CODEX ALIMENTARIUS COMMISSION

E

Food and Agriculture Organization of the United Nations

World Health Organization

Viale delle Terme di Caracalla, 00153 Rome, Italy - Tel: (+39) 06 57051 - E-mail: codex@fao.org - www.codexalimentarius.org

Agenda Item 6

MAS/40 CRD22
ORIGINAL LANGUAGE ONLY

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON METHODS OF ANALYSIS AND SAMPLING

40th Session

Budapest, Hungary, 27 - 31 May 2019

REVISION OF THE GUIDELINES ON MEASUREMENT UNCERTAINTY (CXS 54 - 2004)

Revised by Chair of EWG on the Revision of CXS 54

Codex members and Observers wishing to submit comments on this draft should do so as instructed in CL 2019/16-MAS available on the Codex webpage/Circular Letters: http://www.fao.org/fao-who-codexalimentarius/resources/circular-letters/en/.

Proposal for new work

1. The 39th session of CCMAS (2018) (CCMAS39), agreed to start new work on the revision of the guidelines on measurement uncertainty (CXS 54-2004) and agreed that an EWG chaired by Germany would revise the guidelines.[1]

2. The new work was approved by CAC41 (July 2018).[2]

3. This report reflects the purpose and rationale of the amendment of the *Guidelines on measurement uncertainty* (CXG 54-2004). It also summarizes the work of the EWG after its formation after the 38th session of CCMAS in order to identify improvements and propose changes.

Background

4. As early CCMAS33 (2010), much time has been spent discussing amendments to provide a revised draft serving as a basis of possible improvements. The revision of the guideline originates from the requests for more detailed explanations regarding the impact of measurement uncertainty on analytical test results, sampling procedures, lot assessment and its role in conformity assessment. Some members found it necessary to clarify why measurement uncertainty is important, what kind of influence measurement uncertainty will have on decision-making and its role in conformity assessment of a particular analytical test sample.

5. At CCMAS39, there was general agreement that the guideline needed revision in order to improve and clarify the content. The guideline should not cover how measurement uncertainty would influence the decision-making process regarding conformity assessment. Views were expressed that conformity assessment and the use of uncertainty of analytical results should rest with national governments or agreements between trading partners. It was also noted, that this aspect was not covered by the current CXG 54-2004 and that the *Principles for the use of sampling and testing in international food trade* (CXG 83-2013) stated *"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."*

6. CCMAS acknowledged that measurement uncertainty for the purpose of the guidelines comprised only laboratory samples and would solely concern the uncertainty of analytical test results for laboratory samples, including subsampling. Measurement uncertainty relating to sampling would be covered by the work on the revision of the *General Guidelines on Sampling* (GL50 - 2004).

7. The Committee agreed that the revised CXG 54-2004 covers general aspects on measurement uncertainty and illustrates without recommendation on lot assessment:

(i) the ~~use~~ influence of measurement uncertainty ~~o~~in the interpretation of measurement results.

Commented [GDP1]: This was the original text of REP18_mas39 agreed upon at CCMAS 39

[1] REP18/MAS, para. 61 and Appendix IV

[2] REP18/CAC, para. 66 and Appendix VI

(ii) the relationship between the measurement uncertainty and (given) sampling plans.

8. It was further noted that an information document containing examples would support the revision of CXG 54-2004.The original intention was to keep the Guidelines as simple as possible. By adding a large amount of texts and examples on how to calculate measurement uncertainty in various situations would overload the revised guide and might contradict the original aim.

9. It might be discussed whether CXG 54-2004 should be extended for practical use, providing more than general aspects on measurement uncertainty, as this has been done in the *General Guidelines on Sampling* (CXG 50-2004) for sampling plans and the *Guidelines on Estimation of Uncertainty of Results* (CXG-59-2006) for measurement uncertainty in pesticide analysis. In any case, it was agreed to avoid any kind of overlapping with the CXG 59-2006.

WORK OF THE EWG

10. The EWG chaired by Germany working in English was established to develop the proposed draft revised Guidelines for consideration by CCMAS40.

11. Germany officially invited members and observers to participate in the EWG "Revision of the Guidelines on measurement uncertainty" (CCMAS-GL-mu) via an electronic platform, supplied by the Codex Secretariat. The invitation was sent out in July 2018. The EWG had 43 members. The list of participants is attached as Appendix III.

12. In November 2018, documents were prepared and provided through the electronic platform, asking EWG members for their comments.

Main aspects covered in the revised CXG 54-2004

13. The main aspects to be covered in the revised CXG 54-2004 and supporting information document are as follows:

- An updated CXG 54-2004, which is comprehensive, simple to use and understood by Codex commodity committees. It includes a prioritised combination of general and technical improvements.
- Deals with general aspects of measurement uncertainty.
- The measurement uncertainty comprises only laboratory samples and solely concerns the uncertainty of results for laboratory test samples, including subsampling.
- For improved understanding, an additional part on definition of "measurand", "measurement error", "trueness", "precision", "accuracy" and "measurement uncertainty" has been added.
- Illustrate the ~~use~~ influence of measurement uncertainty ~~io~~n the interpretation of measurement results.
- Illustrate the relationship between the measurement uncertainty and (given) sampling plans.
- A separate information document contains examples, which supports the CXG 54-2004.

Summary of the main changes

14. 11 members[3] commented on the draft guideline CXG 54-2004.

15. Altogether 186 comments were received; 63 technical comments (te), 55 editorial comments (ed) and the remaining were general comments (ge) and suggestions.

16. The chair of the EWG thanks explicitly all members who have critically commented the draft CXG 54-2004 and who gave substantial and fundamental ideas and recommendations which lead to the complete revision of the first draft. All comments were taken into consideration and have been included in the text (Appendix I) as far as possible as long as they were correct and qualified.

- The first draft CXG 54-2004 sent out in November 2018 has been re-drafted completely.
- The introduction and the scope were re-worded and the content modified.
- The chapter "Using the guide" was deleted.
- The chapter "Definitions" was deleted; a modified version has been drafted referring to the respective ISO Standards or guidelines or, for convenient reference, has been provided in the draft itself in cases where the authors were of the opinion that the terms are very important or critical in the context of the draft.

Commented [GDP2]: s. above

[3] Australia, Canada, Honduras, India, Japan, The Netherlands, New Zealand, Norway, Switzerland, the UK and BIPM

- Most of the figures have been deleted because they might have been misleading, irrelevant or wrong; one figure remained.
- A chapter “General considerations” has been included dealing with principle aspects of measurement uncertainty.
- “Uncertainty sources” has been re-phrased to “Uncertainty components”.
- The chapter “Procedures for estimating Measurement Uncertainty” was revised.
- The chapter “The use of analytical results: sampling plans …” has been revised; it has been emphasized that this guide and particularly this chapter does not deal with conformity assessment but exclusively emphasize that measurement uncertainty has an effect on the interpretation of the result and the involved trading partners should agree on how to take this into account.
- The examples have been partly corrected according to comments.
- One example dealing with attribute sampling has been deleted.
- The two remaining examples are shaded in yellow in order to indicate that a decision has to be taken whether they should be included in the draft.
- “Literature” has been revised.

Summary of main changes for information document:

17. The information document (Appendix II) has not been further edited after the first commenting round. The draft CXG 54-2004 has been fundamentally revised after the first commenting round dealing with 186 comments so the content has considerably changed. On the one hand, this has been a very time-intensive process, and on the other hand the information document has to be adapted to the changes made in draft CXG 54-2004. Therefore, it first has to discussed ~~first~~ whether CXG 54-2004 in its present form can be accepted before further work will be put into the information document.

Formatted: Font color: Red

Formatted: Font color: Red, Strikethrough

Summary and conclusion

18. The purpose of the proposed new work is to further revise and amend the document CXG 54-2004, Guidelines on Measurement Uncertainty. It originated from the concern that measurement uncertainty of analytical test results has an impact on decision-making and conformity assessment.

19. It was agreed by the current work assignment (REP18/MAS) that measurement uncertainty deals with laboratory samples. The draft guide does not concern uncertainty which is derived by sampling and the homogeneity of the lot).

20. The draft does not give instructions on conformity assessment. It gives explanations how measurement uncertainty might influence the interpretation of a result and refer to the trading partners involved concerning conformity assessment.

Further points for discussion

21. The following points could be discussed:

- Should the two examples on acceptance sampling be part of the guideline?
- Should the Figure 1 (former Figure 5) be part of the guideline?
- During the revision of the first draft it became more and more obvious how complex the decision making process is. Furthermore, ISO 17025 attaches great importance to the decision making process. It requires that decision rules applied in conformity assessment must be based on the uncertainty of measurement and sampling. Therefore it might be reasonable to think of a guideline to explain the several ISO standards, guides and publications.
- It should be considered whether an adapted version of GL 59, chapter 4 could be included in GL 54

Recommendations

The Committee is invited to:

- consider the proposed draft guidelines as presented in Appendix I; and
- to consider further the points raised in paragraph 21 above.

APPENDIX I

DRAFT REVISED *GUIDELINES ON MEASUREMENT UNCERTAINTY* (CAC/GL 54 – 2004)

(for comments at Step 3 through CL 2019/16-MAS)

Introduction

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 ~~taken into account in conformity assessment~~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 estimation of measurement uncertainty is requisite for making an analytical measurement result metrologically traceable. Accordingly, measurement uncertainty is of utmost importance in ~~testing for regulatory compliance~~analytical testing and subsequent decision-making. It should be noted that, in this guideline, the evaluation of sampling uncertainty is not included.

2. 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 [1]. This standard requires that where necessary for the interpretation of the test results and where applicable measurement uncertainty shall be included in the test report. The ISO/IEC 17025 standard also requires that the measurement uncertainty and its level of confidence must be made available to the user (customer) of the results, on request. ~~Moreover, it is required that decision rules applied in conformity assessment must be based on the uncertainty of measurement and sampling.~~ The use of measurement uncertainty in establishing decision rules must be documented. In summary, the ISO/IEC 17025 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 compliance 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 and the relationship between measurement uncertainty and sampling plans. 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[4] between test portions) and the analysis of a test portion in the laboratory.

4. While the role of chemical analysis in food control often involves *quantitative* analytical measurement results, *qualitative* results are also relevant. For the estimation of the measurement uncertainty associated with qualitative results, a different approach should be applied than for quantitative results, e.g. [3].

Prerequisites

5. Laboratories which perform measurements in chemical analysis 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

---

[4] 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 is the variability between test portions that remains even under the best achievable degree of particle size reduction.** The fundamental variability 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.**

~~The heterogeneity between test portions includes the Fundamental Sampling Error – also called Fundamental Variability – i.e. the variability between test portions that remains even under the best achievable degree of homogenization. The fundamental variability 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 reduced by increasing the mass of the test portions.~~

Formatted: Font: Not Bold

Formatted: Font: 8 pt

Formatted: Font: (Default) Arial, 8 pt

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. Examples and explanations of decision rules can be found in ISO 10576 [4] and JCGM 106:2012 [5].

Terms and definitions

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

7. Guidelines on analytical terminology (CXG 72-2009)

JCGM 200:2012 International vocabulary of metrology – Basic and general concepts and associated terms (VIM)

ISO 3534-1:2006 Statistics – Vocabulary and symbols – Part 1: General statistical terms and terms used in probability

ISO 3534-2:2006 Statistics – Vocabulary and symbols – Part 2: Applied statistics

ISO 2859-1:2014 Sampling procedures for inspection by attributes – Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection

ISO 3951-1:2016 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 6498:2012 Animal feeding stuffs -- Guidelines for sample preparation ISO 10725:2000 Acceptance sampling plans and procedures for the inspection of bulk materials

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

laboratory sample

sample as prepared (from the lot) for sending to the laboratory and intended for inspection or testing

[SOURCE: ISO 6498:2012]

test sample

subsample or sample prepared from the laboratory sample and from which test portions will be taken

[SOURCE: ISO 6498:2012]

test portion

quantity of material drawn from the test sample (or from the laboratory sample if both are the same)

[SOURCE: ISO 6498:2012]

inspection by variables

inspection by measuring the magnitude of a characteristic of an item

[SOURCE: ISO 3951-1:2016]

lot

definite amount of some product, material or service, collected together

[SOURCE: ISO 2859-1:2014]

Alternatively:

A lot is a definite quantity of some commodity manufactured or produced under conditions, which are presumed uniform for the purpose of these Guidelines.

For the goods presumed heterogeneous, sampling can only be achieved on each homogeneous part of this heterogeneous lot. In that case, the final sample is called a stratified sample (see 2.3.3).

NOTE: A continuous series of lots is a series of lots produced, manufactured or commercialised on a continuous manner, under conditions presumed uniform. The inspection of a continuous series of lots can only be achieved at the production or processing stage.

[SOURCE: GL 50/2004]

sample

set of one or more items taken from a lot and intended to provide information on the lot

[SOURCE: ISO 2859-1:2014]

Formatted: Indent: Left: 0.5"

Formatted: English (United States)

Formatted: English (United States)

Formatted: Font: Not Bold

Formatted: Font: Not Bold, English (United States)

Formatted: Font: Not Bold

item

that which can be individually described and considered

[SOURCE: ISO 2859-1:2014]

sample size

number of items in the sample

[SOURCE: ISO 2859-1:2014]

sampling plan

combination of sample size(s) to be used and associated lot acceptability criteria

[SOURCE: ISO 2859-1:2014]

sampling increment

amount of bulk material taken in one action by a sampling device

[SOURCE: ISO 10725:2000]

composite sample

aggregation of two or more sampling increments taken from a lot for inspection of the lot

[SOURCE: ISO 10725:2000]

Formatted: Indent: Left: 0", First line: 0.1"

General considerations

9. 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. It is assumed that any necessary bias correction has been correctly performed. Since all measurement results are subject to error, laboratories are expected to estimate and, if necessary, report the measurement uncertainty associated with every result.

10. Measurements are affected by many influences – e.g. effects which arise in connection with changes in temperature, pressure, humidity or with the judgement 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. The individual components of measurement uncertainty must be identified and quantified, especially repeatability and bias. Some of these components can be evaluated from the statistical distribution of a series of measurement results and characterized by standard deviations. The 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.

11. 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.

Uncertainty components

12. 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 guide [12].

Procedures for Estimating Measurement Uncertainty

13. There are many procedures available for estimating the uncertainty of a measurement result, notably those described in ISO [13] and EURACHEM [12]. The Codex guidelines do not recommend a particular approach for estimating measurement uncertainty, but it is important that whatever approach is used be scientifically acceptable[5]. Choosing the appropriate procedure depends on the type of 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 trials, proficiency studies, validation studies or intra-laboratory quality control samples, or a combination of such data [14], [15].

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

- Modelling (Classical ISO GUM)
  - Bottom-up component-by-component evaluation according to ISO GUM
- Single-lab validation
  - Top-down approach e.g. according to Nordtest TR 537 [15], Eurachem [12] and ISO 21748 [20] (uncertainty of results obtained using the same procedure in a single laboratory varying conditions as described above)
- Interlaboratory validation
  - Top-down approach using the reproducibility standard deviation (uncertainty of results obtained using the same procedure in different laboratories)
- Proficiency testing (PT)
  - Top-down approach using the target reproducibility standard deviation (uncertainty of results obtained by analysing the same sample(s) in different laboratories using different analytical test procedures)

15. 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 a measure of measurement uncertainty. However, one should be aware that usually the matrix mismatch uncertainty component is not adequately taken into account in classical collaborative studies [2]. To overcome this deficiency different matrices and concentration levels – depending on the scope of the method – could be used. In the case of a single-lab validation study, the in-house 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. [2].

16. In addition to the fact that these procedures may vary with regard to the influencing effects included there is also often considerable variation due to random variability of the standard deviation figures (in-house reproducibility, reproducibility, repeatability). Therefore, both the chosen approach for estimating measurement uncertainty (in-house validation, method validation ring trial (collaborative study), bottom up etc.) and the estimated level of confidence of the measurement uncertainty should be provided.

17. Codex recommends that laboratories which perform food testing with quantitative methods should always evaluate measurement uncertainty. In cases where a rigorous evaluation cannot be made, measurement uncertainty should 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.

18. 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 for which limits regarding the values of the major components of measurement uncertainty have been established along with the exact manner in which relevant quantities must be calculated

b. the laboratory uses an official and/or standardized method for which method performance characteristics have already been established, and verifies that it can verifies that the within laboratory performance parameters concord with the official standardized method ~~properly perform the method~~ and that all the critical influences are under control

Formatted: Font: (Default) Arial, 10 pt, Font color: Text 1

[5] 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.

19. Most of the methods used in food testing and recommended in Codex documents are well-recognized methods which have already 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 just described, the evaluation/estimation of measurement uncertainty is considered to have already been successfully performed and any requirements regarding the measurement uncertainty are considered to have been met.

20. The *Guidelines for the Assessment of the Competence of Testing Laboratories involved in the Import and Export Control of Food* (CXG 27-1997) requires laboratories involved in the import/export of foods to comply with the general criteria set forth in ISO/IEC 17025 [1]. The ISO/IEC 17025 [1] standard requires laboratories to use validated methods; it is thus usually recommendable to use data from the interlaboratory or single-lab validation study rather than another approach such as the bottom-up approach. In Section 7.6.2 of the Eurachem guide [12], a procedure for evaluating measurement uncertainty using collaborative study data is provided. The Eurachem guide [12] also references ISO 21748 [20] 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

Measurement uncertainty has several uses including:

- Reporting of measurement results (see ISO 17025):

~~20.~~ 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 %.

~~21.~~ 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 [5].

- ~~Can be used for~~ Assessing the performance of laboratories (see ISO 13528)
- ~~Can be used~~ For the design of acceptance sampling (see ISO 3951 and GL50):
  The determination of sample size and acceptance number for inspection by attributes, and of sample size and acceptability constant for inspection by variables is based on the procedures and the sampling plans provided in ISO standards and/or Codex guidelines. This calculation has to take into account the components of measurement uncertainty.

~~22.~~ • ~~Can be used~~ For conformity assessment, whether the true value of a sample complies with a specification. ~~D~~Details of methods for conformity assessment can be found in:

  - ~~ISO10576 Statistical methods — Guidelines for the evaluation of conformity with specified requirements~~
    ~~This standard describes a method due to Holst et al. based on double sampling.~~
  - JCGM106: 2012 Evaluation of measurement data – The role of measurement uncertainty in Conformity assessment
    This guideline describes a method based on guard-banding.
  - Govindaraju and Jones 2015, Frontiers in Statistical Quality Control.
  - ISO 10576 Statistical methods — Guidelines for the evaluation of conformity with specified requirements
    This standard describes a method due to Holst et al. based on double sampling.
  -

  ~~para 37 provides reference to other procedures that do not rely on measurement uncertainty.~~

- ~~Can be used~~ For a comparison between measurement results and true/reference values (ISO 5725-6)

~~23.~~

How to report ~~The use of~~ measurement uncertainty in ~~reporting~~ test results

~~24.~~21. ~~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 %.~~

Formatted: Font: (Default) Arial, 10 pt, Bold, Font color: Auto
Formatted: Font: (Default) Arial, 10 pt, Bold
Formatted: Heading 2, Justified, Space After: 6 pt
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted: Font: 10 pt, Font color: Text 1
Formatted ...
Formatted ...
Formatted ...
Formatted: Indent: Left: 0.5", No bullets or
Formatted: Font: 10 pt, Font color: Text 1
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted: Font color: Text 1
Formatted: Indent: Left: 0.49"
Formatted: Indent: Left: 0.73"
Formatted: Indent: Left: 0.49"
Formatted: Font color: Auto, English (United Kingdom)
Formatted ...
Formatted ...
Formatted: Font color: Red
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted ...
Formatted: Font color: Red
Formatted ...
Formatted: Font color: Red
Formatted ...
Formatted ...
Formatted: Indent: Left: 0.5", No bullets or

25.22. 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 [5].

The use of measurement uncertainty in conformity assessment

26. The purpose of conformity assessment is to determine whether the true value of a laboratory sample meets the specification.

23. In accordance with ISO/IEC 17025 measurement uncertainty should be taken into consideration when decidingreported to allow for a decision as to whether a *laboratory sample* meets a specification on the basis of an analytical result – possibly? with the exception of cases where there is an immediate health hazard. RK: could this not be included above?

27.24. delete

25. However, ISO/IEC 17025 standard does not say how this information regarding measurement uncertainty is to be should be taken into account. It is clear, however, that it is not sufficient to consider measurement uncertainty as a whole but it is needed to consider method bias, laboratory bias and repeatability separately. RK: This relates to conformity assessment rather than reporting.

Examples of Situations occurring when measurement uncertainty is considered

RK: suggested text:

The figure below illustrates shows s how measurement uncertainty can affect decisions whether the true values conform to specification limits. However this figurediagram is for purposes of illustration of the principle. and [m Measurement] uncertainty intervals such as those in Figure 1 cannot be used as a valid product assessment procedure.

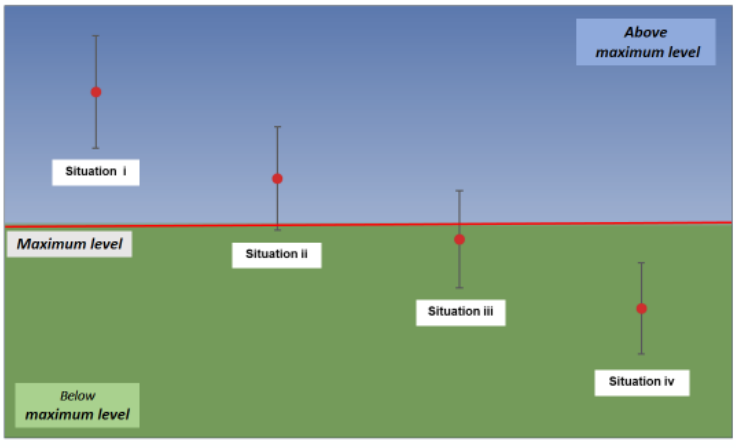
28.

The figure below illustrates situations when measurement uncertainty together with the measurement result is applied in correlation with maximum limits/specified limits. The measurement uncertainty interval used in Figure 1 and its comparison to the maximum level is not intended to be used as a valid product assessment procedure. The influence of the measurement uncertainty on the interpretation of results is illustrated in the diagram below. The diagram shows how the measurement uncertainty can be taken into account when interpreting the analytical result against a legal limit. The actual decision whether the *laboratory sample* meets the specification or not depends on the rules which the different parties involved have agreed to apply.

RK: However I think one role of this guideline is to provide guidance to valid procedures.

The same comment applies to acceptance sampling, e.g. GL83, if I was a producer I would resist attempts to reject batches based on a single result.

There is also a question of the actions taken in the event of non-conformance that also needs to be negotiated, if such negotiation is possible.



26.

Figure 1: Taking into account the expanded measurement uncertainty in the comparison of test results with a Maximum Level. For each situation, the red point represents an individual test result and the vertical bar represents the associated measurement uncertainty interval.

Formatted: Font color: Red
Formatted: Font color: Red
Formatted: Font color: Red
Formatted: Font color: Red, Strikethrough
Formatted: Font color: Red, Strikethrough
Formatted: Font color: Red
Formatted: Font color: Red
Formatted: Font: (Default) Arial, 10 pt, Bold
Formatted: Normal, Indent: Left: 0.25", Don't add space between paragraphs of the same style, No bullets or numbering, Adjust space between Latin and Asian text, Adjust space between Asian text and numbers
Formatted: Font color: Red
Formatted: Font color: Red
Formatted: Font color: Red
Formatted: Font color: Red
Formatted: Font color: Red
Formatted: Font color: Red
Formatted: Font: (Default) Arial, 10 pt, Bold, Font color: Red
Formatted: Normal, Indent: Left: 0.25", Don't add space between paragraphs of the same style, No bullets or numbering, Adjust space between Latin and Asian text, Adjust space between Asian text and numbers
Formatted: Font color: Red, Strikethrough
Formatted: Font: (Default) Arial, 10 pt, Font color: Red, Strikethrough
Formatted: Font color: Red
Formatted: Normal, Left, Space After: 0 pt, No bullets or numbering, Adjust space between Latin and Asian text, Adjust space between Asian text and numbers
Formatted: Font color: Red
Formatted: Font: (Default) Arial, 10 pt
Formatted: No bullets or numbering

27. **Situation i**

28. The analytical result minus the expanded measurement uncertainty exceeds the maximum level. The ~~decision~~conclusion is that it lies above the specification. ~~RK: should these decisions be included? Also, if Raj's procedure is used then the decisions are not made using intervals but [I suppose] on a maximum allowable probability [that the true value of the same exceeds the limit].~~

29. **Situation ii**

30. The analytical result exceeds the maximum level by less than the expanded measurement uncertainty. The interpretation of this result and the actual decision depend on existing agreements between the trading partners. ~~RK: Maybe true, somewhat impractical. Surely the guidelines should give general advice.~~ The standard interpretation here is the outcome is inconclusive, a decision cannot be made to either declare conformity or to declare non-conformity ~~[in case somebody is tempted to make a decision one way or another, going against the science.~~

31. **Situation iii**

32. The analytical result is less than the maximum level by less than the expanded measurement uncertainty. The interpretation of this result and the actual decision depend on existing agreements between the trading partners. The standard interpretation here is the outcome is inconclusive, a decision cannot be made to either declare conformity or to declare non-conformity. ~~RK: an inconclusive outcome~~

33. **Situation iv**

34. The analytical result is below~~less than~~ the maximum level by more than the expanded measurement uncertainty. The decision is that it lies below the specification. ~~RK: below if it a maximum, "within" might be a more general word.~~

35. Note: The measurement uncertainty interval used in Figure 1 and its compaarison to the maximum level is not intended to be used for lot acceptance sampling or conformity assessment but to illustrate the interrelation of the analytical test result and its measurement uncertainty with regard to a maximum level.

36. Note: It is important to note that each of the measurement uncertainty intervals displayed in Figure 1 are obtained from the measurement uncertainty standard deviation as evaluated *at the corresponding measured value*. If the measurement uncertainty is proportional to the measured value, a possible consequence is that the measured value may have to lie *considerably* higher than the Maximum Level (denoted ML in the following) in order for the lower limit of the associated measurement uncertainty interval to lie above ML (*Situation i*). The following example will clarify this point. If the measurement uncertainty interval is obtained from a 30 % relative reproducibility standard deviation value, then the measured value would have to lie above 2.5 times ML in order for the lower limit of the uncertainty interval to lie above ML. (This follows from: X-2*0.3X>ML; X(1-2*0.3)=0.4X>ML; X>2.5 ML; ML/0.4=2.5) An alternative approach (see e.g. [21]) consists in evaluating the measurement uncertainty *at ML*, and to consider that *Situation i* occurs when an individual test result lies above $ML + 2 \cdot u_{ML}$ – where u_{ML} denotes the standard deviation characterizing the dispersion *at ML*. If, as above, the measurement uncertainty interval is obtained from a 30 % relative reproducibility standard deviation value, a test result would only have lie above $(1 + 2 \cdot 0.3) \cdot ML = 1.6 \cdot ML$ (rather than $2.5\ ML$) in order for the lower limit of the associated measurement uncertainty interval to lie above ML (*Situation i*).

37. Note: The implications of situations *i* to *iii* in the case of testing MRL compliance are extensively discussed in the *Guidelines on estimation of uncertainty of results* (CXG 59-2006). 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 is exceeded or that a compliant test result has been obtained, 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 the guideline CXG 83-2013 "Principles for the Use of Sampling and Testing in International Food Trade". It is stated 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".

~~29. **Procedures for conformity assessment**~~

~~30.~~38. ~~Details of methods for conformity assessment can be found in:~~

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font color: Red

Formatted: Font: Bold

Formatted: Normal, No bullets or numbering

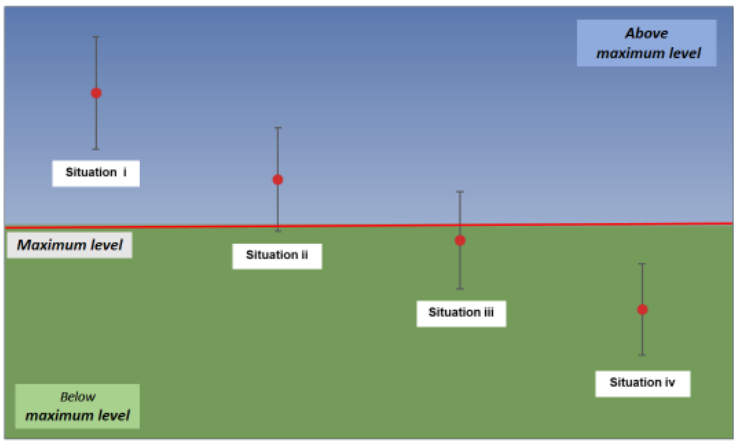
Formatted: Font: (Default) Arial, 10 pt, Bold, Font color: Text 1

- ~~ISO10576 Statistical methods — Guidelines for the evaluation of conformity with specified requirements~~
  ~~This standard describes a method due to Holst et al. based on double sampling.~~
- ~~JCGM106: 2012 Evaluation of measurement data – The role of measurement uncertainty in Conformity assessment~~
  ~~This guideline describes a method based on guard banding.~~

~~• RK: As above, for tidiness I'd like to absorb this para in the text under the conformity assessment bullet point.~~

~~31. There are other techniques, such as:~~

- ~~Fractional Acceptance Numbers for Lot Quality Assurance and Control Charting~~
- ~~K. Govindaraju & G. Jones~~
- ~~Frontiers of Statistical Quality Control 11. Springer (1975) Sven Knoth & Wolfgang Schmid, Editors.~~



~~*Figure 1: Taking into account the expanded measurement uncertainty in the comparison of test results with a Maximum Level. For each situation, the red point represents an individual test result and the vertical bar represents the associated measurement uncertainty interval.*~~

~~**Situation i**~~

~~The analytical result minus the expanded measurement uncertainty exceeds the maximum level. The decision is that it lies above the specification.~~

~~**Situation ii**~~

~~The analytical result exceeds the maximum level by less than the expanded measurement uncertainty. The interpretation of this result and the actual decision depend on existing agreements between the trading partners.~~

~~**Situation iii**~~

~~The analytical result is less than the maximum level by less than the expanded measurement uncertainty. The interpretation of this result and the actual decision depend on existing agreements between the trading partners.~~

~~**Situation iv**~~

~~The analytical result is less than the maximum level by more than the expanded measurement uncertainty. The decision is that it lies below the specification.~~

~~Note: The measurement uncertainty interval used in Figure 1 and its comparison to the maximum level is not intended to be used for acceptance sampling or conformity assessment but to illustrate the interpretation of the analytical test result and its measurement uncertainty with regard to a maximum level.~~

~~Note: It is important to note that each of the measurement uncertainty intervals displayed in Figure 1 are obtained from the measurement uncertainty standard deviation as evaluated *at the corresponding measured value*. If the~~

Formatted: Font color: Red

Formatted: Indent: Left: 0.5", No bullets or

Formatted: Normal, Indent: Left: 0.5", No bullets or numbering

Formatted: Font: (Default) Arial, 10 pt

measurement uncertainty is proportional to the measured value, a possible consequence is that the measured value may have to lie *considerably* higher than the Maximum Level (denoted ML in the following) in order for the lower limit of the associated measurement uncertainty interval to lie above ML (*Situation i*). The following example will clarify this point. If the measurement uncertainty interval is obtained from a 30 % relative reproducibility standard deviation value, then the measured value would have to lie above 2.5 times ML in order for the lower limit of the uncertainty interval to lie above ML. (This follows from $x - 2 \cdot u = 2.5\,ML - 2 \cdot 0.3 \cdot 2.5\,ML = ML$.) An alternative approach (see e.g. [21]) consists in evaluating the measurement uncertainty *at ML*, and to consider that *Situation i* occurs when an individual test result lies above $ML + 2 \cdot u_{ML}$ — where u_{ML} denotes the standard deviation characterizing the dispersion *at ML*. If, as above, the measurement uncertainty interval is obtained from a 30 % relative reproducibility standard deviation value, a test result would only have lie above $(1 + 2 \cdot 0.3) \cdot ML = 1.6 \cdot ML$ (rather than $2.5\,ML$) in order for the lower limit of the associated measurement uncertainty interval to lie above ML (*Situation i*).

Note: The implications of situations *i* to *iii* in the case of testing MRL compliance are extensively discussed in the *Guidelines on estimation of uncertainty of results* (CXG 59-2006). 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 is exceeded or that a compliant test result has been obtained, 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 the guideline CXG 83-2013 "Principles for the Use of Sampling and Testing in International Food Trade". It is stated 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".

The use of measurement uncertainty in (given) sampling plans

32. In the *General Guidelines on Sampling* (CXG 50 - 2004), it is stated that "Codex Methods of Sampling 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". The determination of sample size and acceptance number for inspection by attributes, and of sample size and acceptability constant for inspection by variables is based on the procedures and the sampling plans provided in ISO standards and/or Codex guidelines. While measurement uncertainty may be considered irrelevant for inspection by attributes, its impact on inspection by variables must be accounted for. In the relevant ISO standards, it is assumed that measurement uncertainty is negligible. In the introduction to ISO 3951-1:2013, for instance, it is stated that "[i]t is assumed in the body of this part of ISO 3951 that measurement error is negligible […]".

33. Nonetheless, procedures are provided in ISO 3951-1 and ISO 3951-2 for the case that measurement uncertainty is not negligible. More specifically, in Annex B of ISO 3951-1 [22] and Annex P of ISO 3951-2 [9], procedures for increasing the sample size are presented in the case that the measurement uncertainty σ_m is greater than 10 % of the process standard deviation σ. It is important to note that these procedures are only applicable if "the measurement method is unbiased, i.e. the expected value of the measurement error is zero". In other words, the "measurement uncertainty" σ_m consists mainly of the repeatability component[6].

34. The following examples illustrate how sample size is affected by non-negligible measurement uncertainty in inspection by variables.

35. The measurement uncertainty is to be considered for For **inspection by variables (packages),** if the measurement uncertainty σ_m is non-negligible (greater than one tenth of the sampling standard deviation s or process standard deviation σ), the sample size n must be increased to either $n^* = n \cdot (1 + \gamma^2)$ where $\gamma = \sigma_m/\sigma$ (the process standard deviation σ is known) or $n^* = n \cdot (1 + \tilde{\gamma}^2)$ where $\tilde{\gamma}$ is an estimated upper bound of $\gamma = \sigma_m/\sigma$ (the process standard deviation σ is unknown). The acceptability constant k remains unchanged. For further details, see Annex P in [9]. This procedure is only admissible as long as the laboratory bias is negligible.

36. Example: A lot of 500 items of pre-packaged mineral water is assessed for sodium content. If the measurement uncertainty is not taken into consideration, for an agreed AQL of 2.5 % (maximum concentration 200 mg/L), general inspection level II (default level) and a sample of 30 items should be collected for assessment, (ISO 3951-2, Annex A, Table A1 and Annex B, Table B1). The production is well under control and the control charts give a process standard deviation σ of 2 mg/L. The measurement uncertainty standard deviation σ_m is 1 mg/L and is thus non-negligible. With $\gamma = \sigma_m/\sigma = 0.5$ and $1 + \gamma^2 = 1.25$ the sample size must be increased to 38.

37. If the measurement uncertainty is dominant in the case of **inspection for variables (bulk)**, i. e. when both the standard deviation of the sampling increment σ_s and the standard deviation between test samples σ_p are far less (one tenth or less) than the measurement standard deviation σ_M, which must be known and stable, the measurement

Formatted: Font: Bold

[6] Admittedly, it would be desirable to provide a corresponding procedure for the case that the bias components of measurement uncertainty are nonzero.

uncertainty has an effect on the number of test samples per composite sample n_I as well as the number of measurements per test sample n_M. For further details refer to see Annex B in [18]. For **inspection by variables (bulk)** [10], a *dominant* measurement uncertainty has an effect on the number of test samples per composite sample n_I as well as the number of measurements per test sample n_M. The measurement uncertainty is dominant when both the standard deviation of the sampling increment σ_I and the standard deviation between test samples σ_P are far less (one tenth or less) than the measurement standard deviation σ_M, which must be known and stable, see Annex B in [18]. The number of sample increments per composite sample n_I remains unchanged, no matter whether the measurement uncertainty has no influence on the number of sample increments per composite sample n_I is It remains unchanged, no matter whether the measurement uncertainty is dominant or not.dominant or not. For further details refer to Annex P in [9]. Obviously, a decrease in the measurement uncertainty by the improvement of the method performance could significantly reduce the analytical workload. It should be noted the mass of the increments should be sufficiently large to offset the fundamental sampling error.

38. Example: A lot of wheat bulk material is to be assessed for cadmium content (maximum concentration e.g. 0.1 mg/kg). Since cadmium is a ubiquitous contaminant, cadmium concentrations in the lot are homogeneous, giving very low standard deviations σ_I and σ_P, each estimated as 0.002 mg/kg. Since the concentrations are very low, a relatively high measurement uncertainty is obtained. The corresponding standard deviation σ_M = 0.02 mg/kg is thus dominant. The number of increments per composite sample is n_I = 6, the number of test samples per composite sample is n_I = 1 and the number of measurements per test sample is n_M = 2 (yielding a product $n_I \cdot n_M$ = 2, which can be interpreted as a measure of the analytical workload). The combined overall standard deviation σ_0 is calculated as $\sqrt{\frac{n_I - n_M}{n_I}\sigma_I^2 + n_M\sigma_P^2 + \sigma_M^2} \approx 0.02$ mg/kg and divided by the discrimination interval D (difference between agreed risk-based acceptance and rejection levels, here assumed to be 0.01 mg/kg) in order to obtain the relative standard deviation $d_0 = \sigma_0 / D \approx 2$. In Table B1 in Annex B of [18], this relative standard deviation d_0 is used determine the adjusted number of test samples per composite sample n_I = 6 as well as the adjusted number of measurements per test sample n_M = 3 (yielding a product $n_I \cdot n_M$ = 18). As can be seen, additional laboratory work resulting in a decrease in the measurement uncertainty could significantly reduce the analytical workload. In particular, the mass of the test portions should be large enough to reduce the fundamental sampling error.

Literature

[1] ISO/IEC 17025:201705 General requirements for the competence of testing and calibration laboratories
[2] Jülicher, B. Gowik, P. and Uhlig, S., Analyst, February 1998, Vol. 123 (173–179)
[3] Uhlig et al., Accred Qual Assur (2015) 20:75–83
[4] ISO 10576-1:2003, Statistical methods -- Guidelines for the evaluation of conformity with specified requirements -- Part 1: General principles
[5] JCGM 106:2012, Evaluation of measurement data – The role of measurement uncertainty in conformity assessment
[6] CAC/GL 72-2009, Guidelines on analytical terminology
[7] ISO/IEC Guide 99:2007, International vocabulary of metrology — Basic and general concepts and associated terms (VIM), 2007, also known and available as JCGM 200:2012, JCGM 2012 www.bipm.org
[8] ISO 2859-1:1999, Sampling procedures for inspection by attributes -- Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection
[9] ISO 3951-2:2013, Sampling procedures for inspection by variables -- Part 2: General specification for single sampling plans indexed by acceptance quality limit (AQL) for lot-by-lot inspection of independent quality characteristics
[10] ISO 6498:2012 Animal feeding stuffs -- Guidelines for sample preparation
[11] ISO 3534-1:2006(en), Statistics — Vocabulary and symbols — Part 1: General statistical terms and terms used in probability
[12] EURACHEM / CITAC Guide CG 4, Third Edition (2012) Quantifying Uncertainty in Analytical Measurement
[13] ISO/IEC Guide 98-3:2008, Uncertainty of measurement - Part 3: Guide to the expression of uncertainty in measurement (GUM:1995), 2008; also known and available as JCGM 100:2008, JCGM 2008 www.bipm.org
[14] Eurolab technical Report No. 1/2007. Measurement Uncertainty Revisited: Alternative Approaches to Uncertainty Evaluation. Available as a free download from www.eurolab.org
[15] Nordtest TR 537 ed. 3.1 (2012) Handbook for Calculation of Measurement Uncertainty in Environmental Laboratories
[16] ISO 2859-1:1999 + Cor. 1:2001 + Amd.1:2011 Sampling procedures for inspection by attributes -- Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection
[17] ISO 3951-2:2010 Sampling procedures for inspection by variables -- Part 2: General specification for single sampling plans indexed by acceptance quality limit (AQL) for lot-by-lot inspection of independent quality characteristics, revised in 2013 as ISO 3951-2:2013.
[18] ISO 10725:2000: Acceptance sampling plans and procedures for the inspection of bulk materials
[19] ISO 3534-2:2006 Statistics – Vocabulary and symbols – Part 2: Applied statistics
[20] ISO 21748:2017 Guidance for the use of repeatability, reproducibility and trueness estimates in measurement uncertainty evaluation
[21] ISO 11843-2:2006 Capability of detection – Part 2: Methodology in the linear calibration case
[22] ISO 3951-1:2016 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

APPENDIX II

DRAFT INFORMATION DOCUMENT EXAMPLE PROCEDURES FOR ESTIMATING MEASUREMENT UNCERTAINTY

(for information only)

Introduction

1. Every measurement comes with a particular imprecision. The quality of a measurement result is greatly improved if it comes with the estimation of a measurement uncertainty.

2. Measurement uncertainty is subject to the operator, the instrument used, the environment and any other sources, which may influences the measurement by a certain degree. When the uncertainty in a measurement is evaluated and stated, confidence in data obtained.

3. Such uncertainties can be evaluated and calculated upon by analysis of the measurement process. In practise, the total measurement uncertainty is usually calculated by combining several uncertainty contributions. There are established rules on how to calculate measurement uncertainty and guidelines are published to aid the undertaking.

4. The aim of this information document is to give some examples on the procedures for estimating measurement uncertainty and provide the reader with some references on the general topic.

Measurement procedures

5. In analytical chemistry, each measurement procedure can be subdivided into subsampling, subsample preparation, sample preparation, clean-up, calibration, quantification of the analyte and finally data analysis with evaluation of the measurement result [1]. Figure 1 visualises the single steps:

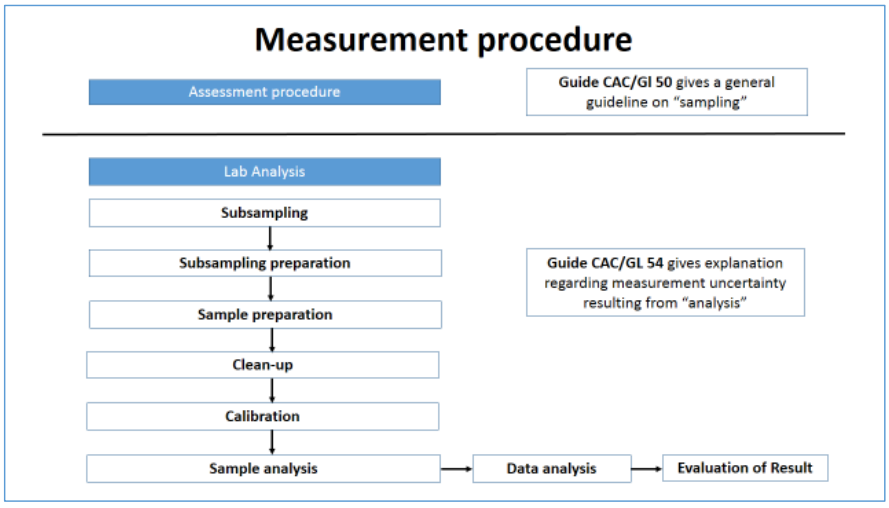


Figure 1: General steps for measurement procedure

Subsampling and subsampling preparation: A mostly prescribed procedure of taking parts from each of the samples, which had been taken from the lot according to the particular sampling plan.

Sample preparation: Most of the subsamples to be measured require treatment before they are going to be analyzed. Freezing, homogenization, dilution and extraction are only some of procedures mentioned. In many cases, analytes have to be converted into measurable compounds (e.g. a colorless sample is converted by addition of defined substances into a colored sample, which can be detected by UV-VIS spectroscopy). Due to possible decomposition or incomplete reaction, that "indirect" method might lead to loss of material or information. Additionally, contamination might also take place at any stage of the procedure and has to be avoided and controlled by analysing blank samples in parallel.

Clean up: extraction, concentration or dilution of the analyte with subsequent clean up procedures to avoid matrix overload.

Calibration of analytical systems: In most cases, analyte-response curves need to be established from which the amount of analyte in question can be determined. Data values need to be confirmed by inclusion of test samples with known concentrations of analytes of interest, e.g. certified reference materials. As a consequence, the purity of the reference material and the any further prepared solution are influencing the measurement uncertainty.

Sample measurement: When the sample is measured, interferences remaining in the final extract (e.g. reagents, matrix) may occur. The experience of the operators can have an impact on the measurement result. Instrument settings as well as the limited stability of the measurement device might cause various results and should be taken into account.

Data analysis: Processing algorithms (mathematical models, which are used to evaluate the results e.g. regression functions used for calibration) might differ from instrument to instrument.

Computational effects: Rounding as well as averaging can lead to inaccuracies in the final result.

Possible Uncertainty Sources

Subsampling:	Representative selection of parts of a lot sample
Storage/transportation:	special storage or shipping conditions with changing environmental condition
Instrumental effects:	detection limits, temperature, gas-pressure controller, gas flow regulator, auto-sampler with possible carry-over effects, time effects (measurement at various time points), also performing equipment maintenance and qualification: IQ (Installation Qualification), OQ (Operation Qualification)
Purity/homogeneity:	partly-inhomogeneous samples, impure substances e.g. reagents and current reference standards, solutions or other used products
Measurement conditions:	Measurement of volumes: volumetric glassware effects for preparing solutions, various masses from weights taken at different times; temperature effects; environmental changes e.g. humidity
Computational effects:	inaccurate calibration models, fitting procedures, rounding procedures
Blank correction:	Like sample, correction for Blank is necessary
Random effects:	By chance for all determination, should be included as a matter of course
Systematic effects:	Operator (experienced, unexperienced)

Table 1: Possible uncertainty sources

6. It might be noticed that not all possible sources of uncertainty will equally account for the uncertainty. In practice, it is likely that only a small number of all possible sources contribute significantly to the uncertainty. Unless there is a large number of contributions, components that are less than one third of the largest need not be evaluated in detail. [1] (EURACHEM step3, 7.2.2.)

Procedures for estimating Measurement Uncertainty

7. Estimation of measurement uncertainty can be conducted by two main strategies:

The “bottom-up” approach, which determines the measurement uncertainty component by component. Every single source of error/uncertainty is separately estimated.

The “top-down” approach where the measurement uncertainty is estimated via error/uncertainty sources based on method performance data, e.g. validation studies, PTs etc.

These approaches refer to different situations:

Modelling (Classical ISO GUM)

- Uncertainty of an individual result of a measurement can be obtained, linked to a particular sample

Single-lab validation

- Typical uncertainty of results obtained using a defined procedure in the laboratory

Interlaboratory validation

- Uncertainty of results obtained using the same procedure in different laboratories

8. The modelling approach calculates the uncertainty for the individual result, on one concrete sample, for one situation. The single-lab validation approach is not linked to a particular sample; it is linked to a procedure. The

interlaboratory approaches obtaining uncertainty results from the same procedure used in different laboratories. This type of approach gives some general uncertainty which can be expected when used in different laboratories.

9. Whichever of these approaches are going to be used, most of the information to calculate the measurement uncertainty is already available from previous studies done in order to validate existing or new methods, QA/QC data or studies, which has been carried out to test laboratory performances [2].

10. Usually there is a lot of data available from proficiency testing data (PT), control chart data, calibration data from instruments, in-house validation data etc. The question remains, how to make the maximum use of these collected data to estimate the measurement uncertainty?

11. All starts with the definition of the measurand. Specifying a measurand is per se not an easy target. A clear definition of a.) an analyzed item or b.) a studied parameter is needed. For example, if the mass fraction of a chemical is to be measured in a batch of two kilo gramms or in a piece of a single apple. It also makes a difference if a total amount of a heavy metal ion should be determined or the amount of its water-soluble salt. If the measurand has been clearly defined, the uncertainty operation can be distinguished between a “single laboratory” approach and “interlaboratory” approach.

12. Single laboratory approaches can be precede by model base or non-model base whereas in the first case component by component is evaluated. This type of practice is laid out in the ISO GUM and is considered as the standard approach for measurement uncertainty. Here the procedure is carefully analyzed, uncertainty sources are looked at component-by-component and then separately quantified. On the other hand, there is the non-model single laboratory described by Nordtest TR537 [3] as well as a single laboratory approach, which includes an orthogonal design of experiments. This type of configuration is based on a statistical model [4] [5].

13. Interlaboratory approaches differ from single laboratory approaches. The interlaboratory approaches examine accumulated data from many laboratories, where each single laboratory does not contribute as much value to the final result. The situation or data from a single laboratory is not looked at and therefore this particular procedure is not highly recommended to establish measurement uncertainty. However, if the uncertainty has to be established for the first time or to preliminary find out more or less what the uncertainty will be this type of procedure can be used. For this purpose, ISO 13528:2015 on “Statistical methods for use in proficiency testing by interlaboratory comparison” describes procedures for robust data analysis [6].

14. In order to consider as many analytical situations as possible, the procedures are developed for different types of analytical methods (standard or in-house methods). Multi-factor experimental designs, analyzed by ANOVA, and Propagation of distributions using a Monte Carlo method are not included in this document but reference to literature is provided [7] [8] [4] [5].

15. This information document does not provide exemplary numerical calculations. It is assumed, that the concerned laboratories do have much experience on application of formulas.

Example Procedures for Estimating Measurement Uncertainty

16. The following procedures for estimation of measurement uncertainty should be regarded as practical examples, which are applicable in many day-to-day situations. They are not prescriptive. To achieve acceptance by both trading partners, the concepts are strictly based on internationally recommended guidelines and standards (JCGM 100:2008: Evaluation of measurement data - Guide to the expression of uncertainty in measurement (GUM) [9], the EURACHEM / CITAC Guide CG 4: Quantifying Uncertainty in Analytical Measurement [1], EURACHEM / CITAC Guide: Use of uncertainty information in compliance assessment [10] and ISO Protocols [11] [12] [13] [14] [15].

17. The development of examples cannot be exhaustive and in special situations, other rational procedures might be applied by agreement. Nevertheless, they do not apply when legal specifications or other internationally accepted guidelines define special rules for the estimation of the measurement uncertainty (e.g. the empirical Thomson-Horwitz equation). In particular, for pesticide residues, the procedures described below do not infringe on provisions in the Guidelines on estimation of uncertainty of results (CXG 59-2006).

18. Measurement uncertainty, which is a parameter of the test result, is based on precision data of the method, taking into account the steps of analysis that may include sub-sampling, sample processing and instrumental analysis. The uncertainty components are combined according to the error propagation rules. Basically, N uncertainty standard deviations $s_{1...N}$ (or relative standard deviations i.e. coefficients of variation $cv_{1...N}$) of the statistical analysis can be combined to the total standard uncertainty u (or relative total standard uncertainty u_{rel}) (GUM 5.1.2, 5.1.5, 5.1.6) :

$u = \sqrt{s_1^2 + s_2^2 + \ldots . + s_N^2}$ or $u_{rel} = \sqrt{cv_1^2 + cv_2^2 + \ldots . + cv_N^2}$ *)

*) The formulas refer to measurands given by the sum and/or the difference of parameters (left) or given by the product and/or the quotient of parameters (right). Since in practice, most of the analytical measurands are given by formulas with products and/or quotients of parameters, in the following text the second formula will be used. For simplicity, the parameters are regarded as non-correlated.

19. This provides the practical advantage that particular precision data from Single-Laboratory method validation or from inter-laboratory method validation (after proving fitness for purpose of the particular test laboratory by verification of that precision data) can be used in combination.

20. The following procedures are ordered by the particular type of the analytical method:

Type I:

- Defining Methods with additional consideration of subsample inhomogeneity and sample preparation variability

Type II:

- Rational Methods (Reference Methods)

Type III:

- Single Laboratory validated Methods (Alternative Approved Methods)
- Combination of repeatability precision of all single steps of analysis
- Precision estimated by series of analysis
- ISO 5752-2 and 5752-3 Approach
- Duplicate Approach

Type IV:

- Tentative methods: Ad-hoc Methods

Type I:

21. For Standard methods, the uncertainty is established utilising appropriate validation including precision data. Generally, these data are based on extensive inter-laboratory method validation, mostly performed according to the IUPAC/ISO/AOAC International Harmonized Guideline [16], ISO 5725-6 (currently under revision) or the AOAC International Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis [17].

22. A basic assumption underlying ISO 5725-1 (currently under revision) is that, for a standard measurement method, repeatability will be not be the same for all laboratories applying the standard procedure. However, the repeatability will be at least approximately the same, so that it is permissible to establish one common average repeatability standard deviation s_r, which will be applicable to any laboratory, even if this is not 100% corresponding to the repeatability of the individual laboratory. Any laboratory should be carrying out a series of measurements under repeatability conditions and verify that the average repeatability standard deviation is applicable under given conditions (ISO 5725-6 (currently under revision)).

23. The reproducibility standard deviation s_R of the standard method is obtained by combining s_r with the between-laboratory standard deviation s_L (ISO 5725-2 (currently under revision)).

Defining Methods with additional consideration of subsample inhomogeneity and sample preparation variability

24. Defining methods achieve comparability between laboratories measuring the same material with no intent to obtain an absolute measure of the true amount of analyte present. Corrections for method bias or matrix effect are ignored by convention.

25. If collaborative trial data are available, at least the repeatability should be evaluated in the particular laboratory and proven to be comparable to that s_r predicted by the collaborative trial and documented in the method i.e. the repeatability standard deviation should be less or equal s_r (EURACHEM Example A6 [1]).

26. A priori, no bias contribution must be considered and it is therefore appropriate to use the relative reproducibility standard deviation (i.e. the coefficient of variation) CV_R values from the collaborative trial or method publication as relative standard uncertainty u_{rel} within the tested range of analyte levels (EURACHEM 7.6.3 [1]).

27. Collaborative trials provide homogenized mostly stabilised material and hence do not cover physical preparation steps (e.g. grinding, drying) of the material. The uncertainty contributions of that analytical part should

be additionally taken into consideration (EURACHEM 7.6.1 [1]), provided that the contribution is significant (i.e. >1/3 CV_R (EURACHEM 7.2.2)).

28. In the case of significant laboratory sample inhomogeneity, the uncertainty contribution of subsampling should be considered. The significance might be assessed by using a homogeneity check like ISO 13528 [6], Annex B by comparing the relative between-subsamples standard deviation cv_s with the relative standard deviation for proficiency assessment CV_σ (σ is used for the estimation of the z-scores) of the standard method. The laboratory sample may be considered to be adequately homogeneous if, $cv_s \leq 0.3\ CV_\sigma$.

29. The between-subsamples standard deviation s_s might be estimated by the procedure given in ISO 13528, Annex B1 and using the formula given in Annex B3. That duplicate test gives information also on the uncertainty contribution of the physical preparation procedure:

30. Select a number g of the subsamples from the laboratory sample at random, where g ≥10.

- Prepare two test portions from each subsample using techniques appropriate to the test material to minimize between-test-portion differences.
- Taking the 2g test portions in a random order, obtain a measurement result on each, completing the whole series of measurements under repeatability conditions.
- Calculate the general average $\bar{\bar{x}}$

$$\bar{\bar{x}} = \frac{\sum_{t=1}^{g} \bar{x}_t}{g} \qquad \text{with} \qquad \bar{x}_t = \frac{x_{t,1} + x_{t,2}}{2}$$

- Calculate the standard deviation s_x of sample averages

$$s_x = \sqrt{\frac{\sum_{t=1}^{g} (\bar{x}_t - \bar{\bar{x}})^2}{g - 1}}$$

- Calculate the within-subsamples standard deviation s_w which is a measure of the physical preparation uncertainty

$$s_w = \sqrt{\frac{\sum_{t=1}^{g} w_t^2}{2g}} \qquad \text{with} \qquad w_t = |x_{t,1} - x_{t,2}|$$

- Calculate the between-subsamples standard deviation s_s with the factor ½ on s_w due to the mean of duplicate analyses being used

$$s_S = \sqrt{s_x^2 - \frac{s_W^2}{2}}$$

- and the relative standard deviation of sample inhomogeneity

$$cv_S = \frac{s_S}{\bar{x}}$$

In case that the sample inhomogeneity is significant ($cv_s > 0.3\ CV_\sigma$), the relative standard measurement uncertainty u_{rel} is given by the combination:

$$u_{rel} = \sqrt{cv_R^2 + cv_S^2}$$

Taking into account the uncertainty contribution of sample preparation (the standard deviation is divided by √2 to correct from a standard deviation for pairwise differences to the standard uncertainty for single values),

$$cv_P = \frac{1}{\sqrt{2}}\frac{s_w}{\bar{x}}$$

the relative standard measurement uncertainty u_{rel} is given by the combination:

$$u_{rel} = \sqrt{cv_R^2 + cv_S^2 + cv_P^2}$$

Note: In formulas for calculating the analytical result, the influence of subsampling differences due to inhomogeneity and preparation variability can be implemented as factors, which are dispersed around 1 (EURACHEM A4.3).

Type II:

Rational Methods (Reference Methods)

31. For rational standard methods, trueness is an issue, which should be considered in the estimation of measurement uncertainty. The current procedure applies to the situation where no bias is to be taken into account. But this assumption should be proven by appropriate recovery experiments.

32. For many rational standard methods, certified reference materials are supplied. As an alternative, samples can be spiked with a known level of the analyte (with preference of matrices, which do not contain the analyte), bearing in mind the different behaviour of the spiked substance and the native counterpart.

33. In a first step, from n recovery experiments on certified reference material or homogenized spiked material (e.g. homogenized samples are split and one portion spiked) with the reference concentration x_{ref} , the found concentrations of the analyte x_i , and the bias b_i , the average laboratory bias $\bar{b}$ is estimated

$\bar{b} = \frac{1}{n}\sum_{i=1}^{n} b_i$ with $b_i = x_i - x_{ref}$

and compared with the standard uncertainty u at the reference concentration (by multiplying u_{rel} with the concentration of the analyte) combined with the certified uncertainty of the reference material or the experimental uncertainty of spiked material estimated by homogeneity tests u_{ref} (see Defining Methods). Laboratory bias can be neglected if

$$|\bar{b}| \leq 2\sqrt{\left(\frac{u^2}{n}\right) + u_{ref}^2}$$

34. Otherwise, the bias is significant (EURACHEM 7.16 [1]) and the analytical result might be corrected for the bias, making due allowance for the uncertainty of the correction. In that case, the standard deviation s_B of the average bias is given by

$$s_B = \frac{1}{\sqrt{n}}\sqrt{\frac{\sum_{i=1}^{n}\left(b_i - \bar{b}\right)^2}{n-1}}$$

35. In case that the matrix might have an impact on the bias, the recovery experiments should be applied on samples from different matrices and the uncertainty contribution of that particular matrix, which corresponds to the sample should be used.

36. Note: It should be avoided to take the effect of bias (this is not the uncertainty of bias) into account by enlarging the “uncertainty” assigned to the result instead of correcting for bias. Evaluating the uncertainty of a measurement result should not be confused with assigning a safety limit to some quantity (Guide to the expression of uncertainty in measurement (GUM), 6.3.1).

Type III:

Single-laboratory Validated Methods (Alternative Approved Methods)

37. Contrary to standard methods, for Single-laboratory validated methods no published standard precision data are available. Therefore, they are subjects of extensive validation procedures. Despite of ad-hoc situations, the validation provides precision data. Ad-hoc methods are methods established to carry out exploratory studies in the short term, or for a short run of test materials. Such methods are typically based on standard or well-established methods within the laboratory, but are adapted substantially; e.g. to study a different analyte [1].

38. In case that the Single-laboratory validated method is a modification of a corresponding standard method, the estimation of precision should focus on the uncertainty contributions of that modification. The uncertainty contributions should be compared to the relative reproducibility standard deviation (i.e. coefficient of variation) CV_R values from the collaborative trial or standard method publication. If the uncertainty contribution of modifications is negligible, it is appropriate to use CV_R as relative standard uncertainty u_{rel} and to proceed according to Procedures 4.1.

39. There are two general approaches to estimate the precision:

- The combination of the repeatability precision of all single steps of analysis (e.g. weighing, drying, extracting, diluting and analytical measurement) with the involved calibrations and other uncertainty sources (e.g. purity of reference standards, experience of test personnel)
- Precision estimated by series of analysis as far as possible over an extended time period allowing natural variation of all impact factors.

40. In practice, a combination of these types is usually necessary and convenient. Therefore, a variance component model offers the possibility of covering various components of the overall uncertainty within one validation experiment, including a randomised sampling scheme [5].

Combination of the repeatability precision of all single steps of analysis

41. The uncertainty components associated with N potential sources of uncertainty are identified, quantified as standard deviations u_i, multiplied with sensitivity coefficients c_i, and combined (GUM 5.1.3):

$$u = \sqrt{\sum_{i=1}^{N} c_i \cdot u_i^2}$$

42. Note: In the case that the different components are not statistically independent, corresponding correlation factors are to be introduced.

43. The sources are for example:

- Standard substances (certified uncertainty/purity)
- Physical/chemical variability (extraction, derivatisation, stoichiometry)
- Application of measuring devices for preparation of the test samples (balances, pipettes, thermometers etc.)
- Application of analytical instruments (stability, calibration, contamination etc.)
- Different experience of staff

44. The procedure begins with the critical reflection of the formula of the measurand i.e. the relationship between the result and the input values. All parameters are to be checked for their uncertainty relevance.

45. Therefore, for example, the uncertainty of the sample preparation is separated into the uncertainties of the individual steps of weighing, homogenizing, drying, extracting, diluting etc., which are to be combined.

46. The uncertainty of weighing itself, for example, is estimated from the separate contributions of calibration and traceability (including certified uncertainty of the weights) and the uncertainty of the reading (analogue/digital-display).

47. Obviously, the subject of this type of estimation is too complex to be sufficiently described in the current paper. Therefore, for further information, reference is made to the JCGM 100:2008: Evaluation of measurement data — Guide to the expression of uncertainty in measurement (GUM) and the EURACHEM / CITAC Guide CG 4: Quantifying Uncertainty in Analytical Measurement.

Precision estimated by series of analysis

48. According to ISO 5725-3, precision estimated in one laboratory is the so-called intermediate precision measure, which is usually smaller than the reproducibility standard deviation based on inter-laboratory method validation and hence more appropriate for the individual laboratory. That intermediate precision condition of measurement includes the same measurement procedure, same location, and replicate measurements on the same or similar objects over an extended period of time, but may include other conditions involving changes like new calibrations, calibrators, operators, and measuring systems.

49. Estimation of precision should take into account all parts of the analysis, which basically would be involved in case of participation on a corresponding inter-laboratory validation of a standard method. That comprises at least the extraction/derivatisation/digestion procedures, which could possibly lead to recovery variation. The complete measurement process also includes calibration and traceability.

50. A typical test sample containing an appropriate amount of analyte (e.g. homogenized and dried or processed to assure stability of the matrix and analyte(s)) might be analyzed several times over a period of time, using different analysts and equipment where possible (e.g. the results of measurements on quality control samples) thus verifying Single-Laboratory reproducibility conditions (EURACHEM 7.7.2) or intermediate precision conditions.

51. The relative intermediate standard deviation cv_{int} estimated by use of the following procedures, like corresponding collaborative trials, does not cover effects of sample preparation and subsample inhomogeneity. In order to take into account these uncertainty components, they should be combined with cv_{int} as described in Procedures 2.1.

52. For the identification and uncertainty estimation of bias, the approaches described in the Procedure 2.1.2 have to be applied.

53. In case that the uncertainty might depend on analyte levels, the precision experiments should be carried out at different levels in any case including the level, which is relevant for compliance assessment. The significance of influence might be checked by the F-test or the Cochran test for homogeneity of the variances from different experiments on different levels of the analyte.

54. Finally, the uncertainty of the calibration standards (which obviously might be much higher than the certified uncertainty of reference material) or of the reference materials (negligible in most cases) should be considered.

ISO 5725-2 and ISO 5725-3 Approach

55. An appropriate norm-consistent approach might be the as-far-as-possible-application of the procedure given in ISO 5725-2 and ISO 5725-3. The reproducibility standard deviation s_R of an inter-laboratory method validation is obtained by combining the mean repeatability standard deviation s_r of all laboratories with the between-laboratory standard deviation s_L.

56. A typical test sample (homogenized and dried) is analyzed over a period of time on n different days by different analysts (with a new extraction/digestion, recalibration). Each of the days, a number of k replicates of the particular extract/digest are measured with the results $x_{j=1...k}$ under repeatability conditions (measurement within a short time, the same instrument and calibration used by the same operator) and the following parameters are calculated:

- Each day i : From the k replicate results $x_{j=1...k}$ the mean value $\bar{x}_i$ and the repeatability standard deviation $s_{r\,i}$ are estimated:

$$\bar{x}_i = \frac{1}{k}\sum_{j=1}^{k} x_j$$

$$s_{r\,i} = \sqrt{\frac{\sum_{j=1}^{k}\left(x_j - \bar{x}_i\right)^2}{k-1}}$$

- From the repeatability standard deviations of the different days $s_{r\,i=1...n}$, the mean repeatability standard deviation $s_{r\,mean}$ is calculated:

$$s_{r\,mean} = \sqrt{\frac{\sum_{i=1}^{n} s_{r\,i}^2}{n}}$$

- The "between-days" standard deviation s_d of the mean values $\bar{x}_{i=1...n}$ of the different days is calculated:

$$s_d = \sqrt{\frac{\sum_{i=1}^{n}(\bar{x}_i - \bar{\bar{x}})^2}{n-1}}$$

with the total mean value $\bar{\bar{x}} = \frac{1}{n}\sum_{i=1}^{n}\bar{x}_i$

- According to ISO 5725-3, the intermediate standard deviation is given by :

$$s_{int} = \sqrt{s_{r\,mean}^2 + s_d^2}$$

Finally, the relative intermediate standard deviation is given by:

$$cv_{int} = \frac{s_{int}}{\bar{\bar{x}}}$$

Duplicate Approach

57. As an alternative to the above-mentioned ISO 5725-2 and ISO 5725-3 approach, the overall run-to-run variation can be performed with a number n of duplicate tests (homogenized samples each divided into two test samples, each of the test samples subjected to complete extraction/digestion and determination procedure including recalibration)(EURACHEM 7.7.2 and A4.4).

58. For each duplicate test i, the relative differences δi rel and the standard deviation of the relative differences sδrel are calculated:

$$\delta_{i\,rel} = \frac{\delta_i}{\bar{x}_i}$$

with $\delta_i = x_{i,1} - x_{i,2}$ and $\bar{x}_i = \frac{x_{i,1}+x_{i,2}}{2}$

$$s_{\delta_{rel}} = \sqrt{\frac{\sum_{i=1}^{n}\left(\delta_{i\,rel} - \bar{\delta}_{rel}\right)^2}{n-1}}$$

with $\bar{\delta}_{rel} = \frac{1}{n}\sum_{i=1}^{n}\delta_{i\,rel}$

- Finally, this standard deviation is divided by √2 to correct from a standard deviation for pairwise differences to the standard uncertainty for single values giving the relative intermediate standard uncertainty:

$$cv_{int} = \frac{s_{\delta_{rel}}}{\sqrt{2}}$$

Type IV:

Ad-hoc Methods (Tentative Methods)

59. In most cases, ad-hoc methods are based on standard or well-established Single laboratory validated methods. They are expanded substantially (e.g. to other analytes or matrices) and will not generally require complete revalidation, but the procedure, which was described in the first paragraph of ISO 5725, Procedures 4.2 is highly recommended. Further information on the evaluation of the measurement uncertainty for ad-hoc methods are given in the EURACHEM Guide (EURACHEM 7.10). In order to get an acceptable statistical power, as many replicates as

practical of the test (including all relevant parts of method) should be performed. The comparison of the resulting relative standard deviation with the relative standard uncertainty of the basic method gives information about the precision equivalence of the ad-hoc method. Where appropriate, the uncertainty of the basic method should be reported.

Literature

[1] *S L R Ellison and A Williams (Eds). Eurachem/CITAC guide: Quantifying Uncertainty in Analytical Measurement, Third edition, (2012).*

[2] *Introductory course on measurement uncertainty available on https://sisu.ut.ee/measurement/uncertainty.*

[3] *Handbook for Calculation of Measurement Uncertainty in Environmental Laboratories. B. Magnusson, T. Näykki, H. Hovind, M. Krysell. Nordtest technical report 537, ed. 3. Nordtest, 2011..*

[4] *Jülicher et al., Analyst, 1998, 123, S. 173-179.*

[5] *Jülicher et al., Analyst, 1999, 124, 537-545.*

[6] *ISO STANDARD 13528:2015 Statistical methods for use in proficiency testing by interlaboratory comparisons.*

[7] *M H Ramsey and S L R Ellison (eds.) Eurachem/EUROLAB/ CITAC/Nordtest/AMC Guide: Measurement uncertainty arising from sampling: a guide to methods and approaches Eurachem (2007).*

[8] *Evaluation of measurement data — Supplement 1 to the "Guide to the expression of uncertainty in measurement" — Propagation of distributions using a Monte Carlo method, JCGM 101:2008.*

[9] *Evaluation of measurement data — Guide to the expression of uncertainty in measurement (GUM), JCGM 100:2008.*

[10] *EURACHEM/CITAC Guide Use of uncertainty information in compliance assessment,* 2007.

[11] *ISO 5725-1:1994 (trueness and precision) of measurement methods and results -- P: General principles and definitionsart 1.*

[12] *ISO 5725-2:1994 Accuracy (trueness and precision) of measurement methods and results -- Part 2: Basic method for the determination of repeatability and reproducibility of a standard measurement method.*

[13] *ISO 5725-3:1994 Accuracy (trueness and precision) of measurement methods and results - Part 3: Intermediate measures of the precision of a standard measurement method.*

[14] *ISO 5725-6:1994 Accuracy (trueness and precision) of measurement methods and results - Part 6: Use in practice of accuracy values.*

[15] *ISO 21748:2010 (revised by ISO 21748:2017), "Guidance for the Use of Repeatability, Reproducibility and Trueness estimates in Measurement Uncertainty Estimation", ISO, Geneva (2010).*

[16] *IUPAC/ISO/AOAC International Harmonized Guideline (7) (Protocol for the Design, Conduct and Interpretation of Method Performance Studies. Pure &Appl. Chem., Vol. 67, No. 2, pp. 331-343, 1995.),.*

[17] *Guidelines for Collaborative Study Procedures To Validate Characteristics of a Method of Analysis, AOAC Official Methods Program, J. AOAC Int. 78(5), 143A–160A(1995).*

APPENDIX III

LIST OF PARTICIPANTS

Argentina
Gabriela Catalani
Punto Focal Codex
Agroindustry Ministry

Australia
Karina Budd
Department of Agriculture and Water Resources

Stacey McIntosh
Department of Agriculture and Water Resources

Richard Coghlan
National Measurement Institute

BIPM
Ralf Josephs
Bureau International des Poids et Mesures
Department: Chemistry

Brazil
Carolina Araújo Vieira
Brazilian Health Regulatory Agency

Ligia Lindner Schreiner

Canada
Thea Rawn
Health Canada

China
Stephen Chung Wai-Cheung
Centre for Food Safety

Colombia
Myriam Rivera Rico
Invima Colombia Pais Miembro Codex

Ecuador
Víctor Hugo Almeida Arteaga
Ministerio de Salud Pública del Ecuador

Egypt
Mariam Barsoum Onsy
Egyptian Organization for Standardization & Qyuali

Germany
Katrin Franks
Chair of EWG
BVL

Steffen Uhlig
Quodata Ltd.

Petra Gowik
BVL – German Federal Office of Food Safety and Consumer Protection

Dorina Bodi
German Federal Institute for Risk Assessment

Honduras
Liza Madrid de Rodriguez
Organismo Hondureno De Acreditacion

Hungary
Erik Maloschik
NEBIH - National Food Chain Safety Office

Andrea Zentai
National Food Chain Safety Office

Kasza Viktor
National Food Chain Safety Office

Kamiran Aron Hamow
Hungarian Academy of Sciences and NEBIH

Zsuzsa Farkas, PhD
National Food Chain Safety Office (NEBIH)

Gabriella Miklos
National Food Chain Safety Office

Attila Nagy DVM
National Food Chain Safety Office

India
Rajesh Rajappan Nair
National Dairy Development Board

Codex Contact Point
Food Safety Standards and Authority of India

Krishna Kumar Sharma
Indian Agricultural Research Institute
International

Iran
Samaneh Eghtedari
ISIRI

Japan
Ministry of Health, Labour and Welfare

Hidetaka Kobayashi
Ministry of Agriculture, Forestry and Fisheries

Kazakhstan
Zhanar Tolysbayeva
The Ministry of Healthcare,México
César Omar Gálvez González
COFEPRIS

Mexico
Tania Daniela Fosado Soriano
Secretaría de Economía

The Netherlands
Henk van der Schee
NVWA

New Zealand
Susan Morris
Ministry of Primary Industries

Roger Kissling
Fonterra Ltd.

Norway
Stig Valdersnes
Institute of Marine Research

Norwegian Codex Contact Point
No Name
Norwegian Food Safety Authority

Switzerland
Erik Konings
Nestec Ltd.

Gerard Gremaud
Swiss Federal Food Safety and Veterinary Office

Thailand
Rungrassamee Mahakhaphong
ACFS

The Republic of Korea
Codex Contact Point
Ministry of Agriculture, Food and Rural Affairs

The Republic of Korea
Yoo Min
Ministry of Food and Drug Safety (MFDS)

UK
Bhavna Parmar
Food Standards Agency UK

USA
Greg Noonan
US FDA