codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

JOINT OFFICE: Viale delle Terme di Caracalla 00100 ROME Tel: 39 06 57051 www.codexalimentarius.net Email: codex@fao.org Facsimile: 39 06 5705 4593

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CL 2004/17 - RVDF
May 2004

TO: Codex Contact Points
Interested International Organizations

FROM: Secretary, Codex Alimentarius Commission
Joint FAO/WHO Food Standards Programme
Viale delle Terme di Caracalla, 00100 Rome, Italy

SUBJECT: **REQUEST FOR COMMENTS/INFORMATION:**

A) RECOMMENDATIONS ON MAXIMUM RESIDUE LIMITS FOR VETERINARY DRUGS (MRLS) ARISING FROM THE 60TH AND 62ND MEETINGS OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

B) PRIORITY LIST OF VETERINARY DRUGS REQUIRING EVALUATION OR REEVALUATION

C) ROUTINE METHODS OF ANALYSIS FOR THE MONITORING OF MAXIMUM RESIDUE LIMITS (MRLS) FOR VETERINARY DRUGS IN FOODS

DEADLINE: **30 August 2004**

COMMENTS:

To:
Secretary
Codex Alimentarius Commission
Viale delle Terme di Caracalla
00100 Rome, Italy
Fax: +39 06 5705 4593
E-mail: codex@fao.org

Copy to:
U.S. Codex Office
Food Safety and Inspection Service
US Department of Agriculture
Room 4861 South Building
1400 Independence Ave., SW
Washington, DC, 2025, USA
Fax: +1 202 720 3157
E-mail: uscodex@usda.gov

A) REQUEST FOR COMMENTS ON MAXIMUM RESIDUE LIMITS FOR VETERINARY DRUGS (MRLVDS) ARISING FROM THE 60TH AND 62ND MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

1. The 60th and 62nd Meetings of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) convened in Geneva, Switzerland from 6 to 12 February and in Rome, Italy, from 4 to 12 February 2004 respectively. They were the 15th and 16th JECFA meetings dealing exclusively with residues of veterinary drugs in foods. The 60th JECFA considered

2. The full reports of the meetings are published in the WHO Technical Report Series. Toxicological monographs summarising the data that were considered by the Committee will be published in *WHO Food Additives Series No. 51 and 53*; residue monographs summarising the data that were considered by the Committee will be published in *FAO Food and Nutrition Paper, No.41/15 and 41/16*.[1]

[1] The Summary and Conclusions of the 60th and 62nd Meeting of the Joint FAO/WHO Expert Committee on Food Additives is also available on Internet at: http://www.fao.org/es/ESN/Jecfa/

3. Governments and interested organizations are invited to comment, as directed above, on the recommendations of the 60th and 62nd JECFA on Maximum Residue Limits for Veterinary Drugs (Annex 1), in conformity with the Procedures for the Elaboration of Codex Standards and Related Texts (see *Codex Alimentarius Procedural Manual*, Thirteenth Edition, pages. 19-21) **not later than 30 August 2004**.

4. These recommendations and comments submitted will be considered by the 15th Session of the Codex Committee on Residues of Veterinary Drugs in Foods (October 2004).

B) REQUEST FOR COMMENTS ON THE PRIORITY LIST OF VETERINARY DRUGS REQUIRING EVALUATION OR REEVALUATION

5. The Codex Committee on Residues of Veterinary Drugs in Foods at its 14th Session (March 2003) agreed to convene the *ad hoc* Working Group on Priorities prior to its next Session under the Chairmanship of Australia to consider proposals for compounds to be evaluated or re-evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (ALINORM 03/31A, para. 115).

6. Governments and interested organizations are invited, as directed above, to make proposals for veterinary drugs to be added to the priority lists for subsequent recommendation to JECFA for evaluation or re-evaluation **not later than 30 August 2004**.

7. Annex 2 to this Circular Letter outlines the selection criteria established by the CCRVDF which should be borne in mind when submitting proposals.

8. Annex 3 is the form on which information is to be provided. Only brief details are required and the form can be retyped if more space is needed under any one heading provided that the general format is maintained. In preparing proposals, member governments should consult with the manufacturer(s) about the existence of appropriate toxicology and residue data and confirm that the manufacturer(s) would be willing to submit data to JECFA and in what year. Proposals submitted should also be listed in priority order.

9. Annex 4 outlines the toxicology and residues studies that are relevant for JECFA consideration. In some cases it is appreciated that not all studies might be available.

C) ROUTINE METHODS OF ANALYSIS FOR THE MONITORING OF MAXIMUM RESIDUE LIMITS (MRLS) FOR VETERINARY DRUGS IN FOODS

10. The Codex Committee on Residues of Veterinary Drugs in Foods at its 14th Session (March 2003) agreed to reconvene the *ad hoc* Working Group on Methods of Analysis and Sampling under the co-chairmanship of Canada and the Netherlands to continue its work on the review and recommendation of methods of analysis and sampling and the updating of methods validation procedures (ALINORM 03/31A, para. 109).

11. A major purpose of the *Ad-hoc* Working Group on Methods of Analysis and Sampling 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.

12. Governments and interested organizations are invited to submit information, as directed above, on routine methods of analysis for the monitoring of MRLs in foods **not later than 30 August 2004**.

13. It is requested that the technical information be summarized to facilitate technical review. A suggested data format for the summary information is outlined in Annex 5 to this Circular letter. Additional technical data may be appended to the basic summary and countries are encouraged to attach additional relevant information to the summary data.

14. Annex 6 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 1. 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.

ANNEX 1

RECOMMENDATIONS ON MAXIMUM RESIDUE LIMITS FOR VETERINARY DRUGS (MRLVDS) ARISING FROM THE 60TH AND 62ND MEETINGS OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

Keys for List of Maximum Residue Limits for Veterinary Drugs:

- Step - indicate current step;
- JECFA - meeting number of the Joint FAO/WHO Expert Committee on Food Additives where the MRLVD was recommended / considered;
- ALINORM - indicates Session number of the CCRVDF where the MRLVD was considered and Appendix number of its report where the MRLVD is contained.

RECOMMENDATIONS ARISING FROM 60th JECFA MEETING

ANTIMICROBIAL AGENTS:

NEOMYCIN

Acceptable Daily Intake: The ADI of 0-60 µg/kg bw established at the 47th Meeting of the Committee (WHO TRS 876, 1998) was maintained.

Residue Definition: Neomycin

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 60th JECFA [a]	Step	JECFA	ALINORM
Cattle	Liver	15000	500	6	52, 58	12V, 13IV, 14IV
Cattle	Kidney	20000	10000	6	52, 58	12V, 13IV, 14IV
Cattle	Milk	500	1500	6	52, 58	12V, 13IV, 14IV

[a/] The MRL of 500 µg/kg for cattle muscle and fat and all other MRLs recommended at the 47th meeting of the Committees were maintained.

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ANTIMICROBIAL AGENTS:

IMIDOCARB

Acceptable Daily Intake: 0-10 µg/kg bw (established at the 50th Meeting of the Committee - WHO TRS 888, 1999).

Residues: Imidocarb free base

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 60th JECFA	Step	JECFA	ALINORM
Cattle	Muscle		300	3		
Cattle	Liver		1500	3		
Cattle	Kidney		2000	3		
Cattle	Fat		50	3		
Cattle	Milk		50	3		

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INSECTICIDES:

DICYCLANIL

Acceptable Daily Intake: 0-7 µg/kg bw (established at the 54th Meeting of the Committee - WHO TRS 900, 2001).

Residues: Dicyclanil

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 60th JECFA	Step	JECFA	ALINORM
Sheep	Muscle	200	150	6	54	13V, 14IV
Sheep	Liver	400	125	6	54	13V, 14IV
Sheep	Kidney	400	125	6	54	13V, 14IV
Sheep	Fat	150	200	6	54	13V, 14IV

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TRICHLORFON (METRIFONATE)

Acceptable Daily Intake: The Committee amended the ADI for trichlorfon from 0-20 µg/kg to 0-2 µg/kg bw.

Residues: The Committee confirmed the MRL for cows's milk and the guidance levels for muscle, liver, kidney and fat of cattle recommended at the 54th meeting (WHO TRS 900, 2001).

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PRODUCTION AID:

CARBADOX

Acceptable Daily Intake: The Committee confirmed the opinion, expressed at it 36th Meeting (WHO TRS 1990), that an ADI could not be established.

Residues: The Committee decided to withdraw the MRLs of carbadox recommended at the 36th meeting (WHO TRS 799, 1990).

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 60th JECFA	Step	JECFA	ALINORM
Pig	Muscle	5	withdrawn	(1993)	36	
Pig	Liver	30	withdrawn	(1993)	36	

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RECOMMENDATIONS ARISING FROM 62nd JECFA MEETING

ANTIMICROBIAL AGENTS:

CEFUROXIME

Acceptable Daily Intake: The temporary ADI established at the 58th Meeting of the Committee (WHO TRS 911, 2002) was withdrawn.

Residues: The temporary MRL for cattle milk was withdrawn.

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	milk	50 T [1/, 2/]	withdrawn	5	58	14IV

[1/] Results of studies to (i) identify the residues in milk and clarify whether the residues other than parent compound are due primarily to metabolism or to non-metabolic decomposition of parent cefuroxime and, (ii) characterize their toxicological significance of non-parent residues in milk are required for evaluation in 2004.

[2/] The recommended MRL is temporary because the ADI is temporary.

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FLUMEQUINE

Acceptable Daily Intake: The Committee re-established an ADI of 0-30 µg/kg bw.

Residues: Flumequine

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	Muscle	500	500	6	42, 48, 54	11V,12IV,13IV,14IV
Cattle	Liver	500	500	6	42, 48, 54	11V,12IV,13IV,14IV
Cattle	Kidney	3000	3000	6	42, 48, 54	11V,12IV,13IV,14IV
Cattle	Fat	1000	1000	6	42, 48, 54	11V,12IV,13IV,14IV
Black tiger shrimp (*P. monodon*)	Muscle	-	500 T [a]	3		-
Chicken	Muscle	500	500	6	42, 48, 54	11V,12IV,13IV,14IV
Chicken	Liver	500	500	6	42, 48, 54	11V,12IV,13IV,14IV
Chicken	Kidney	3000	3000	6	42, 48, 54	11V,12IV,13IV,14IV
Chicken	Fat	1000	1000	6	42, 48, 54	11V,12IV,13IV,14IV
Pig	Muscle	500	500	6	42, 48, 54	11V,12IV,13IV,14IV
Pig	Liver	500	500	6	42, 48, 54	11V,12IV,13IV,14IV
Pig	Kidney	3000	3000	6	42, 48, 54	11V,12IV,13IV,14IV
Pig	Fat	1000	1000	6	42, 48, 54	11V,12IV,13IV,14IV
Sheep	Muscle	500	500	6	42, 48, 54	11V,12IV,13IV,14IV
Sheep	Liver	500	500	6	42, 48, 54	11V,12IV,13IV,14IV
Sheep	Kidney	3000	3000	6	42, 48, 54	11V,12IV,13IV,14IV
Sheep	Fat	1000	1000	6	42, 48, 54	11V,12IV,13IV,14IV
Trout	Muscle	500	500[b]	6	42, 48, 54	11V,12IV,13IV,14IV

[a/] The MRL is temporary; the following information is requested by 2006: (1) A detailed description of a regulatory method, including its performance characteristics and validation data; (2) Information on the approved dose for treatment of black tiger shrimp and the results of the residue studies conducted at the recommended dose.

[b] Muscle including normal proportion of skin.

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LINCOMYCIN

Acceptable Daily Intake: 0-30 µg/kg bw (established at the 54th meeting of the Committee - WHO TRS 900, 2001).

Residues: The MRLs that were recommended by the 54th (WHO TRS 900, 2001) and 58th (WHO TRS 911, 2002) Meeting of the Committee were not reconsidered and maintained.

MRL for cattle tissues were considered but not recommended by the 62nd meeting.

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PIRLIMYCIN

Acceptable Daily Intake: The Committee established an ADI of 0-8 µg/kg bw.

Residues: Pirlimycin

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	Muscle		100	3		
Cattle	Liver		1000	3		
Cattle	Kidney		400	3		
Cattle	Fat		100	3		
Cattle	Milk		100	3		

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INSECTICIDES:

CYHALOTHRIN

Acceptable Daily Intake: The Committee established a permanent ADI of 0-5 µg/kg bw.

Residues: Cyhalothrin

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	Muscle	20 T	20	6	54, 58	13III, 26th CAC
Cattle	Liver	20 T	20	6	54, 58	13III, 26th CAC
Cattle	Kidney	20 T	20	6	54, 58	13III, 26th CAC
Cattle	Fat	400 T	400	6	54, 58	13III, 26th CAC
Cattle	Milk	30 T	30	6	54, 58	13III, 26th CAC
Pig	Muscle	20 T	20	6	54, 58	13III, 26th CAC
Pig	Liver	20 T	20	6	54, 58	13III, 26th CAC
Pig	Kidney	20 T	20	6	54, 58	13III, 26th CAC
Pig	Fat	400 T	400	6	54, 58	13III, 26th CAC
Sheep	Muscle	20 T	20	6	54, 58	13III, 26th CAC
Sheep	Liver	20 T	20	6	54, 58	13III, 26th CAC
Sheep	Kidney	20 T	20	6	54, 58	13III, 26th CAC
Sheep	Fat	400 T	400	6	54, 58	13III, 26th CAC

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CYPERMETHRIN AND ALPHA-CYPERMETHRIN

Acceptable Daily Intake: The Committee established a common ADI of 0-20 µg/kg bw for both cypermethrin and alpha-cypermethrin.

Residues: Total of cypermethrin residues (resulting from the use of cypermethrin or alpha-cypermethrin as veterinary drugs).

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	Muscle		50	3		
Cattle	Liver		50	3		
Cattle	Kidney		50	3		
Cattle	Fat		1000	3		
Cattle	Milk		100	3		
Sheep	Muscle		50	3		
Sheep	Liver		50	3		
Sheep	Kidney		50	3		
Sheep	Fat		1000	3		

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DORAMECTIN

Acceptable Daily Intake: 0-1 µg/kg bw (established at the 58th meeting, WHO TRS 911, 2002).

Residues: Doramectin.

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	Milk		15[a]	3		

[a] The Committee noted that (1) on the basis of a 15 µg/kg MRL for doramectin in whole milk in cattle, the milk discard times would be approximately 240 hours based on the studies using the pour-on treatment. Milk discard times would be approximately 480 hours following treatment using the injection formulated dose; (2) in milk containing 4 per cent milk fat, the residues in milk would be equivalent to 375µg/kg (15 µg/kg ÷ 0.04+= 375 µg/kg). This is higher than the 150 µg/kg MRL in fat tissue; 93) the discard time necessary to accommodate the recommended MRL in milk is unlikely to be consistent with good veterinary practice.

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PHOXIM

Acceptable Daily Intake: 0-4 µg/kg bw (established at the 52nd Meeting of the Committee - WHO TRS 893, 2000).

Residues: The MRLs for sheep, pigs and goats that were recommended by the fifty eight (WHO TRS 911, 2002) meeting of the Committee were not reconsidered and maintained.

The temporary MRLs for cattle that were recommended by the 52nd (WHO TRS 893, 2000) and 58th (WHO TRS 911, 2002) meeting of the Committee were withdrawn.

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	Muscle	50 T 1/	withdrawn	6	52, 58	12V, 13II, 26th CAC
Cattle	Liver	50 T 1/	withdrawn	6	52, 58	12V, 13II, 26th CAC
Cattle	Kidney	50 T 1/	withdrawn	6	52, 58	12V, 13II, 26th CAC
Cattle	Fat	400 T 1/	withdrawn	6	52, 58	12V, 13II, 26th CAC
Cattle	Milk	10 T 1/	withdrawn	6	52, 58	12V, 13II, 26th CAC

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PRODUCTION AIDS:

MELENGESTROL ACETATE

Acceptable Daily Intake: 0-0.03 µg/kg bw (established at the 54th meeting of the Committee (WHO TRS 900, 2001).

Residues: Melengestrol acetate.

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	Liver	2 T	5	6	54, 58	13V, 14IV
Cattle	Fat	5 T	8	6	54, 58	13V, 14IV

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RACTOPAMINE

Acceptable Daily Intake: 0-1 µg/kg bw.

Residues: Ractopamine

Species	Tissue	Current MRL (µg/kg)	MRLs(µg/kg) recommended by 62nd JECFA	Step	JECFA	ALINORM
Cattle	Muscle		10	3		
Cattle	Liver		40	3		
Cattle	Kidney		90	3		
Cattle	Fat		10	3		
Pig	Muscle		10	3		
Pig	Liver		40	3		
Pig	Kidney		90	3		
Pig	Fat		10	3		

ANNEX 2

CRITERIA FOR THE INCLUSION IN, OR EXCLUSION FROM, SUBSTANCES IN THE PRIORITY LIST

In order to be placed on the CCRVDF priority list for the development of a maximum residue limit, the candidate veterinary drug, when used in accordance with good veterinary practices, should meet some, but not necessarily all, of the following criteria:

1) Use of the drug will have potential to cause public health and/or trade problems;

2) Drug available as commercial product, and;

3) Commitment that a dossier will be available.

ANNEX 3

FORMAT FOR PRESENTATION OF INFORMATION ON COMPOUNDS TO BE INCLUDED INTO THE CCRVDF PRIORITY LIST

1. Proposal for Inclusion Submitted by (Country):
2. Drug Name:
3. Trade Names:
4. Chemical Names:
5. Names and Addresses of Basic Producers:
6. Justification for Use:
7. Veterinary Use Pattern:
8. Countries Where Drug is Registered:
9. National Maximum Residue Levels:
10. Commodities for Which the Need for Establishing Codex MRLs Is Required:
11. List of Data (Toxicology, Metabolism, Residue) Available:
12. Date Data Could be Submitted to JECFA:

ANNEX 4

DATA REQUIREMENTS FOR EVALUATION BY JECFA

1. Identify
   - Chemical name
   - Synonyms
   - Structural formula
   - Molecular formula
   - Other information on identity:
     + molecular weight
     + specification of technical material
     + degree of purity
     + qualitative and quantitative composition of impurities
2. Data relevant to the toxicological evaluation of the substance, including:
   i. pharmacokinetic, metabolic and pharmacodynamic studies in experimental and food-producing animals, and in humans when available;
   ii. short-term toxicity, long-term toxicity/carcinogenicity, reproductive toxicity and developmental toxicity studies in experimental animals and genotoxicity studies;
   iii. special studies designed to investigate specific effects, such as those on mechanisms of toxicity, no-hormonal-effect levels, immune responses or macromolecular binding;
   iv. for compounds with antimicrobial activity, studies designed to evaluate the possibility that the compound might have an adverse effect on the microbial ecology of the human intestinal tract, and;
   v. Studies providing relevant data on the use of and exposure to the drug by humans, including studies of effects observed after occupational exposure and epidemiological data following clinical use in humans.
3. Data relevant to the evaluation of residues in food-producing animals, including:
   i. chemical identity and properties of the drug;
   ii. its use and dosage range;
   iii. as for the toxicological evaluation, pharmacokinetic and metabolic studies in experimental animals, target animals, and humans when available;
   iv. residue-depletion studies with radiolabelled drug in target animals from zero withdrawal time to periods extending beyond the recommended withdrawal time (these studies should provide information on total residues, including free and bound residues, and major residue components to permit selection of a marker residue and target tissue);
   v. residue-depletion studies with unlabelled drug for the analysis of marker residue in target animals and in eggs, milk and honey (these should include studies with appropriate formulations, routes of application and species, at doses up to the maximum recommended);
   vi. a description of the analytical procedures used by the sponsor for the detection and determination of parent drug residues with information on validation and performance characteristics, and;
   vii. A review of routine analytical methods that may be used by regulatory authorities for the detection of residues in target tissue.

ANNEX 5

FORMAT FOR PRESENTATION OF SUMMARY INFORMATION ON ANALYTICAL METHODS

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. Are 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

ANNEX 6

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
*Instrumental 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