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# Comparison of ISO-GUM and Monte Carlo methods for the evaluation of measurement uncertainty: Application to direct cadmium measurement in water by GFAAS

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## ABSTRACT

The propagation stage of uncertainty evaluation, known as the propagation of distributions, is in most cases approached by the GUM (Guide to the Expression of Uncertainty in Measurement) uncertainty framework which is based on the law of propagation of uncertainty assigned to various input quantities and the characterization of the measurand (output quantity) by a Gaussian or a *t*-distribution. Recently, a Supplement to the ISO-GUM was prepared by the JCGM (Joint Committee for Guides in Metrology). This Guide gives guidance on propagating probability distributions assigned to various input quantities through a numerical simulation (Monte Carlo Method) and determining a probability distribution for the measurand.

In the present work the two approaches were used to estimate the uncertainty of the direct determination of cadmium in water by graphite furnace atomic absorption spectrometry (GFAAS). The expanded uncertainty results (at 95% confidence levels) obtained with the GUM Uncertainty Framework and the Monte Carlo Method at the concentration level of 3.01 μg/L were ±0.20 μg/L and ±0.18 μg/L, respectively. Thus, the GUM Uncertainty Framework slightly overestimates the overall uncertainty by 10%. Even after taking into account additional sources of uncertainty that the GUM Uncertainty Framework considers as negligible, the Monte Carlo gives again the same uncertainty result (±0.18 μg/L). The main source of this difference is the approximation used by the GUM Uncertainty Framework in estimating the standard uncertainty of the calibration curve produced by least squares regression. Although the GUM Uncertainty Framework proves to be adequate in this particular case, generally the Monte Carlo Method has features that avoid the assumptions and the limitations of the GUM Uncertainty Framework.

## 1. Introduction

The importance of measurement uncertainty and traceability for ensuring the reliability of analytical assays is well recognized. In ISO/IEC 17025, standard procedures presupposing the evaluation of uncertainty and the application of traceability in analyses are included [1].

In order to establish an international consensus for the estimation of measurement uncertainties, ISO has developed and published the Guide to the Expression of Uncertainty in Measurement (GUM) [2], which has been widely accepted and followed [3–5]. The GUM Uncertainty Framework combines the estimates and their associated standard uncertainties of various input quantities through a linear approximation of the measurement equation, in order to determine an estimate and its associated overall standard uncertainty [6].

The GUM Uncertainty Framework exhibits, however, some important limitations, which have been described in detail [7,8], comprising model linearization, assumption of normality of measurand derived from the application of Central Limit Theorem and computation of the effective degrees of freedom.

In order to overcome these handicaps of the GUM Uncertainty Framework, a supplement to GUM was recently developed [9], where the Monte Carlo Method (MCM) is described as an alternative procedure for the estimation of uncertainties. The MCM is a numerical procedure for solving mathematical problems by means of simulating random variables and is applied as a practical alternative to GUM Uncertainty Framework in cases where the latter is

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not applicable or its validity is not clear [7]. The aforementioned methods are fundamentally different in the fact that GUM Uncertainty Framework is a deterministic one based on the mathematical combination of probability distributions, whereas MCM is a probabilistic one performing the combination of probability distributions by numerical simulation [10].

There are several commercial software packages appropriate to carry out Monte Carlo analysis, which however, have not been able to apply the MCM in an adaptive way resulting in lack of direct control over the quality of the results obtained [7,10].

MATLAB [11] is a mathematical program for general purposes, which was used in developing the examples included in Supplement 1 of the GUM, allowing control over all MCM possibilities.

This study illustrates in detail a comparison between two methods to calculate uncertainties: the GUM approach, which is widely used and the MCM approach, which has not been widely applied yet, as it is considered an alternative method to estimate uncertainties. Specifically, both methods are compared in the direct determination of cadmium in water by graphite furnace atomic absorption spectrometry (GFAAS). Through the implementation of MATLAB, MCM is applied in an adaptive way controlling all of its possibilities.

## 2. Methodology

### 2.1. Principles of GUM Uncertainty Framework

The Guide to the Expression of Uncertainty in Measurement (GUM), currently available as ISO/IEC Guide 98-3:2008 establishes consistent and transferable rules for evaluating and expressing uncertainty in measurement. There exist various guides on the practical implementation of GUM, e.g. a Eurachem/CITAC guide for Quantifying Uncertainty in Analytical Measurement, which intends to demonstrate how the concepts of ISO-GUM may be applied to chemical measurements [5].

The GUM Uncertainty Framework estimates the overall uncertainty by identifying, quantifying and combining all the sources of uncertainty associated with the measurement (bottom up approach). It is based on the concept of a measurement equation:

$$Y = f(X_1, X_2, \ldots, X_n) \tag{1}$$

where $Y$ corresponds to the measurand (analytical result) and $X_i$ to the parameters or individual factors that have an influence on the measurand.

An estimate $y$ of the measurand $Y$ is determined by substituting the estimates $x_1, x_2, \ldots, x_n$ for $X_1, X_2, \ldots, X_n$ in Eq. (1). Thus:

$$y = f(x_1, x_2, \ldots, x_n) \tag{2}$$

The standard uncertainty of $y$, $u(y)$ (combined uncertainty), is obtained by appropriately combining the standard uncertainties of the input estimates $x_1, x_2, \ldots, x_n$, denoted by $u(x_1), u(x_2), \ldots, u(x_n)$. This is performed using the so-called "law of propagation of uncertainty" which is based on a first-order Taylor series approximation of Eq. (1). Thus:

$$Y = f(X_1, X_2, \ldots, X_n) \approx y(x_1, x_2, \ldots, x_n) + \sum_{i=1}^{n} c_i X_i \tag{3}$$

where $c_i$:

$$c_i = \frac{\partial f}{\partial x_i} = \left.\frac{\partial f}{\partial X_i}\right|_{x_1, x_2, \ldots, x_n} \tag{4}$$

These partial derivatives (sensitivity coefficients), describe how the estimate $y$ varies with changes in the values of the factors $x_1$, $x_2, \ldots, x_n$. Therefore, a change caused by the standard uncertainty $u(x_i)$ leads to a variation $u_i(y)$ of the estimate $y$ (contribution to uncertainty $u(y)$ from $u(x_i)$):

$$u_i(y) = c_i u(x_i) \tag{5}$$

The law of propagation of uncertainty when $X_1, X_2, \ldots, X_n$ are mutually uncorrelated leads to the expression:

$$u^2(y) = \sum_i c_i^2 u^2(x_i) = \sum_i u_i^2(y) \tag{6}$$

Standard uncertainties $u(x_i)$ may be evaluated either by observation of repeated experiments (Type A evaluation) or by other means (Type B).

In a Type A evaluation the standard uncertainty $u(x_i)$ is calculated as the standard deviation $s(x_i)$ of the mean of m measurements:

$$u(x_i) = s(\overline{x_i}) = \frac{s(x_i)}{\sqrt{m}} \tag{7}$$

The degrees of freedom associated with Type A standard uncertainties based on $m$ measurements are $\nu_i = m - 1$.

In a Type B evaluation the standard uncertainty $u(x_i)$ is evaluated by scientific judgment based on information such as previous measurement data, experience with or general knowledge of materials and instruments involved, manufacturer's specifications, calibration data, etc. When Type B uncertainties are used, it may be necessary to convert a confidence interval into a standard uncertainty, using information about the distribution of the value and the degrees of freedom. If no information is available, the distribution can be assumed to be rectangular and the degrees of freedom $\nu_i$ associated may be taken to be infinite.

The expanded uncertainty $U$, which provides a confidence interval within which the value of the measurand is expected to lie, is obtained by multiplying the combined standard uncertainty $u(y)$ by a coverage factor $k$ depending on the level of confidence required:

$$U = ku(y) \tag{8}$$

For normal distribution, a value $k = 2$ corresponds to an approximate confidence level (coverage probability) of 95%, and $k = 3$ of 99.7%.

However, in some cases the evaluation of a Type A standard uncertainty may not be based on a large number of readings, which could result in the coverage probability being significantly less than 95% if a coverage factor of $k = 2$ is used. In this case it is more correct to use as a coverage factor the two-sided $t$ tabulated value for the level of confidence chosen and the effective degrees of freedom, $\nu_{eff}$, calculated using the Welch–Satterthwaite formula [2,5,12]:

$$\nu_{eff} = \frac{u^4(y)}{\sum_i u_i^4(y)/\nu_\iota} \tag{9}$$

where $\nu_i$ corresponds to the degrees of freedom of $u(x_i)$. The value of $k$, often denoted as $k_p$, where $p$ is the confidence probability, will now give an expanded uncertainty, $U_p$, that maintains the coverage probability at approximately the required level $p$ (usually 95%).

### 2.2. Principles of Monte Carlo Method

The Monte Carlo Method is general [13], in the sense that it can be used to estimate the uncertainty of $Y$ under complex assumptions about the relationships between $Y$ and the factors $X_i$ and the distributions of the factors [7,10,14,15]. The MCM actually combines and propagates distributions rather than propagating uncertainties as in the GUM Uncertainty Framework. Uncertainty evaluation is based on a probabilistic approach that combines the whole distribution of the factors and is not just based on their means and standard deviations.

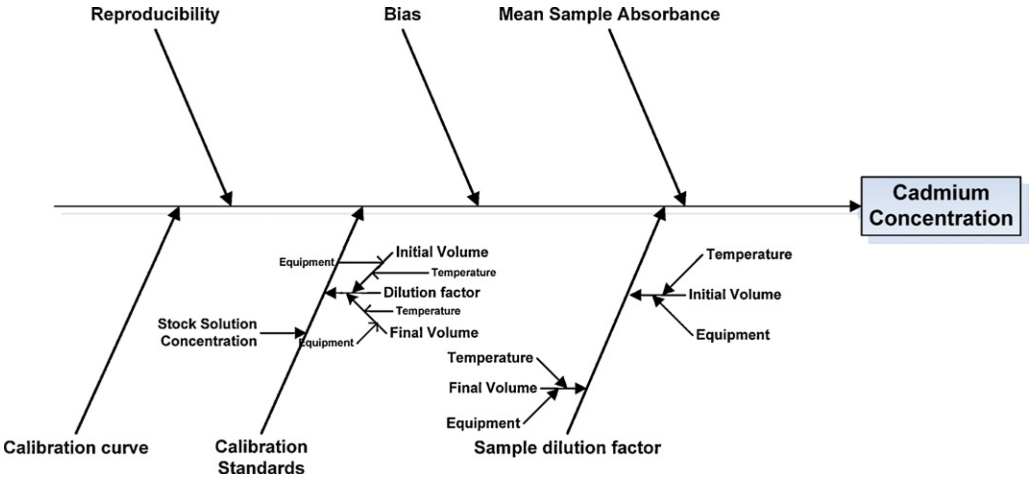

**Fig. 1.** Cause and effect diagram.

The Monte Carlo Method consists of simulating draws from the distribution of the measurand, based on simulated draws from the distributions of the factors.

With $g(X_i)$ denoting the distribution of the factor $X_i$, $i = 1, \ldots, n$, the uncertainty of $Y$, which is a function of the factors as shown in (1), is given by:

$$u(Y) = \sqrt{\int (Y - E(y))^2 g(X_1) \ldots g(X_n) dX_1 \ldots dX_n} \tag{10}$$

where $E(Y)$:

$$E(Y) = \int Y g(X_1) \ldots g(X_n) dX_1 \ldots dX_n \tag{11}$$

With $x_1^{(j)}, x_2^{(j)}, \ldots, x_n^{(j)}$, $j = 1, \ldots, M$, denoting a sample of size $M$ from the distributions of the factors, a Monte Carlo sample from the distribution of the measurand is obtained from Eq. (2) evaluated at the draws, i.e.

$$y^{(j)} = f(x_1^{(j)}, x_2^{(j)}, \ldots, x_n^{(j)}) \tag{12}$$

Then, the expected value of $Y$ is estimated by the average of the draws

$$m = \frac{1}{M} \sum_{j=1}^{M} y^{(j)} \tag{13}$$

and the overall standard uncertainty $u(y)$ is estimated by the sample standard deviation of the draws, that is

$$u(y) = \sqrt{\frac{1}{M-1} \sum_{j=1}^{M} (y^{(j)} - m)^2} \tag{14}$$

Confidence intervals for $y$ can be obtained and other statistical information can be drawn from the sample $y^{(1)}, y^{(2)}, \ldots, y^{(M)}$. For example, a 95% confidence interval for $Y$ can be obtained by taking the 2.5 and 97.5 percentiles of the sample.

### 2.3. Instrumentation and measurement procedures

The determination of dissolved cadmium in water samples was carried out in an accredited, according to ISO/IEC 17025:2005 [1], laboratory (Lab. of Environmental Chemistry, University of Athens) in accordance to the standard method ISO 15586:2003 [16]. The water samples are initially filtered through filters with a nominal pore width of 0.45 μm inside a laminar flow cabinet providing controlled air quality. The filtrate is preserved by the addition of 60% nitric acid ultrapure (Merck, Darmstadt, Germany) in order to obtain a pH <2 (0.5 mL conc. nitric acid in 100 mL sample). The preserved water samples are maintained in cool conditions (1–5 °C) in accordance with ISO 5667-3 [17] until analysis. At least one blank sample is prepared in parallel, in the same way to the samples.

For the preparation of cadmium calibration solutions a stock cadmium solution of 1000 ± 2 mg/mL (NIST traceable; Merck, Darmstadt, Germany) is initially used. Water used was 18.2 MΩ cm Milli-Q (Millipore, Bedford, MA, USA). From the stock solution intermediate cadmium solutions of 10 mg/L and 100 μg/L are prepared in class A volumetric flasks of 100 mL. For the preparation of cadmium calibration solutions with concentrations of 0.2, 0.4, 0.6, 0.8 and 1.0 μg/L, 200, 400, 600, 800 and 1000 μL of the intermediate cadmium standard solution of 100 μg/L are respectively pipetted in class A volumetric flasks of 100 mL.

Cadmium determination was carried out with the employment of graphite furnace atomic absorption spectrometry (GFAAS) with Zeeman background correction (SpectrAA 640Z; Varian, Mulgrave, Victoria, Australia). A sample volume of 20 and 5 μL chemical modifier (15 μg Pd and 10 μg $Mg(NO_3)_2$; Merck, Darmstadt, Germany) are injected with an autosampler directly into the graphite furnace. Graphite tubes used are pyrolytically coated and cadmium measurements were made at 228 nm, slit width 0.5 mm. All measurements were carried out with at least two replicates. The calibration curve is produced with least square linear regression and peak area.

The calculation of the methods' trueness and precision was carried out with the use of the certified reference material (CRM) BCR 610 (groundwater; 2.94 ± 0.08 μg/L Cd; EC-JRC-IRMM, Geel, Belgium). From the participation of the laboratory in three rounds of a Proficiency Testing Scheme, the $z$-score of cadmium determination in water samples was determined varying from −0.1 to 0.0.

## 3. Results and discussion

### 3.1. Mathematical modelling and identification of uncertainty sources

The identification of all relevant uncertainty sources for a complex analytical procedure is best done by drafting a cause and effect diagram sometimes known as an Ishikawa or 'fishbone' diagram [18]. The main parameters influencing the measurand (cadmium concentration of water sample) are represented by the main branches of the diagram. Further factors are added to the diagram, considering each step in the analytical procedure (Fig. 1).

**Table 1**
Mathematical model equations.

| |
|---|
| $C = C_{obs}F + \delta_{rep} + \delta_{bias}$ |
| $F = \frac{V_{10}}{V_{1.667}}$ |
| $C_{obs} = \frac{A_{obs} - B_0}{B_1}$ |
| $A_{obs} = \frac{A_{obs1} + A_{obs2} + \cdots + A_{obs10}}{10}$ |
| $B_1 = \frac{\sum_{i=1}^{6}\sum_{j=1}^{2}[(C_{stdi} - \bar{C}_{std})(A_{stdij} - \bar{A}_{std})]}{\sum_{1}^{6} 2(C_{stdi} - \bar{C}_{std})^2}$ |
| $B_0 = \bar{A}_{std} - B_1 \cdot \bar{C}_{std}$ |
| $\bar{C}_{std} = \frac{2\sum_{1}^{6} C_{stdi}}{12}$ |
| $\bar{A}_{std} = \frac{\sum_{i=1}^{6}\sum_{j=1}^{2} A_{stdij}}{12}$ |
| $C_{work1} = \frac{C_{bulk}V_1}{V_{100}}$ |
| $C_{std1} = 0$ |
| $C_{std2} = \frac{C_{work2}V_{0.2}}{V_{100}}$ |
| $C_{std3} = \frac{C_{work2}V_{0.4}}{V_{100}}$ |
| $C_{std4} = \frac{C_{work2}V_{0.6}}{V_{100}}$ |
| $C_{std5} = \frac{C_{work2}V_{0.8}}{V_{100}}$ |
| $C_{std6} = \frac{C_{work2}V_{1}}{V_{100}}$ |
| $V_{100} = V_{100(20)}[1 + a(T - 20)]$ |
| $V_{0.2} = V_{0.2(20)}[1 + a(T - 20)]$ |
| $V_{0.4} = V_{0.4(20)}[1 + a(T - 20)]$ |
| $V_{0.6} = V_{0.6(20)}[1 + a(T - 20)]$ |
| $V_{0.8} = V_{0.8(20)}[1 + a(T - 20)]$ |
| $V_{1} = V_{1(20)}[1 + a(T - 20)]$ |
| $C_{work2} = \frac{C_{work1}V_1}{V_{100}}$ |
| $V_{10} = V_{10(20)}[1 + a(T - 20)]$ |
| $V_{1.667} = V_{1.667(20)}[1 + a(T - 20)]$ |

The concentration $C$ of cadmium in the sample solution, which after being diluted is determined by atomic absorption spectrometry, is calculated by the following equation:

$$C = C_{obs}\,F + \delta_{rep} + \delta_{bias} \tag{15}$$

where $C_{obs}$ is the cadmium concentration obtained by GFAAS, $F$ is the 6-fold dilution factor of the sample and $\delta_{rep}$, $\delta_{bias}$ are quantities that equal zero and are included just to account for reproducibility and bias components of uncertainty. The cadmium concentration $C_{obs}$ is calculated using a calibration curve (absorption against concentration) which is constructed by linear least square regression using duplicate measurements of 6 calibration standards. The sample is measured 10 times and the mean absorbance $A_{obs}$ of the 10 absorbance measurements is used to obtain $C_{obs}$.

The equations that comprise the mathematical model of the measurement are presented in Table 1. Various quantities are defined in Table 2.

### 3.2. Application of GUM uncertainty framework

The sources taken into account for the application of the GUM Uncertainty Framework were reproducibility, mean absorbance of the sample, calibration curve, dilution factor and bias. Table S1 (supplemental material) presents the method of estimation as well as the mathematical formulas used for the estimation of the standard uncertainties of the various factors.

Concerning the calibration curve uncertainty (Table S1, supplemental material), it is necessary to point out that each one of the reference values $C_{stdi}$ may have uncertainties which propagate through to the final result. In practice, uncertainties in these values are usually small compared to uncertainties in the system responses $A_{ij}$ and may be ignored. Therefore the usual uncertainty calculation procedures for $C_{obs}$ [19–21] only reflect the uncertainty in the absorbance and not the uncertainty of the calibration standards, nor the inevitable correlations induced by successive dilution from the same stock. In this work the uncertainty of the calibration standards is sufficiently small to be neglected [5].

Bias was estimated analyzing a Certified Reference Material (BCR-610). Accounting for the uncorrected bias (significant or not) in the uncertainty estimation is a quite controversial matter. The ISO-GUM appears to rather discourage inclusion of bias in the uncertainty, stating in the note to clause 6.3.1: “Occasionally one may find that a known correction for a systematic effect has not been applied to the reported result of a measurement, but instead an attempt is made to take the effect into account by enlarging the ‘uncertainty’ assigned to the result. This should be avoided; only in very special circumstances should corrections for known systematic effects not be applied to the results of a measurement. Evaluating the uncertainty of a measurement result should not be confused with assigning a safety limit to some quantity”. Generally in chemical measurements, increasing measurement uncertainty to account for bias is certainly better than applying a doubtful correction or, even worse, ignoring the bias. A range of different approaches to account for uncorrected bias have been proposed [22,23]. In this work the result was not corrected ($\delta_{bias} = 0$) and the standard uncertainty of the “zero” bias correction was calculated (Table S1, supplemental material).

Having quantified all the main uncertainty contributions, the standard uncertainty of the measurand (cadmium concentration), $u(C)$, can be estimated using the law of propagation of uncertainty (Eqs. (4)–(6)).

$$u(C) = \sqrt{\left(\frac{\partial C}{\partial C_{obs}}u(C_{obs})\right)^2 + \left(\frac{\partial C}{\partial F}u(F)\right)^2 + \left(\frac{\partial C}{\partial \delta_{rep}}u(\delta_{rep})\right)^2 + \left(\frac{\partial C}{\partial \delta_{bias}}u(\delta_{bias})\right)^2 + \left(\frac{\partial C}{\partial A_{obs}}u(A_{obs})\right)^2} \tag{16}$$

where $u(C_{obs})$, $u(F)$, $u(\delta_{rep})$, $u(\delta_{bias})$, $u(A_{obs})$ are the standard uncertainties of $C_{obs}$, $F$, $\delta_{rep}$, $\delta_{bias}$, $A_{obs}$.

Fig. 2 and Table S2 (supplemental material) present the uncertainty budget for the measurand. The calculations give a combined uncertainty $u(C)$ equal to 0.10 μg/L.

The expanded uncertainty $U(C)$ may be obtained by multiplying the combined standard uncertainty $u(C)$ by a coverage factor $k$ depending on the level of confidence required ($k = 1.96$ for 95% level of confidence). The resulting expanded uncertainty is 0.20 μg/L. Therefore the measurement result is 3.01 ± 0.20 μg/L Cd.

Using as a coverage factor the two-sided $t$ tabulated value for the 95% level of confidence and the effective degrees of freedom, $\nu_{eff}$, calculated using the Welch–Satterthwaite formula (Eq. (9)) does not change the resulting expanded uncertainty. The Welch–Satterthwaite formula gives 265 effective degrees of freedom which corresponds to a coverage factor $k_p$ equal to 1.97.

### 3.3. Application of Monte Carlo Method

In our application of the Monte Carlo Method the model equation, as well as the interim equations which specify the relationships between cadmium concentration and the factors, are those given in Table 1. In order to validate the results of the GUM Uncertainty Framework, firstly we follow a Monte Carlo approach in which only the factors considered to be random by the GUM Uncertainty Framework are simulated from the respective prob-

**Table 2**
List of quantities of Table 1.

| Quantity | Units | Definition |
|---|---|---|
| $C$ | μg/L | Cadmium concentration of the water sample (measurand) |
| $C_{obs}$ | μg/L | Cadmium concentration obtained by GFAAS |
| $F$ | – | Dilution factor of the sample |
| $V_{10}$ | μL | Volume of the 10 mL volumetric flask used for the dilution of the sample |
| $V_{1.667}$ | μL | Volume (1.667 mL) of the sample pipetted for dilution |
| $\delta_{rep}$ | μg/L | Reproducibility component of the uncertainty of C |
| $\delta_{bias}$ | μg/L | Bias component of the uncertainty of C |
| $A_{obs}$ | AU | Mean absorbance of the sample solution |
| $A_{obs1}$ | AU | Absorbance of the 1st measurement of the sample solution |
| $A_{obs2}$ | AU | Absorbance of the 2nd measurement of the sample solution |
| $A_{obs3}$ | AU | Absorbance of the 3rd measurement of the sample solution |
| $A_{obs4}$ | AU | Absorbance of the 4th measurement of the sample solution |
| $A_{obs5}$ | AU | Absorbance of the 5th measurement of the sample solution |
| $A_{obs6}$ | AU | Absorbance of the 6th measurement of the sample solution |
| $A_{obs7}$ | AU | Absorbance of the 7th measurement of the sample solution |
| $A_{obs8}$ | AU | Absorbance of the 8th measurement of the sample solution |
| $A_{obs9}$ | AU | Absorbance of the 9th measurement of the sample solution |
| $A_{obs10}$ | AU | Absorbance of the 10th measurement of the sample solution |
| $B_o$ | AU | Calculated best fit intercept of the calibration curve |
| $B_1$ | AU/(μg/L) | Calculated best fit slope(gradient) of the calibration curve |
| $A_{stdij}$ | AU | Absorbance of the *j*th measurement of calibration standard *i* |
| $\bar{A}_{std}$ | AU | Mean absorbance of all calibration standards |
| $C_{stdi}$ | μg/L | Concentration of the calibration standard *i* |
| $C_{std1}$ | μg/L | Concentration of the calibration standard 1 |
| $C_{work1}$ | μg/L | Cadmium concentration of the working solution 1 |
| $C_{bulk}$ | μg/L | Cadmium concentration of the stock solution |
| $C_{work2}$ | μg/L | Cadmium concentration of the working solution 2 |
| $V_1$ | μL | Volume (1 mL) of the stock solution pipetted for preparing working solution 1<br>Volume (1 mL) of the working solution 1 pipetted for preparing working solution 2<br>Volume (1 mL) of the working solution 2 pipetted for preparing calibration standard 6 |
| $V_{100}$ | μL | Volume of the 100 mL volumetric flask used for the preparation of working solutions and calibration standards |
| $C_{std2}$ | μg/L | Concentration of the calibration standard 2 |
| $V_{0.2}$ | μL | Volume (0.2 mL) of the working solution 2 pipetted for preparing calibration standard 2 |
| $C_{std3}$ | μg/L | Concentration of the calibration standard 3 |
| $V_{0.4}$ | μL | Volume (0.4 mL) of the working solution 2 pipetted for preparing calibration standard 3 |
| $C_{std4}$ | μg/L | Concentration of the calibration standard 4 |
| $V_{0.6}$ | μL | Volume (0.6 mL) of the working solution 2 pipetted for preparing calibration standard 4 |
| $C_{std5}$ | μg/L | Concentration of the calibration standard 5 |
| $V_{0.8}$ | μL | Volume (0.8 mL) of the working solution 2 pipetted for preparing calibration standard 5 |
| $C_{std6}$ | μg/L | Concentration of the calibration standard 6 |
| $\bar{C}_{std}$ | μg/L | Mean concentration of all calibration standards |
| $T$ | °C | Temperature |
| $V_{100(20)}$ | μL | Volume of the 100 mL volumetric flask used for the preparation of working solutions and calibration standards at 20 °C |
| $V_{0.2(20)}$ | μL | Volume (0.2 mL) of the working solution 2 pipetted for preparing calibration standard 2 at 20 °C |
| $V_{0.4(20)}$ | μL | Volume (0.4 mL) of the working solution 2 pipetted for preparing calibration standard 3 at 20 °C |
| $V_{0.6(20)}$ | μL | Volume (0.6 mL) of the working solution 2 pipetted for preparing calibration standard 4 at 20 °C |
| $V_{0.8(20)}$ | μL | Volume (0.8 mL) of the working solution 2 pipetted for preparing calibration standard 5 at 20 °C |
| $V_{1(20)}$ | μL | Volume (1 mL) of the stock solution pipetted for preparing working solution 1 at 20 °C<br>Volume (1 mL) of the working solution 1 pipetted for preparing working solution 2 at 20 °C<br>Volume (1 mL) of the working solution 2 pipetted for preparing calibration standard 6 at 20 °C |
| $V_{10(20)}$ | μL | Volume of the 10 mL volumetric flask used for the dilution of the sample at 20 °C |
| $V_{1.667(20)}$ | μL | Volume (1.667 mL) of the sample pipetted for dilution at 20 °C |
| $\alpha$ | μL/(μL °C) | Thermal expansion coefficient of water |

ability distributions. The remaining factors are set equal to their mean values. Next, we design the complete Monte Carlo approach which takes into account all the random quantities affecting the measurand, including those that have non-standard distributions and/or affecting concentration in a non-linear way. In Table 3 the probability distributions we assume for the various factors are shown. The second column of the table reports whether the respective factor is considered as random by the GUM Uncertainty Framework (YES) or not (NO).

We have used Matlab to implement the Monte Carlo Method of drawing samples from the distributions of the factors in order to obtain a Monte Carlo sample from the distribution of cadmium concentration using equations of Table 1. The Matlab code developed to implement the Monte Carlo approach which includes only the factors taken into account by the GUM Uncertainty Framework is shown in Program S3 (supplemental material). This code simulates vectors of values from the appropriate distributions of the factors and then performs calculations with vectors in order to produce samples of draws from the interim quantities. Finally, it returns a vector of cadmium concentration values. As input, the code takes the number $N$ of draws to be simulated, which is significant in Monte Carlo simulation. As $N$ becomes larger, the accuracy of the Monte Carlo estimates increases. In the applications presented in this paper we have used $N = 10^6$ which is a sufficiently large value, noting however that since the program is very fast, even larger values of $N$ can be easily used.

The Matlab code of Program S3 (supplemental material) simulates samples from the distributions of $V_{1.667(20)}$, $V_{10(20)}$, $T$, $A_{obsi}$, $\delta_{rep}$ and $\delta_{bias}$ and then uses these draws to obtain a sample of $C$. Note that, under this approach, the values of $C_{stdi}$ and $A_{stdi}$ are fixed (non-

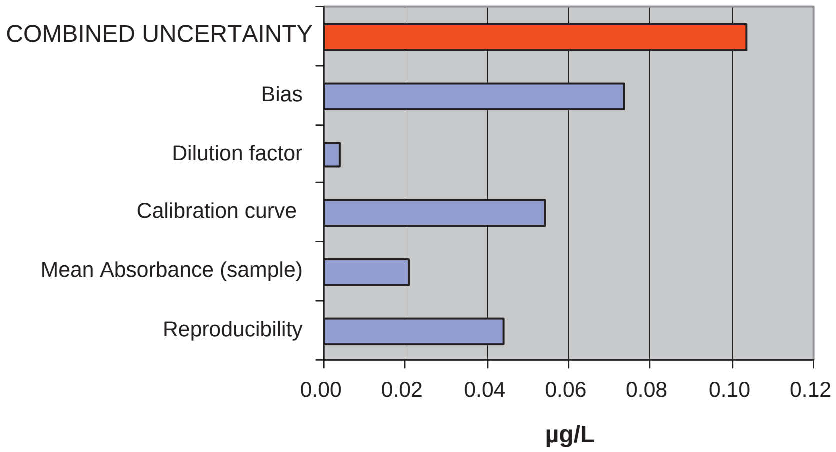

**Fig. 2.** Combined uncertainty of the measurand and uncertainty contributions.

random) and therefore the estimates $B_0$ and $B_1$ of the calibration curve are constant across Monte Carlo samples.

Summary statistics for a sample of $N = 10^6$ draws from the distribution of cadmium concentration obtained using the program S3 (supplemental material) provide a mean value of 3.02 µg/L, a standard uncertainty of 0.09 µg/L and a 95% confidence interval range of 2.84–3.19 µg/L.

The above results suggest that the GUM Uncertainty Framework overestimates the uncertainty of cadmium concentration. The Monte Carlo approach concludes that the distribution of the measurand is symmetric around a mean value of 3.02 µg/L but with a standard uncertainty about 10% smaller than the value of the GUM Uncertainty Framework estimate. This difference is consistent with Herrador et al. [8] who applied Monte Carlo and GUM for the determination of clenbuterol by HPLC with a coulometric electrode array system. Investigating the possible sources of this difference we have found that the main uncertainty contributions obtained by the GUM Uncertainty Framework and the Monte Carlo Method are very similar, apart from the standard uncertainty of $C_{obs}$ which is estimated quite differently under the two different methods. Within the GUM Uncertainty Framework $u(C_{obs})$ is estimated by the right-hand side of Eq. (16). However, this estimate is based on the absorbance values of the measurements used to produce the calibration curve ($A_{stdij}$) and not on the absorbance values

**Table 3**
Distributions of factors.

| Quantity | GUM | Distribution | Mean value | Standard uncertainty |
|---|---|---|---|---|
| $\delta_{rep}$ | YES | Normal | 0 | 0.044 |
| $\delta_{bias}$ | YES | Normal | 0 | 0.074 |
| $A_{obs1}$ | YES | Rectangular | 0.0562 | 0.00121 |
| $A_{obs2}$ | YES | Rectangular | 0.0556 | 0.00121 |
| $A_{obs3}$ | YES | Rectangular | 0.055 | 0.00121 |
| $A_{obs4}$ | YES | Rectangular | 0.0554 | 0.00121 |
| $A_{obs5}$ | YES | Rectangular | 0.0552 | 0.00121 |
| $A_{obs6}$ | YES | Rectangular | 0.0545 | 0.00121 |
| $A_{obs7}$ | YES | Rectangular | 0.0549 | 0.00121 |
| $A_{obs8}$ | YES | Rectangular | 0.0564 | 0.00121 |
| $A_{obs9}$ | YES | Rectangular | 0.055 | 0.00121 |
| $A_{obs10}$ | YES | Rectangular | 0.0564 | 0.00121 |
| $A_{obs11}$ | NO | Rectangular | −0.0001 | 0.00121 |
| $A_{obs12}$ | NO | Rectangular | 0.0015 | 0.00121 |
| $A_{obs21}$ | NO | Rectangular | 0.0217 | 0.00121 |
| $A_{obs22}$ | NO | Rectangular | 0.023 | 0.00121 |
| $A_{obs31}$ | NO | Rectangular | 0.0431 | 0.00121 |
| $A_{obs32}$ | NO | Rectangular | 0.0443 | 0.00121 |
| $A_{obs41}$ | NO | Rectangular | 0.0632 | 0.00121 |
| $A_{obs42}$ | NO | Rectangular | 0.0671 | 0.00121 |
| $A_{obs51}$ | NO | Rectangular | 0.086 | 0.00121 |
| $A_{obs52}$ | NO | Rectangular | 0.0848 | 0.00121 |
| $A_{obs61}$ | NO | Rectangular | 0.1141 | 0.00121 |
| $A_{obs62}$ | NO | Rectangular | 0.1135 | 0.00121 |
| $C_{bulk}$ | NO | Rectangular | 1,000,000 | 1154.701 |
| $T$ | YES | Rectangular | 20 | 1.7320 |
| $V_{100(20)}$ | NO | Rectangular | 100,000 | 7.1014 |
| $V_{0.2(20)}$ | NO | Normal | 200 | 0.25 |
| $V_{0.4(20)}$ | NO | Normal | 400 | 0.5 |
| $V_{0.6(20)}$ | NO | Normal | 600 | 0.75 |
| $V_{0.8(20)}$ | NO | Normal | 800 | 1 |
| $V_{1(20)}$ | NO | Normal | 1000 | 1.25 |
| $V_{10(20)}$ | YES | Normal | 10,000 | 1.8974 |
| $V_{1.667(20)}$ | YES | Normal | 1667 | 2.09 |

of the measurements of the sample solution ($A_{obsi}$) which are used to obtain $C_{obs}$. On the other hand, the Monte Carlo Method draws samples from the distribution of $C_{obs}$ by simulating the quantities $A_{obsi}$, $i = 1, \ldots, 10$, from their respective rectangular distributions. $C_{obs}$ is given as

$$C_{obs} = \frac{A_{obs} - B_0}{B_1} \tag{17}$$

where $A_{obs}$ is the mean of absorbance measurements whereas $B_0$, $B_1$ are constants. Therefore, the variance of $C_{obs}$ can be computed analytically as the variance of the random variable $A_{obs}$, i.e. the mean of 10 independent random variables following different rectangular distribution as specified in Table 3. The theoretical variance of this random variable is 0.00001, equal to the Monte Carlo estimate of the variance of $C_{obs}$. This value, compared to the estimate of var($C_{obs}$) = 0.00008 obtained by the GUM Uncertainty Framework, is significantly smaller. It is noteworthy that the GUM Uncertainty Framework also includes an explicit uncertainty contribution for $A_{obs}$, which in the Monte Carlo Method has been incorporated in the uncertainty of $C_{obs}$. However, in this particular application, this contribution appears to be negligible compared to the uncertainty contribution of $C_{obs}$. Furthermore the various uncertainty contributions are taken into account differently under the two methods. The Monte Carlo Method directly estimates $C$ using the draws and the standard uncertainty of $C$ is estimated from Eq. (14), while in the GUM Uncertainty Framework the uncertainty contributions are combined using the approximate equation (16). For this reason, although the estimates of the variance of $C_{obs}$ under the two approaches differ by a factor of 8, the final estimates of the variance of $C$ are much closer to each other.

The Monte Carlo Method can also take into account the factors that affect the measurand in a non-linear way and/or have non-standard distributions. Hence, we have also considered a complete Monte Carlo approach using all the distributions of Table 3. Under this approach, all the quantities involved in equation 15 and the interim equations of Table 1, including all volumes, concentrations, absorbances and the estimates of the calibration curve parameters, are random, i.e. different across Monte Carlo samples. The Matlab code that implements this approach is shown in Program S4 (supplemental material).

Summary statistics for a sample of $N = 10^6$ draws from the distribution of cadmium concentration obtained using the program S4 (supplemental material) provide a mean value of 3.01 μg/L, a standard uncertainty of 0.09 μg/L and a 95% confidence interval range of 2.83–3.19 μg/L.

The distribution of $C$ obtained by the complete Monte Carlo approach is symmetric around a mean value of 3.01 μg/L but with a standard uncertainty almost equal to the estimate obtained by the simple Monte Carlo approach. These results suggest that the uncertainty associated with the measurement of cadmium concentration in a sample of water estimated by Monte Carlo, continues to be smaller than that estimated by the GUM Uncertainty Framework, even after taking account of the additional sources of uncertainty.

## 4. Conclusions

The expanded uncertainty results (at 95% confidence levels) obtained with the GUM Uncertainty Framework and the Monte Carlo Method were ±0.20 μg/L and ±0.18 μg/L, respectively. This difference is not important when considering the type of the analysis and it does not affect any decision related to the “fitness for purpose” of the method. However, the result of the Monte Carlo Method can be considered as more reliable, since, unlike GUM Uncertainty Framework, it involves almost no assumptions and approximations. In particular, the observed difference of the two approaches may be attributed mainly to the approximation used by GUM Uncertainty Framework in estimating the standard uncertainty of the calibration curve produced by least squares regression.

Overall, the Monte Carlo Method is a practical tool for applying the principle of propagation of distributions and does not depend on the assumptions and the limitations required by the law of propagation of uncertainties (GUM Uncertainty Framework), thus reducing the risk of an unreliable measurement uncertainty estimation, particularly in cases of complicated measurement models, without the need to evaluate partial derivatives. However, the MCM requires programming expertise or use of certain commercial software packages to carry out Monte Carlo Analysis.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.talanta.2010.11.059.

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