CODEX ALIMENTARIUS
INTERNATIONAL FOOD STANDARDS

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World Health Organization

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GUIDELINES ON PERFORMANCE CRITERIA FOR METHODS OF ANALYSIS FOR THE DETERMINATION OF PESTICIDE RESIDUES IN FOOD AND FEED

CAC/GL 90-2017

Adopted in 2017.

OBJECTIVE

1. The purpose of these guidelines is to define and describe the performance criteria, which should be met by methods to analyse pesticide residues in foods and feed (hereafter referred to as food). It addresses the characteristics/parameters to provide scientifically acceptable confidence in the analytical method that is fit for the intended use and may be used to reliably evaluate pesticide residues for either domestic monitoring and/or international trade.

2. This document is applicable to both single residue methods and multi-residue methods (MRMs) that analyse target compounds in all food commodities per the residue definition.

3. These guidelines cover qualitative and quantitative analyses, each having their own method performance criteria. Performance criteria of methods for analyte identification and confirmation are also addressed.

PRINCIPLES FOR THE SELECTION AND VALIDATION OF METHODS

A. Defining the Purpose of the Method and Scope

4. The intended purpose of the method is usually described in a statement of scope, which defines the analytes (residues), the matrices, and the concentration ranges. It also states whether the method is intended for screening, quantification, identification, and/or confirmation of results.

5. In regulatory applications, the maximum residue limit (MRL) is expressed in terms of the residue definition. Residue analytical methods should be able to measure all components of the residue definition.

6. *Fitness-for-purpose* is the extent to which the performance of a method meets the end-user's needs, and matches the criteria (data quality objectives) agreed between the laboratory and the end-user (or client) of the data, within technical and resource constraints. *Fitness-for-purpose* criteria could be based on some of the characteristics described in this document, but ultimately will be expressed in terms of acceptable combined uncertainty[1].

7. Selection of methods is based on analytes and the intended purpose of the analyses[2].

B. Supplementing other Codex Alimentarius Commission Guidelines

8. The Codex Alimentarius Commission (CAC) has issued a guideline[3] for laboratories involved in the testing of foods for import/export which recommends that such laboratories should:

   (a) use internal quality control procedures, such as those described in the "Harmonized Guidelines for Internal Quality Control in Analytical Chemistry Laboratories;"

   (b) participate in appropriate proficiency testing schemes for food analysis which conform to the requirement laid out in "The International Harmonized Protocol for Proficiency Testing of (Chemical) Analytical Laboratories (Pure Appl. Chem., vol 78, No. 1, pp.145-186, 2006);" and

   (c) whenever available, use methods which have been validated according to principles provided by the CAC.

9. The analytical methods should be used within the internationally accepted, approved, and recognized laboratory Quality Management System[4] to be consistent with the principles in the document for quality assurance (QA) and quality control (QC) referenced above.

C. Method Validation

10. The process of method validation is intended to demonstrate that a method is *fit-for-purpose*. This means that when a test is performed by a properly trained analyst using the specified equipment and materials and exactly following the method protocol, accurate, reliable, and consistent results can be obtained within specified statistical limits for sample analysis. The validation should demonstrate the identity and concentration of the analyte, taking into account for matrix effects, provide a statistical characterization of recovery results, and indicate if the frequency of false positives and negatives are acceptable. When the method is followed using suitable analytical standards, results within the established performance criteria should be obtained on the same or equivalent sample material by a trained analyst in any experienced residue testing laboratory. To ensure method performance remains appropriate over time, method validation should be continuously assessed (e.g. recovery spikes).

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1 Harmonized IUPAC Guidelines For Single-Laboratory Validation of Methods of Analysis, Pure & Appl. Chem., 74(5), 2002; 835 – 855

2 OECD Guidance Document on Pesticide Residue Analytical Methods, ENV/JM/MONO (2007)17

3 *Guidelines for the Assessment of the Competence of Testing Laboratories Involved in the Import and Export Control of Food* (CAC/GL 27-1997)

4 General requirements for the competence of testing and calibration laboratories, ISO/IEC 17025 (2005).

PERFORMANCE PARAMETERS FOR ANALYTICAL METHODS

11. The general requirements for the individual performance criteria of a method are summarized below[1,5]

A. Method Documentation

12. After validation, the method documentation should provide, in addition to performance criteria (data quality objectives), the following information:

    (a) Identity of the analytes included in the residue definition.

    (b) Concentration range covered by the validation;

    (c) Matrices used in the validation (representative commodity categories, e.g., similar agricultural products based on characteristics including moisture, fat, and sugar content, pH);

    (d) Protocol describing the equipment, reagents, detailed step-by-step procedure including permissible variations (e.g. "heat at 100 ± 5 °C for 30 ± 5 min"), calibration and quality procedures, special safety precautions required, and intended application and critical uncertainty requirements;

    (e) quantitative result of the expanded measurement uncertainty (MU) for the method should be calculated in the validation procedure and reported, if required.

B. Selectivity

13. Ideally, selectivity should be evaluated to demonstrate that no interferences occur which significantly affect the analysis. It is impractical to test the method against every potential interferant, but it is required that common interferences are checked by analysing a reagent (process) blank for every batch of reagents. When reagents and/or solvents are changed between batches of samples, additional reagent blank evaluations could be performed. Background levels of plasticizers, septa bleed, cleaning agents, reagent impurities, laboratory contamination, carry-over, etc. tend to show up in reagent blanks and must be recognized by the analyst when they occur. Also, analyte-to-analyte interferences must be known by checking individual analytes in mixed standard solutions. Matrix interferences are evaluated by analyses of samples known to be free of the analytes and a matrix blank is required with each batch of samples or a standard addition approach to quantification is adopted (see Section E).

14. As a general principle, selectivity should be such that interferences have no impact on method performance. The ultimate test of selectivity involves the rates of false positives and negatives in the analyses. To estimate rates of false positives and negatives during method validation, an adequate number of blanks per matrix [not from the same source] should be analysed along with spiked matrices at the analyte reporting level.

C. Calibration

15. With the exception of errors in preparation of calibration materials, calibration errors are usually a minor component of the total uncertainty, and can be safely assigned into other categories. For example, random errors resulting from calibration are part of the uncertainty, while systematic errors cause analytical bias, both of which are assessed as a whole during validation and on-going quality control. Nevertheless, there are some characteristics of calibration that are useful to know at the outset of method validation because they affect optimization of the final protocol. For example, it must be known in advance whether the calibration curve is linear or quadratic, passes through the origin, and is affected by the sample matrix or not. The described guidelines in this document relate more to validation, which may be more detailed than the calibration undertaken during routine analysis.

16. Replicate measurements are needed to provide an empirical estimate of uncertainty. The following calibration procedures are recommended for the initial method validation:

    (a) determinations at five or more concentrations should be performed (consider multiple injections per concentration);

    (b) the reference standards should be evenly spaced over the concentration range of interest and the calibration range should encompass the entire concentration range likely to be encountered;

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5 OECD Guidance Document for Single Laboratory Validation of Quantitative Analytical Method-Guidance used in support of pre-and post-registration data requirements for plant protection and biocidal products ENV/JM/MONO(2014)20