SAMPLING AND ANALYSIS FOR VERIFYING SAFETY OF FOOD

PROCEDURES FOR ELABORATION AND ENDORSEMENT OF CODEX METHODS

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GENERAL QUESTIONS WHICH NEED TO BE ADDRESSED WHEN CONSIDERING METHODS OF ANALYSIS AND SAMPLING WITHIN CODEX

Role of Codex Committees

Role of CCMAS

Who produces methods of analysis and sampling incorporated in Codex Standards

How are they incorporated

Quality of methods of analysis

General Principles

Do you know data are interpreted i.e. how is the measurement uncertainty estimated and then used?.

Have you ever had problems with experimental data reported to you – e.g. conflicting results from your contractors/laboratories?

Do you participate in, or require contractors to participate in, proficiency testing schemes?

What are tolerances – need to consider both analysis and intentional manufacturing tolerances?

Are you concerned about the use of proprietary methods for Standardisation and official control purposes?

Are you happy with the criteria approach to methods of analysis?

Or, putting this rather more formally:

NEED TO CONSIDER

Analytical Requirements for Food Laboratories as a result of the Codex Alimentarius Commission

Enforcement of Codex “legislation”

Method Validation Requirements in Codex Alimentarius Commission

Methods in Codex “legislation”

Terminology in Codex Alimentarius Commission

Application of Methods of Analysis in the Laboratory

Application of Methods of Analysis in the Laboratory – Measurement Uncertainty estimation and compliance aspects

Types of methods (empirical and rational) - Codex definitions

Method validation (how do we know that a method is “acceptable” – i.e. is it fit-for-purpose?).

Codex requirements where specific methods are prescribed

Codex requirements where method performance criteria are prescribed (criteria approach)

Laboratory quality – accreditation

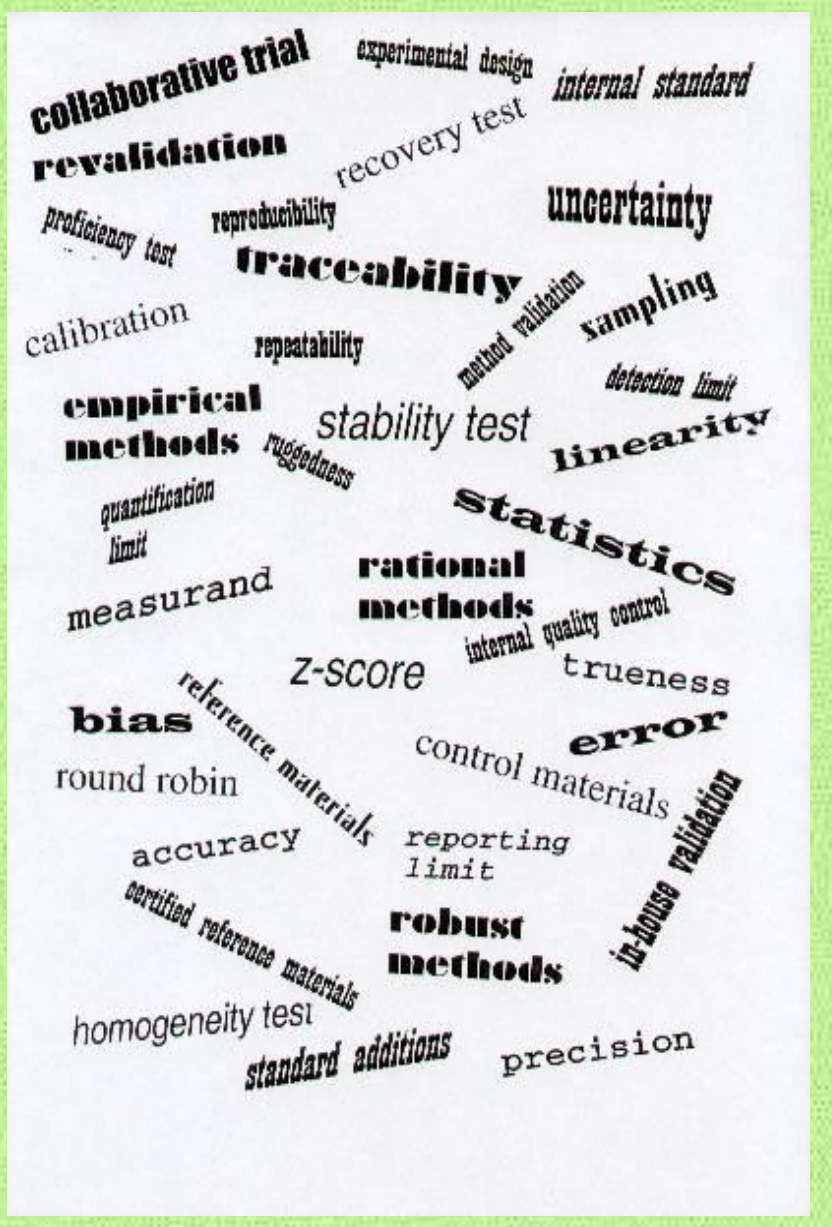
Proficiency testing

Internal Quality Control

Method verification (use of CRMs etc)

Recovery Corrections - Do We Need to Carry Out?

Guidelines for settling disputes over analytical (test) results (CAC/GL 70-2009)


collaborative trial
experimental design
internal standard
revalidation
recovery test
uncertainty
proficiency test
reproducibility
traceability
calibration
method validation
sampling
repeatability
detection limit
empirical methods
stability test
linearity
ruggedness
quantification limit
statistics
rational methods
measurand
internal quality control
z-score
trueness
reference materials
bias
error
round robin
control materials
in-house validation
accuracy
reporting limit
certified reference materials
robust methods
homogeneity test
standard additions
precision

ANALYTICAL REQUIREMENTS FOR FOOD LABORATORIES AS A RESULT OF CODEX ALIMENTARIUS COMMISSION

TYPES OF METHODS OF ANALYSIS IN CODEX

Defining Methods (Type I) (- empirical methods where result is method dependent)

Reference Methods (Type II) (- rational methods where result is independent of method used)

Alternative Approved Methods (Type III) (- rational methods)

Tentative Methods (Type IV) (- either rational or empirical methods)

Specific methods stipulated in Codex standards.

But the “criteria approach” increasingly getting favoured.

WHAT IS THE CRITERIA APPROACH TO METHODS OF ANALYSIS?

WHY INTRODUCE IT?

Traditional Approach (prescribing a specific method of analysis) means:

- The analyst is denied freedom of choice and thus may be required to use an inappropriate method in some situations;

- The procedure inhibits the use of automation;

and

- It is administratively difficult to change a method found to be unsatisfactory or inferior to another currently available.

Traditional Approach (prescribing a specific method of analysis) does:

apply to Codex Type I, II and III methods

and where the method should be “fully validated”.

Criteria Approach (prescribing performance characteristics) means:

- giving greater flexibility than the present traditional procedure adopted by organisations such as Codex

- not being in the situation of having many methods of analysis which are available, which meet requirements as regards method performance characteristics, but which are not considered by Codex because of time constraints.

Considerations

Only applicable to rationale methods, not to empirical methods (i.e. where the result is method dependent) - need to define these better?

Are methods equivalent – or can they be made equivalent? Is it reasonable to force equivalency?

What does empirical (defining) mean?

Units (activities *vs* concentrations) – needed to assess the "quality" of the method.

CHARACTERISATION OF METHODS OF ANALYSIS - CONVERSION OF SPECIFIC METHODS OF ANALYSIS TO METHOD CRITERIA BY THE CCMAS

When a Codex Committee submits a Type II or Type III method to CCMAS for endorsement, it should also submit information on the specified Codex level(s) along with the provision to enable the CCMAS to convert it into suitable generalised analytical characteristics:

1. trueness
2. applicability (matrix, concentration range and preference given to 'general' methods)

3. limit of detection
4. limit of quantification
5. precision; repeatability intra-laboratory (within laboratory), reproducibility inter-laboratory (within laboratory and between laboratories), but generated from method performance study data rather than measurement uncertainty considerations
6. recovery
7. selectivity
8. sensitivity
9. linearity

Then need to assess if satisfactory with respect to:

Range of applicability
Limit of detection
Limit of quantification
Precision
Recovery
Trueness

Approach has been used for many years in some Codex Member Countries (UK since 1994)

GUIDELINES FOR ESTABLISHING NUMERIC VALUES FOR THE CRITERIA

Need to Consider:

applicability (analyte, matrix, conc. range)

selectivity

sensitivity

linearity

precision (s_r and 5_R)

limit of detection (LOD)

limit of quantification (LOQ)

recovery

trueness (bias)

Applicability

The method has to be applicable for the specified provision, specified commodity and the specified level(s) (maximum and/or minimum) (ML). The minimum applicable range of the method depends on the specified level (ML) to be assessed, and can either be expressed in terms of the reproducibility standard deviation (sR) or in terms of LOD and LOQ.

Minimum applicable range:

For ML ≥ 0.1 mg/kg, [ML - 3 sR , ML + 3 sR] For ML < 0.1 mg/kg, [ML - 2 sR , ML + 2 sR]

sR = standard deviation of reproducibility

LoD/LoQ

Limit of Detection (LOD):

For ML ≥ 0.1 mg/kg, LOD ≤ ML · 1/10
For ML < 0.1 mg/kg, LOD ≤ ML · 1/5

Limit of Quantification (LOQ):

For ML ≥ 0.1 mg/kg, LOQ ≤ ML · 1/5
For ML < 0.1 mg/kg, LOQ ≤ ML · 2/5

Precision

For ML ≥ 0.1 mg/kg, HorRat value ≤ 2

For ML < 0.1 mg/kg, the RSD = 22%.

Recovery

Concentration	Ratio	Unit	Recovery (%)
100	1	100% (100 g/100g)	98 – 102
≥10	10^{-1}	≥ 10% (10 g/100g)	98 – 102
≥1	10^{-2}	≥ 1% (1 g/100g)	97 – 103
≥0.1	10^{-3}	≥ 0.1% (1 mg/g)	95 – 105
0.01	10^{-4}	100 mg/kg	90 – 107
0.001	10^{-5}	10 mg/kg	80 – 110
0.0001	10^{-6}	1 mg/kg	80 – 110
0.00001	10^{-7}	100 µg/kg	80 – 110
0.000001	10^{-8}	10 µg/kg	60 – 115
0.0000001	10^{-9}	1 µg/kg	40 – 120

Trueness

Other guidelines are available for expected recovery ranges in specific areas of analysis.

In cases where recoveries have been shown to be a function of the matrix other specified requirements may be applied.

For the evaluation of trueness preferably certified reference material should be used.

EU Tin Performance Criteria*

A: Simple Criteria Approach

Specific methods for the determination of tin contents are not prescribed. Laboratories should use a validated method that fulfils the performance criteria indicated [in Table 3]. The validation should ideally include a certified reference material in the collaborative trial test materials.

[* from first EU Tin Sampling and Analysis Directive]

Table 3: Performance criteria of methods for tin analyses

Parameter	**Value/Comment**
Applicability	Foods specified in Regulation (EC) No…/2003
Detection limit	No more than one 5 mg/kg
Limit of quantification	No more than one 10 mg/kg
Precision	$HORRAT_r$ or $HORRAT_R$ values of less than 1.5 in the validation collaborative trial
Recovery	80% - 105%
Specificity	Free from matrix or spectral interferences

B: Performance Criteria – Uncertainty Function Approach

However, an uncertainty approach may also be used to assess the suitability of the method of analysis to be used by the laboratory. The laboratory may use a method which will produce results with a maximum standard uncertainty given by the following formula:

$$Uf = \sqrt{(CL/2)^2 + (0.1C)^2}$$

where: Uf is the maximum standard uncertainty
CL is the detection limit of the method
C is the concentration of interest

Results with an uncertainty less than that stipulated above will be produced by a method which is equivalent to one meeting the previous performance characteristics.

- The adoption of a more generalised approach would ensure that such methods are brought into the legislative system and does not disadvantage developments being undertaken elsewhere in the analytical community.

Fitness-for-purpose' Approach (Uncertainty Function Approach)

Where a limited number of fully validated methods of analysis exist, alternatively, a fitness-for-purpose' approach may be used to assess the suitability of the method of analysis. Methods suitable for official control must produce results with standard measurement uncertainties less than the maximum standard measurement uncertainty calculated using the formula below:

$$Uf = \sqrt{(CL/2)^2 + (aC)^2}$$

where: Uf is the maximum standard uncertainty

CL is the detection limit of the method

C is the concentration of interest

a is a numeric factor to be used depending on the value of C.

Results with an uncertainty less than that stipulated above will be produced by a method which is equivalent to one meeting the previous performance characteristics.

C (μg/kg)	a
a≤ 50	0.25
1 to 500	0.18
501 to 1,000	0.15
1 ,001 to 10,000	0.12
> 10,000	0.1

PROVISIONS ON THE USE OF PROPRIETARY METHODS IN CODEX STANDARDS

(Added to the Procedural Manual)

Definition of a Proprietary Method of Analysis

For Codex purposes a proprietary method of analysis is one that contains protected intellectual property preventing full disclosure of information about the method and/or where the intellectual property owner restricts the use or distribution of the method or materials for its performance such that no alternative source of these would be available. It does not extend to a method which is subject only to copyright.

REQUIREMENTS

A proprietary method should not be endorsed if there is available a suitable non-proprietary method of analysis which has been or could be endorsed and which has similar or better performance characteristics.

Openness of reagents/system is encouraged

Fully validated requirement is maintained.

If only third-party validated, will be a Type IV method.

Endorsement needs to be reviewed if non-proprietary becomes available.

CONCLUSIONS - 1

Many initiatives over past years have been driving towards “quality”.

Quality of laboratories with appropriate their internal control procedures now required in Codex.

Quality of methods of analysis now defined in Codex.

Stipulation of specific methods of analysis in Codex is becoming less prevalent – being replaced by the “criteria” approach.

This is also leading to a fitness approach.

CONCLUSIONS - 2

Need to understand the method performances characteristics and how they are calculated.

Need to be able to differentiate between rational and empirical (defining) methods.

Potential problems with proprietary methods of analysis.