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EVALUATION OF MEASUREMENT UNCERTAINTY
ANNEX 1.1

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Annex 1 to Guideline "Evaluation of Measurement Uncertainty"
PA/PH/OMCL (18) 145 (in its current version)

Estimation of measurement uncertainty of using Bottom-up approach

When measurand y (*output*) is determined from *input variables* x_1, x_2 , ..., x_n through a functional relationship, i.e., $y = f(x)$, then uncertainties in the x's will propagate through the calculation to an uncertainty in y. Combination of the standard uncertainties ($u(x)$) for each of the input variables gives a combined standard uncertainty ($u_c(y)$) using the appropriate mathematical rule. Usually, the input variables have no relationship with each other, except through their functional relationship which defines the measurand y. However, if there is any correlation between any components then it has to be taken into account by determining the covariance. Bottom up estimation of uncertainty involves estimation of each uncertainty components prior to the calculation of the overall or combined uncertainty. Uncertainty can arise from many possible sources, for which the individual contribution may be needed to be treated individually. In estimation of overall uncertainty it may be necessary to treat each source separately to obtain the individual contribution. When uncertainty is expressed as standard deviation, the uncertainty will be referred as standard uncertainty. Each component to the uncertainty budget should be estimated. However, only a small number of the components contribute significantly to the overall uncertainty. Therefore, it is left to the scientific judgement of the laboratory to decide to consider or not the minor components in the final uncertainty budget. It is typically accepted that components having a value of lower than one third of the major component may be disregarded [1].
Three examples of uncertainty estimation using the bottom-up approach will be given in the present annex and annexes 1.2 and 1.3.

Annex 1.1 Estimation of the measurement uncertainty of concentration of solutions prepared in laboratory

Example: Estimation of the measurement uncertainty for determination of concentration of Thyrotropin Releasing Hormone (TRH) in a solution

This example can be regarded as a stand-alone example, or as part of a more complex estimation, such as the estimation of content of Thyrotropin Releasing Hormone Thyrotropin Releasing Hormone (L-Pyroglutamyl-L-Histidyl-L-Prolinamide, TRH) in a product, for which this standard solution was prepared and used in the quantitation.

1. Description of the analytical procedure (Preparation of solutions):

Preparation of stock solution of TRH
Stock solution is prepared by dissolving 19.5 mg (accurate mass) of Thyrotropin Releasing Hormone certified reference substance in 500 mL volumetric flask (0.105 mM).

Preparation of final solution of TRH
Final solution of TRH (0.0105 mM) is prepared by transferring 10.0 mL of TRH stock solution to a 100 mL volumetric flask and diluting with water up to 100 mL (0.0105 mM).

2. Estimation of the measurement uncertainty

2.1 Step 1. Specification of a measurand

The measurand is the concentration of TRH in the solution, expressed as mol/L, calculated by following formula:

$$\mathrm{C\ (mol/L)} = \frac{m \cdot P_{TRH} \cdot 10}{M \cdot 500 \cdot 100}$$

Where:
m: mass (mg) of the Thyrotropin Releasing Hormone certified reference substance, used for preparation of the stock solution
P_{TRH}: purity of the TRH
M: molar mass of TRH (g/mol)
500, 100: Dilution volumes (mL) of stock solution and final solution, respectively
10: Volume of the stock solution used for dilution (mL)

2.2 Step 2. Identification of uncertainty contributors

Each of the parameters that affect the value of the measurand are shown as a cause and effect diagram (Fig. 1)

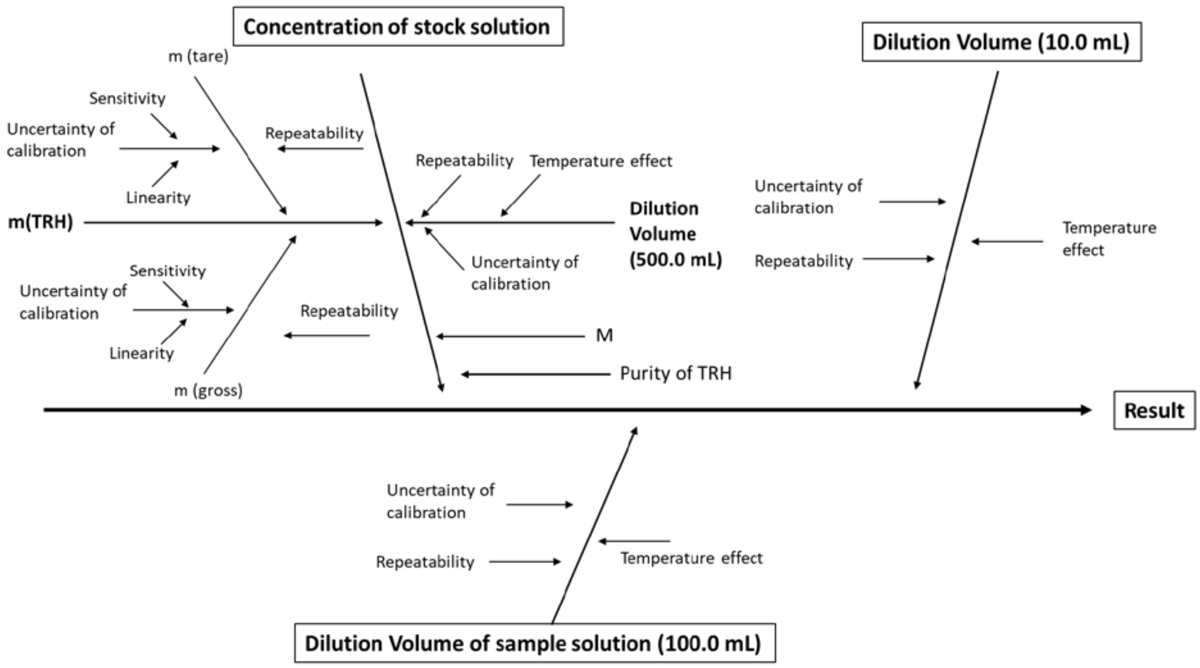

Fig. 1 Cause and effect diagram for determination of TRH concentration

2.3 Step 3. Quantification of uncertainty components

2.3.1 Component 1: Concentration of stock solution

2.3.1.1 *Uncertainty of the mass of TRH*

The purpose is to provide an estimate of uncertainty of the weighed amount of (TRH) in container by the weigh-by-difference method (data are given in Table 1).

Table 1 Weighing records

Mass of TRH + container	36.6 mg
Mass of container	17.1 mg
Mass of THR	19.5 mg

As the weighing process is performed by mass difference, each of the two weighings is subject to run-to-run variability and to the uncertainty in calibration of the balance. The calibration itself has two possible uncertainty sources: the sensitivity and the linearity of the calibration function.

Uncertainty in calibration of the balance

The external calibration of the balance states that the maximum difference from the actual mass on the scale pan and the reading of the scale is within ± 0.08 mg at level of confidence of approximately 95%, i.e., *k* = 2 following a normal distribution.

$$u(bcal) = \frac{0.08\,mg}{2} = 0.04\ \mathrm{mg}$$

Sensitivity

Since the two consecutive masses were done using the same balance over a short period of time, the sensitivity of the balance is neglected. [1, 2].

Uncertainty of measurement of the balance (balance usage) taken from repeated weighings (repeatability)

Weigh-to-weigh variability, 0.09902 mg, was estimated by means of a Shewhart control chart [3].

$$u(brep) = 0.09902\ \mathrm{mg}$$

Calculation of the Standard Uncertainty in Weighing Process, $u(mass)$:

$$u(mass) = \sqrt{2 \cdot u(bcal)^2 + u(brep)^2} = \sqrt{2 \cdot (0.040)^2 + (0.09902)^2} = 0.11402\ \mathrm{mg}$$

It has been conventionally assumed that the $u(bcal)$ has to be taken into account twice because of two weighings involved (the tare and the gross mass) as each is an independent observation and the linearity effects are not correlated [1]. It has been conventionally assumed $u(brep)$ is to be counted only once [4].

The relative standard uncertainty of measurement of the mass of the standard substance is:

$$\frac{u(m_{st})}{(m_{st})} = \frac{0.11402\,mg}{19.5\,mg} = 0.00585$$

2.3.1.2 ***Purity of TRH***

The supplier quotes the purity of TRH in the certificate of analysis as 97% ± 3%, without information on level of confidence and distribution.

In case of purity a rectangular distribution is assumed [1], so the uncertainty of the purity was divided by square root of 3 to obtain the standard uncertainty $u(\mathrm{P_{TRH}})$ *as*:

$$u(\mathrm{P_{TRH}}) = \frac{3\ \%}{\sqrt{3}} = 1.73\ \%$$

The relative standard uncertainty of measurement of the purity of TRH is:

$$\frac{u(\mathrm{Pst})}{(\mathrm{Pst})} = \frac{1.73\ \%}{97\ \%} = 0.0178$$

Calculation of standard Uncertainty for mass of TRH:

Table 2 provides summary of the calculated values for uncertainties for the weighing process.

Table 2 Summary of Values of Uncertainties for the mass of TRH:

Description	**Value x**	***u(x)***	***u(x)/x***
Purity of TRH	97%	1.73%	0.0178
Mass of TRH	19.5 mg	0.11402 mg	0.00585

$$\frac{u(mTRH)}{m_{TRH}} = \sqrt{(0.0178)^2 + (0.00585)^2} = 0.0187$$

The uncertainty must be calculated in the same unit, i.e., mg, as the result.

$$u(mTRH) = 0.0187\ \cdot 19.5\ \mathrm{mg}\ = 0.3654\ \mathrm{mg}$$

2.3.1.3 ***Uncertainty of the dilution volume of the standard solution***

Volume Calibration

According to the manufacturer certificate, the uncertainty of measurement of the volumetric flask is stated as 500.0 mL ± 0.12 mL, at a temperature of 20 °C, without any information regarding the level of confidence or distribution. A triangular distribution is assumed, because the actual volume is more likely to be at the center than at the extremes of the range [1].

Therefore the uncertainty of the calibration of volume is:

$$u(Vcal) = \frac{0.12}{\sqrt{6}} = 0.05\ mL$$

Repeatability of the Volume Measurements (run-to-run variation)

A series of ten fill-and-weigh exercises on the volumetric flask (500 mL) presented a standard deviation of 0.03 mL. This value is to be used in the final calculation directly.

$$u(Vrep) = 0.03\ mL$$

Temperature Effect

The volumetric flask has been calibrated at 20°C whereas the laboratory temperature varies between 16 °C and 24 °C (20 °C ± 4 °C). The uncertainty from this effect is calculated for the target volume (500 mL) from the estimate of temperature variation and the coefficient of volume expansion, i.e. 0.00021 per 1 °C [1, 2].

$$\text{Volume expansion} = 500\ \text{mL} \cdot 4^{\circ}\text{C} \cdot \frac{0.00021}{1\ ^{\circ}\text{C}} = 0.420\ \text{mL}$$

Assuming rectangular distribution, the uncertainty for temperature variation is:

$$u(VT) = \frac{0.420}{\sqrt{3}} = 0.2425\ mL$$

Calculation of the Standard Uncertainty of dilution volume of the stock solution *u(Vstock).*

$$u(Vstock) = \sqrt{u(Vcal)^2 + u(Vrep)^2 + u(VT)^2}$$

$$u(Vstock) = \sqrt{0.05^2 + 0.03^2 + 0.2425^2} = 0.249\ \text{mL}$$

The relative standard uncertainty of dilution volume of the standard solution is:

$$\frac{u(Vst)}{(\text{Vst})} = \frac{0.249\ \text{mL}}{500.0\ \text{mL}} = 0.0005$$

Calculation of standard uncertainty for Preparation of Stock solution

Table 3 provides summary of the calculated values for uncertainties for the preparation of stock solution.

Table 3 Summary of values of uncertainties for preparation of stock solution

Description	**Value x**	***u(x)***	***u(x)/x***
Mass of TRH	19.5 mg	0.3654 mg	0.0187
Dilution Volume	500 mL	0.249 mL	0.0005

Considering uncertainties in weighing and volume preparation the standard uncertainty of preparation of the stock solution is:

$$\frac{u(Cstock)}{C_{stock}} = \sqrt{(0.0187)^2 + (0.0005)^2} = 0.0187$$

The concentration of stock solution is calculated as:

$$C_{stock} = \frac{m_{st} \cdot P_{st}}{100} = \frac{19.5\ \text{mg} \cdot 0.97}{500\ \text{mL}} = 0.038\ \text{mg/mL} = 0.038\ \text{g/L}$$

The uncertainty of the concentration of the stock solution is:

$$u(Cstock) = C_{stock} \cdot 0.0187 = 0.038 \cdot 0.0187 = 0.0007\ g/L$$

2.3.1.4 *Uncertainty of Conversion of TRH concentration from g/L to mol/L*

Table 4 provides standard atomic weights and their quoted uncertainties for the constituent elements of TRH ($C_{16}H_{22}N_6O_4$) [5].

Table 4 Standard atomic weights and quoted uncertainties for the constituent elements of TRH

Element	**Standard Atomic Weight**	**Quoted Uncertainty** *u(e)*	**Standard Uncertainty** *u(e)*/$3^{1/2}$
Carbon C	12.0106	± 0.001	0.0006
Oxygen O	15.9994	± 0.00037	0.00021
Hydrogen H	1.007975	± 0.000135	0.000078
Nitrogen N	14.00674	± 0.00042	0.000245

The molar mass of TRH is:

$$M_{TRH} = 16 \cdot 12.0106 + 22 \cdot 1.007975 + 6 \cdot 14.00674 + 4 \cdot 15.9994 = 362.38309 \text{ g/mol}$$

The standard uncertainty of molar mass of TRH is:

$$u(M_{TRH}) = \sqrt{16 \cdot 0.0006^2 + 22 \cdot 0.000078^2 + 6 \cdot 0.000245^2 + 4 \cdot 0.00021^2} = 0.02536 \text{ g/mol}$$

The relative standard uncertainty of molar mass of TRH is:

$$\frac{u(M_{TRH})}{M_{TRH}} = \frac{0.02536 \text{ g/mol}}{362.38309 \text{ g/mol}} = 0.000007$$

The concentration is converted to mol/L:

$$C_{TRH(\frac{mol}{L})} = \frac{C_{TRH(\frac{g}{L})}}{M_{wTRH}} = \frac{0.038}{362.38309} = 0.000105 \frac{\text{mol}}{\text{L}} = 0.105\, mmol/L$$

Calculation of standard uncertainty for conversion of TRH concentration

Table 5 provides summary of the calculated values for uncertainties for the Molar mass and concertation of TRH.

Table 5 Uncertainty of the conversion of TRH concentration

Quantity	**Value (*x*)**	***u(x)***	***u(x)/x***
Concentration of TRH	0.038 g/L	0.0007 g/L	0.0184
Molar mass of TRH	362.3839 g/mol	0.00189 g/mol	0.000005

Considering uncertainty of calculation of concentration of TRH and uncertainty of molar mass of TRH, the standard uncertainty of conversion of TRH concentration:

$$\frac{u(C_{TRH})}{C_{TRH}} = \sqrt{(0.0184)^2 + (0.000005)^2} = 0.0184$$

The uncertainty of the concentration of the TRH in stock solution (mmol/L) is:

$$u(C_{TRH}) = C_{TRH} \cdot 0.0184 = 0.105 \cdot 0.0184 = 0.001932\, mmol/L$$

2.3.2 Component 2: Preparation of final solution of TRH

2.3.2.1 *Uncertainty of the dilution volume of the sample solution*

Volume calibration

According to the manufacturer certificate, the uncertainty of measurement of the 10 mL pipette is 0.04 mL and for volumetric flask of 100.0 mL the uncertainty of measurement is ± 0.1 mL, at a temperature of 20 ºC, without any information regarding the level of confidence or distribution. A triangular distribution is assumed, because the actual volume is more likely to be at the center than at the extremes of the range [1]. Therefore the uncertainties in calibration of volume are:

$$u(VpipetteCal) = \frac{0.04}{\sqrt{6}} = 0.0163\,mL$$

$$u(VflaskCal) = \frac{0.1}{\sqrt{6}} = 0.0408\,mL$$

Repeatability of the volume measurements

Two series of ten fill -and-weigh exercises on the volumetric flasks present standard deviations of 0.012 and 0.010 mL for the 10 mL pipette and 100 mL volumetric flaks, respectively, to be used in the final calculation directly.

$$u(VpipetteRep) = 0.012\,mL$$

$$u(VflaskRep) = 0.010\,mL$$

2.3.2.2 *Temperature effect*

The volumetric flasks have been calibrated at 20˚C, whereas the laboratory temperature varies between 16 ˚C and 24 ˚C (20 ˚C ± 4 ˚C). The uncertainty from this effect is calculated for the target volume (10 mL and 100 mL) from the estimate of temperature variation and the coefficient of volume expansion, i.e. 0.00021 per 1 ºC [1, 2].

$$\text{Volume expansion(pipette)} = 10\text{ mL} \cdot 4\,^{o}\text{C} \cdot \frac{0.00021}{1\,^{o}\text{C}} = 0.0084\text{ mL}$$

$$\text{Volume expansion (flask)} = 100\text{ mL} \cdot 4\,^{o}\text{C} \cdot \frac{0.00021}{1\,^{o}\text{C}} = 0.084\text{ mL}$$

Assuming rectangular distribution, the uncertainty for temperature variations for pipette and volumetric flask are:

$$u(VpipetteT) = \frac{0.0084}{\sqrt{3}} = 0.00485\text{ mL}$$

$$u(VflaskT) = \frac{0.084}{\sqrt{3}} = 0.0485\text{ mL}$$

Calculation of the Standard Uncertainty of the dilution volume

$$u(Vpipette) = \sqrt{u(VpipetteCal)^2 + u(VpipetteRep)^2 + u(VpipetteT)^2}$$

$$u(Vpipette) = \sqrt{0.0163^2 + 0.012^2 + 0.00485^2} = 0.02081 \text{ mL}$$

$$u(Vflask) = \sqrt{u(VflaskCal)^2 + u(VflaskRep)^2 + u(VpipetteT)^2}$$

$$u(Vflask) = \sqrt{0.0408^2 + 0.01 + 0.0485^2} = 0.06416 \text{ mL}$$

The relative standard uncertainties of the dilution volume are:

$$\frac{u(V_{pipette})}{V_{pipette}} = \frac{0.02081 \text{ mL}}{10 \text{ mL}} = 0.002081$$

$$\frac{u(V_{flask})}{V_{flask}} = \frac{0.06416 \text{ mL}}{100 \text{ mL}} = 0.0006416$$

2.4 Step 4. Calculation of combined standard uncertainty and expanded uncertainty

Combined standard uncertainty is calculated as:

$$\frac{u_c}{\mathrm{C_{TRHfinal}}} = \sqrt{(\frac{u(C_{TRH})}{C_{TRH}})^2 + (\frac{u(V_{pipette})}{V_{pipette}})^2 + (\frac{u(V_{flask})}{V_{flask}})^2}$$

$$\frac{u_c}{\mathrm{C_{TRHfinal}}} = \sqrt{(0.0184)^2 + (0.002081)^2 + (0.0006416)^2} = 0.0185$$

$$u_c = 0.0185 \cdot 0.0105 = 0.000195 \text{ mmol/L}$$

The uncertainty contribution of TRH molar mass to the overall uncertainty is insignificant, therefore it can be neglected.

Expanded uncertainty (k = 2, approximately 95% level of confidence) is:

$U = 2 \cdot u_c = 0.0004 \text{ mmol/L}$

2.5 Reporting of result

The result is expressed as:

C(TRH) = 0.0105 mmol/L ± 0.0004 mmol/L (approximately 95% level of confidence)

3. Estimation of the combined uncertainty using spreadsheet approach

The uncertainty of the final concentration of TRH solution can also be estimated by applying the spreadsheet approach (Table 6 and Table 7). This approach summarizes the relationship between all of the variables that have impact on the uncertainty of the concentration of TRH:

$$\mathrm{C\ (mol/L)} = \frac{m \cdot P_{TRH} \cdot 10}{M \cdot 500 \cdot 100}$$

The following equation is used for the calculation of the combined uncertainty:

$$u_c = \sqrt{\left[\left(\frac{\delta C_{TRH}}{\delta mass}\right)^2 \cdot u^2(mass) + \left(\frac{\delta C_{TRH}}{\delta Purity}\right)^2 \cdot u^2(Purity) + \left(\frac{\delta C_{TRH}}{\delta M}\right)^2 \cdot u^2(M) + \left(\frac{\delta C_{TRH}}{\delta V_{500mL}}\right)^2 u^2(V_{500mL}) + \left(\frac{\delta C_{TRH}}{\delta V_{100mL}}\right)^2 u^2(V_{100mL}) + \left(\frac{\delta C_{TRH}}{\delta V_{10mL}}\right)^2 u^2(V_{10mL})\right]}$$

where, partial derivative ($\frac{\delta C_{TRH}}{\delta xi}$), *i.e.* sensitivity coefficient, is a measure of the sensitivity of the TRH concentration to any changes in the input variables. However, it must be noted that the above equation neglects any correlation between the measured values. The following scheme presents a simple approach, i.e. spread sheet approach for the estimation of the combined uncertainty [1, 2, 6].

Table 6. Components involved in the estimation of the combined uncertainty by the spread sheet approach.

Numerical differentiation by change of the diagonal elements with the absolute standard deviations*						
Quantity	*u*(*Mass*)	*u*(*Purity*)	*u*(*M*)	*u*(*V500*)	*u*(*V100*)	*u*(*V10*)
Mass	*MASS* + *u*(*Mass*)	Mass	Mass	Mass	Mass	Mass
Purity	Purity	*PURITY*+ *u*(*Purity*)	Purity	Purity	Purity	Purity
M	M	M	*M*+ *u*(*M*)	M	M	M
$V_{500\ mL}$	$V_{500\ mL}$	$V_{500\ mL}$	$V_{500\ mL}$	*v500 ML*+ *u*(*V500*)	$V_{500\ mL}$	$V_{500\ mL}$
$V_{100\ mL}$	$V_{100\ mL}$	$V_{100\ mL}$	$V_{100\ mL}$	$V_{100\ mL}$	*v100 mL*+ *u*(*V100*)	$V_{100\ mL}$
$V_{10\ mL}$	$V_{10\ mL}$	$V_{10\ mL}$	$V_{10\ mL}$	$V_{10\ mL}$	$V_{10\ mL}$	*v10 mL*+ *u*(*V10*)
Result	C_{TRH} + $(\partial C_{TRH} / \partial Mass)$ $u(Mass)$	C_{TRH} + $(\partial C_{TRH} / \partial Purity)$ $u(Purity)$	C_{TRH} + $(\partial C_{TRH} / \partial M)$ $u(M)$	C_{TRH} + $(\partial C_{TRH} / \partial V500)$ $u(V500)$	C_{TRH} + $(\partial C_{TRH} / \partial V100)$ $u(V100)$	C_{TRH} + $(\partial C_{TRH} / \partial V10)$ $u(V10)$
ΔC_{TRH}	$(\partial C_{TRH} / \partial Mass)$ $u(Mass)$	$(\partial C_{TRH} / \partial Purity)$ $u(Purity)$	$(\partial C_{TRH} / \partial M)$ $u(M)$	$(\partial C_{TRH} / \partial V500)$ $u(V500)$	$(\partial C_{TRH} / \partial V100)$ $u(V100)$	$(\partial C_{TRH} / \partial V10)$ $u(V10)$
$(\Delta C_{TRH})^2$	$[(\partial C_{TRH} / \partial Mass)$ $u(Mass)]^2$	$[(\partial C_{TRH} / \partial Purity)$ $u(Purity)]^2$	$[(\partial C_{TRH} / \partial M)$ $u(M)]^2$	$[(\partial C_{TRH} / \partial V500)$ $u(V500)]^2$	$[(\partial C_{TRH} / \partial V100)$ $u(V100)]^2$	$[(\partial C_{TRH} / \partial V10)$ $u(V10)]^2$
Index	$[(\partial C_{TRH} / \partial Mass)$ $u(Mass)]^2/\Sigma(\Delta C_{TRH})^2$	$[(\partial C_{TRH} / \partial Purity)$ $u(Purity)]^2/$ $\Sigma(\Delta C_{TRH})^2$	$[(\partial C_{TRH} / \partial M)$ $u(M)]^2/$ $\Sigma(\Delta C_{TRH})^2$	$[(\partial C_{TRH} / \partial V500)$ $u(V500)]^2/$ $\Sigma(\Delta C_{TRH})^2$	$[(\partial C_{TRH} / \partial V100)$ $u(V100)]^2/$ $\Sigma(\Delta C_{TRH})^2$	$[(\partial C_{TRH} / \partial V10)$ $u(V10)]^2/$ $\Sigma(\Delta C_{TRH})^2$
$u(C_{TRH})$ = $\mathbf{\Sigma\Delta(C_{TRH})^2]^{1/2}}$						
Index (relative contribution of each uncertainty to the combined uncertainty) = $[(\partial C_{TRH}/\partial x_i)\ u_{xi}]^2 / \Sigma(\Delta C_{TRH})^2$						

Table 7 Estimation of the combined uncertainty by the spread sheet approach

Quantity	Value	u(x)	Unit
Weight	19.5	0.1140	*mg*
v_{500}	500	0.2492	*mL*
Purity	0.97	0.0173	
Mw	362.384	0.0019	*g/mol*
v_{10}	10	0.0208	*mL*
v_{100}	100	0.0642	*mL*

C = (Weigt x Purit x 10) / (Mw x 500 x 100) =(19.5 . 0.97 . 10) /(362.3 . 500 . 100)=0.014 mM

u(x)	0.114039293	0.2491987	0.01732051	0.001892	0.02083715	0.0641768
Quantity	***Weight***	***v_{500}***	***Purity***	***Mw***	***v_{10}***	***v_{100}***
Weight	**19.614**	19.5	19.5	19.5	19.5	19.5
v500	500	**500.249**	500	500	500	500
Purity	0.97	0.97	**0.987**	0.97	0.97	0.97
Mw	362.384	362.384	362.384	**362.386**	362.384	362.384
v10	10	10	10	10	**10.0208**	10
v100	100	100	100	100	100	**100.064**
C_{TRH}	**0.010439205**	**mg/L**				

C_{TRH}	**0.01050**	**0.01043**	**0.01063**	**0.01044**	**0.01046**	**0.01043**
ΔC_{TRH} = ci . u(xi)	0.0000611	-0.0000052	0.0001864	0.000000	0.0000218	-0.0000067
$(ci . u(x_i))^2$	**3.72713E-09**	**2.704E-11**	**3.4747E-08**	**2.97E-15**	**4.7316E-10**	**4.483E-11**
Indexes	***9.6%***	***0.1%***	***89.1%***	***0.0%***	***1.2%***	***0.1%***
$\Sigma[c_i . u(x_i)]^2$	**3.90188E-08**					

$u(C_{TRH})$=	**0.000198**		***$u(C_{TRH})$ =***	***$\{\Sigma[ci . u(xi)]^2\}1/2$***
$U_{Expanded}$	**0.000395**	***k=2***		

$$u_c = 0.0002 \text{ mmol/L}$$

$$C_{TRH} = 0.0108 \text{ mmol/L} \pm 0.0004\text{mmol/L} \ (k = 2, \text{approximately } 95\% \text{ level of confidence})$$

The contribution of each uncertainty source to the combined uncertainty is depicted in figure 2. As seen the purity of THR is the major uncertainty source.

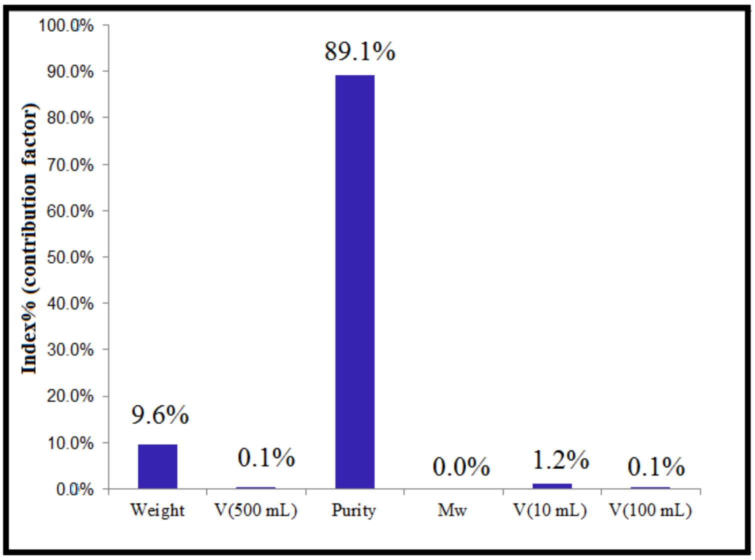

Fig. 2 Contribution of each uncertainty source to the combined uncertainty

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