codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 6 **CX/MAS 10/31/06**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON METHODS OF ANALYSIS AND SAMPLING
Thirty-first Session
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GUIDANCE ON UNCERTAINTY OF SAMPLING

(Prepared by the United Kingdom)

BACKGROUND

At the twenty-ninth Session of CCMAS there was discussion on the preparation of guidance on (analytical) 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 this request to CCMAS for consideration.

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 (Analytical) Measurement Uncertainty 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 the significance of the text that has already been adopted by the Commission.

It was agreed that this activity would be a "New Work Item" for CCMAS. This was approved by the Codex Commission in 2008. It was made explicit that the "New Work Item" would only cover measurement uncertainty derived from analysis.

However, it was also recognised that "measurement uncertainty" included uncertainty derived from sampling as well as from analysis, but that it would be best to treat each aspect separately at the present time.

The topic was discussed at the 30th Session of CCMAS where:

- It was appreciated that sampling is part of the measurement process and needs to be recognised as such.

- It was appreciated that the topic was important but needed to be considered in more detail before it should be progressed as "new work". New international guidance in the area had been published, and in particular the EURACHEM/EUROLAB/CITAC/Nordtest Guide on the Estimation of Measurement Uncertainty Arising from Sampling and the Nordtest Handbook for sampling planners.

- It was considered especially critical for the Committee to decide whether sampling uncertainty should be taken into account when assessing compliance, or to follow the non-scientific approach, but pragmatic approach, of defining sampling uncertainty as zero.

- Several delegations supported the development of an overarching document on measurement uncertainty combining analytical and sampling uncertainty in order to address uncertainty as a whole on a scientific basis. But other delegations expressed the view that it was premature to undertake new work at this stage on uncertainty of sampling as priority should be given to progress on analytical measurement uncertainty.

It was agreed that the documents should be redrafted by an electronic working group led by the Delegation of the United Kingdom, open to all members and observers and working in English. The document was circulated all participants at the thirtieth Session of CCMAS and a number of comments were received. Comments were prepared by delegates from Argentina, Australia, Chile, Cuba, the International Dairy Federation, Japan, The Netherlands, New Zealand, NMKL and the USA and sent to the UK for consideration since the thirtieth Session of CCMAS.

The comments received are often in conflict with each other, some delegates wanting to combine formally with the analytical measurement uncertainty topic at this time, other delegates wishing to keep separate.

SAMPLING IN CODEX

"Methods of sampling" have had a long and troubled history within Codex. The majority of the work described within Codex is based on the use of acceptance sampling plans, and is frequently very complex. As a result Codex Commodity Committees frequently refer to the use of CAC/GL 5 0-2004 (the Codex General Guidelines on Sampling) but then do not progress further than that. They do not choose from the options given in 50-2004 as should happen. With the publication of the EURACHEM/EUROLAB/CITAC/Nordtest *Guide on the Estimation of Measurement Uncertainty Arising from Sampling;* and Nordtest handbook for sampling planners on sampling quality assurance and uncertainty estimation *Uncertainty from sampling,* it was considered that it would be unwise to ignore this area of measurement uncertainty. To do so will result in the same issues and confusion that have already arisen when analytical measurement uncertainty has been considered.

As stated above sampling has long been recognised as part of the measurement process, when the measurand (or true value to be determined) is defined in terms of the sampling target (e.g., a batch/lot of material) rather than in terms of the laboratory sample. Several methods have been proposed to estimate measurement uncertainty arising from all steps in the measurement process, including the primary sampling. Once an estimate of the uncertainty has been made, it is necessary to address whether that level of uncertainty is acceptable in order to decide whether the measurements are fit for the purpose for which they are intended. (One approach to this question, not discussed in this paper, is to designate this optimal value of uncertainty, as the point that minimises the overall financial loss to the user of the measurements).

However, for Codex purposes it is possible to pre-define a fit-for-purpose value for the measurement uncertainty, including both the "analytical" and "sampling", such that any sampling plan which is developed will meet that criterion. Clearly this then becomes an iterative process.

Thus as a result of the international activities it is critical for CCMAS to recognise that a decision has to be taken as to whether sampling uncertainty should be taken into account when assessing compliance, or whether it wishes to take the simplistic route of defining sampling uncertainty as being zero following the use of defined sampling procedures. In addition it could suggest that Codex Commodity Committees recommend the maximum uncertainty that is fit-for-purpose.

There it has been agreed that the existing Codex Guidelines on Measurement Uncertainty be re-drafted to include explanatory notes explaining the significance of the Guidelines to Codex Committees. It is suggested that the same approach be taken with respect to extending those Guidelines to include measurement uncertainty including sampling uncertainty. The arguments/discussion about sampling uncertainty are given in the explanatory notes to the Guidelines.

The explanatory notes are written to help non-specialists, and in particular to emphasise that as a result of the consequence of the adoption of the text "The Use of Analytical Results: Sampling Plans, Relationship between the Analytical Results, the Measurement Uncertainty, Recovery Factors and Provisions in Codex Standards" in the Procedural Manual there are consequences for other Codex Committees, which was the original concern with the subject. The explanatory notes have therefore been written with this objective in mind and statistical considerations have been kept to a minimum.

A simple procedure is outlined for the estimation of uncertainty though to give such information is not the primary objective of the draft revised guidelines.

Various definitions have been suggested for "measurement uncertainty" but since the last Session of CCMAS Codex has adopted formal analytical terminology and this has been used in the draft Guidelines.

Some concern was expressed by exporting countries that they would be disadvantaged by the procedures now given in the Procedural Manual. In fact because of the consequence of taking measurement uncertainty into account when establishing "beyond reasonable doubt" it is importing countries that have to be most concerned that the value of the specification in the Codex Standard is negotiated with the measurement uncertainty being appreciated.

MAGNITUDE OF SAMPLING UNCERTAINTY

Work has been carried out to estimate the sampling uncertainties which are likely to arise in the food sector. These are given in the following table. There it will be seen that there is a considerable range in the values of uncertainty derived from sampling, in some cases being over 100% of the observed (mean) value. Clearly this is not sustainable or acceptable when considering "official" or contractual work.

In practice sampling has been carried out in areas where there is a considerable variability by taking a sufficiently large sample from a lot and defining that to be representative of the lot. In the case of aflatoxins in peanuts, as an example, 30kg is frequently taken using at least 100 incremental units and suitably combining these.

Consideration should be given to whether this should be introduced as a "default" approach if the uncertainty of sampling is found to be too large to be acceptable.

Although work is being carried out to be able to predict the uncertainty from sampling it is not completed and is unlikely to result in a generalized equation such as the Horwitz Equation when considering analytical variability.

Product	Analyte	Units	mean conc	U_{meas}%	U_{samp}%	U_{anal}%
Pistachio nuts	Total aflatoxin	µg kg^{-1}	0.86	70.5	45.02	54.19
Wheat	N	% m/m	2.13	2.08	2.03	0.47
	Molybdenum (Mo)	mg kg^{-1}	0.48	13.60	12.08	6.25
	Lead (Pb)	mg kg^{-1}	0.017	93.68	76.47	54.12
Coffee(Green)	Moisture	% m/m	11.98	2.46	1.65	1.82
	Nickel (Ni)	mg kg^{-1}	4.83	31.33	22.36	21.95
Spreadable fats	Fat	% m/m	57.78	1.09	1.70	1.38
Sausages	Meat	% m/m	69.17	11.28	10.03	3.33
	Fat	% m/m	21.36	13.56	12.94	4.06
	Moisture	% m/m	55.89	5.25	5.08	1.35
Infant milk	Zinc (Zn)	µg kg^{-1}	49931	17.4	0.00	17.41
	Lead (Pb)	µg kg^{-1}	4.815	52.8	0.00	52.79
	Copper (Cu)	µg kg^{-1}	2806	13.9	4.52	13.17
	Cadmium (Cd)	µg kg^{-1}	4.654	44.5	10.49	43.23
	Arsenic(As)	µg kg^{-1}	10.29	63.51	45.50	44.31
	Tin(Sn)	µg kg^{-1}	358.8	108.23	105.47	24.29
Infant wet meals	Zinc (Zn)	µg kg^{-1}	4019.5	33.1	21.47	25.18
	Lead (Pb)	µg kg^{-1}	4.884	107.7	54.14	93.16
	Copper (Cu)	µkg^{-1}	493	33.9	31.61	12.25
	Cadmium (Cd)	µg kg^{-1}	7.575	43.7	32.61	29.04
Butter (frozen)	Fat	% m/m	82.92	0.54	0.52	0.14
	Moisture	% m/m	15.755	2.53	2.47	0.53
	Peroxide value	meq. kg^{-1}	0.083	63.3	57.83	26.02
Lettuce (glasshouse)	Nitrate	mg kg^{-1}	4408	16.4	14.48	7.62
			3148.3	35.3	35.16	3.42
			3117.5	19.8	19.64	2.71
Tuna (fresh)	Mercury (Hg)	mg kg^{-1}	0.257	21.79	21.01	6.23
Tomatoes (tinned)	Tin (Sn)	mg kg^{-1}	6.455	79.44	75.17	25.69
	Tin (Sn)	mg kg^{-1}	74.26	20.55	19.66	6.01
Butter (fresh)	Moisture	% m/m	15.41	0.78	0.67	0.39
			15.41	1.12	1.04	0.39
Peanut	Aflatoxin	µg kg^{-1}	20		228.00	70.80
			20		114.00	44.80
Coffee (green)	Ochratoxin A	µg kg^{-1}	5		111.60	13.28
Hazelnuts	Aflatoxin (total)	µg kg^{-1}	10		263.80	10.40

GUIDELINES ON MEASUREMENT UNCERTAINTY INCLUDING UNCERTAINTY FROM SAMPLING

The existing Guidelines on Measurement Uncertainty have been retained as far as possible but expanded to also consider uncertainty derived from sampling – the objective of this paper is to help appreciate the consequences of their potential adoption by Codex.

RECOMMENDATIONS

It is recommended that the Committee:

- notes the publication of the EURACHEM/EUROLAB/CITAC/Nordtest Guide on the "Estimation of Measurement Uncertainty Arising from Sampling" and the Nordtest handbook.
- discusses the issue of uncertainty and sampling and decides whether it should develop recommendations in the area in the same way that it already has for [Analytical] Measurement Uncertainty.
- discusses whether sampling uncertainty should be taken into account when a lot is assessed for compliance with a Codex specification.
- discusses the situation when the magnitude of the uncertainty derived from sampling is deemed to be not "fit-for-purpose" and whether a pragmatic approach should be developed in such situations.
- whether it should prepare Guidance for Codex Committees on sampling uncertainty, possibly through the preparation of general guidelines an initial draft of which are attached.

ANNEX: PROPOSED DRAFT REVISED GUIDELINES ON MEASUREMENT UNCERTAINTY INCLUDING UNCERTAINTY FROM SAMPLING AND EXPLANATORY NOTES ON THE SIGNIFICANT OF THE GUIDELINES (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, 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 (K=2) within which the true value would be found (in other cases can be increased as K=3 (99%)). 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

Non-negative parameter characterising the dispersion of the values being attributed to a measurand, based on the information used.

Notes:

Measurement uncertainty includes components arising from systematic effects, such as components associated with corrections and the assigned values of measurement standards, as well as the definitional uncertainty. Sometimes estimated systematic effects are not corrected for but, instead associated measurement uncertainty components are incorporated.

The parameter may be, for example, a standard deviation called standard measurement uncertainty (or a given multiple of it), or the half-width of interval having a stated coverage probability.

Measurement uncertainty comprises, in general many components. Some of these components may be evaluated by Type A evaluation of measurement uncertainty from the statistical distribution of the values from a series of measurements and can be characterized by experimental standard deviations. The other components which may be evaluated by Type B evaluation of measurement uncertainty can also be characterized by standard deviations, evaluated from assumed probability distributions based on experience or other information. In general, for a given set of information, it is understood that the measurement uncertainty is associated with a stated quality value attributed to the measurand. A modification of this value results in a modification of the associated uncertainty.

Reference:

VIM, International Vocabulary of Metrology – Basic and general concepts and associated terms, 3rd edition, JCGM 200: 2008

This definition for Measurement Uncertainty adopted by the Codex Alimentarius Commission.

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 of an analytical result including uncertainty from sampling may be estimated by a number of procedures, notably those described by EURACHEM (5) and Nordtest (6). These Guidelines do not recommend any particular approach.

4. 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.

5. EURACHEM/EUROLAB/CITAC/Nordtest *Guide on the Estimation of Measurement Uncertainty Arising from Sampling.* Downloadable from: http://www.eurachem.org/guides/UfS_2007.pdf

6. Nordtest handbook for sampling planners on sampling quality assurance and uncertainty estimation *Uncertainty from sampling* (Based upon the EURACHEM international guide *estimation of measurement uncertainty arising from sampling).* Downloadable as Report 604 from: http://www.nordicinnovation.net/nordtestfiler/tr604.pdf

EXPLANATORY NOTES TO THE CODEX GUIDELINES ON MEASUREMENT UNCERTAINTY INCLUDING SAMPLING UNCERTAINTY

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

INTRODUCTION

In the Procedural Manual it is stated in the section dealing with: "The Use of Analytical Results: Sampling Plans, Relationship between the Analytical Results, The Measurement Uncertainty, Recovery Factors and Provisions in Codex Standards":

Issues Involved

There are a number of analytical and sampling considerations which prevent the uniform implementation of legislative standards. In particular, different approaches may be taken regarding sampling procedures, the use of measurement uncertainty and recovery corrections.

At present there is no official guidance on how to interpret analytical results in the framework of Codex. Significantly different decisions may be taken after analysis of the "same sample". For example some countries use an "every-item-must-comply" sampling regime, others use an "average of a lot" regime, some deduct the measurement uncertainty associated with the result, others do not, some countries correct analytical results for recovery, others do not. This interpretation may also be affected by the number of significant figures included in any commodity specification.

It is essential that analytical results be interpreted in the same way if there is to be harmonization in the framework of Codex.

It is stressed that this is not an analysis or sampling problem as such but an administrative problem which has been highlighted as the result of recent activities in the analytical sector, most notably the development of International Guidelines on the Use of Recovery Factors when Reporting Analytical Results and various Guides prepared dealing with Measurement Uncertainty.

Recommendations

It is recommended that when a Codex Commodity Committee discusses and agrees on a commodity specification and the analytical methods concerned, it states the following information in the Codex Standard:

1. Sampling Plans

The appropriate sampling plan, as outlined in the Guidelines for Sampling (CAC/GL 50-2004), Section 2.1.2 Guidelines on Sampling to control conformity of products with the specification. This should state:

- whether the specification applies to every item in a lot, or to the average in a lot**,** or the proportion non-conforming;
- the appropriate acceptable quality level to be used;
- the acceptance conditions of a lot controlled, in relation to the qualitative/quantitative characteristic determined on the sample.

2 Measurement Uncertainty

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.

3 Recovery

Analytical results are to be expressed on a recovery corrected basis where appropriate and relevant, and when corrected it has to be so stated.

If a result has been corrected for recovery, the method by which the recovery was taken into account should 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.

4 Significant Figures

The units in which the results are to be expressed and the number of significant figures to be included in the reported result.

The Explanatory Notes given below will help with the interpretation of the above, particularly with respect to section 2, measurement uncertainty.

EXPANATORY NOTES

1. Introduction

It is widely accepted that repeat analyses of the same sample will almost always produce varying results. These variations may be due to e.g. changes in the operating conditions, and an inhomogeneous sample from which only a small test portion is taken. Persons responsible for producing, appraising and interpreting the results of chemical analyses will be familiar with terms such as reproducibility and repeatability - both are measures of this random variability. They will also be familiar with the use of 'reference materials' and terms such as 'bias' and 'recovery', which are used to check if analytical results are systematically higher or lower than they should be, when compared to a known reference value. The random variability and systematic effects in analytical results are characterised as analytical uncertainty.

Chemical analysis is usually the end part of the measurement process, following the taking of samples (sampling) and grinding, blending and treatment of samples in preparation for chemical analysis (physical preparation). The term 'measurement' (as in measurement uncertainty) encompasses the whole procedure. Each step in the measurement process will introduce variability in the final measurement result, the measurement uncertainty. The International Standards Organization defines uncertainty of measurement as 'parameter, associated with the result of a measurement that characterises the dispersion of the values that could reasonably be attributed to the measurand' (ISO GUM 1993).

The Codex General Guidelines on Sampling (CAC/GL 5 0-2004) are based on the principals of acceptance sampling. They are designed to ensure that fair and valid sampling procedures are used when food is being tested for compliance with a particular Codex commodity standard. These Guidelines make the distinction between sampling error and measurement error. For the purpose of the Guidelines measurement error (caused by the measured value of the characteristic failing to accurately represent the true value of the characteristic within the sample) is analogous to analytical uncertainty. Like analytical uncertainty, sampling error (caused by the sample failing to accurately represent the population from which it was collected) has input from both systematic and random effects. The CAC Guidelines advise it is desirable that the sampling errors associated with any sampling plan, as well as measurement errors associated with analysis, should be quantified and minimised. Laboratories are required, as part of 3rd party accreditation, to participate in inter- laboratory trials, data from these and other internal quality control measures allow the estimation of analytical uncertainties. Methods for estimating sampling uncertainty have been published.

The Eurachem/EUROLAB/CITAC/Nordtest Working Group on Uncertainty from Sampling was formed in September 2003. This Working Group includes representatives from a wide range of disciplines, including those from the food sector. The Eurachem Working Group has prepared guidance for the evaluation of uncertainties in measurement arising from the process of sampling. This guidance is applicable to all chemical measurements that require the taking of a sample. It provides guidance on the assessment of the uncertainty of the measurement that is caused by the process of sampling, and any physical preparation of the sample prior to analysis, and how this can be combined with estimates of uncertainty arising from the analytical process. The guide was developed in

collaboration with relevant international bodies and will be updated as experience is gained in their use.

The Guide looks firstly at the methods of estimating uncertainty and uses real case studies to exemplify each. The role of measurement uncertainty in the decision making process is also addressed, as is the assessment of fitness for purpose. The second part of this document examines whether it is a good idea to set global fitness for purpose criteria for sampling uncertainty. This document is focussed on measurement processes that result in quantitative data. Qualitative data (e.g. yes / no responses) are not addressed.

In addition Nordtest has prepared a handbook for sampling planners on sampling quality assurance and uncertainty estimation *Uncertainty from sampling,* which is based upon the EURACHEM Guide *estimation of measurement uncertainty arising from sampling,* but which is rather more "practical".

, 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.

2. What is Measurement Uncertainty?

Even ignoring sampling 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 present Codex Measurement Uncertainty 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.

The values "U" or "2u" need to take into account the total uncertainty including that contributed by the sampling uncertainty. This will probably make the value of "U" rather large than if the sampling uncertainty is ignored.

3. 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 or when the uncertainty affects compliance to a specification limit, for example a Codex Standard (the Codex Alimentarius Commission has developed Guidelines which require laboratories involved in the import/export of foods to be accredited). As Codex is concerned with goods moving in international trade it would be anticipated that the request will be made.

4. 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.

5. 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.

The same applies when sampling is also taken into account. No sampling procedure will be exactly replicated when applied to the same batch.

6. Procedures for Estimating Measurement Uncertainty

There are many procedures available for estimating the measurement uncertainty of a result.

The Codex guidelines for analytical measurement uncertainty 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. 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:

'However, with respect to total measurement uncertainty there are several ways of estimating sampling uncertainty but both Guides (Eurachem and Nordtest) include the "duplicate method" which has been found to be broadly applicable across the food sector.'

7. The duplicate method – general principles

A sampling protocol (detailing, how many samples, how to sample, sample mass etc.) is a prerequisite for all food surveys, assessments etc. The duplicate method requires a second (duplicate) sample to be taken for 10% (or a minimum of 8) of the total number of sampling targets. This second 'duplicate' sample should be taken to represent the ambiguity in interpreting the protocol, what this means is perhaps better explained using the examples.

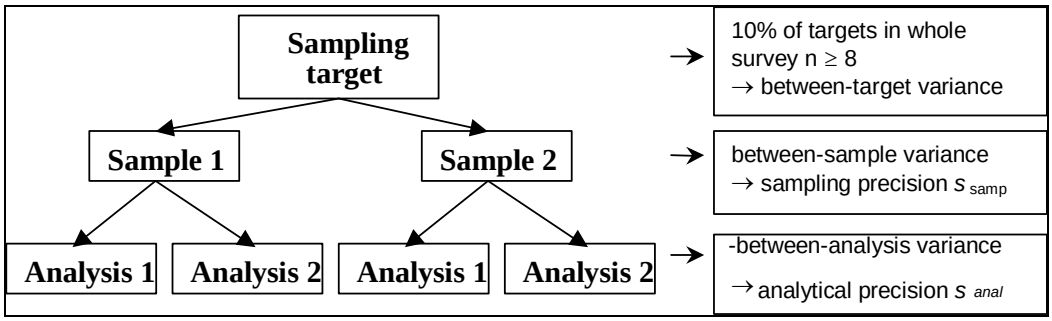
The duplicate samples are then each subject to independent physical preparation (i.e. they are not combined). Two analytical test portions are drawn from each of the duplicate 'prepared' samples.

All test portions are anonymised (so it is unclear which are duplicates) and subsequently analysed in a randomised order.

Statistical procedures are applied to the resultant data to separate out between-target variances, sampling (or within-target) variances and analytical variances.

The inclusion of certified reference materials (CRM) and /or spike samples within the analytical run will allow the systematic effects of analysis to be quantified. This is generally routine in most laboratories. As described, the duplicate method does not permit the estimation of systematic effects from the sampling process. When the duplicate method of uncertainty estimation is utilised, the costs will increase by 10% for sampling and 30% for analysis.

Details of the procedure are given in the EURACHEM and Nordtest Guides. It is illustrated diagrammatically below using a balanced experimental design for the empirical estimation of uncertainty.



8 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.

9. Values of Measurement Uncertainty Estimations

Stipulating information on the anticipated values of measurement uncertainty estimations is frequently not appreciated. 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) analytical measurement 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.

However, for total measurement uncertainties it has not yet been possible to "predict" what the uncertainties are likely to be. Experimental work has suggested that for a range of systems within the food sector the sampling uncertainty is between equal to the analytical uncertainty to 4 times the analytical measurement uncertainty.

In situations where the total measurement uncertainty is obviously too large to be acceptable, i.e. if it is greater than 100% of observed (mean) value, this will be considered not sustainable or acceptable when considering "official" or contractual work.

In practice sampling has been carried out in areas where there is a considerable variability by taking a sufficiently large sample from a lot and defining that to be representative of the lot. In the case of aflatoxins in peanuts, as an example, 30kg is frequently taken using at least 100 incremental units and suitably combining these.

Consideration should be given to whether this should be introduced as a "default" approach if the uncertainty of sampling is found to be too large to be acceptable.

Although work is being carried out to be able to predict the uncertainty from sampling in the food sector it is not completed and is unlikely to result in a generalized equation such as the Horwitz Equation when considering analytical variability, and which has been used to predict the uncertainty values given in the table above,

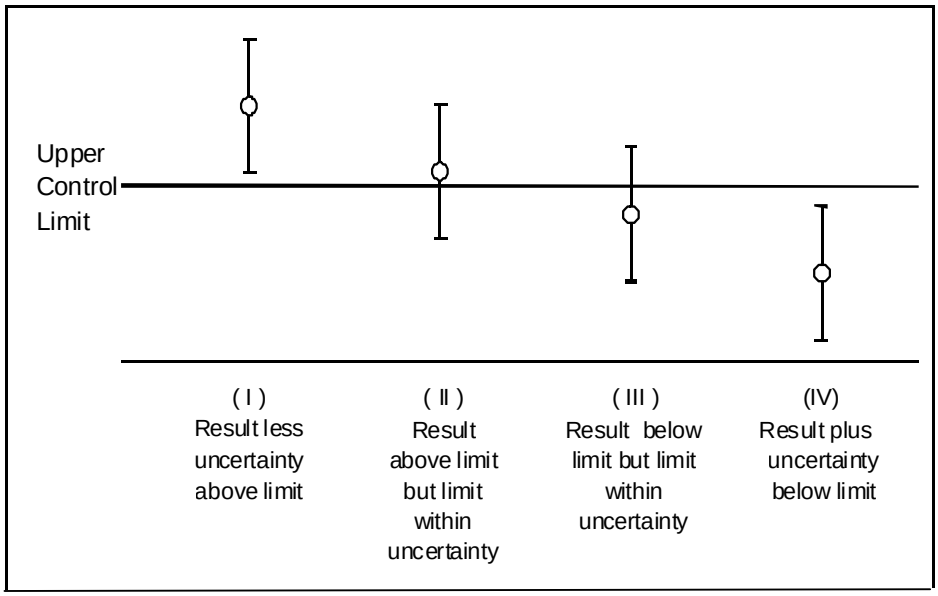
10. Significance of the Section in the Procedural Manual of the "use of analytical results: sampling plans, relationship between the analytical results, the measurement uncertainty, recovery factors and provisions in Codex Standards" (from Codex Procedural Manual, 18th Edition)

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

10.1 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 total 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 total 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.

However, if the total measurement uncertainty is to be taken into account, the "error bars" become very much greater. This means that there is much more chance of situations *II and III* occurring. In addition, there are two other possibilities if the total measurement uncertainty is separated into both analytical and sampling uncertainties, i.e. when a sample would be considered non-compliant in situation *I* if only the measurement uncertainty derived from analysis was considered but considered compliant if the total measurement uncertainty from both sampling and analysis was considered.. Similarly in situation *IV* when the sample is always considered compliant if only the analytical measurement uncertainty was considered, but where there was a chance that the sample was non-compliant if the total uncertainty was considered.

10.2 Enforcement Situation

The significance of this section in the Procedural Manual is that the laboratory at importation will deduct the measurement uncertainty. 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. If sampling uncertainty is taken into account then without an alteration to a (maximum) control level, more samples will be deemed to be compliant with the control level.

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.

By using the total uncertainty to assess compliance it means that the situation II will occur more frequently than previously.

10.3 Action to be taken by Authority Setting the Specification Level

In order to protect the consumer either:

i) The total measurement uncertainty when estimated must not be significantly greater that the analytical uncertainty when estimated alone, or

ii) The (maximum) specification level must be reduced to take into account the increased value of the total measurement uncertainty as compared to the analytical measurement uncertainty.

11 Useful References

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

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

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 2 1748:2004 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

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)

EURACHEM/EUROLAB/CITAC/Nordtest *Guide on the Estimation of Measurement Uncertainty Arising from Sampling*. Downloadable from: http://www.eurachem.org/guides/UfS_2007.pdf

Nordtest handbook for sampling planners on sampling quality assurance and uncertainty estimation *Uncertainty from sampling* (Based upon the EURACHEM international guide *estimation of measurement uncertainty arising from sampling)*. Downloadable as Report 604 from:
http://www.nordicinnovation.net/nordtestfiler/tr604.pdf

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.

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

Validation of Chemical Analytical Methods. NMKL Procedure No 4, 3rd Version, 2009

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).