CODEX ALIMENTARIUS COMMISSION

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World Health Organization

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Agenda Item 5 **CX/MAS 23/42/7 Add.1**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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INFORMATION DOCUMENT: GUIDELINES ON MEASUREMENT UNCERTAINTY (CXG 54-2004)

Comments in reply to CL 2023/14-MAS

Comments of Australia, Brazil, Canada, Chile, Egypt, European Union, Iraq, Japan, Mauritius, New Zealand, Paraguay, Philippines, Singapore and ICUMSA

Background

1. This document compiles comments received through the Codex Online Commenting System (OCS) in response to CL 2023/14-MAS issued in April 2023. Under the OCS, comments are compiled in the following order: general comments are listed first, followed by comments on specific sections.

Explanatory notes on the Annex

2. The comments submitted through the OCS are hereby attached as **Annex I** and presented in table format.

Annex I

GENERAL COMMENTS	
General comments a. We believe the information document serves the purpose of supporting the revision of CXG 54 and its implementation by providing further explanation of the theory, some calculated examples but also references more detailed discussions in published standards or journal articles. b. We have suggested some modifications to the text to align more with the GUM and hopefully make the document clearer. c. There are some minor editorial changes required, as outlined under specific comments.	**Australia**
Considering the complexity for laboratories to apply the principles expressed in the document, Brazil supports its adoption as an informative document. Regarding the text, we identified the need of updating some references as listed below: • Footnotes 2, 3 and 5 - pages 3, 4 and 9: the reference number for VIM document should be replaced from 7 to 8. • Footnote 4 - page 8: the reference number should be replaced from 10 to 11. • List of references: - The last version of the document “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 [5]” is 2019. - The last version of the documents “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 [14]” and “ISO TS 23471, Experimental designs for the evaluation of uncertainty – Use of factorial designs for determining uncertainty functions [20] and “ISO 13528:2015, Statistical methods for use in proficiency testing by interlaboratory comparison [22]” is 2022.	**Brazil**
Chile considers that the document is adequate in its content, however, it is not clear if the document could be understood by all who consult it, because terminology is used that requires referring to the standards or attached bibliography, for a better comprehension. It would be important that, after the approval of the document, the CCMAS could organize an on-line workshop for its dissemination and better understanding among the different member countries.	**Chile**
Egypt suggests endorsement of this document from CCMAS 42	**Egypt**
The European Union and its Member States (EUMS) congratulate Germany for doing an excellent job that provides the technical background necessary for the estimation of measurement uncertainty and the examples for illustrating different use cases; it will certainly support the guidance provided by CXG 54. The content of the information document explains in a comprehensive manner relevant approaches to estimate measurement uncertainty (top-down and bottom-up), the models and assumptions governing those approaches and provides practical examples how to evaluate uncertainty components. Even if a note regarding sub-sampling has been added to the current version of the information document, it could still profit from a stronger focus on test methods validated by collaborative study as methods endorsed by CCMAS and included in CXS 234-1999 have to be validated by multi-lab studies. Method performance data resulting from collaborative studies do in a number of cases not include certain uncertainty sources. It would be an advantage if the document described how to identify additional influential factors on the measurement result, e.g., preparation steps related to transforming a laboratory sample into the test portion, sub-sampling from the laboratory sample, matrix variation, etc., that were not adequately covered in the collaborative study (reconciliation of potential uncertainty sources with the available collaborative study results) and quantify the	**European Union**

uncertainty component arising from them. Lastly, it should briefly describe when and how to combine those additional standard uncertainties with the performance parameters (sr and sR) of the collaboratively trialed method. As some endorsed methods do not have the concerned commodity in their scope (e.g. AOAC 968.31, which has been validated for canned tomatoes, lima beans, and potatoes, but which also endorsed for Ca in canned strawberry), guidance and an example should be provided how to assess uncertainty due to the matrix mismatch. A paragraph on the role of certified reference materials for estimating measurement uncertainty, particularly the uncertainty of bias correction, would strengthen the information document as well.	
Agree with no comments	**Iraq**
Germany has done a good job documenting some of the more detailed technical information underpinning the CXG 54 Guidelines that makes this information more accessible than (say) providing references to papers. In particular the document includes a range of useful examples that show how some of the calculations are done and some information is provided on the role of measurement uncertainty in acceptance sampling, that supports CXG 50. We think the reference in 9.1 to Section) should refer to Section 8	**New Zealand**
Estamos de acuerdo en general con el documento.	**Paraguay**
The Philippines agrees on the proposed draft information document prepared by Germany on the GUIDELINES ON MEASUREMENT UNCERTAINTY (CXG 54-2004) and agrees to publish on the Codex website. Rationale: The Information document was updated to take into account the comments received during CCMAS41. This document provides the information on how different approaches for the evaluation of measurement uncertainty relate to one another and have information regarding the best procedure to adopt in any given case. Furthermore, this new document provides information and clarifies basic understandings which are important for the correct evaluation and interpretation of measurement uncertainty. We also agree on the new note added at the end of Section 3 regarding the case that precision depends on concentration.	**Philippines**
“The examples presented on pages 15 to 16 of CL 2023/14/OCS-MAS offer valuable insights into the determination of sample sizes in the presence of measurement uncertainty.”	**Singapore**
The symbols described in the paragraphs throughout the document are raised (superscripts). This isn't typical and looks odd. It would be better if the symbols were in line with the text. This starts from section 2, where "Y" is raised relative to the text around it. "...in most cases a measurand Y is..."	**ICUMSA**
SPECIFIC COMMENTS	
1. Introduction	
<u>This document provides information on example procedures to estimate measurement uncertainty. Since procedures are not limited to what are written in this document, Members may use other procedures for the estimation of measurement uncertainty than those described in this document.</u>A measurement result should always be accompanied by information regarding its uncertainty. Such information provides an indication of the quality of the measurement result and allows meaningful comparison to other measurement results or reference values. Without a statement of measurement uncertainty, a measurement result is essentially incomplete and cannot be properly interpreted. Rationale To clarify the nature of this document (information document), not a Codex guideline or standard.	**Japan**

A measurement result should ~~always~~ ideally be accompanied by information regarding its uncertainty. Such information provides an indication of the quality of the measurement result and allows meaningful comparison to other measurement results or reference values. Without a statement of measurement uncertainty, a measurement result is essentially incomplete and cannot be properly interpreted.	**Mauritius**
A measurement result should **always** be accompanied by information regarding its uncertainty. Such information provides an indication of the quality of the measurement result and allows meaningful comparison to other measurement results or reference values. Without a statement of measurement uncertainty, a measurement result is essentially incomplete and cannot be properly interpreted. As per ISO 17025, clause 7.6, we need to identify contributions to MU. We need to evaluate MU or an estimate based on an understanding of the theoretical principles or practical experience of the performance of the method As per clause 7.8.3.1, test reports shall however, where necessary for interpretation of test results, include, where applicable, the measurement uncertainty presented in the same unit as the measurand or in a term relative to the measurand when: it is relevant to the validity or application of test results a customer's instruction so requires or MU affects conformity to a specification limit In view of above we are proposing alternate wording	
This document provides ~~guidance~~ information regarding those sources of uncertainty which originate in the laboratory itself, i.e. in connection with the procedures and conditions starting with the laboratory sample and ending with the measurement result. In particular: the question of sampling uncertainty and the extent to which laboratory samples are representative of the content in the container will not be addressed. Such questions are addressed in CXG 50-2004 [13]. Again, this is not a guidance but to provide information.	**Japan**
This document provides guidance regarding those sources of uncertainty which originate in the laboratory itself, i.e. in connection with the procedures and conditions starting with the laboratory sample and ending with the measurement result. In particular: the question of sampling uncertainty and the extent to which laboratory samples are representative of the content in the container will not be ~~addressed~~addressed in this information document. Such questions are addressed in CXG 50-2004 [13].	**Mauritius**
Measurement uncertainty is defined as a parameter "…that characterizes the dispersion of the values that could reasonably be attributed to the measurand", see 2.2.3 in GUM [1]. This document aims to clarify what is meant ~~in~~ by this definition and to provide the information which is necessary to understand how different approaches for the evaluation of measurement uncertainty relate to one another. This should allow the reader to make informed decisions regarding the best procedure to adopt in any given case.	
2. Top-down versus bottom-up approaches	
2.1 Monte Carlo method (MCM). It is suggested to clearly distinguish in the document what refers to the Monte Carlo Method (MCM); as this would make it easier to understand	**Chile**
The uncertainty values of the individual variables are taken from the certificates of the reference standard substances of materials, while the uncertainty values for the variables are obtained from the regression analysis (residual standard deviation).	

Strictly speaking, the ordinary minimum squares method used in Chemical Metrology assumes that the X axis has no uncertainty, the random error is only attributable to the instrument (Y axis). Of course, this is not correct. Formally, if one wanted to incorporate the uncertainty of the calibrants, a linear regression with error in both axes should be used. That would be rigorous, but the proposed approximation can be accepted without major modifications. The CCQM gas metrology group uses this type of regression with uncertainty in both axes	
3. Basic model for the top-down approach	
True value The 'estimation by averaging' should be done with caution, thus suggest the following amendment. 'It can be estimated by averaging e.g. across methods, samples and laboratories, but must be done with caution, as in practice, unless participants for an interlaboratory study are chosen based on both expertise and similar methodologies, an average bias of zero is difficult to achieve.' 2. Section 3, sub-section on individual term 'True value', first paragraph, third sentence. Suggested following amendment, 'However, it is crucial to note that in the GUM [1], measurement uncertainty is defined without any reference to a true value; rather, it is defined as a parameter "... that characterizes the dispersion of the values which could reasonably be attributed to the measurand", see 2.2.3 in GUM [1].' 3. Section 3, sub-section on individual term 'True value', first paragraph, last sentence. Either the last sentence is removed, as a discussion of reference material usage is better left when defining or discussing method biases. Alternatively, if retained suggest the following amendment. 'If a certified reference material and associated values is available, it will suggest a range where the true value might be, and give along with a reference uncertainty value, for inclusion the latter can be included in the uncertainty of bias correction.	**Australia**
Method bias (average across labs and matrices) When talking about method bias or laboratory bias from page 5 and 14, would it be a prerequisite that laboratories participating in the validation process through interlaboratories are (i) ISO accredited ones adopting the same/latest methods (ii) accredited for the test (iii) working in the recommended conditions both environmental and equipment use (iv) including any deviation that are permissible by the relevant ISO methods to ensure having all the deviations that could be met. These are important as we see from PT results, that even ISO accredited laboratories sometimes do not fall within the acceptable z scores. Thus it is important to define the laboratories to be involved for comprehensiveness.	**Mauritius**
Method bias (average across labs and matrices) 'Method bias (average across labs and matrices)' first sentence. Suggest amendment 'The method bias across both labs and matrices can be estimated by averaging across laboratories and matrices, but only becomes meaningful if an estimate of bias is available from use of a certified reference material.'	**Australia**
Laboratory bias 'Laboratory bias' last sentence. Suggest that if a definition of 'Laboratory standard deviation' is required it should be done separately, as bias and variance are not interchangeable. Thus removed the third second sentence from this paragraph. 'The corresponding component of total variability is called the laboratory standard deviation.'	

Repeatability error 'Repeatability error','Note regarding the case that the precision depends on the concentration level:' Second last sentence in paragraph. We suggest the '...relatively high precision...' as high or low could be misinterpreted and suggest amendment to '...relatively highpoor precision...'.	
5. Relation between measurand and validation data	
The conditions under which validation data can be used to support a measurement uncertainty estimate can be stated as follows: We suggest that the conditions under which validation data can be used to support a measurement uncertainty estimate, should include 'precision and bias' and not just 'precision'. Thus, suggest following amendments ' and the measurand is included in the scope of the validation and plus precision and bias within the laboratory which is evaluating measurement uncertainty is comparable to the method's precision and bias as characterized in the validation study then... the precision and bias estimates from the validation study can be used in the calculation of measurement uncertainty. In order to check and provide evidence of competence in the application of the method and to ensure adequate precision and bias in the laboratory which is evaluating measurement uncertainty, it may be necessary to perform a verification study.'	**Australia**
7. Uncertainty sources in the top-down and bottom-up approaches	
Sources of uncertainty are conveniently classified under six main headings: Sources are described in ISO 19036 as follows: technical, matrix and distributional uncertainties- taking test portion from lab or test sample preparation of initial suspension serial dilution inoculation incubation, (technical operations and calculations- equipment, culture media and reagents) counting of colonies and/or detection of growth confirmation Are these all covered in the present document?	**Mauritius**
8. Requirements regarding data size	
In the case that different uncertainty sources are *simultaneously* taken into consideration, say in the bottom-up approach, the requirement regarding data size can be applied via the Satterthwaite formula. More specifically: take the case that 2 different uncertainty sources are included in the calculation of the combined uncertainty, and . Say that each was obtained by applying the formula for the sample standard deviation on the basis of and measurement results, respectively. The number of degrees of freedom for the combined uncertainty can then be computed as We suggest alignment with the GUM, with a reference for further information. Thus, amend to 'In the case that different uncertainty sources are simultaneously taken into consideration, say in the bottom-up approach, the requirement regarding data size can be applied via the Welch-Satterthwaite formula see [1] Annex G, G.4.1.' We also suggest amending all the other uses of the 'Satterthwaite formula' to 'Welch-Satterthwaite formula'.	**Australia**

In the case that prior information is used for an individual value (Type B variable) and that no information regarding data size is available, it is suggested to use ; the uncertainty which corresponds to this data size is intended to reflect the fact that, in the case of Type B variables, distributional assumptions are often based on “educated guesses.” We would consider the ni = 7 could be conservatively low in some cases. Thus suggest the amendment ‘... suggest to use ni > 7; the...’. This would also require the amendment in Table 1, by replacing ‘=’ with’>’, thus ‘Not available, Take n4 > 7 .	
Add a sentence to the end of this section (Section 8). ‘We would suggest users of the Welch-Satterthaite formula refer to the GUM [1] Annex G for a discussion on the formula and the range in which the calculated degrees of freedom should fall, since incorrect implementations commonly give answers outside of this range.’	
9.1 Procedure for characterizing in-house variation	
PROCEDURE FOR CHARACTERIZING IN-HOUSE VARIATION It is suggested that a statement be added to clarify that the equations in 9.1 are general for Section 9 and not specific to in-house variation since the formulas in Section 9.1 for characterizing in-house variation can also be applied to Sections 9.2 (across matrices) and 9.3 (between labs). For example, variability between the matrices (Smatrix) and labs (Slab) are calculated in the same way as between days (SD) in Table 4.	**Canada**
PROCEDURE FOR CHARACTERIZING IN-HOUSE VARIATION Suggest a reference is provided for the computation equations after table 2.	**Australia**
As explained in Section ~~0~~8, it is recommended that, at a minimum, different in-house measurement conditions (e.g. different days) be represented in the data set.	**Canada**
9.2 Procedures for characterizing variation across matrices (matrix mismatch)	
PROCEDURES FOR CHARACTERIZING VARIATION ACROSS MATRICES (MATRIX MISMATCH) Procedure 2, sentence 1. We believe more than one measurement result within each laboratory is required for separation of sr and slab. Thus suggest the following amendment ‘If PT data are available, and a sufficient number of participants (ideally, at least 12) have used the same method and replicate measurement results within each laboratory – then thisese data can be used to characterize variation across laboratories.’	**Australia**
9.4 Procedures for characterizing fundamental variability	
PROCEDURES FOR CHARACTERIZING FUNDAMENTAL VARIABILITY The fundamental variability Section (9.4) seems to be quite general, and thus some more details could be given. For example, might it be helpful to explain the Horwitz SD value, particularly for users new to this type of work?	**Canada**
Fundamental variability is a subcomponent of the repeatability error term from the basic model in Section 3 and denotes the irreducible variation between samples which remains even under the highest achievable degree of homogeneity. **Fundamental variability reflects heterogeneity at the level of the sample’s constituent particles;** it has an influence on the uncertainty of measurement results when the target analyte is located on sparsely distributed carrier particles. Fundamental variability appears twice: first, during sampling, and second, during subsampling in the laboratory, i.e. extraction of a test portion after homogenization of the laboratory sample. In practice, nonnegligible fundamental variability can be reduced by	**Chile**

modifying the testing procedure in two respects: first, by finer grinding or comminuting or mixing of the test material, and second, by increasing the test portion size. Chile has doubts if this is equivalent to the fundamental error of Pierre Gy's Theory?	
$s_F = \sqrt{\frac{k}{(k-1)} \cdot (s_1^2 - s_2^2)}$ If s12/s22 is less than 2.17, does that mean fundamental variability is not significant and SF doesn't need to be estimated? If this understanding is correct, please provide a statement clarifying this, so that the reader understands what to do if the condition is <2.17.	**Canada**
10. Influence of measurement uncertainty on sampling plans: examples	
This modified procedure is taken from current stage of development of Annex B of ISO/WD ISO 3951-6 [15]. Specific Comments – editorial 14. Section 2, paragraph 9, second sentence. For clarity suggest explaining the acronym used in the quotation using square brackets. Thus amend to 'This can briefly described as "repeated sampling from the PDFs[probability density functions] for the and the evaluation of the model in each case," see 5.9.1 in [3].' 15. Section 3, last paragraph, second sentence. The reference is not consistent with the Reference section. Suggest amendment to "This approach is described in Uhlig (20232) [25] and..." 16. Section 9.1, paragraph 4, first sentence. The text reference appears incorrect as "Section 0" but correctly linked to Section 8. Thus, amend to "As explained in Section 08, it is	**Australia**
Procedures for bulk sampling are provided in ISO 10725:2000 **[17].** As in the case of sampling from packages, these procedures are only valid under the assumption that there is no method bias. Modified procedures for the case that there is a method bias are currently being developed. For now, the discussion is limited to the case that there is no bias. Please clarify if the procedures described at the end of Section 10 are specific to bulk sampling. It is suggested to have a subsection or subheading before text that is pertinent to bulk sampling. For instance, the second example at the end of Section 10 does not appear to use the general guidelines summarized earlier in the same section. Please clarify which criteria and variables in the example apply specifically to this scenario (i.e., bulk sample of wheat), or provide more details if they are more broadly applicable in other scenarios.	**Canada**
References Section 'Reference'. While we all seek to implement an information document with the most recent research, the reference [23], [24], & [25] articles have not undergone peer review and unless specifically required should not be included	**Australia**
ISO 5725-2~~:1994~~: 2019, 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.	**Chile**

outdated versions of ISO standards are mentioned in the references, which would be important to correct.	
ISO 3951-1:~~2016~~2022, 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. outdated versions of ISO standards are mentioned in the references, which would be important to correct.	
~~ISO/WD 3951-6:2019, Sampling procedures for inspection by variables — Part 6: Specification for single sampling plans indexed by limiting quality (LQ).~~ The committee in Chile searched in ISO and only found "ISO/DIS 3951-6 Sampling procedures for inspection by variables — Part 6: Specification for single sampling plans for isolated lot inspection indexed by limiting quality (LQ)" also indicates that it is standard under development, that is, it is not yet official: https://www.iso.org/standard/78827.html	
ISO TS 23471:2022, Experimental designs for the evaluation of uncertainty – Use of factorial designs for determining uncertainty functions.	
ISO 13528:~~2015~~2022, Statistical methods for use in proficiency testing by interlaboratory comparison. Current version 2022	