codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 8 **CX/MAS 09/30/9**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON METHODS OF ANALYSIS AND SAMPLING
Thirtieth Session
Balatonalmádi, Hungary, 9 - 13 March 2009

PROPOSED DRAFT REVISED GUIDELINES ON MEASUREMENT UNCERTAINTY
(At Step 3 of the Procedure)

(Prepared by the United Kingdom)

BACKGROUND

At the twenty-ninth Session of CCMAS there was discussion on the preparation of guidance on measurement uncertainty and uncertainty of sampling. This arose because a number of delegations had previously requested of the Commission further guidance in order to address measurement uncertainty following the adoption of the text on "The Use of Analytical Results: Sampling Plans, Relationship between the Analytical Results, the Measurement Uncertainty, Recovery Factors and Provisions in Codex Standards". The Commission had referred to the CCMAS this request

The Delegation of the United Kingdom had prepared a paper to aid discussion. After extensive discussion the Committee agreed that, subject to the approval of the Commission, the Delegation of the United Kingdom, with the assistance of an electronic working group open to all members and observers and working in English, would prepare a Proposed Draft Revision of the Guidelines for comments at Step 3 and consideration by the next session.

There was general agreement that explanatory notes on the significance on the current Guidelines on Measurement Uncertainty (CAC/GL 54-2004) would be the appropriate way forward. These could then address of text as that have already been adopted by the Commission.

The Delegation of the United Kingdom circulated all participants at the twenty-ninth Session of CCMAS of its intended approach. Some comments were received. In the light of the comments the current Guidelines have been revised by including explanatory notes. These are given in the attached draft revision of CAC/GL 54-2004. It should be noted that the draft:

- does take due note of the texts that have already been developed by CCMAS and adopted by the Commission,
- does not recommend particular procedures for estimating measurement uncertainty. There are many texts which already cover those considerations,
- does not consider uncertainty derived from sampling, and
- has been written in a style not for metrological experts but routine providers of analytical data, customers of laboratories reporting analytical data and delegates to Codex Commodity Committees.

If only a single delegation has made a comment without comment from others, then it will not necessarily been taken into account in the Explanatory Notes. This particularly applies when comments were made about already adopted Codex texts, e.g. the use of recovery factors.

RECOMMENDATIONS

It is recommended that:

- the Committee discusses whether the draft explanatory notes to the existing Codex Guidelines in Measurement Uncertainty meet the concerns of delegations following the adoption by the Commission of the text on "The Use of Analytical Results: Sampling Plans, Relationship between the Analytical Results, the Measurement Uncertainty, Recovery Factors and Provisions in Codex Standards", and
- whether there are additional considerations that should be addressed.

The Proposed Draft Revised Guidelines are hereby circulated at Step 3 for comments and consideration by the 30th Session of the Committee on Methods of Analysis and Sampling. Governments and international organizations wishing to provide comments should do so in writing, preferably by email, to the Secretary, Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, FAO, Viale delle Terme di Caracalla, 00153 Rome, Italy, Fax: +39 (06) 5705 4593, E-mail: codex@fao.org, with a copy to the Hungarian Codex Contact Point, Hungarian Food Safety Office, H-1097 Gyáli út 2-6. Budapest Hungary, Fax:+36 13879400, e-mail: HU_CodexCP@mebih.gov.hu, **before 1 March 2009**.

ANNEX: PROPOSED DRAFT REVISED GUIDELINES ON MEASUREMENT UNCERTAINTY (Revised CAC/GL 54-2004)

Introduction

It is important and required by ISO/IEC 17025:2005 that analysts are aware of the measurement 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 control[1], 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 ± 2u or a ± 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 ± 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. ."

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).

[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 metrology - basic and general concepts and associated terms, JCGM 200:2008.

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, 33 1-343.
4. "Precision of Test Methods", Geneva, 1994, ISO 5725, Previous editions were issued in 1981 and 1986.

EXPLANATORY NOTES TO THE CODEX GUIDELINES ON MEASUREMENT UNCERTAINTY

These Explanatory Notes are written not for metrological experts but routine providers of analytical data, customers of laboratories reporting analytical data and delegates to Codex Commodity Committees.

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 Codex Guidelines, most quantitative analytical results take the form of "a ± 2u" or "a ± 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 ± 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 may 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 should lie.

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

Yes, one of the requirements of the Accreditation Standard, ISO 17025:2005 that Codex has adopted by reference is that the measurement uncertainty of a result must be estimated and then made available if requested (the Codex Alimentarius Commission has developed Guidelines which require laboratories involved in the import/export of foods to be accredited[3]). As Codex is concerned with goods moving in international trade it would be anticipated that the request will be made.

3. Does Measurement Uncertainty Apply to both Sampling and Analysis?

Measurement uncertainty applies to the whole measurement process. For analysts only "analytical" measurement uncertainty has been considered but it is now increasingly being recognised that the whole system must be considered, and so "sampling" measurement uncertainty is gaining an increasing importance. However, this guidance only considers "analysis" but may need to be revised as the discussions on measurement uncertainty from sampling are further discussed within Codex.

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

It is the estimation of the measurement uncertainty associated with an analytical result that is important. Measurement uncertainty is not associated with a method, but the values that are obtained in the validation of a method may be used to estimate the uncertainty of a result in some situations. This differentiation between "result" and "validated method" is frequently not appreciated and so causes some confusion. It does mean that different laboratories, even if using the same (validated) method on the "same" sample may report different measurement uncertainties. This is to be expected. As a consequence precision values for a validated method (the repeatability and reproducibility values) cannot to be taken to be the measurement uncertainty without qualification. In particular additional factors such as 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 recognised procedures. All such procedures may be considered to be equally valid. However, the procedure that an individual laboratory uses will have to be considered appropriate by its Accreditation Agency as part of its 17025 accreditation

[3] Guidelines for the assessment of the competence of testing laboratories involved in the import and export control of food (CAC/GL 27-1997)

In general procedures are based on a component-by-component ("bottom-up") approach or on a "top-down" approach using collaborative trial data.

In Codex there is a requirement to use fully validated methods and so it is usually more cost-efficient to use data from the validation rather than using another approach (i.e. the component-by-component approach). The caveats to using such validation data are best described in the Eurachem Guide to quantifying uncertainty in analytical measurement, where in Section 7.6.1 of the Second Edition of the EURACHEM Guide it is stated:

"A collaborative study carried out to validate a published method, for example according to the AOAC/IUPAC protocol or ISO 5725 Standard, is a valuable source of data to support an uncertainty estimate. The data typically include estimates of reproducibility standard deviation, s_R, for several levels of response, a linear estimate of the dependence of s_R on level of response, and may include an estimate of bias based on CRM studies. How this data can be utilised depends on the factors taken into account when the study was carried out. During the 'reconciliation' stage indicated above, it is necessary to identify any sources of uncertainty that are not covered by the collaborative study data. The sources which may need particular consideration are:

- Sampling. Collaborative studies rarely include a sampling step. If the method used in-house involves sub-sampling, or the measurand (see Specification) is estimating a bulk property from a small sample, then the effects of sampling should be investigated and their effects included.
- Pre-treatment. In most studies, samples are homogenised, and may additionally be stabilised, before distribution. It may be necessary to investigate and add the effects of the particular pre-treatment procedures applied in-house.
- Method bias. Method bias is often examined prior to or during interlaboratory study, where possible by comparison with reference methods or materials. Where the bias itself, the uncertainty in the reference values used, and the precision associated with the bias check, are all small compared to S_R, no additional allowance need be made for bias uncertainty. Otherwise, it will be necessary to make additional allowances.
- Variation in conditions: Laboratories participating in a study may tend towards the means of allowed ranges of experimental conditions, resulting in an underestimate of the range of results possible within the method definition. Where such effects have been investigated and shown to be insignificant across their full permitted range, however, no further allowance is required.
- Changes in sample matrix. The uncertainty arising from matrix compositions or levels of interferents outside the range covered by the study will need to be considered.

Each significant source of uncertainty not covered by the collaborative study data should be evaluated in the form of a standard uncertainty and combined with the reproducibility standard deviation S_R in the usual way.

For methods operating within their defined scope, 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."

These Explanatory Notes are not intended to describe the available procedures for the estimation of measurement uncertainty, but procedures have been developed by:

- ISO, in the ISO Guide to the expression of uncertainty in measurement
- Eurachem through the Eurachem Guide to quantifying uncertainty in analytical measurement, where both the component-by-component approach and the use of collaborative trial data are described.
- ISO, in the ISO TS 21748 – Guide To The Use Of Repeatability, Reproducibility And Trueness Estimates In Measurement Uncertainty Estimation
- The concept set by (EU) Commission Decision 2002/657/EC Implementing Council Directive 96/23/EC Concerning The Performance Of Analytical Methods And The Interpretation Of Results
- Using results from internal quality control data, as developed by the Netherlands Food Inspection Service.
- The Nordic Committee on Food Analysis

The use of collaborative trial data as first described in ISO 5725 critical differences approach is not endorsed as an approach as it concentrates only on the method validation study and not on how the method is subsequently used in the laboratory.

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 schemes, as an example, will be developed.

References for the procedures given above are listed in section 11.

6. Considerations when Estimating Measurement Uncertainty within the Context of Codex

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 which have to be implemented by control laboratories. In particular, such laboratories have to be:

- accredited to an Internationally recognised Standard (now with ISO/IEC 17025 Standard); such accreditation is aided by the use of internal quality control procedures,
- participate in proficiency schemes, and
- use validated methods.

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 "fully 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.

8. Values of Measurement Uncertainty Estimations

Stipulating information on the anticipated values of measurement uncertainty estimations is frequently not supported by analysts. However, the users of analytical data and the customers of the laboratories producing such data frequently ask for such information. 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 not be unreasonable to anticipate that the (expanded) uncertainties reported by laboratories would be of the following orders:

Concentration	Expanded Uncertainty	Range of Acceptable Concentrations*
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%	56 to 144µg/kg

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

For microbiological analyses, where it is frequently stated that results within the range of +/- 0.5 log units are acceptable, then the range of actual counts that this equates to is frequently much larger than customers of analytical data appreciate (or require).

It would be expected that the reported measurement uncertainties by all laboratories would not significantly exceed the value estimated from the reproducibility standard deviation (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 values less that the values given above.

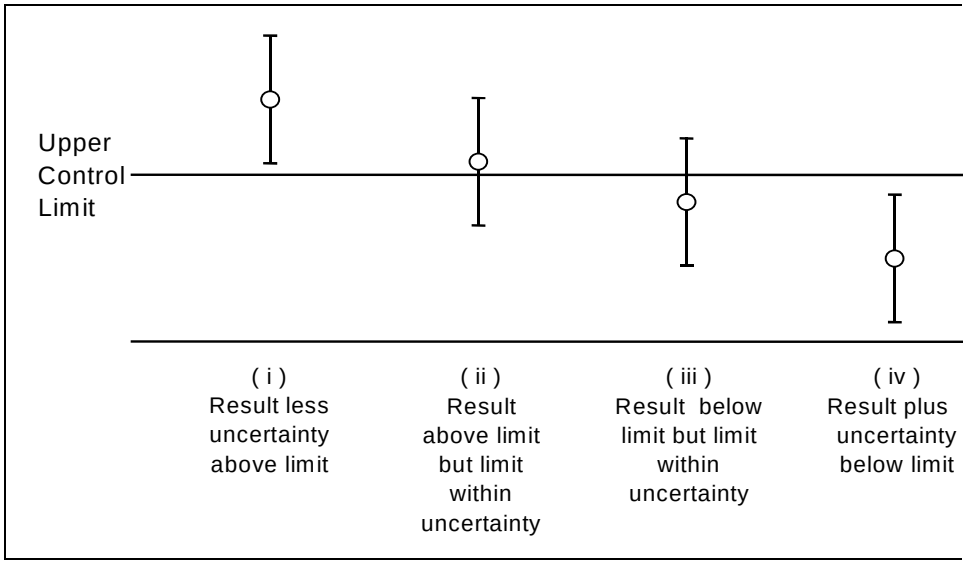
9. Significance of the Section in the Procedural Manual of the "use of analytical results: sampling plans, relationship between the analytical results, the measurement uncertainty, recovery factors and provisions in Codex Standards" (from Codex Procedural Manual, 17th Edition)

This section attempts to explain the significance of the adopted Codex text with respect to the measurement uncertainty and recovery in particular.

9.1 Measurement Uncertainty

It is stated that an allowance is to be made for the measurement uncertainty when deciding whether or not an analytical result falls within the specification. This requirement may not apply in situations when a direct health hazard is concerned, such as for food pathogens. This does mean that it is important for Codex Commodity Committees, when setting specifications, to recognise that there is a difference between the numeric value in the specification and numeric value at which the specification will be enforced. Put simply this difference equates to the measurement uncertainty of the result obtained by the "enforcing laboratory". Thus, when enforcing a maximum limit, the enforcement laboratory (normally the importer) will have to deduct the value of the measurement uncertainty before deciding whether the sample meets the specification.

This is best illustrated diagrammatically, where the figure below illustrates four different situations:



Situation I

The analytical result together with the measurement uncertainty exceeds the maximum level. All authorities will consider the sample as being non-compliant with the specification.

Situation II

The analytical result exceeds the maximum level by less than the measurement uncertainty. Some authorities would have accepted the sample as being compliant with the specification, if they routinely take into account the measurement uncertainty. Others would have ignored the measurement uncertainty and so would not accept the sample. The effect of the accepted text is that all authorities will accept the result as being compliant (i.e. the result is not non-compliant *"beyond reasonable doubt"*).

Situation III

The analytical result is below the maximum level by less than the measurement uncertainty. In general authorities will consider the sample to be compliant with the specification, but would probably be wary of future samples.

Situation IV

The analytical result is less than the maximum value by an amount greater than the measurement uncertainty. All authorities will consider the sample as being compliant without any hesitation.

It should be noted that the above situation will have to be interpreted with sensitivity in some instances. However, the risk of inadequate protection of the consumer may be reduced by a suitable selection of the specification – thus it is essential that the significance of measurement uncertainty deduction from the analytical result before assessing compliance is appreciated.

9.2 Recovery

It is stated that analytical results are to be expressed on a recovery corrected basis where appropriate and relevant, and when corrected it has to be stated.

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.

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 shall be expressed on an recovery-corrected basis or not.

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

10. Use of Measurement Uncertainty and Definition of a Dispute Situation

TO BE DEVELOPED IN VIEW OF THE DISPUTE SITUATION PAPER. BUT SUITABLE TEXT MAY BE ALONG THE LINES:

A dispute will arise when considering a Codex specification, which is a maximum value, if:

- the export certificate states that the analytical result to which its associated measurement uncertainty is then added is less than the Codex specification (i.e. "x + U" < L, where x is the reported analytical result, U is the expanded uncertainty and L is the Codex specification, which is a maximum limit) and so the sample meets the Codex specification, and

- the import certificate states that the analytical results to which its associated measurement uncertainty is then deducted is still greater than the Codex specification (i.e. "x – U" > L, where x is the reported analytical result, U is the expanded uncertainty and L is the Codex specification, which is a maximum limit) and so the sample does not meet the Codex specification[4].

This assumes that the laboratory at importation will deduct the measurement uncertainty, as implied in Section 5, above, of this guidance. If the value after deduction is still greater than the specification, then it may be stated, ***beyond reasonable doubt***, that the sample is not compliant with the specification.

It is important for the exporter to realise that in order to be sure that the exported product meets the specification the "certificated value" obtained by the producer/exported must have the uncertainty of the result added to it, and for that value to be below the specification.

11. Useful References

A number of references are given below. [NB: these are general references and do need up-dating.]

Methods 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 Secretariat, BAM, Berlin, 2000. This is available as a free download from http://www.eurachem.ul.pt/

[4] Suggested UK definition in comment on the dispute situation paper.

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/TS 21748:2004 Guidance for the Use of Repeatability, Reproducibility and Trueness estimates in Measurement Uncertainty Estimation, ISO, Geneva (2004).

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

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, L221 (2002) 8-36.

T.P.J. Linsinger, R.D. Josephs: Limitations of the application of the Horwitz

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 Secretariat, BAM, Berlin, 2007. This is available as a free download from http://www.eurachem.ul.pt/

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).