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# ESTIMATION OF MEASUREMENT UNCERTAINTY IN PHYSICAL ANALYSIS LABORATORY

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**Abstract**
Many decisions, in all fields of human activities, are based on the results of measurements. Therefore it is essential that such results are reliable. This can be achieved by, among other things, establishing traceability of the results to stated references and providing an estimate of the uncertainty of measurement based on an uncertainty budget including all known uncertainty contributions. In analytical chemistry several sources contribute to the deviation of an individual result from an unknown “true” value. These are sometimes indicated from a laboratory point of view as a ladder of errors including the measurement procedure (method) bias, the lab bias, the run error and the repeatability error. Consistent treatment of measurement bias, including the question of whether or not to correct for bias, is essential for the comparability of measurement results. Several different published approaches to the treatment of uncorrected bias and its uncertainty are critically reviewed with regard to coverage probability and simplicity of execution.
The fundamental document on expression of uncertainty in measurement, the ISO/IEC Guide to the Expression of Uncertainty measurement [1] (GUM), was published in 1993 following the collaborative effort of metrological organization, standardization bodies and scientific societies involved in the science of measurement. The principles of the GUM are recognized to apply to all types of quantitative measurements, in all field of application. A prerequisite for the application of the GUM is that “the result of a measurement has been corrected for all recognized significant systematic effects” (GUM 3.2.4). This implies that when developing a measurement procedure all possible sources of bias should be investigated and if deemed appropriate a correction should be incorporated into the procedure.
**Keywords:** bias, uncertainty, reference material

## 1. Introduction

### *Bias*

Bias is defined in ISO 3534:1993 as the difference between an accepted reference value and the expectation of test results. An accepted reference value is reasonably clear, but the expectation of test results deserves closer consideration. The expectation carries the usual statistical meaning, usually identical with the mean of an infinite number of replicated observations. However, it is important to specify the conditions under which the test results are obtained. Different conditions do not necessarily lead to the same expectation i.e. the same mean value, and this affects the way we think about bias. Using a bias determined on a certified reference material (CRM) under repeatability conditions to correct a measurement on a routine test sample on a later occasion, day-to-day effects and matrix effects would both have to be included in estimating the uncertainty of the correction. This issue is considered further below in relation to experimental determination of bias.

## 2. Method

### *Experimental estimation of bias*

Overall bias is best estimated by repeated analysis of a relevant CRM, using the complete measurement procedure. When the aim is to estimate a bias for a measurement procedure in routine use in a laboratory the within laboratory reproducibility (intermediate precision) conditions are preferred since the variation in time will lead to a better estimate of the bias uncertainty. This is because the conditions include effects like e.g. different personnel, different chemicals and calibrants, change in instrument resolution, instrumental drift, annual instrument service, summer and winter conditions and cross-contamination from different test samples.

Precision and bias estimates obtained using the within-laboratory validation approach are designed as to cover all effects impacting the measurement that would occur under normal operation conditions for the measurement procedure. Therefore, provided that the measurements are under statistical control, uncertainty estimates obtained using this approach is applicable for all measurements within the scope of the measurement procedure. The application range of the uncertainty estimates is determined by the range covered in the validation study and the on-going quality control. Therefore these investigations should include appropriate within-scope variations, e.g. different levels of the measurand and different types of test items.

The accuracy or trueness of an analytical procedure should be evaluated, in terms of bias, through the analysis of either reference materials or spiked samples or by comparison with an alternative method. The approach which is chosen depends on the intended use of the method being validated and the resources available. The following approaches for determining accuracy are listed in order of desirability in terms of providing increased measurement reliability:

- the use of certified reference material;
- the use of a traceable reference material or material prepared ‘in-house’;

- the use of the method when participating in a proficiency testing scheme,
- the use of spiked samples, based on blank or positive samples.

Preference must be given to the use of a certified reference material (CRM) over the use of other reference materials, or a material prepared in the laboratory (in-house material) containing a known amount of the analyte. The reference object will be measured repeatedly (at least n = 6 times, better n>10) under appropriate within-laboratory reproducibility conditions, which correspond to those employed in normal operation.

The first step is to investigate whether the standard deviation of the measurement series is compatible with the previously determined and monitored standard deviation of the measurement procedure. Subsequently, the mean value of the measurement results is compared with the reference value in order to investigate potential bias. The bias observed will be assessed as "unacceptable", "significant but acceptable" or "insignificant".

**3. Results and disscusions**

***GUM treatment of bias***

In the GUM it is assumed (GUM 3.2.3) that a systematic error that

(1) arises from a recognized effect of an influence quantity on a measurement result,

(2) can be quantified and

(3) is significant in size relative to the required uncertainty, should be corrected for.

This is not only a recommendation; it is a pre-condition for application of the GUM implementation of the law of propagation of uncertainty, which assumes that all relevant uncertainty contributions can be treated as contributions to a combined variance.

The basic methodology of the GUM accordingly makes no provision for accommodation of a recognized, but uncorrected, bias. The treatment given is simple in principle; calculate a mean bias, *b*, correct for the mean bias, and estimate the variance of the correction from the range of possible bias. The mean and variance calculations given in GUM F.2.4.5 are based on an assumption of a distribution of possible bias, *b(t)*, over a rectangular distribution of parameter values *t*.

For an estimate of the standard uncertainty for the bias interval we would normally use the root mean square (RMS): $u_b = \sqrt{\frac{\sum b_i^2}{n}}$

It follows that, to the extent that any use of uncorrected bias falls within the scope of the GUM, a simple treatment which uses an assumed correction of zero, an uncertainty contribution based on the RMS bias (equal, for a single observed bias, to the bias itself) and an uncertainty of the bias determination is consistent with the recommendations of GUM F.2.4.5. [1]. According to GUM [1] a measurement result should always be corrected if the bias is significant and based on reliable data such as a CRM.

For every estimation of the uncertainty from the laboratory bias, two components have to be estimated to obtain *u(bias)* [5]:

1) the bias (as % difference from the nominal or certified value)

2) the uncertainty of the nominal/certified value, $u(C_{ref})$ or $u(C_{recovery})$

The uncertainty of the bias, *u(bias)* can be estimated by

$$u(bias) = \sqrt{u_b^2 + u(C_{ref})^2} \quad \text{where} \quad u_b^2 = \frac{\sum (b_i)^2}{n}$$

and if only one CRM is used also the $s_{bias}$ have to be included and *u(bias)* can the be estimated by

$$u(bias) = \sqrt{b^2 + (\frac{s_{bias}}{\sqrt{n}})^2 + u(C_{ref})^2}$$

Suppose now the bias magnitude is known, less than a positive number $b_{max}$, but that the expected bias is zero. Then, [5] suggest treating the bias magnitude as uniformly distributed up to $b_{max}$. This leads to var[*b*]=1/3 $b^2_{max}$ whose square root become the uncertainty component.

***Testing for bias***

If the precision at the reference object is compatible with the procedural precision as determined before, then the deviation of the measured values obtained on the reference object from the reference value is examined and assessed. In principle this can be done for each individual measured value. However, for the sake of simplicity the mean deviation, i.e. the deviation of the mean value will be examined here. It will be first checked whether the deviation of the mean value is acceptable or not.

An unacceptable deviation indicates serious deficiencies of the measurement procedure, which require a detailed investigation of all process steps and devices concerning sources of error, and appropriate corrective actions to eliminate or at least reduce the observed bias. An acceptable deviation matches the expectation regarding the trueness of the procedure and does not require any revision of the measurement procedure. If the deviation of the mean value is acceptable, then it will be tested for (statistical) significance.

A deviation is considered to be significant, indicating significant bias, if the magnitude (absolute value) of the deviation of the mean value $\overline{x_{meas}}$ from the reference value $x_{ref}$ is larger than twice the standard uncertainty of this deviation,

$$\left|\overline{x_{meas}} - x_{ref}\right\rangle 2\sqrt{\frac{s_{meas}^2}{n}}$$

Otherwise the deviation is insignificant [5].

***GUM about uncertainty components due to the bias***

In practice it happens quite often that significant bias is found, but the data are not sufficient for deriving a sound correction. For example, it may be doubtful whether a single-level correction, based on measurements of a single standard, is applicable to the entire measuring range. Then additional measurements, e.g. including another standard, should be made in order to characterize the bias to an appropriate degree. If this is not possible or not practical, a pragmatic alternative is to increase the uncertainty to account for the observed bias instead of attempting any correction [7].

The GUM appears to rather discourage such procedure, 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."* In appreciating this guidance, a key phrase to recognise is that of a "known correction". Certainly systematic effects (i.e. bias) that have been characterised to a degree that the applicable corrections can be considered as known, should be corrected, unless this entails unacceptable expenses. In practice, however, it will often be the expenses for deriving rather than for applying a "known correction" that are prohibitive. Then increasing measurement uncertainty to account for significant bias is most certainly better than applying a doubtful correction or, even worse, ignoring the bias.

**Conclusion**

1. If the representative materials are certified reference materials, the biases can be estimated directly as the differences between the results and the reference values, and the

whole procedure is straightforward. In the more likely event that insufficient number of certified reference materials are available, recovery tests with a range of typical test materials may be resorted to, with due caution. Currently there is very little quantitative information about the magnitude of uncertainties from this source, although in some instances they are suspected of being large.

2. The analysis of a CRM can be used to evaluate the uncertainty in the framework of method validation

3. The evaluation of analytical measurement uncertainty by extended validation experiments gives a realistic view of the method's capability and also offers the chance to use this information in routine analysis.

4. The advanced concept of estimating "expanded combined uncertainty" according to the GUM [1] demands consideration of all significant sources of uncertainty that are inherent in the overall analytical process. The uncertainty in the AQC measurement that is decisive for assurance of analytical trueness provides a significant contribution to the uncertainty in the final result of unknown samples. If this uncertainty is not considered, the use of an "uncertain" CRM would be advantageous because the range for acceptance is wider. In contrast to this paradoxical situation the use of a "certain" CRM is justified by a smaller interval for the combined uncertainty in the analytical result of the unknown sample.

5. It is usual practice to test the significance of the detected bias; if it is not significant it seems to be illogical to correct the raw results of unknown samples.

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