CODEX ALIMENTARIUS
INTERNATIONAL FOOD STANDARDS

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World Health Organization

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GUIDELINES ON MEASUREMENT UNCERTAINTY

CXG 54-2004

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1. Analytical measurement results in food control are used to assess whether food products meet relevant specifications. The accuracy of measurement results is affected by various error components, and it is important to ensure these errors are properly considered. Since the true value of the quantity being measured is unknown, errors cannot be known exactly. The focus thus shifts to an evaluation of the uncertainty associated with a measurement result. All measurement results have an associated uncertainty; the non-estimation of measurement uncertainty does not mean that there is no uncertainty. The evaluation of measurement uncertainty is required to establish the comparability of measurement results. Accordingly, measurement uncertainty is of utmost importance in analytical testing and subsequent decision-making.

2. This Guideline does not provide guidance for the evaluation of the contribution to total uncertainty due to sampling neither does it provide guidance as to how to take measurement uncertainty into account in the specification of sampling plans for acceptance sampling in connection with lot inspection. The Codex Alimentarius Commission has developed *Guidelines for the Assessment of the Competence of Testing Laboratories Involved in the Import and Export Control of Foods* (CXG 27-1997). They recommend that laboratories involved in food control for import/export should adopt the general criteria set forth in ISO/IEC 17025. The latter standard requires that information regarding measurement uncertainty must be provided in test reports insofar as it is relevant to the validity or application of the test results, in response to a customer's request, or when the uncertainty affects conformity to a specification limit.

Scope

3. This Guideline covers general aspects of measurement uncertainty for quantitative analysis, gives definitions of measurement uncertainty and related terminology and clarifies the role of measurement uncertainty in the interpretation of test results in conformity assessment and in specifying sampling plans for the inspection of lots. This guideline does not address the uncertainty component associated with sampling and focuses on uncertainty contributions which arise in connection with obtaining a test sample from the laboratory sample, taking a test portion from a test sample (i.e. the errors due to the heterogeneity[1] between test portions) and the analysis of a test portion in the laboratory.

4. Analytical measurements in food control are often *quantitative*, but *qualitative* test results are also relevant. While an evaluation or estimation of measurement uncertainty is not required for qualitative results, it is recommended that laboratories identify factors which have an influence on such test results and establish quality assurance procedures to control relevant effects.

Prerequisites

5. Laboratories which perform analytical measurements should have effective quality assurance procedures in place (properly trained staff, equipment maintenance, calibration of equipment, reference materials and standards, documentation, participation in proficiency tests, quality control charts etc.), which can be used for the evaluation of measurement uncertainty. Furthermore, sufficient statistical knowledge either by qualified staff or external consultants is recommended, in order to ensure that statistical methods, mathematical formulas and decision rules are correctly applied, and that criteria for producer and consumer risks are met (JCGM 106: and ISO 10576).

Terms and definitions

6. For the purposes of this Guideline, the terms and definitions of the following documents apply:

   - CXG 72-2009 (Guidelines on Analytical Terminology)
   - JCGM 200 International vocabulary of metrology – Basic and general concepts and associated terms (VIM)
   - ISO 3534-1 Statistics – Vocabulary and symbols – Part 1: General statistical terms and terms used in probability
   - ISO 3534-2 Statistics – Vocabulary and symbols – Part 2: Applied statistics
   - ISO 2859-1 Sampling procedures for inspection by attributes – Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection

[1] The heterogeneity between test portions is composed of compositional heterogeneity (CH) and distributional heterogeneity (DH). Both of these lead to random errors when selecting a test portion, known as Fundamental Sampling Error – also called Fundamental Variability – and Grouping and Segregation Error. Fundamental variability results from CH and has a dominant effect on total variability when the “target compound” is predominantly located in a specific fraction of the particles (there is a low number of particles with relatively high concentrations of the target compound). The fundamental variability can be controlled by collecting a sufficient test portion mass. Grouping and segregation error results from DH and is the non-random distribution (spatial or temporal) of the “target compound” within the material from which a test portion is selected. The grouping and segregation error can be controlled through the collection of a sufficient number of random increments to comprise a test portion.

- ISO 3951-1 Sampling procedures for inspection by variables – Part 1: Specification of single sampling plans indexed by acceptance quality limit (AQL) for lot-by-lot inspection for a single quality characteristic and a single AQL
- ISO 6498 Animal feeding stuffs -- Guidelines for sample preparation
- ISO 10725 Acceptance sampling plans and procedures for the inspection of bulk materials
- ISO/IEC 17025 General requirements for the competence of testing and calibration laboratories

7. For convenient reference, the following definitions are provided here:

- **Inspection by variables**: Inspection by measuring the magnitude of a characteristic of an item.
- **Item**: That which can be individually described and considered.
- **Laboratory sample:** Sample as prepared (from the lot) for sending to the laboratory and intended for inspection or testing.
- **Lot:** A lot is a definite quantity of some commodity manufactured or produced under similar conditions.
- **Measurement uncertainty:** Parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand (i.e. the quantity intended to be measured).
- **Sample:** Set of one or more items taken from a lot and intended to provide information on the lot.
- **Sampling plan:** Specified sample size, methodology for the selection of samples and lot acceptability criteria.
- **Sample size:** Number of items in the sample.
- **Test portion:** Quantity of material drawn from the test sample (or from the laboratory sample if both are the same).
- **Test sample:** Subsample or sample prepared from the laboratory sample and from which test portions will be taken

General considerations

8. When a measurement is performed, it is generally assumed that a “true value” of the quantity being measured exists. However, this true value is unknown and is thus only available as a reference value or a conventional true value. For this reason, measurement error cannot be reliably estimated and the focus shifts to the evaluation of measurement uncertainty. Measurement uncertainty is expressed as an interval within which values which can reasonably attributed to the measured quantity will lie with a stated coverage probability. The uncertainty of a measurement result reflects the lack of exact knowledge of the value of the measurand. Since all measurement results are subject to error, laboratories are expected to estimate and, if necessary, report the measurement uncertainty associated with every result.

9. Measurements are affected by many influences – e.g. effects which arise in connection with changes in temperature, pressure, humidity, matrix variability or with the judgment of the analyst. These errors can be classified as either *systematic* or *random*. The term *bias* is often used to refer to a systematic error. Even if all *systematic* error components could be evaluated and corrected for, measurement results would remain subject to random errors which cannot be corrected for, leading to an uncertainty range. An example of the manner in which a random error manifests itself is the dispersion of measurement results observed when measurements are performed within one laboratory under near-identical, i.e. repeatability, conditions. Both systematic and random components of measurement uncertainty should be summarily quantified. Components of measurement uncertainty can be evaluated from the statistical distribution of a series of measurement results and characterized by standard deviations. Other components, which can also be characterized by standard deviations, are evaluated on the basis of distributional assumptions derived from experience or other information. All components of uncertainty, including those arising from systematic effects such as the uncertainty of bias corrections and reference standards, contribute to the dispersion.

10. It is important to note that time and financial resources do not allow for the evaluation and correction of all measurement errors. For this reason, the focus lies on the identification and evaluation of the *main* components of measurement uncertainty. However it is of utmost importance to identify and evaluate systematic components of measurement uncertainty since these cannot be reduced by repeated measurements. Whenever possible test methods should be used that have been validated by collaborative studies. In case that there are two methods with identical measurement uncertainty, the method with lower systematic error should be preferred.

Uncertainty components

11. While performing a measurement, it is important to consider all possible uncertainty components which will influence the result of the measurement. Typical uncertainty components include effects associated with instrumental equipment, analyst, sample matrix, method, calibration, time and environment. These sources may not be independent, in which case the respective correlations should be taken into account in the uncertainty budget – i.e. in the computation of the total uncertainty. Moreover, under certain circumstances, the effect associated with a particular uncertainty component may change over time and a new estimation of measurement uncertainty may be necessary as a result. For more information on this subject, please refer to the EURACHEM / CITAC Guide: Quantifying Uncertainty in Analytical Measurement, Sections 7.3.1, 7.13.2 and 7.13.3.

Procedures for estimating measurement uncertainty

12. There are many approaches available for estimating the uncertainty of a measurement result, notably those described in CGM 100 Evaluation of measurement data – Guide to the expression of uncertainty in measurement and EURACHEM / CITAC Guide CG 4: Quantifying Uncertainty in Analytical Measurement. These Codex Guidelines do not recommend a particular approach for estimating measurement uncertainty, but it is important that whatever approach is used be scientifically acceptable[2]. Among such scientifically acceptable approaches, none may be said to be better than any other – i.e. there is no "hierarchy" among such approaches. Choosing the appropriate approach depends on the type of measurement or analysis, the method used, the required level of reliability, and the urgency of the request for an estimate of measurement uncertainty. In general, procedures are based either on a "bottom-up" approach or on a "top-down" approach, with the latter using data from collaborative studies, proficiency studies, validation studies, intra-laboratory quality control samples, or a combination of such data. For microbiological testing, the procedure described in ISO 19036 follows a "top-down" approach.

13. Most common approaches for the evaluation of measurement uncertainty:

- Modelling (ISO GUM)
    - Bottom-up component-by-component evaluation according to JCGM 100 or according to JCGM 101 (Monte-Carlo Method)
- Single-lab validation
    - Top-down approach e.g. according to Nordtest TR 537, NMKL procedure No. 5, EURACHEM / CITAC Guide: Quantifying Uncertainty in Analytical Measurement (uncertainty of results obtained using the same procedure in a single laboratory under varying conditions)
- Interlaboratory validation
    - Top-down approach using the reproducibility standard deviation (ISO 5725-2, ISO 5725-3 and ISO 21748) (uncertainty of results obtained using the same procedure in different laboratories)
- Proficiency testing (PT)
    - Top-down approach using the standard deviation for proficiency assessment (uncertainty of results obtained by analysing the same sample(s) in different laboratories)

14. These procedures are not equivalent and may produce different estimates of the measurement uncertainty. In the top-down approach, the reproducibility standard deviation obtained from collaborative studies is often used as an estimate of measurement uncertainty. The matrix mismatch uncertainty component should be adequately taken into account during the estimation of measurement uncertainty. Different matrices and concentration levels – depending on the scope of the method – could be used to overcome this deficiency. In the case of a single-lab validation study, intermediate precision (within-lab reproducibility) is used for the estimation of the uncertainty and the laboratory bias is therefore missing with the result that the uncertainty may have been underestimated. Depending on the case, this can be addressed e.g. by estimating and correcting for the bias via a recovery experiment (with the uncertainty of the recovery correction duly taken into account in the uncertainty) or by simulating the laboratory bias by varying influencing effects like analytical instruments, analysts, time span, equipment for sample preparation etc. Certified reference materials can also be used to estimate bias and its uncertainty.

15. In addition to the fact that these procedures may differ depending on the influencing effects included, there is also often considerable variation due to random variability of the standard deviation figures (intermediate

[2] The expression "scientifically acceptable" is used here to mean either that the approach has been previously described in an international standard or guideline or that, upon expert scrutiny, it would be agreed that the approach is appropriate.

precision (within-lab reproducibility), reproducibility, repeatability). Therefore, both the chosen approach for estimating measurement uncertainty (in-house validation, collaborative study, bottom up etc.) and the estimated level of confidence of the measurement uncertainty should be available on request.

16. Almost all uncertainty data are expressed as standard deviations or functions of standard deviations. If a standard deviation is calculated using a small amount of data there is considerable uncertainty in the estimate of measurement uncertainty obtained.

17. The reliability of the measurement uncertainty components should be taken into account in the design of experimental studies and the evaluation of the measurement uncertainty. This is especially important if the estimate of a standard deviation is derived from a low number of tests run by a single laboratory or from a collaborative study conducted with a low number of laboratories.

18. Even if some components of measurement uncertainty cannot be evaluated, such components can often at least be estimated on the basis of principles, experience and "state of the art" knowledge based e.g. on results from comparable laboratories, concentration levels, matrices, analytical methods or analytes.

19. In order to demonstrate that a laboratory is competent in the application of a validated method, there are two possible approaches:

    a. The laboratory uses a validated in-house test method with established limits regarding the major measurement uncertainty components along with the exact manner in which relevant quantities must be calculated.

    b. The laboratory uses a method which has been validated in a collaborative study and thus has established method performance characteristics and verifies that it can meet and/or exceed the within laboratory performance parameters in accordance with the official standardized method and that all the critical influences are under control.

20. Most of the methods used in food testing and recommended in Codex documents are well-recognized methods which have been reliably validated. As long as the laboratory's competence in the application of a validated method has been demonstrated following either one of the two approaches described, the measurement uncertainty evaluation/estimation is considered to have been successfully performed and any requirements regarding the measurement uncertainty are considered to have been met.

21. According to CXG 27, laboratories involved in import and export control of food should comply with ISO/IEC17025. ISO/IEC 17025 requires laboratories to use validated methods (see Section 7.2); thus, data from the interlaboratory or single-lab validation study can be used for the estimation of measurement uncertainty following the top-down approach. In Section 7.6.2 of the EURACHEM / CITAC Guide: Quantifying Uncertainty in Analytical Measurement, a procedure for evaluating measurement uncertainty using collaborative study data is provided. The EURACHEM / CITAC Guide: Quantifying Uncertainty in Analytical Measurement also references ISO 21748 as the primary source for the estimation of uncertainty on the basis of "collaborative study data acquired in compliance with ISO 5725."

Uses of measurement uncertainty

22. Measurement uncertainty has several uses including, but not limited to:

    - Reporting of measurement results (see Section 7.8.3.1 c) in ISO/IEC 17025):

      Typically, the measurement uncertainty is reported as the expanded measurement uncertainty U, i.e. as the standard uncertainty u multiplied by a coverage factor $k = 2$, which for a normal (Gaussian) distribution corresponds to a coverage probability of approximately 95 %. Note: The higher the uncertainty of the standard deviation used for the calculation of the measurement uncertainty, the lower the coverage probability of the latter. In such cases it may be sensible to increase the coverage factor k by taking the corresponding factor of the Student t distribution.

    - For conformity assessment, to assess whether the true value of the tested laboratory sample (i.e. of an individual item) complies with a specification (see paragraphs 25 and 26). Examples and explanations of decision rules can be found in Section 8 of JCGM 106 and in Section 6 of ISO 10576-1. An illustration is provided in Figure 1, below.

- For the design of acceptance sampling plans based on inspection by variables. The determination of sample size and acceptability constant for inspection by variables plans is based on the procedures and the sampling plans provided in ISO standards and/or Codex guidelines, e.g. ISO 3951-2 and CXG 50-2004 (*General Guidelines on Sampling*). When measurement uncertainty is non-negligible in relation to the process standard deviation, the different components of measurement uncertainty should be taken into account in the design of the plan (see for instance Annex P in ISO 3951-2).
- Assessing the performance of laboratories (see Sections 9.6 and 9.7 of ISO 13528)
- For the characterization of certified reference materials
- For comparison between measurement results and true/reference values (ISO 5725-6)

Note 1: *It is important to distinguish between the conformity of an individual item and the conformity of a lot consisting of a number (sometimes a very large number) of items. In the latter case, lot acceptance is determined on the basis of a sample of randomly selected items. The combination of inspection by attributes plans with the classification of each item as conforming or nonconforming via the type of approach described in Figure 1 (see below) does not constitute an effective lot inspection procedure (even if the measurement uncertainty includes a sampling component), as it would require a large increase in sample size to satisfactorily control consumer and producer risks.*

Note 2*: Information regarding the individual components of measurement uncertainty is required in the design of inspection by variables plans (in cases where measurement uncertainty is non-negligible in relation to the process standard deviation). Such information may not be available if the measurement uncertainty is reported as a single number.*

How to report measurement uncertainty in test results

23. In accordance with Section 7.8.3.1 c) and 7.8.6 in ISO/IEC 17025 measurement uncertainty should be reported to allow for a decision as to whether a *laboratory sample* meets a specification on the basis of an analytical result.

24. However, ISO/IEC 17025 does not specify exactly which information should be reported. It is clear, however, that it would be useful to include information as to whether a correction for method bias was applied and whether the contribution corresponding to uncertainty of bias correction is included in the reported measurement uncertainty. The reader is also referred to the ILAC Guidelines ILAC-G17 (Measurement Uncertainty in Testing) and ILAC-G8 (Guidelines on Decision Rules and Statements of Conformity), as well as to the Eurachem / CITAC Guide: Use of Uncertainty Information in Compliance Assessment.

Examples of situations occurring when measurement uncertainty is considered

25. Figure 1 illustrates how measurement uncertainty can affect the decision whether the true value of a laboratory sample (i.e. an individual item) conforms to a specification limit. The procedure illustrated in Figure 1 is not always suitable and is merely intended to illustrate the basic principle only. Measurement uncertainty intervals such as those in Figure 1 cannot be used as a valid conformity assessment procedure.

26. The decision whether the laboratory sample meets the specification or not depends on the rules which the different parties involved have agreed to apply.

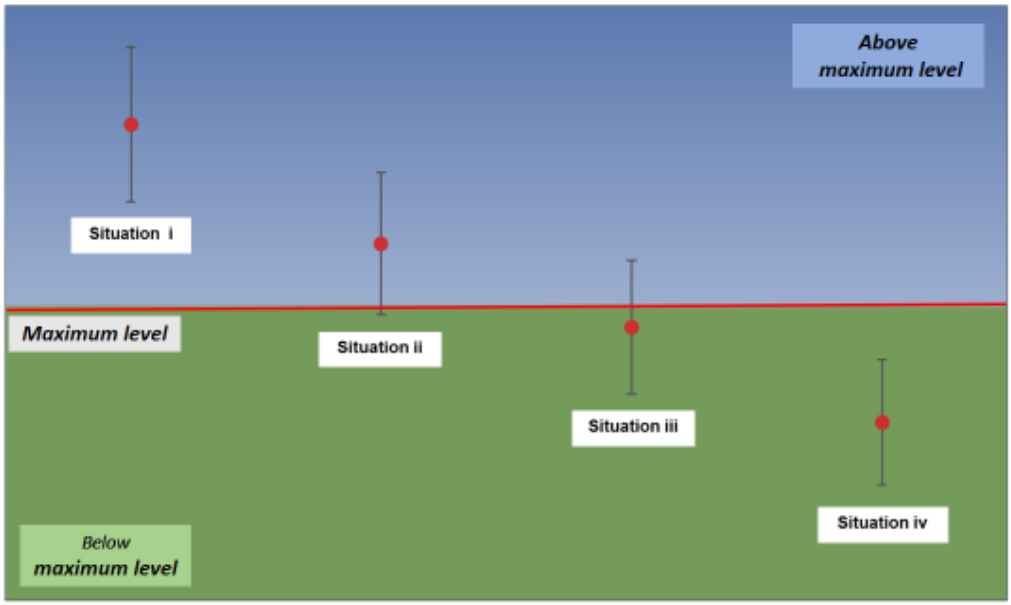

Figure 1: The diagram shows how measurement uncertainty can be taken into account in connection with the conformity assessment of an individual item against a specification. Such a procedure is not suitable for lot inspection. For each situation, the red point represents an individual test result and the vertical bar represents the expanded measurement uncertainty interval.

Situation i

The analytical result minus the expanded measurement uncertainty exceeds the maximum level. The conclusion is that the true value lies above the specification.

Situations ii and iii

The analytical result differs from the maximum level by less than the expanded measurement uncertainty. The standard interpretation here is the outcome is inconclusive. Action on this result depends on existing agreements between the trading partners.

Situation iv

The analytical result is below the maximum level by more than the expanded measurement uncertainty. The decision is that the true value lies below the specification.

Note: The implications of situations i to iii in the case of testing MRL compliance are extensively discussed in CXG 59-2006 (*Guidelines on Estimation of Uncertainty of Results*). If, as in situations ii and iii, it cannot be concluded beyond reasonable doubt (in relation to the consumer and producer risks involved) that the MRL or maximum level is exceeded or that the item is compliant, the decision will depend on national practices and on existing agreements between the trading partners, which may thus have a considerable impact on the acceptance of trade consignments. This question is addressed in Section 4 of CXG 83-2013 (*Principles for the Use of Sampling and Testing in International Food Trade*). It is stated under Principle 5 that “the exporting country and the importing country should agree on how the analytical measurement uncertainty is taken into account when assessing the conformity of a measurement against a legal limit.”