Comprehensive guidance for the process of submission, consideration and endorsement of methods for inclusion in CXS 234

(for internal use by CCMAS)

1. Preamble/Introduction

This document provides integrated guidance on submission to and review of methods of analysis by CCMAS prior to inclusion in the *General Standard for Methods of Analysis and Sampling* (CXS 234 – 1999). This guidance is intended to assist countries and standards development organisations (SDOs) in the submission and review of methods of analysis for inclusion in CXS 234. The methods are primarily intended as international methods for the verification of provisions in Codex standards[1]. This guidance is intended to supplement, and does not replace or supersede, the information found in the *Procedural Manual of the Codex Alimentarius Commission*[2]. The *Procedural Manual* should be utilized to capture all of the requirements associated with the submission and review of methods.

2. Definitions

Definitions used in the description of methods and their performance characteristics should conform to the *Guidelines on Analytical Terminology* (CXG 72 – 2009) and the relevant source (e.g. ISO, VIM, Eurachem, etc.) Other descriptors have been used in Codex discussions such as Identical and Complementary and are defined below:

- Identical (Applies to all types of Codex methods[3])
  - A single method published jointly by two or more SDOs as a single document, or;
  - separate documents containing identical text, or;
  - two or more methods which have the same principle, the same chemicals in the same concentrations, in the same procedure/sequence and the same measuring equipment, but are published by different SDOs and written in differing styles.[4]
- Complementary
  - Two or more methods which are all required to determine the desired result.

Table 2.1: Clarification and Examples on Method Definitions

Name	Meaning	Example	Relevant Type	Separator in CX S234
Identical	1. A single method published jointly by two or more SDOs as a single document, **or** 2. separate documents containing identical text **or** 3. two or more methods which have the same principle, the same chemicals in the same concentrations, in the same procedure/sequence and the same measuring equipment but are published by different SDOs and written in differing styles.	ISO 5534 | IDF 4	All Types	| / /
Complementary	Two or more methods required to determine/calculate the required answer	ISO 5534 | IDF 4 and ISO 1735 | IDF 5	All Types	And

[1] Codex Alimentarius Commission Procedural Manual: *Principles for the establishment of Codex methods of analysis*

[2] Where appropriate and important for context excerpts from the *Codex Alimentarius Commission Procedural Manual* are included within this Guidance.

[3] See footnote 1 and Description of Method Typing (below).

[4] In cases where a standard contains multiple approaches to the determination, but which are not separately identified, comparison with a second method with more prescriptive details will be carried out on a case-by-case basis to determine if the two methods may be considered identical.

Description of Method Typing from Procedural Manual

Methods of Analysis

Definition of types of methods of analysis

(a) Defining Methods (Type I)

Definition: A method which determines a value that can only be arrived at in terms of the method per se and serves by definition as the only method for establishing the accepted value of the item measured.

Examples: Howard Mould Count, Reichert-Meissl value, loss on drying, salt in brine by density.

b) Reference Methods (Type II)

Definition: A Type II method is the one designated Reference Method where Type I methods do not apply. It should be selected from Type III methods (as defined below). It should be recommended for use in cases of dispute and for calibration purposes.

Example: Potentiometric method for halides.

(c) Alternative Approved Methods (Type III)

Definition: A Type III Method is one which meets the criteria required by the Committee on Methods of Analysis and Sampling for methods that may be used for control, inspection or regulatory purposes.

Example: Volhard Method or Mohr Method for chlorides

(d) Tentative Method (Type IV)

Definition: A Type IV Method is a method which has been used traditionally or else has been recently introduced but for which the criteria required for acceptance by the Committee on Methods of Analysis and Sampling have not yet been determined.

Examples: chlorine by X-ray fluorescence, estimation of synthetic colours in foods.

Table 2.2: Guidance on Method Listing in CXS 234

Types	Further explanation	Coexistence with other types	Examples
I	Need validation data.[5]	There can be only one Type I method listed for each commodity and provision (unless complementary or identical. No other Type II or Type III methods can be listed for same commodity and provision.	Determination of nitrogen content by Kjeldahl, determination of fat by Weibull-Berntrop,
II	Need validation data.[4]	There can be only one Type II method listed for each commodity and provision (unless identical or complementary).	Chromatography, spectrophotometry
III	Need validation data.[4]	Multiple Type III methods can be listed for a commodity and provision, but cannot exist without a Type II method.	Chromatography, spectrophotometry
IV	No or insufficient validation data.	Can be listed as alternative to Type I/II/III if deemed useful by CCMAS. More than 1 Type IV method may be listed for each commodity and provision. May be only method type listed when there are no other methods that meet	

[5] Precision figures for methods are an important aspect of assessing the performance of methods and that for newly developed / proposed Type I methods, precision figures should be presented as part of the data reviewed during the endorsement process. Lack of such data would not cause a change in the method type or revocation of a method.

Types	Further explanation	Coexistence with other types	Examples
		the general criteria for selection of methods.	

3. Process for the submission of methods of analysis for provisions in Codex Documents

3.1 Steps in the process

i. Signaling and capturing the need for a method when a new or amended provision or reference to the provision is incorporated in a Codex document.

ii. Initiative of one or more SDOs, Codex Members, or other Codex related entities (e.g. Bureau International des Poids et Mesures, International Oil Council) to identify an existing candidate method or to develop and validate the candidate method.

iii. Submission of the candidate method to the relevant Codex Committee, or directly to CCMAS when the relevant committee has been adjourned. (See Section 3.2 ii).

iv. A candidate method may be submitted directly to CCMAS for review and endorsement, even when the relevant Codex Committee is active. If endorsed, the method will be referred to the relevant Codex Committee for approval prior to submission to CAC.

v. Review of the method suitability (fitness for purpose) by the relevant Codex Committee and submission to CCMAS for review.

vi. Review, assign typing, endorsement of the method by CCMAS including decision on submission of a proposal to CAC for adoption of the method and inclusion in CXS 234, optionally indicating replacement or retyping of already listed method(s) in CXS 234. (See Section 3.4).

vii. Decision on adoption by CAC and inclusion in CXS 234, optionally replacing or editing already listed method(s) in CXS 234.

3.2 Acceptance of methods of analysis

The Codex Committees should submit methods to CCMAS for endorsement in line with the Procedural Manual. Codex standards for products in commercial trade between countries need to be defined by each committee.

i. All proposed methods of analysis must have direct pertinence to the Codex Standard to which they are directed.

ii. Each provision in a standard needs to have an attribute (*e.g.* limit value, maximum or minimum level, a description) and a suitable method of analysis for use should a dispute arise.

iii. When a committee develops a standard, during the development process and before submission of a method to CCMAS, the committee should:

a. Consider the criteria approach in place of recommending specific methods;

b. Determine if a suggested method of analysis is fit for purpose in consultation with relevant trade organizations, referee laboratories, competent authorities and standards development organizations;

c. Determine if there are validation data available for the method and analyte in the commodity or food;

d. Determine if the suggested method of analysis has been studied by one or more SDOs;

e. Consult the appropriate SDOs on the validation and publication status and applicability of the methods;

f. whenever possible, provide information to CCMAS for each individual analytical method proposed, relating to specificity, accuracy, precision (repeatability,

reproducibility) limit of detection, sensitivity, applicability and practicability, as appropriate[6] (see Annex I)

iv. Proposal of methods of analysis to CCMAS for endorsement should be carried out with the knowledge that the methods of analysis meet the above criteria (iii. a-f).

a. Proposals should include the information presented in the template in Annex 1 to allow the Committee to assess and compare the actual analytical performance of the method to the provision specifications in the relevant Codex Standard. CCMAS delegates and observers are expected to review this information prior to endorsing the method for inclusion in CXS 234.

b. Methods of analysis elaborated by international organizations occupying themselves with a food or group of foods are preferred.

c. Methods which have been validated in interlaboratory trials are preferred.

v. Committees are encouraged to offer proposals for the Typing of a method and the Principle (definition of the technique) according to the requirements of CXS 234. CCMAS will confirm these proposals and also consider the advice of relevant SDOs.

vi. Method proposals should be supplied to CCMAS well in advance (60 days**)** of a physical meeting to enable receipt of comments from interested parties.

a. Delegates, SDOs and observers are strongly encouraged to provide written comments in a timely fashion (30 days, prior to the meeting).

3.3 Endorsement by CCMAS of a proposed method of analysis is a multi-stage process:

i. Proposed methods are reported to the committee under Agenda Item 2 and Agenda Item 3 of the CCMAS Provisional Agenda.

ii. Methods together with their Typing and Principle are discussed by the Physical Working Group (PWG) on Methods Endorsement, generally held immediately prior to CCMAS.

1. Delegates and observers are encouraged to review the methods and make any recommendations on possible alternative methods or identical methods in writing prior (30 days) to the PWG and according to CCMAS timelines.

2. If recommendations of alternative methods or identical methods are made during the PWG and not prior to the PWG, discussion and endorsement of these methods may be held for discussion at the next meeting of the committee to allow for adequate review of the recommendations.

iii. The PWG report recommends endorsement and typing or denial of methods to the committee.

iv. CCMAS discusses the report of the Physical Working on Methods Endorsement in plenary.

v. Methods endorsed by CCMAS are forwarded to CAC for adoption, except if methods have been submitted directly to CCMAS and without prior input of the relevant active Codex Committee (Section 3.1 iv).

3.4 Revocation/removal by CCMAS of a method of analysis listed in CXS 234:

CCMAS has agreed (REP16 MAS, Appendix IV) to an on-going periodic (10 years) review of methods. This periodic review is partly intended to capture methods that need to be revoked/removed. Additionally, the following steps are applicable to initiate the revocation/removal of a method outside of the periodic review process:

i. The recognition that a method is obsolete, inappropriate (no longer fit for purpose) or has been withdrawn by the relevant SDO should be brought to the attention of CCMAS by Codex Committee members, member countries, observers and SDOs.

ii. When a method becomes obsolete the committee originally proposing the method of analysis should be informed and should find a replacement and bring it to the attention of CCMAS.

[6] Procedural Manual: *Relations between Commodity Committees and General subject Committees, Methods of Analysis and sampling, normal practices*

iii. The SDO should bring the information directly to CCMAS if the Codex Committee is adjourned or otherwise inactive/unresponsive.

iv. The opinion of the SDO which owns the method should be recognized by CCMAS.

v. Proposals for a replacement are encouraged and will be deliberated by CCMAS.

vi. If CCMAS identifies an obsolete or inappropriate method it should alert the committee (if active) of proposed removal from CXS 234, to allow the committee to respond to the revocation.

3.5 The role of SDOs in Codex Committees

To play a positive role in the maintenance of methods of analysis for use in the Codex system, SDOs wishing to maintain ownership and exercise their rights as methods providers (intellectual property and copyright issues) should undertake the following oversight activities:

i. Have Codex Alimentarius observer status

ii. Follow the activities of relevant Codex committees

iii. Contribute timely written comments on relevant issues

iv. Provide method performance data and other relevant information to the CCMAS during method review

v. Contribute oral comments during plenary proceedings

vi. Inform Codex of changes in SDO activities (for instance in a report/brief news item or through joint contributions of the InterAgency meeting)

vii. Bring to the attention of CCMAS actions at a Codex committee which may lead to a change in requirements for a method of analysis

viii. Bring to the attention of a Codex committee actions by CCMAS which may lead to a change in requirements for a method of analysis

ix. Provide Codex Alimentarius with assistance when deliberations involve technical details or a deeper understanding of analytical issues

x. Encourage horizontal and regional committees to seek the advice of relevant SDOs on analytical issues at all stages of standard development, including contacting those organizations not participating during a discussion.

xi. Ascertain that references in CXS 234 to their standards are correct and kept up to date.

3.6 The role of SDOs at CCMAS in the methods endorsement process

SDOs should be:

i. The provider of accurate information regarding the status of an analytical method and its stage within the organization's method evaluation process (e.g. publication status, SLV, full collaborative study or anecdotal or PT data collection) and its fitness for purpose.

ii. In agreement when methods are "Identical" or have sufficient differences to affect the analytical outcome. SDOs are to provide this assurance to CCMAS.

iii. Able to consider scope and scope extension vs "Codex general methods".

iv. Able to provide advice on method typing as these criteria are specific to Codex, and not generally used by SDOs outside of CCMAS.

3.7 Replacement of Type I methods

This sub-section is applicable to the replacement of a Type I method with a new Type I or with Type II/III method(s).

i. Codex committee, either through members or consultation with SDO, proposes to replace an existing Type I method

ii. The new method may be an empirical or rational method

iii. The new method is referred, reviewed and endorsed as outlined in sub-section 3.1

iv. As part of the endorsement a time frame to complete the change is established

v. If adopted by the Commission, the new method would replace the older method in CXS 234 at designated date.

3.8 Selection of Type II methods from multiple Type III methods

It is not uncommon that several analytical methods are proposed for a single commodity – provision combination. However, only one of these can be designated as the reference method (Type II method).

In the event of multiple Type III methods for the same provision-commodity combination, it is expected that these methods, although they might use different approaches, should result in equivalent decisions (compliant vs non-compliant).

Considerations for choosing a Type II methods among multiple Type III methods[7]

- As the scope of methods of analysis are aligned with various matrices from many groups of commodities (Codex Procedural Manual, General Criteria for the Selection of Methods of Analysis, Recommended Methods of Analysis and Sampling (CXS 234-1999), the method explicitly validated for the commodity stated in the Codex provision should be preferred: e.g. if a method for copper in infant formula is required, a method specifically validated for this commodity should be preferred to a method validated for milk powder.
- The method validated for more than one matrix from a specific commodity[8] should be preferred. For example, a method validated for milk-based, and soy protein-based infant formulas should be preferred to a method validated only for milk-based infant formula.
- The method with the best selectivity should be preferred.
- The method with the best precision data (if this precision difference is relevant to the question asked) should be preferred.
- The method where a certified reference material, preferably from a matrix similar to that used in the scope of the method, was included in the validation should be preferred.
- The method should be practicable and applicable under normal laboratory conditions.

Validation of the decision guidance is provided in Annex II.

3.9 Type IV methods and their transitioning to other method types

i. New candidate methods may only be typed as Type I, II or III when submitted with a full set of validation data, e.g. precision data obtained in conformity with internationally accepted standards. With the submission of other lesser validation data these methods will be listed as Type IV.

ii. Existing Type I methods without a full set of validation data are to be considered on a case-by-case basis by the relevant SDO(s) on:

    a. the feasibility of collecting and submitting the missing validation data to Codex

    b. the availability of an alternative candidate-method to become the Type I method

    c. the rationale for keeping the existing Type I method in place as is

    d. the rationale for retyping the method or revocation of the method.

iii. A method typed as Type IV may be retyped after the submission of acceptable validation data from the SDO, or method owner, to CCMAS. A method should not remain as Type IV indefinitely.

iv. Where two methods are proposed as Type I for a particular provision, the relevant SDOs shall determine if the methods are Identical (in which case they can both be listed) or if, based on the performance data or other information, one better meets the required criterion than another. In cases where there is a regional preference for one method over another,

[7] In some situations, CCMAS may decide not to apply these selection considerations, e.g. for ethical, economic or safety reasons. This decision must be duly justified.

[8] Different matrices belonging to one commodity. E.g infant formula includes milk-based, soy-based, hydrolyzed protein based.

the relevant Codex committee should decide, and provide justification on, which method to put forward to CCMAS.

4.0. Presentation of methods for incorporation into CXS 234

CXS 234 is a summary document that contains all the methods of analysis that cover provisions contained in Codex Standards but excludes methods for pesticides and veterinary drugs in food, the assessment of micro biological quality and safety in food, and the assessment of specifications for food additives. In time this will be the sole reference for these methods.

i. Information required:

   a. An attribute in a Codex standard with a limit/range of values or a characteristic (authenticity)

   b. A suitable method for the analysis, preferably from an accepted SDO

   c. Principle

   d. Codex Typing

   e. Assurance that sufficient testing has been carried out to generate precision data

   f. Validation data that prove fitness for purpose[9]

ii. Correct use of separators between methods presented in CXS 234 (as per Table 2.1).

iii. If separator is not applicable (e.g. not Identical), methods should be listed in separate rows.

[9] Degree to which data produced by a measurement process enables a user to make technically and administratively correct decisions for a stated purpose. *Guidelines on Analytical Terminology* (CXG 72-2009)

Annex I

Template for submissions of methods for Endorsement of Methods of Analysis and Sampling

Executive Summary (if long document)

Insert a brief summary of the submission and the recommendations to CCMAS.

Agenda Item #3: Endorsement of Methods of Analysis Provisions and Sampling Plans in Codex Standards

Codex Committee on ….

Methods of analysis for provisions in the Standard for .... (CXS….)

Method(s) for provision 1

- If relevant, reminder of the decision from Codex Committee.
- Title and description of Method A. Scope, validated matrice(s). Indicate where the method is published, and where the validated data/report of collaborative study is published.
- Description of the principle (including reagents, standards, temperatures, equipments…)
- If other methods are already listed in CXS 234, brief description of current method(s) (method B), and how the new proposed method compares to it.

Include a Summary table of the validation data for each attribute (repeatability, reproducibility, recovery and limit of quantitation, if data is not protected by copyright). The table and/or text above may include other relevant information from the collaborative study.

Attribute – XXX	**Method A**	**Method B**
Matrices, samples used in collaborative study		
Concentration range of matrices validated		
Repeatability (RSD_r or s_r)		
Reproducibility (RSD_R or s_R)		
Recovery range from SLV/MLT		
Accuracy (Certified materials)		
Limit of Quantitation		
CXS XX provision 1		

[Note: SLV refers to Single Laboratory Validation. MLT refers to Multi-Laboratory Testing studies (i.e. collaborative studies).]

Summary of proposed changes in CXS 234, including retyping of existing methods and recommendations to CCMAS

Table 1. Recommended Methods of Analysis and Sampling (CXS 234-1999)

Commodity	**Provision**	**Method**	**Principle**	**CXS**	**Proposed Type**
Commodity	Provision	**New method A**	**Principle**		**II**
		Existing method B retyped	Principle		~~II~~ **III**
		Existing method C no change	Principle		III
		~~Existing method proposed to be removed~~	~~Principle~~		~~III~~

Recommendations to CCMAS

XXX recommends CCMAS to take the following actions:

1. Endorse Method A as Type II for the determination of attribute(s) in commodity A and reclassify the following existing Type II methods as Type III:
    a. Method B
    b. Method C

Annex 2

Validation of the decision guidance for the selection of a Type II method from multiple Type III methods.

Validation of the decision guidance (Section 3.8)

To test the selection guidance, the following commodity-provision combinations with multiple Type III methods included in CXS-234 were used:

- Sodium and Potassium in infant formula (1 Type II and 3 Type III methods)
- Copper in milkfat products (1 Type II, 2 Type III methods)

Table 1: Selection guidance for Type II methods

Provision and Commodity	Method	Principle	Type	Type II				
				validated for commodity	validated for larger panel matrices	best selectivity	best precision data	certified reference material included pref. Similar matrix scope
Sodium/ Potassium in infant formula	AOAC 2015.06	ICPMS	Type II	x	x		x	x
	AOAC 2011.14	ICPOES	Type III	x	x			x
	ISO 8070 IDF 119	FAAS	Type III Was Type II	no, milk products only	x			x milk powder
	AOAC 986.24	ICPOES	Was Type III					?
Copper in milkfat products	AOAC 2015.06	ICPMS	Type II	yes, butter	x	x		yes, infant formula
	ISO 5738 IDF 76	photometry	Type III	yes, butter, butterfat	x		x	no
	AOAC 2011.14	ICPOES	candidate Type III	yes, butter	x			yes, infant formula

Considerations selection Type II method Sodium/Potassium in infant formula:

- AOAC 986.24 cannot be considered as Type II because of difference in analytical steps as compared to other Type III methods, which may have implications on the results. In addition, this method has 'Safety concerns' (Perchloric acid destruction). Method is rightfully revoked by the SDO and CXS-234.
- ISO 8070 | IDF 119, has an option to use dry ashing as a sample preparation, which is not appropriate for the determination of sodium. In addition, the method is not validated for Infant Formula. In conclusion, this method has several drawbacks as compared to the other 2 candidate Type II methods: AOAC 2011.14 and AOAC 2015.06.
- Comparing AOAC 2015.06 and AOAC 2011.14, which are both validated on the same samples, AOAC 2015.06 has better precision data and therefore should be preferred as Type II method. (MAS40/ CRD05 for precision data)

Considerations selection Type II method Copper in milkfat products:

- The validation of AOAC 2011.14 does not cover the range of the provision and consequently cannot be considered as Type III method. (MAS40/CRD06 for precision data)
- Although ISO 5738 | IDF 76 based on photometry seems to have better precision data, AOAC 2015.06 based on ICP-MS has a better selectivity and therefore should be preferred as Type II.

Conclusions

From the examples of Sodium and Potassium in infant formula and Copper in milkfat products, the guidance (see Section 3.8) is suitable for the selection of the appropriate Type II method when multiple Type III methods exist, and may therefore support CCMAS in the process of consideration and endorsement of methods for inclusion in CXS234.