VAM SEMINAR: CURRENT ISSUES IN METHOD VALIDATION

WHERE WE ARE WITH RESPECT TO METHOD REQUIRMENTS AND VALIDATION IN THE FOOD SECTOR

Roger Wood, Food Standards Agency,UK
c/o Institute of Food Research,
Norwich Research Park, Colney, Norwich NR4 7UA

Will cover:

SCOPE

1. These guidelines provide a framework for the implementation of quality assurance measures to ensure the competence of testing laboratories involved in the import and export control of foods.

2. These guidelines are intended to assist countries in the application of requirement for trade in foodstuffs in order to protect the consumers and to facilitate fair trade.

REQUIREMENTS

3. The following criteria shall be adopted by laboratories involved in the import and export control of foods:

- Compliance with the general criteria for testing laboratories laid down in ISO/IEC Guide 25: 1990 “General requirements for the competence of calibration and testing laboratories”; [i.e. effectively accreditation],

- Participation in appropriate proficiency testing schemes for food analysis which conform to the requirements laid down in “The International Harmonised Protocol for the Proficiency Testing of (Chemical) Analytical Laboratories”, Pure and Applied Chemistry 65 (1993) 2132-2144; [already adopted for Codex purposes by the CAC at its 21st Session in July 1995]

- Whenever available, use methods of analysis which have been validated according to the principles laid down by the CAC, and

- Use internal quality control procedures, such as those described in the “Harmonised Guidelines for Internal Quality Control in Analytical Chemistry Laboratories”, Pure and Applied Chemistry 67 (1995) 649-666

4. The bodies assessing the laboratories referred to above should comply with the general criteria for laboratory accreditation, such as

REGULATION (EC) No 882/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 29 April 2004

on official controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules.

Article 11

Methods of sampling and analysis

1. Sampling and analysis methods used in the context of official controls shall comply with relevant Community rules or,

(a) if no such rule exist, with internationally recognised rules or protocols, for example those that the European Committee for standardisation (CEN) has accepted or those agreed in national legislation; or

(b) in the absence of the above, with other methods fit for the intended purpose or developed in accordance with scientific protocols

2. Where paragraph 1 does not apply, validation of methods of analysis may take place within a single laboratory according to an internationally accepted protocol.

3. Wherever possible methods of analysis

Article 12

Official laboratories

1. The competent authority shall designate laboratories that may carry out the analysis of samples taken during official controls.

2. However, competent authorities may only designate laboratories that operate and are assessed and accredited in accordance with the following European Standards:

- EN ISO/IEC 17025 on “General requirements for the competence of testing and calibration laboratories”;

- EN 45002 on “General criteria for the assessment of testing laboratories”;
- EN 45003 on “Calibration and testing laboratory accreditation system – General requirements for operation and recognition”,

taking into account criteria for different testing methods laid down in Community feed and food law.

3. The accreditation and assessment of testing laboratories referred to in paragraph 2 may relate to individual tests or groups of tests.

4. The competent authority may cancel the designation referred to in paragraph 1 when the conditions referred to in paragraph 2 are no longer fulfilled.

ANNEX III: CHARACTERISATION OF METHODS OF ANALYSIS

- Methods of analysis should be characterised by the following criteria:

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.

Criteria Approach (prescribing performance characteristics) means:

- This “criteria” approach gives greater flexibility than the present procedure adopted by organisations such as Codex and the EU
- In some areas of food analysis there are many methods of analysis which are available, which meet requirements as regards method charactchara i 90 -5.2.4(er)5.4(04 .4(i 90 -5.2.o72(he p5T4w[o()s0 -5.T4wfdP5.4(o) p5n(v)7(ailab903(l)-[3U.9(e a)-5.Trnd th90 th90 thTD0.002n5.86

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

Horwitz Values

The precision values are calculated from the Horwitz equation, i.e.:

$RSD_R = 2^{(1-0.5\log C)}$

where:

RSD_R is the relative standard deviation calculated from results generated under reproducibility conditions [($s_R / \bar{x}$) x 100]

C is the concentration ratio (i.e. 1 = 100g/100g, 0.001 = 1,000 mg/kg)

The mathematical form of the function

The functional form of the Horwitz relationship is more easily perceived if the traditional trumpet is replaced by a mathematically equivalent relationship between predicted reproducibility standard deviation σ_H and concentration c, namely

$$\sigma_H = 0.02c^{0.8495}$$

- 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.

THE RELATIONSHIP BETWEEN THE FINAL ANALYTICAL RESULT AND THE SAMPLING, THE MEASUREMENT UNCERTAINTY AND THE RECOVERY FACTOR USED TO OBTAIN THAT RESULT

These factors affect the relationship between the final analytical result and the provisions in legislation

Decisions taken by those responsible for the enforcement of legislation directly affect decisions as to whether a lot is in compliance with that legislation.

SCIENTIFIC CO-OPERATION TASK 9.1

"PREPARATION OF A WORKING DOCUMENT IN SUPPORT OF THE UNIFORM INTERPRETATION OF LEGISLATIVE STANDARDS AND THE LABORATORY QUALITY STANDARDS PRESCRIBED UNDER DIRECTIVE 93/99/EEC"

was initiated to identify differences amongst Member States.

Two countries may have different national rules for the interpretation of results from lots.

Country A requires: that each and every item in the lot meets the specification. In this example it means that all 1,000 units, if analysed separately, would have to be less than 2.0 mg/kg. Here a significant number of units are greater than 2.0 mg/kg so the lot would be deemed to be in non-compliance with the legal specification and so would be rejected, but Country B requires: that the mean value of the characteristic in the lot is to be less than the legal specification. In this case the mean value is 1.9 mg/kg so the lot would be deemed to be in compliance with the legal specification.

Consequence: the two countries A and B will make different judgements as to compliance with a legal specification on essentially the same lot. This is unacceptable and can only be avoided if the sampling procedures are elaborated at the same time as the commodity standard is elaborated. In addition it should also be noted that the number of units to be analysed also influences the decision on compliance.

REPORTING OF RESULTS WITH RESPECT TO THEIR MEASUREMENT UNCERTAINTY

All analytical results should be reported in the form "a ± b" where "a" is the best estimate of the true value of the concentration of the measurand (the analytical result) and "a-b" to "a+b" is the range within which the true value is estimated, with a given probability, to fall. The value of "b" is known as the "measurement uncertainty" and may be estimated by the analyst in a number of different ways.

The estimation of the value of "a" is dependent on: the accuracy of the method of analysis used, how well the analyst uses that method, i.e. whether the analytical system is "in control".

The value of the measurement uncertainty "b" is dependent on:

- **the inherent precision of the method of analysis used**
- **the number of analytical replicates that are carried out.**

The more replicates the less the value of the measurement uncertainty.

REPORTING OF RESULTS BY FOOD CONTROL ANALYSTS

The procedure adopted by some food control analysts is to report samples as containing "not less than "a" – "b"" in situations where the statutory limit is a maximum permissible concentration. Thus, in any enforcement situation the maximum benefit is given to the food producer. This is consistent with the requirement to prove ***beyond reasonable doubt*** that a limit h4Q932 TD5fT*n8 s-6.894.6( )]TJnG1 1 Tf17.5(are carriedt)8(.4.6x)1387entsare

Other food analysts may report the value "a"

without taking into account any measurement

uncertainty considerations.

Similar considerations identified in Codex Alimentations Commission

Section on
"The Use of Analytical Results: Sampling, Relationship Between the Analytical Results, the Measurement Uncertainty, Recovery Factors and the Provisions in Codex Standards"
to be included in Procedural Manual

ISSUES INVOLVED

There are a number of analytical and sampling considerations which prevent the uniform implementation of legislative standards. In particular, different approaches may be taken regarding sampling procedures, the use of measurement uncertainty and recovery corrections.

At present there is no official guidance on how to interpret analytical results

2. Measurement Uncertainty

That an allowance is to be made for the measurement uncertainty when deciding whether or not an analytical result falls within the specification. This requirement may not apply in situations when a direct health hazard is concerned, such as for food pathogens.

3. Recovery

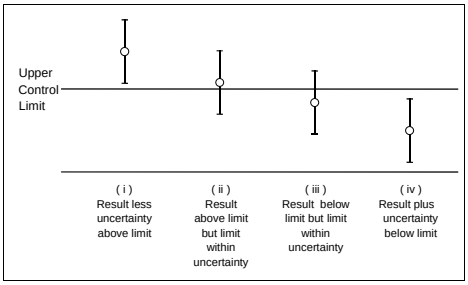
Where relevant and appropriate the analytical results are to be reported on a recovery corrected basis and that the recovery should be quoted in any analytical report. Analytical results are to be expressed on a recovery corrected basis where appropriate and relevant, **and when corrected it has to be so stated.**

In all cases it has to be stated when the result is corrected for recovery.

If a result has been corrected for recovery, the method by which the recovery was taken into account should be stated. The recovery rat-7.7(n coat)57.8(r)5en i(1u5(e)0cC821Te2bn5.8(r)5en c77(d) ( )-7.8)5en 326.9(e)st an9.4.8(a)89(e)stnep836(a)3mct

4. Significant Figures

The units in which the results are to be expressed and the number of significant figures to be included in the reported result.



This means that the legal specification and enforcement limit are different.

This should be appreciated when specification is being set.

UNCERTAINTY OF SAMPLING

Draft EURACHEM Guide

Codex paper

UNCERTAINTY OF SAMPLING

Example 1 – Nitrate concentration in glasshouse

Example 3 – Moisture in wholesale butter

Mean = 15.754 % (m/m)

Analytical uncertainty: 0.0421 % (m/m)

Sampling uncertainty: 0.1947 % (m/m)

Measurement uncertainty: 0.1992 % (m/m)

FUTURE

Codex looking at the dispute situation

IUPAC looking at qualitative analysis

Inter-Agency Members (ISO, CEN etc) looking at making more method validation information available.

- Need to appreciate that sampling and its uncertainty will become a real issue

But what is the cost to him?

It will be essential for him to develop and appreciate statistical skills in order to be able to use this new-found freedom effectively.