

GUIDELINES ON MEASUREMENT UNCERTAINTY

CAC/GL 54-2004

Introduction

It is important and required by ISO/IEC 17025:1999 that analysts are aware of the uncertainty associated with each analytical result and estimates that uncertainty. The measurement uncertainty may be derived by a number of procedures. Food analysis laboratories are required, for Codex purposes, to be in control¹, use collaboratively tested or validated methods when available, and verify their application before taking them into routine use. Such laboratories therefore have available to them a range of analytical data which can be used to estimate their measurement uncertainty.

These guidelines only apply to quantitative analysis.

Most quantitative analytical results take the form of “ $a \pm 2u$ or $a \pm U$ ” where “ a ” is the best estimate of the true value of the concentration of the measurand (the analytical result) and “ u ” is the standard uncertainty and “ U ” (equal to $2u$) is the expanded uncertainty. The range “ $a \pm 2u$ ” represents a 95% level of confidence where the true value would be found. The value of “ U ” or “ $2u$ ” is the value which is normally used and reported by analysts and is hereafter referred to as “measurement uncertainty” and may be estimated in a number of different ways.

Terminology

The international definition for Measurement Uncertainty is:

"Parameter, associated with the result of a measurement, that characterises the dispersion of the values that could reasonably be attributed to the measurand"²

NOTES:

1. The parameter may be, for example, a standard deviation (or a given multiple of it), or the half-width of an interval having a stated level of confidence.
2. Uncertainty of measurement comprises, in general, many components. Some of these components may be evaluated from the statistical distribution of results of a series of measurements and can be characterised by experimental standard deviations. The other components, which can also be characterised by standard deviations, are evaluated from assumed probability distributions based on experience or other information.
3. It is understood that the result of a measurement is the best estimate of the value of a measurand, and that all components of uncertainty, including those arising from systematic effects, such as components associated with corrections and reference standards, contribute to the dispersion. .”

¹ As outlined in Codex GL 27-1997 “Guidelines for the Assessment of the Competence of Testing Laboratories Involved in the Import and Export of Food”

² International vocabulary of basic and general terms in metrology, ISO 1993, 2nd Edition.

Recommendations

1. The measurement uncertainty associated with all analytical results is to be estimated.
2. The measurement uncertainty of an analytical result may be estimated by a number of procedures, notably those described by ISO (1) and EURACHEM (2). These documents recommend procedures based on a component-by-component approach, method validation data, internal quality control data and proficiency test data. The need to undertake an estimation of the measurement uncertainty using the ISO component-by-component approach is not necessary if the other forms of data are available and used to estimate the uncertainty. In many cases the overall uncertainty may be determined by an inter-laboratory (collaborative) study by a number of laboratories and a number of matrices by the IUPAC/ISO/AOAC INTERNATIONAL (3) or by the ISO 5725 Protocols (4).
3. The measurement uncertainty and its level of confidence must, on request, be made available to the user (customer) of the results.

References

1. "Guide to the Expression of Uncertainty in Measurement", ISO, Geneva, 1993.
2. EURACHEM/CITAC Guide Quantifying Uncertainty In Analytical Measurement (Second Edition), EURACHEM Secretariat, BAM, Berlin, 2000. This is available as a free download from <http://www.eurachem.ul.pt/>
3. "Protocol for the Design, Conduct and Interpretation of Method Performance Studies", ed. W. Horwitz, *Pure Appl. Chem.*, 1995, 67, 331-343.
4. "Precision of Test Methods", Geneva, 1994, ISO 5725, Previous editions were issued in 1981 and 1986.

EXPLANATORY NOTES

1 What is Measurement Uncertainty?

It is not always appreciated that analytical results are variable, and just how large that variability may be, particularly when low concentrations of a measurand (i.e. ppb levels) are being determined. As stated in the Guidelines, “most quantitative analytical results take the form of “ $a \pm 2u$ ” or “ $a \pm U$ ” where “ a ” is the best estimate of the true value of the concentration of the measurand (the analytical result) and “ u ” is the standard uncertainty to 68% level of confidence and “ U ” (equal to $2u$) is the expanded uncertainty to 95% level of confidence.. The range “ $a \pm 2u$ ” represents a 95% level of confidence in which the true value would be found. The value of “ U ” or “ $2u$ ” is the value which is normally used and reported by analysts, normally referred to as “measurement uncertainty” and may be estimated in a number of different ways. ”

In food analysis it is the (approximately) 95% probability (i.e. $2u$) which is used to calculate the expanded uncertainty. Other sectors may specify a different probability.

Thus measurement uncertainty can be regarded as the variability around the reported results which is quantified as the value “ U ” when considering the expanded uncertainty and within which the “true” result may be expected to lie.

2 Does the Measurement Uncertainty have to be Estimated in Codex?

Yes, one of the requirements of the ISO/IEC 17025:2005 Standard that Codex has adopted by reference is that the measurement uncertainty of a result shall be estimated and then made available if requested. The Codex Alimentarius Commission has developed Guidelines CAC/GL 27-1997 that require laboratories involved in the import/export of foods to comply with general criteria in ISO/IEC 17025. As Codex is concerned with goods moving in international trade it would be anticipated that the request for measurement uncertainty estimates will be made.

3 Does Measurement Uncertainty Arise From both Sampling and Analysis?

Measurement uncertainty applies to the whole measurement process. However, this guidance only considers analytical measurement uncertainty.

In many cases uncertainty of sampling is as large as or larger than analytical measurement uncertainty. Uncertainty of sampling is often the overriding factor in conformity assessment procedures. Sampling procedures in the *General Guidelines on Sampling* are designed to take account of uncertainty of sampling.

4 What is the Relationship between Measurement Uncertainty, the Analytical Result and the Method Used to Obtain the Result?

The uncertainty of test results is not associated with the method of analysis. However, the estimates of analytical performance characteristics that are obtained in the validation and/or in quality control of a method may be used to estimate the uncertainty of a result in some situations. The differentiation between measurement uncertainty associated with the result and precision obtained during the validation of the method is frequently not appreciated. As a consequence precision demonstrated for a validated method (the repeatability or reproducibility standard deviation) cannot be used as the sole estimate of the measurement uncertainty without qualification. In particular additional factors such as uncertainty associated with bias, matrix effect, and competence of laboratory must be considered.

5 Procedures for Estimating Measurement Uncertainty

There are many procedures available for estimating the measurement uncertainty of a result. The Codex guidelines do not recommend any particular approach, but it is important that whatever approach is used, the procedure is scientifically credible. No one approach may be said to be better than any other provided the procedure used is appropriate and credible - i.e. there is no “hierarchy” of the procedures.

In general, procedures are based on a component-by-component (“bottom-up”) approach or on a “top-down” approach using data from collaborative trials, proficiency studies, validation studies or intra-laboratory quality control samples, or a combination of such data.

In the *Guidelines for the Assessment of the Competence of Testing Laboratories Involved in the Import and Export Control of Foods* (CAC/GL 27-1997) there is a requirement to use validated methods and so it is usually more cost-efficient to use data from the method validation studies rather than using another approach (i.e. the component-by-component approach).

Users of validation data should note that sources of uncertainty that are not or only partly covered by validation studies include³:

- Sampling
- Pre-treatment
- Method bias
- Variation in conditions
- Changes in sample matrix
- Imprecision in estimating method or laboratory bias

For methods operating within their defined scopes, when the reconciliation stage shows that all the identified sources have been included in the validation study or when the contributions from any remaining sources have been shown to be negligible, then the reproducibility standard deviation s_R , adjusted for concentration if necessary, may be used as the combined standard uncertainty.

It is recognised that further procedures for the estimation of measurement uncertainty are being developed, and that, in this evolving situation, further recommendations will be made as to acceptable procedures. It is anticipated that procedures based on results obtained from participation in proficiency testing programmes, as an example, will be developed.

6 Considerations when Estimating Measurement Uncertainty within the Context of Codex

It is important that the requirement to estimate measurement uncertainty does not impose any unnecessary additional workloads on laboratories.

When deciding on which procedure is to be used when estimating measurement uncertainty within the Codex context it is important to recognise that Codex has adopted a number of formal quality assurance measures that have to be implemented by control laboratories. In particular, such laboratories should:

- be in compliance with an internationally recognised standard (now with ISO/IEC 17025:2005 Standard); such compliance is aided by the use of internal quality control procedures,
- participate in proficiency testing programmes, and
- use validated methods.

³ EURACHEM/CITAC Guide on the Use of uncertainty information in compliance assessment EURACHEM Secretariat, BAM, Berlin, 2007. This is available as a free download from <http://www.eurachem.org/>

It is essential that the information provided as a result of these requirements being implemented is used by laboratories when estimating their measurement uncertainties in order to avoid unnecessary work being carried out by laboratories. In Codex, where there is a high emphasis being placed on the use of “validated” methods of analysis, i.e. methods which have been validated through collaborative trials, information obtained from such trials can be used in many situations.

In addition, information derived from internal quality control procedures may also be used to estimate uncertainties in some situations.

This section re-emphasises that for the analyst it is important that no unnecessary duplication of existing work is undertaken.

7 Values of Measurement Uncertainty Estimates

Stipulating information on the anticipated values of measurement uncertainty estimates is frequently not supported by analysts. The users of analytical data and the customers of the laboratories producing such data frequently ask for such information regarding the level of uncertainty that may be expected for test results. They have concerns that some laboratories underestimate the size of their uncertainties and so report unrealistically small uncertainties to their customers.

For chemical analyses, using the values of s_R from collaborative trials, it would be reasonable to anticipate that the (expanded) uncertainties reported by laboratories would be approximately the following:

Nominal Concentration	Typical Expanded Uncertainty	Expected Range of Results*
100g/100g	4%	96 to 104g/100g
10g/100g	5%	9.5 to 10.5g/100g
1g/100g	8%	0.92 to 1.08g/100g
1g/kg	11%	0.89 to 1.11g/kg
100mg/kg	16%	84 to 116mg/kg
10mg/kg	22%	7.8 to 12.2mg/kg
1mg/kg	32%	0.68 to 1.32mg/kg
< 100µg/kg	44%	0.56 x concentration to 1.44 x concentration µg/kg

* this effectively means that values falling within these ranges may be regarded as being of the same analytical population.

It would be expected that the reported measurement uncertainties by any laboratory would not significantly exceed the value estimated from the s_R at the concentration of interest if the laboratory is in “analytical control”. Very experienced laboratories carrying out any particular analysis on a regular basis would be expected to obtain uncertainty values less than the values given above.

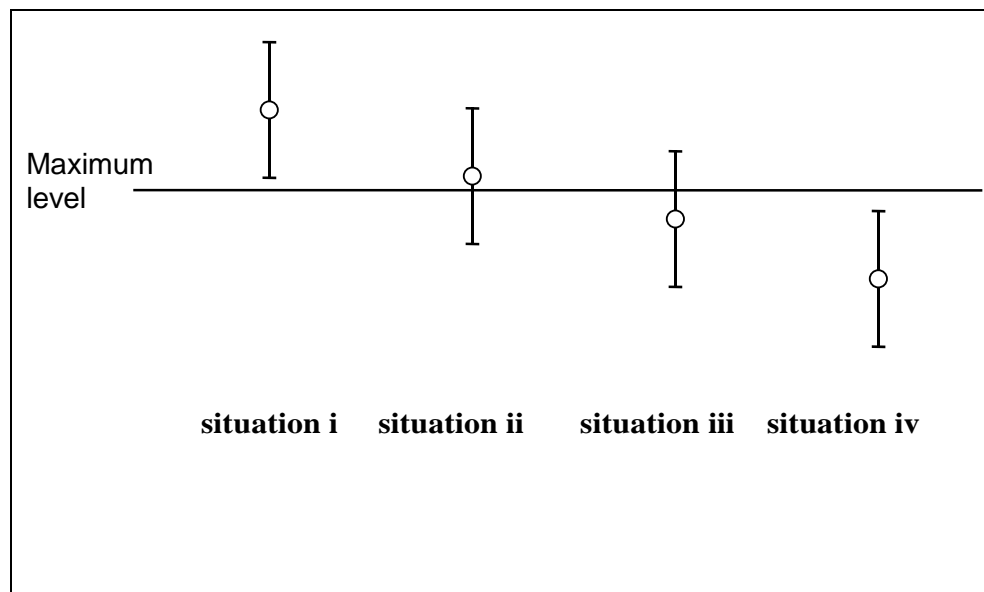
8. Relationship between analytical results, measurement uncertainty and recovery factors

This section attempts to explain the significance of analytical results and their associated measurement uncertainties and recoveries.

8.1 Measurement Uncertainty

It is important that measurement uncertainty is considered when deciding whether or not a sample meets the specification. This consideration may not apply when a direct health hazard is concerned. The significance of this can be illustrated by an example shown in the diagram below, which shows the simplest case when decisions are made based on a single test sample.

The example shown here is one where the test result is compared against the specification consisting of a maximum level. It illustrates how the concept of measurement uncertainty could be taken into account when interpreting analytical results on a tested sample.



This diagram demonstrates the importance of defining clear guidelines to allow unambiguous interpretation of analytical results with respect to their measurement uncertainties.

Situation i

The analytical result minus the expanded measurement uncertainty exceeds the maximum level. The result indicates that the measured analyte in the test sample is above the specification.

Situation ii

The analytical result exceeds the maximum level by less than the expanded measurement uncertainty.

Situation iii

The analytical result is less than the maximum level by less than the expanded measurement uncertainty.

Situation iv

The analytical result is less than the maximum level by more than the expanded measurement uncertainty.

&2 Recovery

The Codex Alimentarius Commission has adopted the IUPAC Guidelines on the use of recovery information by reference (see CAC/GL 37-2001).

Analytical results should be expressed on a recovery-corrected basis where appropriate and relevant, and when corrected they have to be stated as such.

If a result has been corrected for recovery, the method by which the recovery was taken into account should also be stated. The recovery rate is to be quoted wherever possible. The uncertainty of measurement should include the uncertainty associated with the recovery correction or be quoted in conjunction with the stated recovery.

When laying down provisions for standards, it will be necessary to state whether the result obtained by a method used for analysis within conformity checks is expressed on a recovery-corrected basis or not.

9 Useful References

These references are provided for information purposes only.

Guides for the Estimation of Measurement Uncertainty

Guide 98, Guide to the Expression of Uncertainty in Measurement (GUM) ISO, Geneva (1995)

EURACHEM/CITAC Guide Quantifying Uncertainty in Analytical Measurement (Second Edition), EURACHEM 2000. This is available as a free download from <http://www.eurachem.org/>

Analytical Methods Committee of the Royal Society of Chemistry “Uncertainty of Measurement - Implications of its use in *Analytical Science*”, *Analyst*, 1995, **120** (9), 2303-2308

ISO 21748:2010 Guidance for the Use of Repeatability, Reproducibility and Trueness estimates in Measurement Uncertainty Estimation, ISO, Geneva (2010)

NIST Technical note 1297 (1994 Edition): “Guidelines for Evaluating and Expressing the Uncertainty of NIST Measurement Results”

NMKL Procedure No. 5, 2nd edition (2003): “Estimation and Expression of Measurement Uncertainty in Chemical Analysis”

UKAS (United Kingdom Accreditation Service) 2000 The Expression of Uncertainty in Testing Edition 1, UKAS Publication ref: LAB 12

Eurolab technical Report No. 1/2007. Measurement Uncertainty Revisited: Alternative Approaches to Uncertainty Evaluation. Available as a free download from www.eurolab.org

Nordtest report TR 537. Handbook for Calculation of Measurement Uncertainty in Environmental Laboratories. Available as free downloads from www.nordtest.org (although this handbook is directed towards environmental analyses, the approaches and examples described are applicable to the results from tests on foods and feeds)

Procedures for the Validation of Analytical Methods and Method Performance

“Precision of Test Methods”, Geneva, 1994, ISO 5725, Previous editions were issued in 1981 and 1986. (not adopted by Codex)

“Protocol for the Design, Conduct and Interpretation of Method Performance Studies”, ed. W. Horwitz, *Pure Appl. Chem.*, 1995, 67, 33 1-343 (adopted by Codex)

European Commission Decision 2002/657/EC implementing directive 96/23/EC Concerning the Performance of Analytical Methods and the Interpretation of Results, Off J Eur Comm, L22 1 (2002) 8-36

Validation of Chemical Analytical Methods. NMKL Procedure No 4, 4th Version, 2010

Accreditation etc

ISO/IEC 17025:2005, General Requirements for the Competence of Testing and Calibration Laboratories, ISO, Geneva (2005)

EURACHEM Guidance Document No. 1/WELAC Guidance No. WGD 2: “Accreditation for Chemical Laboratories: Guidance on the Interpretation of the EN 45000 series of Standards and ISO/IEC Guide 25”

Z., Ben-David, H., Mates, A. 2001 Proficiency testing as tool for ISO 17025 implementation in National Public Health Laboratory: a mean for improving efficiency. *Accreditation & Quality Assurance*, **6**: 190-194

NMKL Procedure No. 3 (1996) “Control charts and control samples in the internal quality control in chemical food laboratories” Örnemark, U., Boley, N., Saeed, K., van Berkel, P.M., Schmidt, R., Noble, M., Mäkinen, I., Keinänen, M., Uldall, A., Steensland, H., Van der Veen, A., Tholen, D. W., Golze, M., Christensen, J.M., De Bièvre, P., De Leer, W. B (ed). 2001

Proficiency testing in analytical chemistry, microbiology, and laboratory medicine – working group discussions on current status, problems, and future directions. Accreditation & Quality Assurance, **6**: 140-146

Compliance

EURACHEM/CITAC Guide on the Use of uncertainty information in compliance assessment EURACHEM, 2007. This is available as a free download from <http://www.eurachem.org/>

Terminology

ISO (2nd ed., 1993) VIM “International Vocabulary of Basic and General Terms in Metrology”. Geneva

ISO Guide 99, International Vocabulary of Basic and General Terms in Metrology, 3rd Ed., VIM3, ISO, Geneva (2008)