Evaluation of uncertainty of reference materials

Abstract Certification of reference materials is far more than just characterisation of a selected homogeneous batch of material. From the perspective of the ISO Guide on the Expression of Uncertainty in Measurement (GUM) all uncertainty sources relevant to the user of an individual certified reference material (CRM) sample at a moment in time should be part of the CRM uncertainty. This not only includes the full uncertainty of the batch characterisation (rather than the statistical variation), but also all uncertainties related to possible between-bottle variation, instability upon long-term storage and instability during transport to the customer.

Key words Certified reference materials · Uncertainty · Characterisation · Uncertainty analysis

Introduction

The accurate and traceable determination of a mean value of a quantity (content, amount) in a sample or a batch of material can be obtained in various ways, such as carrying out a number of independent repetitions using a primary method of analysis [1], comparing the results of a limited number of reference methods, or comparing the results of various independent methods applied in a series of laboratories. These three different methods are used by various producers to certify the values assigned to their reference materials (RMs), whereby this assignment is done using quite similar statements, but these statements may sometimes have very different meanings. Moreover, it must also be realised that the certification of a RM is much more than just carrying out a series of precise and accurate measurements traceable to the SI or to any other system of units, to written or agreed standards or to an artefact, such as, e.g. the primary WHO materials to which several clinical RMs are traceable. The certification of a RM involves, in the first instance, the preparation of a larger number of homogeneous, stable and adequately packaged samples which are all representative of the complete batch, as well as the proper assessment of their homogeneity and stability. Ignoring this is not only one of the main reasons why problems occur with certified reference materials (CRMs), but also why they are the subject of needless discussions about primary, secondary, consensus, working, etc. RMs. This distinction in classes of RMs mainly exists in the mind of some metrologists, but is fully absent in the existing ISO-REMCO Guides. The latter only differentiate between (just) RMs and CRMs, whereby a RM is defined as “a material or substance one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus,
the assessment of a measurement method, or for assigning values to materials", and a CRM is just “a RM with a certificate in which the certified values are accompanied by an uncertainty at a stated level of confidence” [2].

What is a CRM user interested in?

CRMs are sometimes forced into a hierarchical system depending on the fact that there certified values were determined using a primary method of analysis or are based on “less traceable” measurements obtained in a laboratory intercomparison. In reality, such a differentiation is meaningless, considering that very often the uncertainty component which originates from the characterisation of the RM is dominated by uncertainty components originating from several other sources such as insufficient guarantee of absence of inhomogeneity and/or instability. Therefore, it is not correct when producers certify their RMs just considering the results of their accurate and traceable determinations of the mean value of the content of the CRM batch, knowing that their customers (users) are only interested in the mean value of the single bottle they ordered on condition that it is received on the day of dispatch.

The ongoing revision of the ISO-Guide 35 [3] - which constitutes a complete rewriting - is therefore a unique opportunity to reconsider the production of CRMs. It will consider production as an integrated process of correct preparation, positive demonstration of homogeneity and stability, and accurate and traceable characterisation, and thus of full implementation of the principles laid down in the Guide to the Expression of Uncertainty in Measurement (GUM) [4]. This means that all components of uncertainty of “the sample on the desk of the user” should be properly evaluated and accounted for. Thereby, it must be strongly emphasised that the inability to demonstrate between bottle variation or instability during storage or transportation, as well as confining the uncertainty of the batch characterisation to the statistical between-laboratory variation is no longer acceptable. Ignoring this is one of the major causes of the so-called “Jorhem paradox” discussed at BERM-7 [5] where it was (rightly) found unacceptable that “results found to be unacceptable for user laboratories are good enough to be used in the certification of the CRM”, even if it is statistically just logic [6]! The consequence is, however, that one will have to accept - just as was the case for testing laboratories introducing GUM - that uncertainties of CRMs will increase “from fiction to reality”: an idea which is apparently difficult for many analysts to become accustom to, and which, moreover, may confuse those who tend to deal with these aspects. A CRM producer should include in an uncertainty statement everything that reasonably attributes (GUM) to the uncertainty of the measurand, i.e. the property value to be certified. This ends where accidents and incidents start: if something happens to a CRM during transport that goes beyond what can be foreseen, it is not part of an uncertainty statement, as the information on the certificate will stipulate under what conditions the certificate (and the CRM) are valid.

Uncertainty analysis in the preparation of a CRM

From the reasoning given above, it becomes apparent that the certification of a RM includes far more than just the characterisation of the material. This step, often carried out as a collaborative study between multiple laboratories, is crucial for the quality of the material as a CRM, but it is generally insufficient.

From the perspective of EURACHEM Guide [7] as well as from GUM [4], a producer should include all uncertainty sources that are relevant to the package sold to the customer. Internal consistency of the uncertainty analysis requires the inclusion of the (residual) uncertainty from the experiments carried out for homogeneity and stability testing. So, even if the producer cannot demonstrate any inhomogeneity or instability, there is still a (small) uncertainty budget to be included. Usually, this budget will be small, but in cases where only poorly repeatable methods of measurement are available, this contribution may be of significance.

A further consequence of this is that it really “pays off” in terms of uncertainty if a sufficient number of replicate measurements is carried out in homogeneity and stability testing. The use of methods with good linearity, selectivity and repeatability will also greatly contribute to reducing the uncertainty from these experiments. These factors are all in the hands of the producer. Implementing them correctly and consistently will reduce the costs of “after sales” of a CRM producer, not to speak of the subsequent damage due to wrongly certified RMs.

This way of thinking may seem new, but those who have already gained experience with inhomogeneous and/or instable RMs have already developed ways to deal with these aspects. A CRM producer should include in an uncertainty statement everything that “reasonably attributes” (GUM) to the uncertainty of the measurand, i.e. the property value to be certified. This ends where accidents and incidents start: if something happens to a CRM during transport that goes beyond what can be foreseen, it is not part of an uncertainty statement, as the information on the certificate will stipulate under what conditions the certificate (and the CRM) are valid.

What is important in the preparation of a CRM?

Good measurements carried out on bad quality candidate RMs are a nonsense and a complete waste of time and money! Therefore, extreme care should be taken not only to prepare a stable and homogeneous base material, but also to sample it in a tight and inert containment [8]. Matrix CRMs require in general to be clean and dry, to be transformed into an optimal physi-