# Key rules for uncertainty evaluation

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## Overview

- ISO recommendations
- Standard uncertainty – definition
- Rules for conversion
- Combining uncertainties
- Expanded uncertainty

## ISO recommendations for uncertainty evaluation

ISO 'Guide to the expression of uncertainty in measurement (GUM)'

- Uncertainties arise from several contributions
- Two ways of evaluating uncertainty components
  - statistical (Type A) and otherwise (Type B)
  - should be treated in the same way
- Express as standard deviations
- Combine by '.. the usual method for the combination of variances'
- Multiply by a (stated) factor if required
  - coverage factor ($k$)

The ISO Guide to the Expression of Uncertainty in Measurement ('the GUM') is the primary document applicable to uncertainty estimation.

[Full reference, BIPM, IEC, IFCC, ISO, IUPAC, IUPAP, OIML JCGM 100:2008, Evaluation of measurement data – Guide to the expression of uncertainty in measurement (GUM 1995 with minor corrections) (www.bipm.org). (Printed as ISO/IEC Guide 98-3:2008. ISO, Geneva)]

The basic recommendations implemented by the ISO guide are:

1. The uncertainty in the result of a measurement generally consists of several components which may be grouped into two categories according to the way in which their numerical value is estimated:

   **Type A**. Those which are evaluated by statistical methods

   **Type B**. Those which are evaluated by other means (modelling, reading from certificates etc.)

   Note that this does not describe the effects that cause the uncertainty (e.g. 'systematic' or 'random' effects), but the method of evaluation.

2. The components in category A are characterised by estimated variances $s_i^2$ (or standard deviations $s_i$) and their degrees of freedom $\nu_i$.

3. The components in category B should be characterised by quantities $u_j^2$, which may be considered approximations to the corresponding variances, the existence of which is assumed. The quantities $u_j^2$ may be treated like variances and the quantities $u_j$ like standard deviations.

4. The combined uncertainty should be characterised by the numerical value obtained by applying the usual method for the combination of variances. The combined uncertainty and its components should be expressed in the form of standard deviations.

5. If for particular applications, it is necessary to multiply the combined uncertainty by a factor to obtain the required level of confidence, the multiplying factor must always be stated.

## Uncertainty components

- Uncertainty in a result will arise from several contributions
- Uncertainty contributions combined to give a ‘total’ uncertainty
  - uncertainty components must be expressed in the same form to allow combination
  - express as standard deviations => standard uncertainty (*u*)

- BUT…uncertainty information comes in different forms so may need to convert
  - standard deviations - use as is
  - confidence intervals - convert
  - expanded uncertainties - convert
  - stated ranges - convert

When we intend to combine different contributions to form an overall estimate of uncertainty, it is reasonable to expect that the different contributions should be in the same basic form.

ISO principles use the fact that standard deviations can be combined rigorously to provide combined standard deviations. Thus, combination of uncertainties by ISO principles requires all the contributions to be expressed as standard uncertainties. A ‘standard uncertainty’ is simply an uncertainty expressed as a standard deviation.

Given that we encounter uncertainty information in several different forms, we need some rules for converting the different forms into standard deviations. Those rules are summarised on the following slides.

## $u(x)$ from a standard deviation $s$

- For uncertainties associated with single results
  - use the standard deviation $s$

Example: the random component of the uncertainty associated with the determination of creatinine in serum was estimated as 2 µmol L$^{-1}$ (standard deviation of 10 results obtained from the analysis of a QC material)

- For uncertainties associated with a mean of $n$ observations
  - convert to standard deviation of the mean

$$s/\sqrt{n}$$

If the data are already expressed as a standard deviation, and the uncertainty associated with a single result is required, then no conversion is required.

Note that if the uncertainty estimate is associated with the mean of $n$ results than it is the standard deviation of the mean, rather than the standard deviation, that is required.

The standard deviation of the mean is obtained by dividing the standard deviation by $\sqrt{n}$.

## $u(x)$ from a confidence interval

- Example:
  A frozen human serum reference material is stated by the supplier to contain:
  0.346 ± 0.007 mmol $L^{-1}$ creatinine
  with a level of confidence of not less than 95%
- Rule:
  Divide the half-range (0.007 mmol $L^{-1}$) by 1.96

$$\bar{x} \pm \frac{t \times s}{\sqrt{n}}$$

A confidence interval is calculated from:

$$\bar{x} \pm \frac{t \times s}{\sqrt{n}}$$

where $t$ is the student's $t$ value for a given level of confidence, which can be obtained from statistical tables. To obtain $s/\sqrt{n}$ from this expression we therefore need the appropriate value of $t$. To obtain the correct value of $t$ we need to know the degrees of freedom ($\nu$) and the level of confidence.

However, statements of the type shown on the slide are generally given without specifying degrees of freedom. Under these circumstances, it is acceptable to use the 95% ($\alpha$ = 0.05) 'large sample' value for $t$ which is 1.96.

If a different confidence level is quoted, use the relevant value of $t$. For example, for 99% confidence ($\alpha$ = 0.01), the value would be 2.58.

If the total number of results used to calculate the confidence interval is given, a more accurate value for the standard uncertainty can be calculated. From statistical tables find the Student $t$ value at the given confidence level for $\nu = n-1$, then divide the confidence interval by this $t$ value to give a standard uncertainty. However, for most purposes, use of the value 1.96 provides an adequate approximation.

## $u(x)$ from an expanded uncertainty

- Example:

  The certificate for a CRM (whole blood) states a certified tacrolimus concentration of:

  7.82 ± 0.25 µg $L^{-1}$

  where the reported uncertainty is an expanded uncertainty, calculated using a coverage factor of $k$=2.3, which gives a level of confidence of approximately 95%
- Rule:

  Divide the expanded uncertainty by the coverage factor, $k$

$$u(x) = \frac{U(x)}{k}$$

Note that $U(x)$ is the expanded uncertainty and $u(x)$ is the standard uncertainty.

The concept of 'expanded uncertainty' is explained in more detail in a later slide.

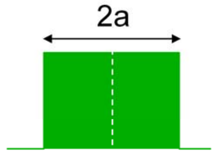
## $u(x)$ from a stated range

A range ($\pm a$) is given without an estimate of the distribution or confidence level. No reason to expect values close to mean are more likely than values at the extremes.

Assume rectangular distribution

divide $a$ by $\sqrt{3}$

$$u(x) = \frac{a}{\sqrt{3}}$$

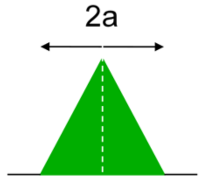



A range ($\pm a$) is given without an estimate of the distribution or confidence level. Values close to mean are more likely than values at the extremes.

Assume triangular distribution

divide $a$ by $\sqrt{6}$

$$u(x) = \frac{a}{\sqrt{6}}$$




In some situations the only information available is a value and an associated range. This type of information often relates to equipment specifications or the purity of pure substance reference materials. For example, the specification for a 50 mL volumetric flask is 50±0.06 mL.

Where only the stated range is given, the analyst has to choose a suitable distribution to represent the data. A rectangular distribution assumes that values can occur anywhere within the stated range (with equal probability) but not outside of the range. For the example of the 50 mL volumetric flask, assuming a rectangular distribution implies that the actual volume of the liquid in a given flask when it is filled to the calibration mark could be anywhere from 49.94 mL to 50.06 mL.

It is easy to calculate a standard uncertainty from a rectangular distribution. If the stated range is ±a, the standard uncertainty is $a/\sqrt{3}$.

If there is information to suggest that values closer to the middle of the stated range are more likely than values at the extremes, then a triangular distribution should be assumed.

If the range is ±a, the standard uncertainty from a triangular distribution is $a/\sqrt{6}$.

It is usually acceptable to use a rectangular distribution to obtain an initial estimate of the uncertainty associated with, for example, manufacturing tolerances. Such uncertainties do not generally make a significant contribution to the overall uncertainty associated with results from multi-stage test methods so the choice of distribution for stated ranges is not usually critical.

Note that the Eurachem/CITAC Guide, 'Quantifying uncertainty in analytical measurement' assumes a triangular distribution for the tolerances associated with volumetric glassware. The argument in this case is that in an effective manufacturing process, the actual value is probably more likely to be close to the nominal value than at the extremes of the permitted range.

## Exercise – Calculating standard uncertainties

In each case identify:

- Type of data (confidence interval, stated range…)
- Appropriate conversion factor

## Exercise – Calculating standard uncertainties

- The manufacturer's specification for a Class A 100 mL volumetric flask is ±0.1 mL
- The standard deviation of the volume of water delivered from a 1 mL automatic pipette (obtained from weighing the liquid from repeat dispensings) was calculated as 0.0004 mL
- The purity of a creatinine reference material is given by the supplier as (99.7 ± 0.3)%
- The certificate of analysis accompanying a frozen human serum certified reference material (CRM) states that the certified value for creatinine is 3.1 ± 0.5 mg $kg^{-1}$
  - The quoted uncertainty is the half-width of the expanded uncertainty calculated using a coverage factor, *k*, of 2.6, which gives a level of confidence of approximately 95%

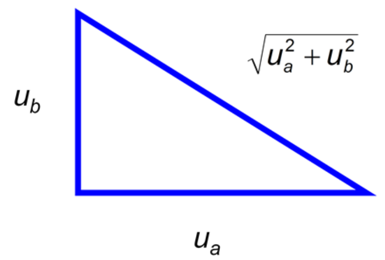
## Combination of uncertainties (1)

- Addition or subtraction

$$y = a + b - c + \ldots..$$

Uncertainties are combined as standard deviations

$$u(y) = \sqrt{u(a)^2 + u(b)^2 + u(c)^2 + \ldots.}$$




Most analytical methods involve several steps and a number of parameters contribute to the final result. Each step or parameter will have an associated uncertainty. The way the uncertainties are combined depends on the form of the equation(s) used in the calculation.

The mathematical expression for combining uncertainties is:

$$u(y(a,b,\ldots.)) = \sqrt{\left(\frac{\partial y}{\partial a}\right)^2 u(a)^2 + \left(\frac{\partial y}{\partial b}\right)^2 u(b)^2 + \ldots.}$$

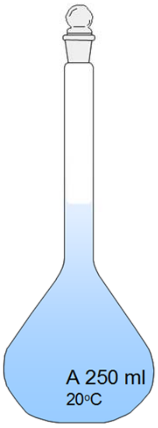
The form of the differential terms determines whether it is appropriate to combine the uncertainties as variances or relative variances. In cases where the calculation of the final result involves only addition or subtraction, the differential terms will all be equal to 1. The full expression therefore simplifies so that uncertainties are combined as variances.

This simplest rule for combination of uncertainty contributions, as shown on the slide, is known as the root-sum-of-squares rule.

This rule only applies when all the uncertainties ($u_a$, $u_b$ etc.) are expressed as standard deviations in the end result (and are therefore in the same units), and when the individual effects are independent.

Note that due to the way uncertainty contributions are combined, the combined uncertainty will be dominated by the largest uncertainty components. A contribution is often considered negligible if it is below a third of the largest uncertainty, though some authorities prefer a factor of five.

## Combination of uncertainties – Example 1




- 250 mL volumetric flask filled to the mark with 0.1M hydrochloric acid
  - manufacturer's specification: **±0.15 mL**
  - precision of filing flask to line – standard deviation of results from 10 fill-and-weigh experiments: **0.012 mL**
- Uncertainty in the volume:

$$u(v) = \sqrt{\left(\frac{0.15}{\sqrt{3}}\right)^2 + 0.012^2} = 0.087\,\text{mL}$$

Before combining the uncertainties they need to be expressed as standard uncertainties. The manufacturer's tolerance needs to be converted to a standard uncertainty, following the rules described previously. Assuming a rectangular distribution, the stated range is divided by $\sqrt{3}$.

The estimate of the uncertainty associated with the precision of filling the flask to the calibration line is expressed as a standard deviation and can therefore be used directly in the calculation.

## Combination of uncertainties (2)

- Product or quotient

$$y = \frac{a \times b}{c}$$

- Uncertainties are expressed as relative standard deviations

$$\frac{u(y)}{y} = \sqrt{\left(\frac{u(a)}{a}\right)^2 + \left(\frac{u(b)}{b}\right)^2 + \left(\frac{u(c)}{c}\right)^2}$$

Where terms are multiplied or divided, the differential terms in the basic expression shown on the previous page will be equal to *y*/*a*, *y*/*b*, etc. The uncertainties are therefore expressed as relative standard deviations before being squared and combined. This leads to the uncertainty in *y* also expressed as a relative standard deviation, i.e. $u(y)/y$.

**Further rules**

If the equation is a measured quantity multiplied by an exact number B,

$$q = \mathrm{B}x$$

B has no uncertainty so the uncertainty in *q* is B times the uncertainty in *x*

$$u(q) = \mathrm{B}\,u(x)$$

If, in the equation to calculate a result there is a variable raised to a power,

$$q = x^{\mathrm{n}}$$

the uncertainty in *q* is calculated from:

$$\frac{u(q)}{q} = \mathrm{n}\frac{u(x)}{x}$$

## Combination of uncertainties – Example 2

- Standard solution prepared by dissolving 18.96 mg of dopamine hydrochloride in 0.1M hydrochloric acid and making up to volume in a 100 mL volumetric flask

$$c\left(\text{mmol L}^{-1}\right) = \frac{m \times p}{v \times M} \times 1000$$

- m = mass of dopamine hydrochloride (mg)
- p = purity of dopamine (expressed as a ratio between 0 and 1)
- v = final volume of the solution (mL)
- M = molar mass of dopamine hydrochloride

This examples illustrates the calculation of the uncertainty associated with the concentration of a standard solution prepared in a laboratory. The uncertainty in the concentration will have contributions from the uncertainties associated with each of the quantities used in the calculation of the concentration: mass, purity, volume and molar mass.

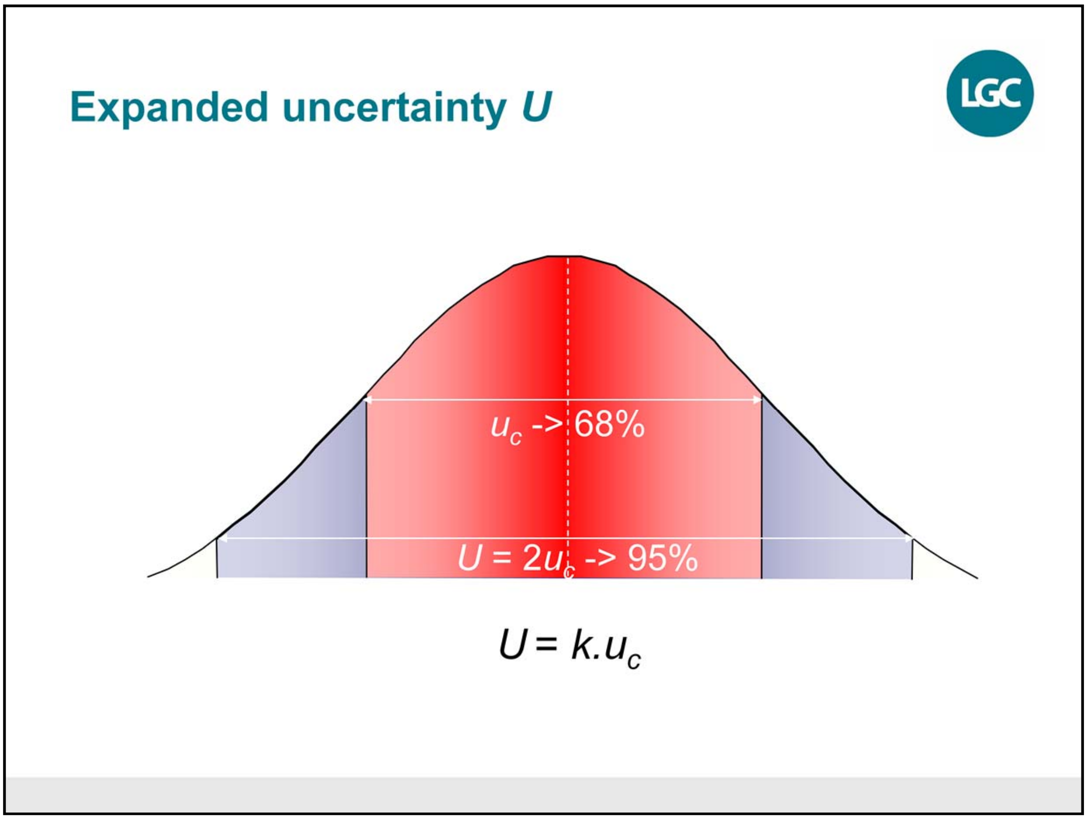
| Parameter | Value $x_i$ | Standard uncertainty $u(x_i)$ | Relative uncertainty $u(x_i)/x_i$ |
|---|---|---|---|
| Mass (m) | 18.96 mg | 0.0286 mg | 0.00151 |
| Purity (p) | 0.99 | 0.00577 | 0.00583 |
| Volume (v) | 100 mL | 0.0621 mL | 0.000621 |
| Molar mass (M) | 189.64 g mol$^{-1}$ | 0.0039 g mol$^{-1}$ | 0.0000206 |
| $c = \frac{m \times p}{v \times M} \times 1000$ | 0.990 mmol L$^{-1}$ | $\frac{u(c)}{c} = \sqrt{\left(\frac{0.0286}{18.96}\right)^2 + \left(\frac{0.00577}{0.99}\right)^2 + \left(\frac{0.0621}{100}\right)^2 + \left(\frac{0.0039}{198.64}\right)^2}$ $= 0.00605$ | |
| | $u$(c) | **0.990 x 0.00605 = 0.0060 mmol L$^{-1}$** | |

The standard uncertainties shown in the table have been calculated from different sources of information:

- Mass – standard uncertainty calculated from information on balance calibration certificate and standard deviation of replicate weighings of a check weight;
- Purity – manufacturer's specification, converted to a standard uncertainty (rectangular distribution assumed);
- Volume – standard uncertainty calculated from manufacturer's specification and data from precision (fill-and-weigh) experiment;
- Molar mass – standard uncertainty calculated from IUPAC data on atomic weights.

Since the calculation of the concentration involves multiplication and division, the standard uncertainties are combined as relative values. This gives the combined uncertainty expressed as a relative value (0.00605). To express the uncertainty as a standard uncertainty (in units of mmol L$^{-1}$) the relative uncertainty is multiplied by the concentration of the solution.

The solution therefore has a concentration of 0.99 mmol L$^{-1}$ with a standard uncertainty of 0.0060 mmol L$^{-1}$.




For a normal distribution, a range of ±σ only includes about 68% of the possible values.

In ordinary statistics, the confidence interval is a range which includes a specified (usually 95%) fraction of the possible values. The confidence interval is typically calculated by multiplying the observed standard deviation *s* by Student's *t*. For 95% confidence and for large numbers of degrees of freedom, *t* is close to 2.

By analogy, the standard uncertainty *u* needs expanding to give a range with a high probability of including the right answer. The ISO Guide recommends that *u* be expanded by a coverage factor *k*. *k* is usually expected to be based on the Student *t* value corresponding to the number of degrees of freedom associated with the uncertainty estimate. In most cases, a reasonable number of degrees of freedom is assumed, so **for most practical purposes, *k* is set equal to 2**.

## Summary

- Uncertainty in a result will arise from several contributions
- Uncertainty contributions combined to give a ‘total’ uncertainty
  - uncertainty components must be expressed in the same form to allow combination
  - express as standard deviations => standard uncertainty (*u*)
  - contributions may need converting
- Standard uncertainties are then combined:
  - as standard deviations:

$$u(y) = \sqrt{u(a)^2 + u(b)^2 + u(c)^2 + ....}$$

  - as relative standard deviations:

$$\frac{u(y)}{y} = \sqrt{\left(\frac{u(a)}{a}\right)^2 + \left(\frac{u(b)}{b}\right)^2 + \left(\frac{u(c)}{c}\right)^2}$$

**Answers to Exercise**

*The manufacturer's specification for a Class A 100 mL volumetric flask is ±0.1 mL.*

Answer:

The manufacturer's specification is a stated range. Assuming a rectangular distribution, the standard uncertainty in the volume is:

$0.1/\sqrt{3} = 0.0577$ mL.

(Note that if a triangular distribution is assumed the standard uncertainty is $0.1/\sqrt{6} = 0.0408$ mL)

*The standard deviation of the volume of water delivered from a 1 mL automatic pipette (obtained from weighing the liquid from repeat dispensings) was calculated as 0.0004 mL.*

Answer:

The value given is a standard deviation which is the correct form for a standard uncertainty. No conversion is required.

*The purity of a creatinine reference material is given by the supplier as (99.7 ± 0.3)%.*

Answer:

The specification for the purity is a stated range. Assuming a rectangular distribution, the standard uncertainty associated with the purity is:

$0.3/\sqrt{3} = 0.173\%$.

*The certificate of analysis accompanying a frozen human serum certified reference material (CRM) states that the certified value for creatinine is 3.1 ± 0.5 mg kg$^{-1}$.*

*The quoted uncertainty is the half-width of the expanded uncertainty calculated using a coverage factor, k, of 2.6, which gives a level of confidence of approximately 95%.*

Answer:

An expanded uncertainty is converted to a standard uncertainty by dividing by the stated coverage factor. The standard uncertainty is therefore:

$0.5/2.6 = 0.192$ mg kg$^{-1}$.