codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 12(b) **CX/RVDF 01/13**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Thirteenth Session, 4-7 December 2001
Charleston, South Carolina, USA

CONSIDERATION OF THE IDENTIFICATION OF ROUTINE METHODS OF ANALYSIS FOR VETERINARY DRUG RESIDUES IN FOODS

Governments and international organizations wishing to submit comments on the following subject matter are invited to do so **no later than 1 October 2001** as follows: U.S. Codex Office, Food Safety and Inspection Service, US Department of Agriculture, Room 4861, South Building, 14th and Independence Avenue, S.W., Washington, DC 20250, USA (Fax No: +1.202.720.3157; e-mail: uscodex@usda.gov), with a copy to the Secretary, Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, FAO, Viale delle Terme di Caracalla, 00100 Rome, Italy (Telefax: +39.06.5705.4593; E-mail: Codex@fao.org).

1. The 12th Session of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) agreed to reinstate its *ad hoc* Working Group on Methods of Analysis and Sampling under the Chairmanship of Canada and the United States (ALINORM 01/31, paras. 102-109).

2. The *ad hoc* Working Group on Methods of Analysis (WG) of the CCRVDF requests your assistance in identifying analytical methods that may be suitable for the monitoring of maximum residue limits (MRLs) in food. This request is a continuation of the analytical method information collection that commenced at the 10th session of the CCRVDF.

3. The chief purpose of the CCRVDF *ad hoc* Working Group on Methods of Analysis and Sampling (WG) is to specify analytical methods that can be fully recommended for the measurement of the MRLs for the food residues of veterinary drugs promulgated by the CCRVDF. The availability of the technical specifications of potential methods along with sufficient validation and performance information is necessary to objectively evaluate an analytical method.

4. Phase I of the data collection effort was to determine the extent of analytical methods that were in use in countries for food control purposes. This initial request was based on the premise that analytical methods in use in countries for the monitoring of animal drug residues may also provide a scientific basis for recommending methods for CCRVDF use. It was also anticipated that the availability of this information would have the added benefit of helping to conserve technical resources and reduce the time needed for recommending an analytical method for monitoring of MRLs.

5. Therefore, the WG's initially requested countries to identify the existence and type of analytical method that was in use for a list of animal drugs that was provided. The specific technical information requested was the Species, the Matrices, The Scientific Principle of the Method, (e.g. HPLC, GC, MS etc), the LOQ and whether the method was used as a Screening, Quantitative or Confirmatory method.

6. The following countries responded to the initial request for analytical method information: Australia, Botswana, Brazil, Canada, Costa Rica, Denmark, Finland, France, Germany, Japan, Kenya, Malaysia , Malta, Mexico, New Zealand, Poland, Slovak Republic, South Africa, Switzerland, Thailand, United Kingdom, and the United States of America. A summary of the number of analytical methods that were reported by these countries as being used for selected animal drugs is in Attachment 1. The WG greatly appreciates the work of these countries in responding to the request for information. Phase I of the survey, initial data gathering, is complete.

7. This request initiates Phase II of the project and is an invitation to countries to provide a detailed information on analytical methods, validation and method performance data for the drugs listed in Attachment 1.

8. It is requested that the technical information be summarized to facilitate technical review. A suggested data format for the summary information is outlined in Attachment 2. Additional technical data may be appended to the basic summary and countries are encouraged to attach additional relevant information to the summary data.

9. Attachment 3 outlines scientific issues that are commonly considered in the development and validation of analytical methods. This information is intended to be of help to countries in selecting and organizing information for completion of the suggested method summary as specified in Attachment 2. An effort was made to keep this outline to a minimum and the list is therefore, not a complete exposition of technical issues. The scientific experts of responding countries are invited to emphasize additional scientific issues that they deem relevant.

10. It is hoped that you will be able to help in this endeavor to gather needed, relevant method performance information on analytical methods. Your efforts could help in the more timely provision of fully recommended analytical methods for veterinary drug residues in food which would be of use to all of us interested in food safety.

Attachment 1

SUM OF ANALYTICAL METHODS REPORTED BY RESPONDING COUNTRIES

Drug	Number of Methods
Alpha cypermethrin	2
Abamectin	4
Albendazole	13
Azaperone	7
Benzyl penicillin	20
Carazolol	7
Carbadox	6
Ceftiofur sodium	4
Chloramphenicol	22
Chlortetracycline	24
Clenbuterol	7
Closantel	1
Cyfluthrin	1
Cypermethrin	5
Danofloxacin	4
Dexamethasone	5
Diclazuril	
Dihydro-streptomycin	12
Diminazine	1
Doramectin	4
Enrofloxacin	10
Eprinomectin	2
Estradiol	8
Febantel	7
Fenbendazole	13
Fluazuron	2
Flubendazole	3
Flumequin	1
Gentamicin	7
Imidocarb	1
Isometimidium	
Ivermectin	14
Levamisole	11
Moxidectin	5
Neomycin	13
Nicarbazin	4
Olaquindox	1
Oxfendazole	12
Oxytetracycline	21
Procaine penicillin	9
Progesterone	6
Sarafloxacin	3

Spectinomycin	5
Spiramycin	5
Streptomycin	13
Sulphadimidine	27
Testosterone	10
Tetracycline	22
Thiabendazole	11
Thiamphenicol	1
Tilmicosin	10
Trenbolone Acetate	16
Triclabendazole	2
Zeranol	13

Attachment 2

CODEX COMMITTEE FOR RESIDUES OF VETERINARY DRUGS IN FOOD

***Ad Hoc* Working Group on Methods of Analysis and Sampling**
Analytical Method Information Summary

A. Descriptive Information

1. Name of drug or chemical:_____

2. Drug or chemical class:_____
(e.g. antimicrobial, anthelmintic, etc)

3. Veterinary Use:_____

4. Analyte(s) measured:_____
(specify if metabolite)

5. Intended use of the method:

    a. Screening _____
    b. Routine_____
    c. Reference_____
    d. Confirmatory_____

6. Test matrix_____
(e.g. muscle, kidney, urine, etc)

7. Summary of principal steps in sample preparation:
_____
_____

8. Summary of principal steps in extraction procedure:
_____
_____

9. Summary of principal steps in analyte clean-up procedure:
_____
_____

10. Measurement procedure:

    a. Chemical

        1. Instrumentation _____
        2. Detector system _____
        3. Chromatographic column _____
        (if applicable)

b. Immunochemical/Immunoassay

1. Technique: _____
(e.g. Elisa, RIA, Immunochromatog, etc)

2. Critical reagents: _____
_____
(e.g. antibody specificity and availability)

3. Special equipment required: _____

c. Microbiological

1. Technique:_____

2. Organism: _____

3. Media: _____

4. Special equipment required:_____

11. Sample/Analyte Stability
Warning (if applicable): _____

12. Literature References available: _____
_____
_____

13. Contact for Information:

a. Name_____
b. Country_____
c. Affiliation_____
d. Address_____
_____
e. Telephone_____
f. FAX_____
g. Email_____

B. Method Performance

1. a. Limit of Detection (LOD) (mg/kg)_____
How was LOD determined?_____
_____

b. Limit of Quantification (LOQ) (mg/kg)_____
How was LOQ determined?_____
_____

c. Method sensitivity_____
(The smallest difference in concentration that can be measured)

2. JECFA MRL_____

3. Is analytical data corrected for recovery? Yes____ No_____

4. How is recovery estimated _____
(e.g. external standard; internal standard. etc)

5. Accuracy

a. Concentration(s) tested _____
b. Concentration(s) measured _____
c. Recovery (%) _____

6. Precision using fortified control tissue

a. Concentration(s) tested _____
b. Repeatability (within lab CV) _____
c. Reproducibility (between lab CV) _____

7. Precision using tissue containing incurred drug residues

a. Concentration(s) tested _____
b. Repeatability (within lab CV) _____
c. Reproducibility (between lab CV) _____

8. Selectivity of the method

This information is often referenced as "Specificity". Selectivity refers to the ability of the method to provide accurate measurement of the analyte of interest when other chemicals or drugs are also resident in the laboratory sample. Data of interest in this regard are the effects of:

a. Drugs of similar structure _____
or drug class or other veterinary _____
drugs that may also be used along _____
with the analyte of interest _____.

b. Contaminants that are likely to be present in the sample
_____

9. Type of Validation studies

   a. Single laboratory _____
   b. Multi-laboratory _____
   c. AOAC or other official procedure _____

C. Information relevant to laboratory implementation

1. Training and experience recommended for analyts
2. Critical steps in the method
3. Information on availability of unusual reagents or equipment
4. Special reagent or sample stability concerns
5. Reagent handling and safety concerns (if any)
6. Literature references or other useful information

Attachment 3

OUTLINE OF SCIENTIFIC ISSUES COMMONLY CONSIDERED IN THE DEVELOPMENT AND VALIDATION OF ANALYTICAL METHODS

1. Determinative (Quantitative) Method

   A. Purpose of the Method
      *Scope of application (intended use)
      *Target tissue
      *Marker residue (analyte)
      *Limit of quantification (LOQ), Limit of Detection (LOD) or other Lowest Validated Level

   B. Experimental data
      *Reagents (purity, strength, grade)
      *Apparatus and Equipment
      *Analytical Standards (quality, concentration and solvents)
      *Tissue Samples (procedure for preparation for analysis)
      *Analyte Extraction Procedures
      *Analyte Clean-up
      *Instumental Procedures and Calibrations
      *Calculations

   C. Quality Assurance
      *Storage Stability of the Analyte in Tissue
      *Quality Control Samples
      *System Suitability Criteria
      *Readiness to perform assessment
      *Data Acceptability Criteria

2. Confirmation Procedure
   *Sample preparation
   *Instrumental procedures and calibrations
   *Standards employed
   *Criteria for positive identification

3. Validation considerations
   *Accuracy
   *Recovery
   *Precision (repeatability and reproducibility)
   *Sensitivity and LOQ
   *Specificity