16 February 2016

# Codex Committee on Methods of Analysis and Sampling (37th Session) Budapest, Hungary, 22-26 February 2016

## European Union comments on Agenda item 4:

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

***Mixed Competence***
***Member States Vote***

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.