*Trace*CERT™ – Traceable Certified Reference Materials. Reliability is a matter of proper uncertainty calculation

Part 5 – This is the fifth and final article in the series on Certified Reference Materials to appear in Analytix.

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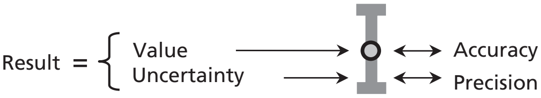
In addition to the concept of traceability as it applies to analytical chemistry, the concept of uncertainty is also poorly understood. It is not uncommon for chemists to hesitate when they are asked for the uncertainty budgets of their measurement values. Although there are published guidelines on how to deal with this issue [1–2], admittedly the calculation of uncertainty can be a real challenge. As is true for makers of fine watches, who must know how even the smallest component contributes to the overall mechanism, it is crucial for analysts to have a detailed understanding of the entire measurement process in order to calculate a true and reliable uncertainty budget. It is not possible to present in this short article a comprehensive discourse on the subject. However, we will use this space to provide some basic understanding and show how we calculate and report the uncertainty values for our *Trace***CERT**™ reference materials.

Uncertainty vs. error

Confusion often arises because of the incorrect use of the terms uncertainty and error. Whereas error is not quantifiable, being a blunder or a mistake, uncertainty can be estimated or calculated and therefore expressed as an actual number. The uncertainty characterizes the variability that can reasonably be attributed to the measurand, the physical parameter being quantified by measurement. Consequently, each measurement result consists of two components: the *value* (predominantly the average of replicate measurements) and the *uncertainty* (the attributed variability), as shown in **Figure 1**.

Figure 1 A measurement value without an uncertainty budget is not a measurement result

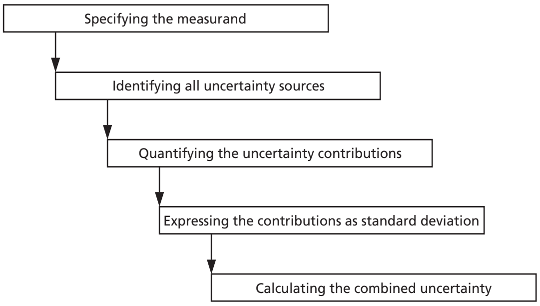


Calculating the uncertainty budget: Empiric vs. bottom-up

Generally, there are two approaches to obtain an uncertainty budget for a measurement: the empiric approach and the so-called "bottom-up" approach. The empiric approach is based on historical data, such as proficiency test performance (round robins), control charts or validation data. Hence, uncertainties calculated by the empiric approach are based on actual experience. The empiric approach is also called the top-down estimation. Typically it is not necessary to know in detail all of the influence parameters since the uncertainty estimation is based on the analysis of the whole process. In some cases the empiric approach may lead to meaningful results. However, because it is based on a snapshot in time, it cannot be assumed to be representative of future measurements.

A more sophisticated approach is the so-called "bottom-up" approach. Here, the uncertainty of a process or a measurement is calculated by summing all contributing influence parameters. Hence, all the details of the process must be identified and quantified individually **(Figure 2).** Obviously, the bottom-up approach is much more challenging and, in some cases, is not even possible due to lack of information. However, there is greater confidence in uncertainty calculations that use the bottom-up approach since by definition all sub-processes at the actual time of measurement are fully known and understood.

Figure 2 Step-by-step procedure of an uncertainty evaluation by the bottom-up approach



Combined uncertainty, u_c

After specification of the measurand and identification of the influence parameters, the individual influence parameters (contributors to the uncertainty budget) must be quantified. There are many different ways input data on the individual influence parameters of a process can be obtained. They might include min/max tolerance values from instrument specifications, nonlinearity data, any repeatabilities, and so forth. However, for these various data to be summed they must be first converted to standard deviation values (SD). Only SDs can be added by applying mathematical rules to get the combined uncertainty. Besides triangular or rectangular distributions, there are other methods to convert data into SDs [1]. After all influence parameters are converted to SDs, the combined uncertainty u_c can be calculated by applying the mathematical rules of uncertainty propagation. **Figure 3** shows the two basic algorithms. With the help of a cause-effect (Ishikawa or fishbone) diagram, like that shown in **Figure 4**, the influence parameters can be visualized to give an overview of the uncertainty determination. This tool is very helpful, especially when analyzing highly-complex processes.

Figure 3 Uncertainty propagation rules. In the case of additive parameters the absolute uncertainties are combined (square root of the sum of the squared contributions). In the case of multiplicative contributions the relative uncertainty contributions are combined

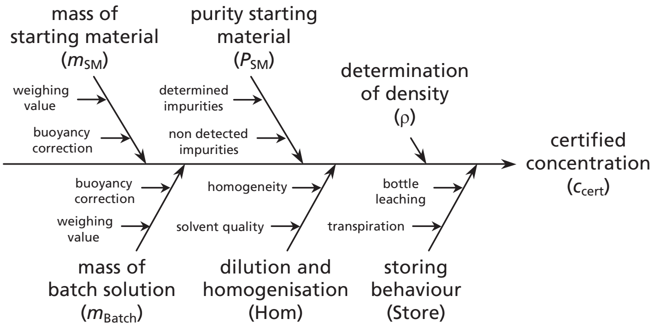
Additive parameters:

$$M = a + b \qquad u_c(M) = \sqrt{u^2(a) + u^2(b)}$$

Multiplicative parameters:

$$M = a \cdot b \qquad \frac{u_c(M)}{M} = \sqrt{\left(\frac{u(a)}{a}\right)^2 + \left(\frac{u(b)}{b}\right)^2}$$

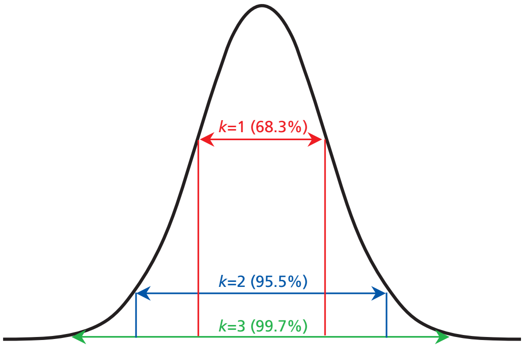
Figure 4 Cause effect diagram of the preparation procedure of *Trace***CERT**™ reference materials. Only first and second order influence parameters are shown



Expanded uncertainty, U

Since the combined uncertainty, u_c, is a single standard deviation, the associated confidence level is only 68% (based on a Gaussian distribution, **Figure 5**). However, because a reported uncertainty value is meaningful only when the underlying level of confidence is adequate, it is quite common to expand u_c with an expansion factor, k, equaling 2. Assuming that a Gaussian distribution is fulfilled, the reporting of a double SD (k=2) leads to a confidence level of 95%. It is therefore important avoid at all costs citing an uncertainty value based on a single SD since it can lead to misunderstandings and overly-optimistic uncertainty values. Instead, it is recommended to report the expanded uncertainty, U, which is equal to $k \cdot u_c$, where k is the number of standard deviation units (expansion factor).

Figure 5 Gaussian distribution showing the increase in confidence level with increasing expansion factor, *k* (number of standard deviation units)

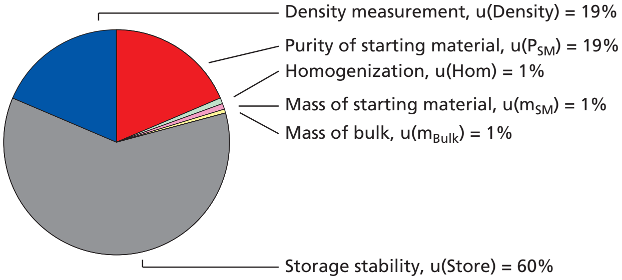


Evaluation of *Trace*CERT™ CRM uncertainties

In the previous four installments of this series of technical articles on *Trace***CERT**™ reference materials, we discussed the manufacturing, analysis and storage effects [3]. Without going into mathematical details, in this article we want to give an overview of the key influence parameters to the uncertainty calculation of *Trace***CERT**™ CRMs and discuss their relevance to the overall uncertainty budget. In **Figure 4**, the identified key influence parameters are shown as a cause-effect diagram. Each of the primary parameters (vertical arrows) is composed of a set of secondary parameters (horizontal arrows). For clarity, we have shown only the major effects. It should be noted that most of the secondary influence parameters comprise multiple minor influence parameters (tertiary parameters). For example, the secondary influence parameter "weighing value" (left upper corner in **Figure 4)** is made up of the following contributions: repeatability of weighing, readability, nonlinearity and eccentric load of balance, uncertainties of the calibration weights and temperature coefficient. This is a good example of how the bottom-up approach for uncertainty calculation is only possible with a deep understanding of the details of the measurement process.

Of course not all of the influence parameters are of equal importance in terms of their contribution to the overall uncertainty budget. Only when the whole uncertainty calculation is done can the relevance of the individual parameters be analyzed. **Figure 6** shows the primary influence parameters of the uncertainty budget of a *Trace***CERT**™ Ultra, a CRM for ICP calibration, including the storage effects. By including the storage effects into the uncertainty budgets of all *Trace***CERT**™ products, we can guarantee that the certified value is not only within specification at the time of production, but also when the bottle is first opened by the end-user. Two major contributions will be explained in more detail in the next section: the uncertainty calculation of the starting material purity statement and the storage effect contribution.

Figure 6 Partitioning of the uncertainty budget of *Trace***CERT**™ Ultra reference materials relative to the total uncertainty (expanded uncertainty usually is 0.2% relative to the certified value)



Uncertainties of starting material purity and storage effects

We discussed in a previous article of this series how the "100% minus sum of impurities" approach is the best method for the characterization of materials with high purity (>99.8%). In this case, the found trace impurities and an estimated contribution from the non-found impurities (below detection limit, DL) are subtracted from 100%. These two different impurities (real found and below DL) are also treated in separate ways in terms of their contribution to the uncertainty budget. For the real found impurities, an individual uncertainty contribution is considered for each element. For trace analysis with ICP-OES or ICP-MS, these contributions are typically in the range of several percent relative to the found value. For all the unfound impurities (below DL) a contribution of half of the DL is applied to the uncertainty budget.

The storage effects arise primarily from the loss of solvent by transpiration through the container wall [3]. Hence, the associated uncertainty contribution of this effect depends to a great extent on the container and the packaging material (aluminized bag vs. "naked" bottle). Long-term studies have yielded maximum transpiration rates for each individual type of bottle/packaging under various storage conditions and solvent systems. These data are considered in the uncertainty budget, and also are used to calculate the expiry date and the maximum storage temperature for the product.

We hope that this series of technical articles gave you an inside look into the production, testing and certification of our *Trace***CERT**™ reference materials. Since buying an analytical standard is a matter of trust, it is our intention to bring as much transparency as possible to our customers. As a consequence of the continuous improvement in our production of certified reference materials and our extensive experience in the CRM field, our laboratories will soon be accredited by the Swiss Accreditation Service according to both EN-ISO/IEC 17025 (general requirements for the competence of testing and calibration laboratories) and also ISO Guide 34 (general requirements for the competence of reference material producers). We look forward to supplying your need for CRMs, in terms of application, composition and quality, long into the future.

To view the entire *Trace***CERT**™ line, please visit our web site **www.sigmaaldrich.com/tracecert**

References

1] Quantifying uncertainty in analytical measurement, Eurachem/CITAC Guide, second edition, **2000.**

2] Guide to the expression of uncertainty in measurement (GUM), ISO, Geneva, corrected edition, **1995.**

3] *Trace*CERT™ – Traceable Certified Reference Materials. Part 1: Analytix, Vol. 5, **2006** and Part 2–4: Analytix, Vol. 1–3, 2007, available at **www.sigmaaldrich.com/analytix**