CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 7 **CRD07**

ORIGINAL LANGUAGE ONLY

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON METHODS OF ANALYSIS AND SAMPLING

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(Comments of ICC and AOECS)

Agenda Item 7: Methods of analysis for precautionary allergen labelling

ICC, the International Association for Cereal Science and Technology, and AOECS, the Association of European Coeliac Societies, thank the EWG for their hard work on this very important “Discussion Paper on Analysis for Precautionary Labelling”. We kindly ask the EWG and CCMAS to consider our comments:

Section 1 – Introduction

In December 2023, CAC46 adopted at Step 5 the Proposed Draft Revision of the General Standard for the Labelling of Prepackaged Foods (CXS 1-1985) relevant to Allergen Labelling, 2. DEFINITION OF TERMS:

"Food allergen" means a food or ingredient (or substance or processing aid) used in food, usually a protein or protein derivative that can elicit IgE-mediated or other specific immune-mediated reaction in susceptible individuals."

Therefore, the wording in the Introduction “allergic response” does not reflect the second part of the definition of terms and needs to be changed to “immune-mediated reactions”.

To explain “other immune-mediated reaction”, coeliac disease is described in 2. DEFINITION OF TERMS:

"Coeliac disease" means a chronic immune-mediated intestinal disease in genetically predisposed individuals induced by exposure to dietary gluten proteins that come from wheat, rye, barley and triticale (a cross between wheat and rye). "

Later on in chapter 4.2.1.4 after "Cereals containing gluten" a footnote is inserted with the explanation “includes spelt, Khorasan and other specific cereals containing gluten”.

The “allergen action level” for wheat and further gluten containing cereals had already been adopted by CAC in July 2008 in CXS 185-1979 in 2.1.1 Definition of “Gluten-free foods: ….the gluten level does not exceed 20 mg/kg in total, based on the food as sold or distributed to the consumer“.

The “currently available test method” has been used since 2008 as a Type 1 method as already confirmed in Section 5 later on.

Section 2 – Terminology

The attempt of setting a common terminology is a good starting point however without practical guidance or advice how to characterize each term makes the use of this discussion paper difficult. Different ELISA methods can only be compared if the way of characterization of performance parameters is similar or in best case identical.

Some major aspects to consider are:

- For LoD, LoQ, recovery and precision only matrix containing extracts shall be used; these matrix will allow to state an assay applicability (also called method claim)
- The difference between ruggedness and robustness is not clear because ruggedness is also called stability in this discussion paper; stability of a test kit is normally a sum of experiments characterizing for real-time, in-use, transport, and freezing stability (see clinical guideline CLSI EP25, 2023)
- Sensitivity: a calibration graph for antibody-based system is seldom linear therefore a “slope” does not apply.

- The mandatory use of incurred samples is missing which is a fundamental requirement by AOAC and EN.
- The term precision need to be specified because e.g. if only repeatability is given as a performance parameter, a user is not able to judge if the method is useful for his requirements.
- The difference between extraction efficiency and recovery is not clear. Maybe the more common term recovery should be used only.

Section 2 and Section 3 could be merged to reach a more practical guidance. Nevertheless minimum requirements for the extent of each performance characteristic need to be mention somewhere. EN 17855 could be used as a basis.

Section 4 - Confirmatory methods

What is the main outcome of this section? It describes the status quo quite well but it is not clear what the practical consequences are. It should be kept in mind that a positive result for an ELISA and a negative result of a confirmatory method on the same sample could be the result of a lower sensitivity of the confirmatory method. What will be the outcome when one method measures a concentration above the threshold and the other below? In case of a precautionary label, it seems advisable to use a PAL when in doubt. If so, the need of a confirmatory method is questionable. In the case above, the result of the confirmatory method will not have any impact on the PAL, as it will be applied whether the confirmatory method is positive or negative.

In case of an existing Type I method, the need of a confirmatory method is in any case not given, as the Type I method per definition delivers the “correct” result and will overrule any other method.

In any case it must be avoided that a product labelled “gluten-free” may have a PAL statement “may contain wheat”. This will confuse

- the coeliac population, the prevalence is 1 %-2 % world-wide
- the dermatitis herpetiformis patients who need also a gluten-free diet and
- the population suffering from “Non-Coeliac-Gluten/Wheat-Sensitivity”, the estimated prevalence is between 1 % and 13 %.

Section 6 - Codex Method Typing for ELISA methods

The implications of these two subchapters need to be discussed in great detail because bringing every ELISA kit on Codex Type I method level will not only produce a lot of work at Codex level but also suddenly will lead to the question what will happen in case of differences between two methods. It also contradicts the purpose of a Type I method. Not the Codex system needs to be adjusted to this discussion paper, but the discussion paper to the existing Codex system.

Section 7 - Best Practice Guidance Documents and References

EN 17855 can be added to the document because the ratification was completed on April 8, 2024. It also contains minimum requirements for the LoQ of methods derived out of reference doses/action levels. This document also contains definitions for each allergen and an informative Annex how to perform a validation study.

It is also suggested to mention the new AOAC guideline, which is close to publication.

Appendix I

The list of methods in Appendix I implicates, that all methods listed are comparable and have the same status of validation. We should only mention methods that have undergone an external validation e.g. AOAC PTM or AOAC OMA. At least, an additional row can be added, that states if any external validation is available. Furthermore, it is not clear if the LoQ stated in the tables are derived out of experiments that are state-of-the-art. Good descriptions of how to characterize for an LoQ are given in EN 17855, EN 17254, EN 17644 and the new AOAC Guideline on Validation of methods to determine allergens including gluten.

There are many duplications in Appendix I that inflates the table. The authors statet that this is the result of a questionnaire but for final publication this should be resolved.

We volunteer to set up a new table based on the comments above and others that may come.

Regarding the Background-Information in point 3

It is written:

- Currently available test methods and validation status for the priority allergens listed in CX/FL 23/47/5 Appendix I and noting the validated scope (food matrices, processed food) of these methods.

- Required information for method evaluation and validation, including antibodies used (if ELISA), cross-reactivity, assay applicability, selectivity, stability (ruggedness), calibration procedures, sensitivity, range of quantification, LOD/LOQ, accuracy/trueness, extraction efficiency, precision, robustness, applicability, recovery and practicability, and whether it reports total protein. Validation requirements for the testing of allergens in foods including accuracy/trueness, extraction efficiency, precision, robustness, applicability, recovery and practicability.

Bullet point 2 mentions the required information for method evaluation and validation. Without minimum requirements for these, a list as in Appendix I (bullet point 1) is not reasonably possible now. Proposal: To use minimum criteria from EN 17855 and EN 17254 for “screening” of all methods listed in the actual Appendix I and to select those that fulfil the minimum requirements.

It is further written in the next bullet point that confirmatory methods should be considered. In case of PCR methods these can be used as an identification tool e.g. almonds vs. apricot seeds. It depends on the definition of a confirmatory method if PCR is a confirmatory method.