codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 7a) and b) **CX/MAS 01/8**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON METHODS OF ANALYSIS AND SAMPLING
Twenty-Third Session
Budapest, Hungary, 26 February - 2 March 2001

MEASUREMENT UNCERTAINTY

PROGRESS REPORT BY RELEVANT ORGANIZATIONS (EURACHEM)
and
RELATIONSHIP BETWEEN THE ANALYTICAL RESULT, THE MEASUREMENT UNCERTAINTY AND THE SPECIFICATION IN CODEX STANDARDS[1]

Background

The 22nd Session of the Committee on Analysis and Sampling considered measurement uncertainty and decided to defer further discussion on this question pending the publication of the EURACHEM Guide so as to avoid duplication with the work of other international bodies (ALINORM 99/23, paras. 41- 46).

Agenda Item 7a refers to Progress Report by Relevant Organizations. The report provided by EURACHEM following the publication of the *Guide Quantifying Uncertainty in Analytical Measurement* is included in the present document. Other international organizations are invited to inform the Committee of their activities in this area.

At the 22nd Session of the Committee, the Delegation of the United Kingdom, supported by several delegations, proposed that guidance should be prepared on the interpretation of analytical results in relation to the compliance with the specifications in Codex Standards since there were differences in the treatment of analytical errors in the interpretation of results. The Committee agreed to request the United Kingdom, in collaboration with Finland, France, Ireland, Netherlands and the United States, to prepare a paper on this issue for consideration by the Committee at its next Session. It also agreed that since the issue involved measurement uncertainty, it would be discussed under the agenda item for measurement uncertainty (ALINORM 99/23, para.70).

The discussion paper addressing this question is attached. The Committee is invited to consider how it wishes to proceed in this area, in the light of the information provided in the document and the EURACHEM *Guide*.

[1] Prepared by the United Kingdom

MEASUREMENT UNCERTAINTY

RELATIONSHIP BETWEEN THE ANALYTICAL RESULT, THE MEASUREMENT UNCERTAINTY AND THE SPECIFICATION IN CODEX STANDARDS

INTRODUCTION

In quantitative chemical analysis many important decisions are based on the results obtained by a laboratory and so it is therefore important that an indication of the quality of the results reported is available. Analytical chemists are now more than ever coming under increased pressure to be able to demonstrate the quality of their results by giving a measure of the confidence placed on a particular result to demonstrate its fitness for purpose. This includes the level that the result would be expected to agree with other results irrespective of the method used. "Measurement Uncertainty" (MU) is a useful parameter which gives this information, and one that is increasingly accepted in the food analysis Community.

Measurement Uncertainty terminology together with its estimation has been discussed at both the 21st and 22nd Sessions of the Codex Committee on Methods of Analysis and Sampling[1, 2]. At those Sessions it was noted that:

1. the concept of the introduction of measurement uncertainty as developed by the component-by-component ISO/EURACHEM[3,4] approach is increasingly being discussed and implemented in other sectors of analytical chemistry and may well therefore have an impact on the work of CCMAS. In particular, accreditation agencies are increasingly demanding that measurement uncertainty be quoted on many of results obtained under accreditation conditions and that such results should have a formal estimate of the measurement uncertainty attached to them.

2. The term "measurement uncertainty" is increasing being used. Whereas analytical chemists appreciate exactly what the term measurement uncertainty is, others may not do so.

3. Analysts using Codex approved or endorsed methods of analysis are using methods of analysis which have been fully collaboratively tested. There is an argument to state that if a laboratory has to comply with the four Codex principles relation to laboratory quality (i.e. that laboratories should use validated methods of analysis, become accredited to ISO/IEC Guide 25, participate in proficiency testing schemes and introduce appropriate internal quality control procedures) then it is unnecessary for the laboratory to undertake a further estimate of the measurement uncertainty according to the component-by-component approach.

The Committee agreed at its 22nd Session[5] that "it would defer discussion on this item to a future Session of CCMAS pending the publication of the EURACHEM Guide".

This paper up-dates participants to the 23rd Session of CCMAS on the current situation with regard to Measurement Uncertainty, opens further discussion points and makes recommendations which participants may wish to discuss and possibly accept.

DEVELOPMENTS SINCE THE 22nd SESSION OF CCMAS

Since the 22nd Session of CCMAS there have been a number of developments which are of interest to delegates, namely:

- the ISO/IEC Guide 25 has now been replaced by ISO/IEC 17025[6]. This latter Standard makes extensive reference to measurement uncertainty. The

- the second edition of the EURACHEM Guide to Quantifying Uncertainty in Analytical Measurement[7] has now been published

- there has been some international discussion on the relationship between the analytical result, the measurement uncertainty and the specification in legislation.

These are commented on below.

ISO/IEC 17025: NOMENCLATURE

The replacement of ISO/IEC Guide 25 by ISO/IEC 17025 should be noted. Codex has endorsed the use of the ISO/IEC Guide 25 and will presumably likewise endorse the use of 17025, the replacement accreditation standard, when that is discussed. This latter Standard makes extensive reference to measurement uncertainty. Not withstanding the misgivings of many delegates to the 21st and 22nd Sessions of CCMAS it is now unreasonable to expect the term "measurement uncertainty" to be replaced by another, albeit a possibly more appropriate term.

EURACHEM/CITAC GUIDE QUANTIFYING UNCERTAINTY IN ANALYTICAL MEASUREMENT (SECOND EDITION)

THE SECOND EDITION OF THE GUIDE IS AVAILABLE AS A FREE DOWNLOAD FROM HTTP://WWW.VTT.FI/KET/EURACHEM

The first version of the Guide, which was published in 1995, has been very widely used and two successful workshops on its utilisation have been held since its publication. Following from these workshops and the many helpful comments the Working Group has received on the contents of the first edition, many significant changes and improvements have been made in this second edition.

The format of the Guide is very similar to that of the first edition with chapters 1 and 2 dealing with the scope and the concept of uncertainty as before. Chapter 3, Analytical Measurement and Uncertainty, is completely new and covers the process of method validation and conduct of experimental studies to determine method performance and their relationship to uncertainty estimation. There is also a new section on traceability. The chapter on uncertainty estimation in the previous guide has been considerably expanded and split into four separate chapters, dealing with the four steps involved in estimating uncertainty. Step 1 deals with the specification of the measurand, Step 2 with identifying the uncertainty sources, Step 3, which has been considerably expanded to cover the use of existing method validation data, deals with quantifying the uncertainty and Step 4 covers the calculation of the combined uncertainty. The examples have been completely revised and new ones added. They are now all in a standard format, which follow the four steps described above. They all utilise the cause and effect diagram as an aid to identifying the sources of uncertainty and to ensuring that all the significant ones are included in the evaluation of the uncertainty. In addition a web site has been set up (www.measurementuncertainty.org) which contains an indexed HTML version of the Guide. This site hosts a discussion forum on the application of the guide and has a section for the publication of additional examples.

Of particular interest to CCMAS are the changes dealing with the use of method performance data and in particular the use of method validation data, from both collaborative validation studies and from in-house studies. There are new sections dealing with the use of method performance data show that in many cases such data gives all, or nearly all information required to evaluate the uncertainty. These new sections are of particular interest to CCCMAS in view of the importance that is attached to method validation through the Codex General Principles on Methods of Analysis and Sampling, and the importance that is thus placed on Codex adopting methods which are "fully validated" through collaborative trial.. An important aspect is the use of cause and effect diagrams as an aid in both method validation and uncertainty evaluation. By using these diagrams it is possible to determine whether there are any components of uncertainty that are not covered by the validation data. In most cases a good validation study will provide all of the necessary data and it is possible to justify the use of an appropriate statistic, such as S_R, to determine the uncertainty. This was demonstrated in CX/MAS 98/7, as discussed at the 22nd Session of CCMAS.

Indeed, Sections 7.6.1 to 7.6.3 of the Second Sedition of the Guide explicitly state:

7.6.1 "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 (section 7.2), 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.

7.6.2 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 (section 8)

7.6.3 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 such as those discussed in section 7.6.1 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."

To the delegates to CCMAS this should be reassuring.

RELATIONSHIP BETWEEN THE ANALYTIAL RESULT, THE MEASUREMENT UNCERTAINTY AND THE SPECIFICATION IN CODEX STANDARDS

There are a number of analytical and sampling issues which prevent the uniform implementation of legislative standards; in particular sampling procedures, the use of recovery factors and the treatment of the measurement of uncertainty when evaluating analytical results.

The first two issues will be addressed in other papers prepared for the 23rd Session of CCMAS, the last is addressed in this paper.

Work outside of CCMAS has shown that at the present time there is no common interpretation of analytical results across some members of the Codex Alimentarius Commission. This is best demonstrated by example.

A sample for which there is a legislative limit (e.g. a Codex limit) of, say, 4 µg/g for a contaminant may be interpreted as containing 3 µg/g on analysis in one Member State but 10 µg/g in another. This is because some countries correct analytical results for recovery, others do not; some countries take note of measurement uncertainty when interpreting analytical results, others do not.

With respect to measurement uncertainty all countries should, in future, be in the position to report results in the form a ± b where "a" is the analytical result and "b" is the measurement uncertainty, i.e. the "range" within which the true result will fall.

Taking the example above, two countries A and B will report a sample as containing 7 ± 4 μg/g of a contaminant, both on the same basis with respect to recovery.

These two countries may have different national rules for the interpretation of results with respect to compliance, i.e.

Country A requires	That the analytical result is to be reported as "not less than 3 μg/g", i.e. it is not beyond reasonable doubt that the analytical result exceeds the statutory limit of 4 μg/g, and so the sample is deemed to be compliant with the statutory limit.
Country B requires	That the measurement uncertainty is not taken into account when the assessing whether the sample is compliant with the specification. In this case a result of 7 μg/g would be reported and so the sample would be deemed to be non-compliant
Consequence	The two countries A and B will make different judgements as to compliance with a Codex specification on essentially the same sample

This situation can only be avoided if a common approach to the use of the estimated measurement is adopted within Codex. Within any one single country the problems are reduced in that a common approach and understanding is taken by both the control authorities and the food manufacturer. However, for food moving in international trade there will not be this common understanding.

CONCLUSIONS and RECOMMENDATIONS

It is important that analysts are aware of the uncertainty associated with each analytical result and reports that uncertainty. The measurement uncertainty may be derived by a number of procedures. In particular, because food analysis laboratories are required to use collaboratively tested methods for Codex purposes, estimations derived such validation work may be used.

It is therefore recommended that delegates of the 23rd Session of CCMAS consider the issue of measurement uncertainty in the light of both this paper and the papers discussed at previous Sessions of CCMAS. Participants are invited to consider the formulation of recommendations which are to be progressed through the Codex Alimentarius system with a view to adoption by governments as guidelines. These may be:

1. The measurement uncertainty/reliability associated with all analytical results is to be quantified and available to the user of the analytical results.

2. For Codex purposes it is now accepted that the term "measurement uncertainty" should be used.

3. The measurement uncertainty of an analytical result may be estimated through data produced in a method-performance study, or where this information is not available, through the use of internal quality control and method validation. These values may be used to estimate the measurement reliability of an analytical result.

4. The need to undertake an additional formal evaluation of a method of analysis using the ISO component-by-component approach in addition is not required if information obtained through a collaborative trial or other similar exercises is available.

5. That the Committee discusses and recommends whether the measurement uncertainty of an analytical result should be taken into account when deciding whether a sample is in compliance with a Codex specification for goods moving in international trade.

REFERENCES

1. "Measurement Uncertainty And Its Effect On Analytical Chemists", Paper for the Twenty-first Session Codex Committee On Methods Of Analysis And Sampling, Budapest, 10 - 14 March 1997, CX/MAS 97/7, FAO, Rome.

2. Measurement Uncertainty And Its Effect On Analytical Chemists", Paper for the Twenty-second Session Codex Committee On Methods Of Analysis And Sampling, Budapest, 23 - 27 November 1998, CX/MAS 98/7, FAO, Rome.

3. "Guide to the Expression of Uncertainty in Measurement", ISO, Geneva, 1993.

4. "Quantifying Uncertainty in Analytical Measurement", EURACHEM Secretariat, Laboratory of the Government Chemist, Teddington, UK, 1995, EURACHEM Guide.

5. "Report of the Twenty-Second Session of the Codex Committee on Methods of Analysis and Sampling", Budapest, 23-27 November, 1998, ALINORM 99/23, FAO, Rome

6 International Standard ISO/IEC 17025 "General Requirements for the Competence of Testing and Calibration Laboratories"" ISO/IEC, 1999

7. 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.vtt.fi/ket/eurachem.