	K factor
H <sub>2</sub> -SQ	7	<sup>56</sup> Fe	0.024	1.417 $\pm$ 0.021
O <sub>2</sub> -SQ	60	<sup>57</sup> Fe	3.4	
He-SQ	11	<sup>56</sup> Fe	0.045	1.351 $\pm$ 0.016
NH <sub>3</sub> /He-SQ	35/6	<sup>57</sup> Fe	2.6	
H <sub>2</sub> -MS/MS	9	<sup>56</sup> Fe	0.025	1.313 $\pm$ 0.014
O <sub>2</sub> -MS/MS	80	<sup>57</sup> Fe	2.3	
He-MS/MS	11	<sup>56</sup> Fe	0.030	1.085 $\pm$ 0.029
NH <sub>3</sub> /He-MS/MS	50/7	<sup>57</sup> Fe	0.035	
		<sup>56</sup> Fe	0.021	1.150 $\pm$ 0.018
		<sup>57</sup> Fe	0.80	
		<sup>56</sup> Fe	0.03	1.115 $\pm$ 0.019
		<sup>57</sup> Fe	0.8	
		<sup>56</sup> Fe	0.03	1.160 $\pm$ 0.016
		<sup>57</sup> Fe	0.66	
		<sup>56</sup> Fe	0.028	1.038 $\pm$ 0.052
		<sup>57</sup> Fe	0.026	



**Fig. 2.** (a) <sup>57</sup>Fe/<sup>56</sup>Fe ratio versus concentration. (b) Regression slopes for lines in (a) versus dead time.

K values and optimum flow rate of cell gases are given in Table 2 and Fig. 1. Except the NH<sub>3</sub>/He cell gas in single quad mode, all other cell gases in single quad mode did not provide as accurate ratio measurement as in MS/MS mode. As removal of molecular interferences on <sup>56</sup>Fe is easier to minimize with almost each cell gas even in the single quad mode, the critical point of this optimization was to minimize the interferences on <sup>57</sup>Fe isotope. Both background equivalence concentration and isotope ratio measurements at optimum tune parameters for each analysis mode proved that the best reaction cell gas was the mixture of NH<sub>3</sub>/He using SQ or MS/MS mode of the instrument. Single quad mode was preferred for IDMS applications due to getting higher signal intensities which provided better %RSD for isotope ratio measurement resulting in lower measurement uncertainty. Although the molecular interferences on both isotopes were down to approximately 30 ng/L, all the measured intensities were corrected systematically for background which was measured before and after each mass bias solution measurement.

**Table 3**  
Comparison of different co-precipitation methods in terms of procedural blank levels and limit of detection values.

Method	Reagent	Instrument	Removal of Interference	Sample Intake, g	Preconcentration	Blank, ng/L	LOD, ng/L	Reference
Single IDMS	Double N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub> assisted Mg(OH) <sub>2</sub> co-precipitation	Agilent 8800 ICP-MS/MS	Single Quad- NH <sub>3</sub> /He	5.0	1.0	9	11	This Study
Q-ICP-MS	Triple N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub> assisted Mg(OH) <sub>2</sub> co-precipitation	Varian 820-MS ICP-MS	H <sub>2</sub> cell gas	10	10	204	33	[36]
External calibration	NH <sub>3</sub> assisted Mg(OH) <sub>2</sub> co-precipitation	Perkin Elmer-Sciex Elan DRC II	NH <sub>3</sub> cell gas	50	10	7.9	5.5	[64]
Additional calibration Q-ICP-MS	NH <sub>3</sub> assisted Mg(OH) <sub>2</sub> co-precipitation	Perkin Elmer-Sciex Elan DRC II	NH <sub>3</sub> cell gas	50	10	11.7	5.0	[35]
Standard addition calibration Q-ICP-MS	NH <sub>3</sub> assisted Mg(OH) <sub>2</sub> co-precipitation	Thermo Finnigan MAT Element 2	Medium Resolution	15–30	7.5–15	6.3	3.0	[30]
Single IDMS	Double NH <sub>3</sub> assisted Mg(OH) <sub>2</sub> co-precipitation	Thermo Finnigan MAT Element 2	Medium Resolution	50	500	0.89	0.11	[29]
Single IDMS	NH <sub>3</sub> assisted Mg(OH) <sub>2</sub> co-precipitation	Thermo Finnigan MAT Element 2	Medium Resolution	1.4	14	6.8	9.0	[32]
Single IDMS	Double NH <sub>3</sub> assisted Mg(OH) <sub>2</sub> co-precipitation	Thermo Finnigan MAT Element 2	Medium Resolution	14	140	2.5	2.8–3.4	[32]

**Table 4**  
Results of CASS 6, NMIA MX014 and UME CRM 1206.

	Certified Value, ng/g ( <i>k</i> = 2)	Single IDMS		Double IDMS		Triple IDMS	
		Measured Value, ( <i>k</i> = 2)	Recovery, %	Measured Value, ( <i>k</i> = 2)	Recovery, %	Measured Value, ( <i>k</i> = 2)	Recovery, %
<b>CASS -6</b> ( <i>n</i> = 5) ERM Application Note 1	1.53 ± 0.12	1.521 ± 0.032 No significant difference	99.4 ± 1.9	1.525 ± 0.027 No significant difference	99.6 ± 1.8	1.536 ± 0.038 No significant difference	100.4 ± 2.4
<b>NMIA MX014</b> ( <i>n</i> = 4) ERM Application Note 1	21.7 ± 0.32	21.32 ± 0.26 No significant difference	99.0 ± 0.2	21.60 ± 0.14 No significant difference	99.5 ± 0.1	21.70 ± 0.14 No significant difference	100.0 ± 0.2
<b>UME CRM 1206</b> ( <i>n</i> = 12)		12.70 ± 0.16		12.728 ± 0.084		12.732 ± 0.062	

### 3.2. Detector dead time

One of the parameters that affect accuracy of isotope ratio measurements is detector dead time which is related to the detector response time, and may lead to counting losses if not determined accurately [51]. Detector dead time corresponds to a short time needed for the recovery of the ion impact for which the ion counting system is “blind” to the next coming ion. In order to achieve good counting statistics, the intensity of enriched isotope should be increased and the intensity of ion with higher abundant isotope can easily be affected by the dead time of the multiplier. Therefore, it is necessary to determine dead time of the instrument special to the analytes to provide high accuracy isotope ratio measurements independent of analyte concentration [52,53]. In this study, determination of detector dead time was performed as the Method 2 described by Nelms et al. [52]. This method was basically based on plotting the measured  $^{57}\text{Fe}/^{56}\text{Fe}$  isotope ratios versus Fe concentration for different dead time values. Dead time correction obtained ( $\tau = 34$  ns) was automatically applied by ICP-MS/MS software (Fig. 2).

### 3.3. Mass bias correction

As the transmittance efficiency of masses is different in ICP-MS, measured isotope ratios (*r*) are always biased [51], and this bias becomes a more critical issue as the relative mass difference between two isotopes gets higher [54]. Different rate of transmittance of ions stems from the different parts of mass spectrometers and mostly due to the space charge effect [50]. As it is mentioned by Vanhaecke et al. reaction/collision cell gases may result in heavy mass bias effect [55]. In order to correct the bias, an isotopically certified reference material (iCRM) or a standard with natural isotopic abundance should be used. In the absence of an iCRM, a natural abundance standard can be preferred and isotopic composition data provided in IUPAC [56] must be used as reference for the calculation of a mass bias correction factor (*K*). The measured isotope ratios are corrected for mass bias when  $R_y$ ,  $R_x$ ,  $R_{xy}$  and/or  $R_{zy}$  are not measured at the same time or some of them are taken from a certificate (e.g.  $R_y$ ) or IUPAC tables (e.g.  $R_x$ ) [50].

In this study, mass bias solution was prepared from seawater sample itself by applying co-precipitation procedure so that the matrix of sample blends and mass bias solution are matched as much as possible. Besides matching the matrix, elemental concentration in the unknown sample was also matched in the mass bias solution. Bracketing approach was applied for measurement of mass bias correction solution by introducing mass bias solution every three sample blends [46] and weighted correction factors were applied. This mass bias correction is more critical parameter especially in single IDMS application as  $R_y$  and  $R_x$  was taken from the certificate of IRMM 620 and IUPAC, respectively. However, it was observed that this correction could be neglected as long as exact isotope ratio match is achieved between sample and calibration blends in the application of double/triple IDMS. The relative standard deviation of matrix matched mass bias solution measured

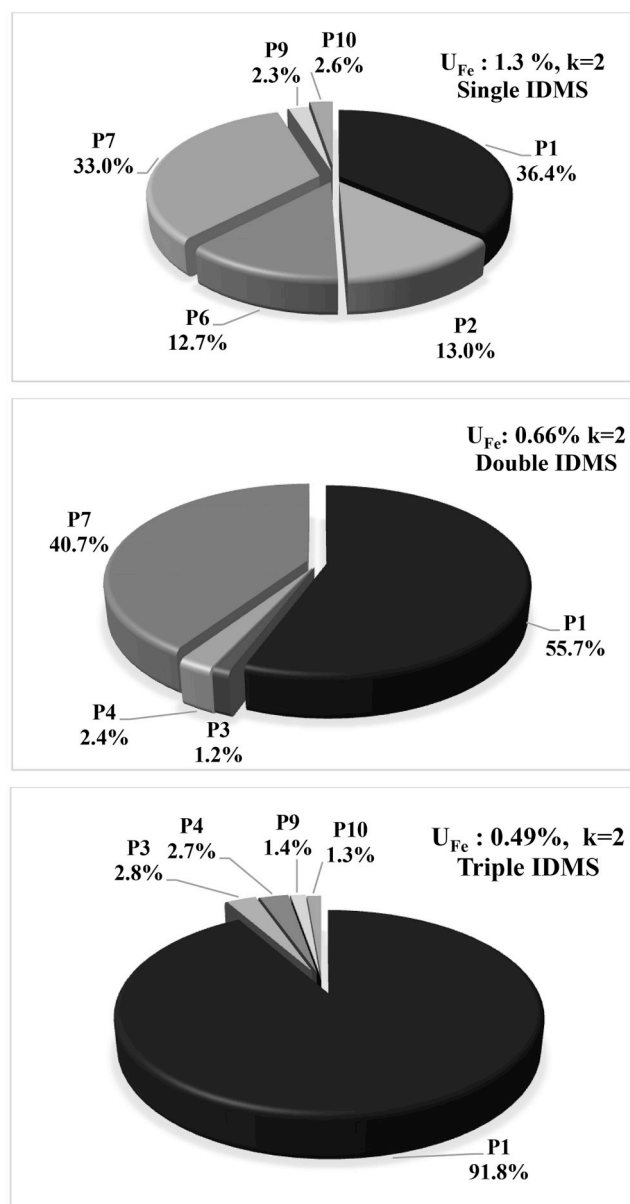
along the sequence last in 4 h is 0.7% (*n* = 8) which is a sign of stability of isotope ratio measurement by ICP-MS/MS.

### 3.4. Determination of procedural blank and limit of detection for TEA assisted $\text{Mg}(\text{OH})_2$ co-precipitation method

Procedural blanks were determined within each IDMS approaches, separately. In order to determine procedural blank level of TEA assisted co-precipitation method, a 90- $\mu\text{L}$  aliquot of TEA was added to 15 mL polyethylene centrifuge tubes which were cleaned as described in Section 2.2, and spiked by appropriate amount of iCRM (IRMM 620). Solutions were evaporated at 110 °C in an ISO Class 4 clean fume hood placed in ISO Class 6 clean chemistry laboratory. After the evaporation, 1.0 mL of 5.0% (v/v) sub-boiled  $\text{HNO}_3$  was added to the vial and diluted to 5.0 g with deionized water. The signals of procedural blank blend were evaluated with and without background corrections. The procedural blank level and limit of detection (defined as 3 times the standard deviation of blanks) without applying background correction for single IDMS were found as 48 ng/kg (0.86 nM) and 41 ng/kg (0.73 nM), respectively. However, as the background correction were applied to all sample and calibration blends systematically background corrected values were used in the calculations. Typical concentration of procedural blank and limit of detection which were determined by single IDMS were found to be 9 ng/kg (0.16 nM) and 11 ng/kg (0.20 nM), respectively. As seen in Table 3, procedural blank level of the proposed method is approximately 20 times lower than the recently published results in which TEA was used as a reagent for the first time to perform  $\text{Mg}(\text{OH})_2$  precipitation [36]. Although the procedural blank levels of TEA assisted co-precipitation technique are mostly compatible with the techniques of  $\text{NH}_3$  assisted  $\text{Mg}(\text{OH})_2$  co-precipitation in the literature, J. Wu et al. have been demonstrated that lower detection limits can be succeeded by the latter [29,32]. On the other hand, it has advantages over  $\text{NH}_3$  assisted  $\text{Mg}(\text{OH})_2$  co-precipitation technique for some other heavy metals such as Cd, Cu, Ni, Co, and Zn with higher recoveries [36,57]. Moreover, as one of the most preferable technique for determination of trace elements in seawater is the commercially available automated system called as seaFAST [23] by the routine analysis laboratories or to use of resin called as Nobias-chelate PA-1 with combination of offline automated trace metal extraction/pre-concentration systems should be also overviewed. It is noted that although 0.14 nmol/L [24] and 0.25 nmol/L [58] which are very comparable procedural blank levels with TEA assisted  $\text{Mg}(\text{OH})_2$  coprecipitation technique were also reported, much more lower procedural blank levels seems to be achieved by using Nobias-chelate PA-1 based on the literature [59–62].

### 3.5. Establishment of measurement accuracy

In order to demonstrate the trueness of the method, seawater certified reference materials were analyzed for the determination of their iron contents. One of the certified reference materials is from National



**Uncertainty Contribution Parameters**

P1	Sample preparation (Weighing)
P2	Uncertainty on IUPAC (col 9) isotopic abundance of Fe
P3	Uncertainty on $^{56}\text{Fe}/^{57}\text{Fe}$ ratio of sample blends
P4	Uncertainty on $^{56}\text{Fe}/^{57}\text{Fe}$ ratio of calibration blends
P5	Uncertainty on $^{56}\text{Fe}/^{57}\text{Fe}$ ratio of K for calibration blends
P6	Uncertainty on $^{56}\text{Fe}/^{57}\text{Fe}$ ratio of K for sample blends
P7	Uncertainty on intermediate precision
P8	Uncertainty on $^{56}\text{Fe}/^{57}\text{Fe}$ ratio of procedural blank blends
P9	Uncertainty on background correction
P10	Other

**Fig. 3.** Uncertainty budgets of single, double and triple IDMS.

Research Council, Canada (NRCC), CASS 6 Nearshore Seawater Certified Reference Material for Trace Metals and other Constituents. This CRM is one of the most suitable one in order to establish the measurement trueness of the method due to lower level of Fe in seawater matrix with a

relatively high precision if compared with the candidate certified reference material. As the pH of CASS 6 is also 1.6, no pH adjustment was applied, and the first co-precipitation step was performed by adding the proportional amount of TEA (20  $\mu\text{L}$  for 2.0 g of CASS 6) with respect to sample amount used. As amount of Mg varies for each seawater matrix, the second co-precipitation step was applied by addition of TEA dropwise until solutions developed visible turbidity. The second reference material used for this purpose was NMIA MX014 which has been produced by National Measurement Institute of Australian Government as coastal sea water matrix certified reference material. The mass fraction of this material relatively higher than the candidate certified reference material. The pH of 1.0 g MX014 was adjusted to pH 1.6 by adding ultrapure water just before applying co-precipitation procedure as its pH was approximately 0.7, and the same co-precipitation strategy was applied as described for the former CRM preparation.

The evaluation of measured results for CASS 6 and MX014 were performed by taking account of measurement uncertainty and combined uncertainty of CRMs as described in ERM Application Note 1 [63]. As summarized in Table 4, this comparison proved that there is no significant difference between the measurement results and certified reference values for each calibration strategies.

Moreover, repeatability (within day precision) and intermediate precision (day-to-day precision) of the all the calibration approaches were evaluated using the results of UME CRM 1206. The data set consisted of ten replicates per day (two days for single IDMS, three days for double/triple IDMS). This evaluation was performed by one way ANOVA analysis. Relative standard uncertainty of within day precision was found as 0.16%, 0.19% and 0.20% for single, double and triple IDMS, respectively. On the other hand, as the within day precision of all three approaches were similar, relative standard uncertainty of intermediate precision for single and double IDMS were calculated as 0.37% and 0.21%, respectively. As day-to-day precision was smaller than the within day precision ( $MS_{\text{between}} < MS_{\text{within}}$ ), this value could not be calculated for triple IDMS. However, relative standard deviation of average values of three day was found to be 0.13%. The intermediate precision of calibration approaches was taken into account in the estimation of measurement uncertainty.

### 3.6. Measurement results and uncertainty budgets of UME CRM 1206 characterization

One of the purposes of applying three different IDMS approach was to establish the most accurate value for the certification of Fe in UME CRM 1206. As there was no significant difference between the measurement results of two CRMs and certified values, all three data set of UME CRM 1206 were compared in terms of closeness of the average values and their uncertainties. Characterization measurements were performed using three unit of candidate certified reference material and four independent sub-sample per unit.

The average value of single IDMS was found to be  $(12.70 \pm 0.16)$  ng/g. The relative expanded uncertainty ( $k = 2$ ) of 1.3% is in the typical range 1–2% as expected for single IDMS applications [30]. Main contribution to total uncertainty budget resulted from weighing (36.4%), precision on isotope ratio measurements of mass bias correction solution (12.7%), IUPAC values (13.0%) and intermediate precision (33.0%). It was mentioned by the authors [42,44] that the uncertainty of double IDMS approach is expected to be the smaller than single IDMS as all isotope abundance and atomic weight data cancel out in the equation of double IDMS. A dramatic reduction in the uncertainty of measurements was also observed in this study. As seen in Fig. 3 and Fig. 4, the uncertainty budget of double IDMS is 0.66% ( $k = 2$ ) which is approximately half of the single IDMS uncertainty budget. It was established that the main contribution to double IDMS measurement uncertainty budget resulted from weighing (55.7%) and intermediate precision (40.7%). The measurement uncertainty of triple IDMS might be expected to be larger than double IDMS as a second series of

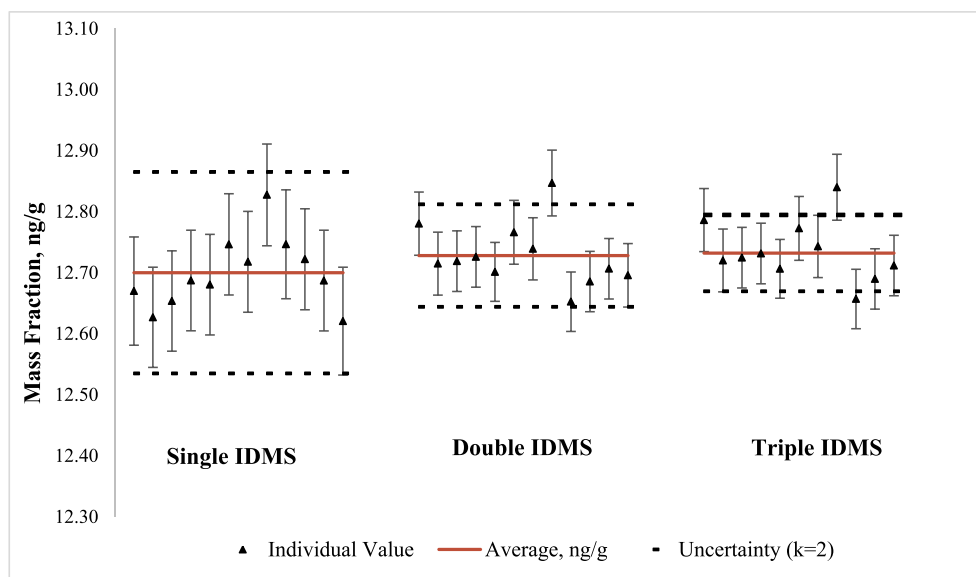


Fig. 4. Graphical representation of obtained results for UME CRM 1206.

calibration blend are introduced to the measurement [42]. However, relative expanded measurement uncertainty was improved by applying triple IDMS which was calculated as 0.49%. Gravimetric sample preparation step of all blends was the main contributor to total uncertainty budget (91.8%). Therefore, measurement uncertainty of IDMS applications can be improved by applying metrological gravimetry principles using substitution weighing against E2 class mass standards. However, this is only applicable to single IDMS practically since the procedure of metrological weighing takes quite long time for double and triple IDMS.

Although, the mean values of three approaches are compatible within their respective uncertainties (Fig. 4), the intermediate precision and the resulting uncertainty budget of triple IDMS is superior to single and double IDMS. Therefore, the value of triple IDMS ( $12.732 \pm 0.062$  ng/g) measurements is assigned as the characterization value of UME CRM 1206.

### 3.7. Establishment of metrological traceability

Validation of a method including uncertainty estimation and the description of the traceability chain of analytical results is a must to assess the quality of measurement. Isotope dilution mass spectrometry technique can be used to assign the certified value of reference materials as its operation is well described and understood so that complete uncertainty statement can be written in terms of SI units and traceability chain can be clearly established in terms of the mole and the kilogram throughout the shortest possible way. In this study, traceability of Fe amount content was established by use of calibrated and SI traceable balance, iCRM (IRMM 620) and NIST SRM 3126a.

The measurement results of iron by single IDMS is traceable to SI unit mole via IRMM 620 iCRM used in preparation of sample blends, and to kg via SI traceable calibrated balance used to prepare the sample blends and also metrological control of IRMM 620 for weight loss during its shelf life. As the traceability to kg was achieved in a same way of single IDMS for double and triple IDMS measurements, traceability to mole was established through IRMM 620 and NIST SRM 3126a for double IDMS. On the other hand, traceability to mole in triple IDMS application is established to SI units via only NIST SRM 3126a.

## 4. Conclusion

For the reference measurements of iron in candidate seawater certified reference material, UME CRM 1206, single, double and triple

IDMS coupled with TEA assisted  $\text{Mg}(\text{OH})_2$  co-precipitation have been successfully applied without applying preconcentration to the samples and CRMs. Comparison of calibration approaches and the application of TEA assisted  $\text{Mg}(\text{OH})_2$  co-precipitation with IDMS for Fe is reported for the first time in this study. The procedural blank levels and detection limits of the method are comparable with  $\text{NH}_3$  assisted  $\text{Mg}(\text{OH})_2$  co-precipitation techniques. The investigation of single, double and triple IDMS measurements reveals that the lowest expanded uncertainty was achieved by triple IDMS which was 0.49% ( $k = 2$ ) as all the measurement results were in agreement within their uncertainties. Beside this advantage, triple IDMS compensates the risk of contamination of iCRM by the preparation of a third blend series with moderate isotope ratio which provides lower intermediate precision.

## Conflict of Interest

None.

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