CODEX ALIMENTARIUS COMMISSION

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 4, 6, 7, 9 **MAS/37 CRD/16**

ORIGINAL LANGUAGE ONLY

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON METHODS OF ANALYSIS SAMPLING

Thirty-seventh Session
Budapest, Hungary, 22 – 26 February 2016

(comments submitted by European Union)

Agenda item 4: Discussion Paper on Development of Procedures/Guidelines for Developing Equivalency to Type I Methods (CX/MAS 16/37/4)

The European Union and its Member States (EUMS) acknowledge the efforts of the delegation of the United States of America for compiling useful information in this Discussion Paper. However, the EUMS regret that the discussion paper has not been circulated to the members of the electronic working group, as agreed at the last CCMAS session, before being discussed in plenary.

In case the document is discussed in plenary or in an in-session working group, the EUMS wish to refer to the note of caution expressed by the Committee at its 36th Session, namely that the current concept of Type I methods should not be changed, as it might lead to unintended implications, in particular in case of settling those disputes which involve the application of Type I methods. However, outside the Codex context, the concept of method equivalence can indeed be of help to method developers for identifying suitable methods that might lead to the replacement of existing methods if applicability and equivalency or even superiority of the alternative can be proven.

Demonstrating equivalence among other method types (e.g. Type II versus Type III) could be of interest in certain cases, but as already pointed out in the discussion paper, provisions for establishing Numerical Criteria with respect to Type II-IV methods already exist in the Codex system and, therefore, establishing equivalency between such methods may not be advantageous. For these reasons the Committee is invited to reflect on the added value if further work in this area is pursued.

The EUMS would also like to submit the following specific comments:

The two one-sided t-test (TOST), which is described in ASTM E2935 – 14 Standard Practice for Conducting Equivalence Testing in Laboratory Applications, is recommended in the discussion paper (paragraph 19). Unfortunately, no considerations have been given to existing alternative approaches such as principles described in ISO 16140 (Microbiology of food and animal feeding stuffs – Protocol for the validation of alternative methods) and ISO 8196 (Milk – Definition and evaluation of the overall accuracy of alternative methods of milk analysis) and NF V03-110 (Analyse des produits agricoles et alimentaires - Protocole de caractérisation en vue de la validation d'une méthode d'analyse quantitative par construction du profil d'exactitude) for demonstrating equivalence of alternative testing methods.

In laboratory medicine certain regression techniques (Bland-Altman, Deming, Passing-Bablock) are frequently used to assess equivalency of methods, and they could be included in the discussion paper as well. For example, useful guidance has been published by the Clinical and Laboratory Standards Institute (CLSI): EP9-A2 Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline.

The TOST test uses the bias between two methods for equivalence testing. It is questionable whether a bias is the appropriate measure or whether it would not be more adequate to use the variability of this bias across and within matrices and precision data instead. Furthermore, the computation of the theta is not statistically sound as well as the statistical test as such. Therefore, other, more sophisticated software packages (R, SAS, PROLabPlus, mqVal) should be considered to be used as well. An explanation as to the respective merits of the different approaches is also recommended.

Finally, the EUMS believe that terms like e.g “sufficient power” or “sample set” need to be defined.

Agenda Item 6: Discussion paper on criteria for endorsement of biological methods used to detect chemicals of concern (CX/MAS 16/37/6)

The European Union and its Member States (EUMS) would like to thank Chile and France for chairing the electronic working group tasked with the development of criteria for endorsement of biological methods used to detect chemicals of concern and appreciates the work done so far.

The eWG recognised that most methods endorsed to quantify vitamins have now been replaced by chromatographic methods and therefore the question is if the biological methods will be kept endorsed in the coming years by the CCMAS.

The same would apply to other biological methods for which the same question would apply.

The eWG foresees a high probability that most of the methods would not be kept as endorsed by the CCMAS and therefore questions whether there is a real need to establish criteria for endorsement of biological methods. The EUMS are of the opinion that the bioassays used for the determination of vitamins are still useful and applied in many laboratories and do not see the immediate need for eliminating them from STAN-234; however, given the existence of methods based on physico-chemical principles, re-typing them, for example as Type III instead of Type II, is appropriate.

The eWG also highlighted the need to continue working on two issues of the original assignment (CCMAS36):

- Identify to which classes of methods the criteria approach applies, and
- recommend criteria to endorse each class of biological methods defined.

These are critical issues which for the moment remain unresolved.

The EUMS believe that the recommendations of the eWG to the CCMAS regarding the re-evaluation of the list of biological methods, in particular those involving animals, and with a view to the typing of the remaining methods for the determination of vitamins are reasonable; the EUMS support these recommendations. The EUMS would encourage the re-establishment of the eWG to continue its work, in particular on the two remaining issues.

Agenda item 7: Review and update of methods in Codex STAN 234-1999 (CX/MAS 16/37/7)

The European Union and its Member States (EUMS) would like to thank Brazil and Japan for the excellent work done for preparing the document outlining how to revise and update the methods of analysis and related texts in a single source document/database.

The EUMS can support the proposal to CCGP, presented in the recommendations, to split the section "Methods of Analysis and Sampling" in two separate sections and can in principle support the new text proposed for the section on methods of analysis. The exact wording of the text will need some clarification. In case the proposal for splitting the section is accepted, the Committee needs to decide how to word the remaining sampling chapter.

The EUMS can also support the other recommendations made by the eWG to CCMAS.

A correction of the status of the Codex Commodity Committees presented in Table II should be done so that CCMMP and CCS are both reported as Active* (working by correspondence).

Concerning the proposed preamble, the EUMS would like to thank the Codex Secretariat for providing a clear text. The EUMS can support the proposal of the Codex Secretariat, although the Committee is invited to reflect whether the name of the standard should be changed, since the lists contain only methods of analysis.

Agenda item 9: Procedures for determining uncertainty of measurement results (CX/MAS 16/37/9)

The European Union and its Member States (EUMS) would like to thank Germany and New Zealand for chairing the electronic working group tasked with the development of procedures for determining uncertainty of measurement results including sub-sampling, sample processing and analysis.

The procedures to be developed by the eWG are intended to complement the Guidelines on Measurement Uncertainty (GL 54-2004), which already contain Explanatory Notes and further useful references, which are provided for information purpose only. The Guidelines on Estimation of Uncertainty of Results (GL 59-2006) already explain that next to the analytical part (extraction, clean-up, analysis) physical sample preparation can contribute to a significant amount to the uncertainty of measurement.

The EUMS welcome that guidance is made available on how to estimate uncertainty contributions of certain steps of a measurement process, notably sample processing and sub-sampling.

The text could profit from providing concrete examples to illustrate how the described concepts could be applied to relevant commodities. In addition, more details on how to practically estimate the various

uncertainty components, for example those mentioned in paragraph 23 or 23, would be helpful (perhaps as an annex).

The terminology used for explaining the possible approaches for estimating uncertainty components (reproducibility precision) for in-house developed methods should be aligned with the definitions given in the International vocabulary of metrology — Basic and general concepts and associated terms (VIM). The advantages of using the TOST procedure for checking whether new and old calibration standards produce equivalent results may need further clarification.

The EUMS would welcome that the eWG continues its work and further refines the text. The Committee should also consider how the document can then be incorporated into the relevant Codex text.