codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

JOINT OFFICE: Via delle Terme di Caracalla 00100 ROME: Tel. 57971 Telex: 610181 FAO I. Cables Foodagri Facsimile: 6799563

ALINORM 89/31A

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX ALIMENTARIUS COMMISSION
Eighteenth Session
Geneva, 3-12 July 1989

REPORT OF THE THIRD SESSION OF THE CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Washington, D.C., 31 October - 4 November 1988

NOTE: This document incorporates Codex Circular Letter 1988/53-RVDF.

W/Z 4076

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CX 4/60.2

CL 1988/53-RVDF
December 1988

TO: - Codex Contact Points
- Interested International Organizations

FROM: Chief, Joint FAO/WHO Food Standards Programme, FAO, Via delle Terme di Caracalla, 00100 Rome (Italy)

SUBJECT: Distribution of the Report of the Third Session of the Codex Committee on Residues of Veterinary in Foods (ALINORM 89/31A)

The report of the Third Session of the Codex Committee on Residues of Veterinary Drugs in Foods is attached. It will be considered in conjunction with the Report of the Second Session of the Codex Committee on Residues of Veterinary Drugs in Foods by the 18th Session of the Codex Alimentarius Commission to be held in Geneva from 3-12 July 1989.

A. MATTERS OF INTEREST TO THE COMMISSION ARISING FROM THE REPORT OF THE SECOND (ALINORM 89/31) AND THIRD (ALINORM 89/31A) SESSIONS OF THE CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

The following matters will be brought to the attention of the 18th Session of the Codex Alimentarius Commission:

1. Proposed Draft MRLs for Veterinary Drugs in Foods at Step 5; ALINORM 89/31A, Appendix V.

2. Definitions for "Maximum Residue Level" and "Good Practices in the Use of Veterinary Drugs"; ALINORM 89/31A, Appendix III.

3. Procedures for the Elaboration of Codex Maximum Residue Levels for Veterinary Drugs in Foods; ALINORM 89/31A, Appendix IVA.

4. Procedures for the Elaboration of Codex Maximum Residue Levels for Veterinary Drugs in Foods - Introduction; ALINORM 89/31A, Appendix IVB.

5. Procedures for the Acceptance of Codex Maximum Residue levels for Veterinary Drugs in Foods; ALINORM 89/31A, Para. 65.

B. DOCUMENTS OF INTEREST TO BE ELABORATED FOR DISTRIBUTION AND GOVERNMENT COMMENT PRIOR TO THE NEXT MEETING OF CCRVDF

1. Glossary of Terms and Definitions (Canada); see ALINORM 89/31A, Paras. 82-86.

2. Code of Practice for the Control of the Use of Veterinary Drugs (United Kingdom); see ALINORM 89/31A, Paras. 88-91.

3. Guidelines for the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods (United States); see ALINORM 89/31A, Paras. 115-120.

C. REQUEST FOR COMMENTS AND INFORMATION

1. Compendium of Veterinary Drugs - ALINORM 89/31A, Paras. 39-41

The Committee agreed to request Governments and international organizations to review the data summarized in the draft compendium and to send corrections, comments and further data.

2. Survey on Intake Studies - ALINORM 89/31A, Para. 87

The Committee agreed to request Governments and international organizations to submit information requested in the Intake Study questionnaire, with special emphasis given to those studies which provide useful information for the determination of MRLs based on the ADI.

3. Methods of Analysis and Sampling - ALINORM 89/31A, Appendix VI

The Committee agreed to request Governments and international organizations to submit comments regarding the working papers on methods of analysis and sampling, including regulations concerning cross-border shipments of biological samples used for validation of methods for veterinary drugs, and methods of analysis for the compounds to be evaluated at the 34th JECFA session (please see method criteria outlined in Para. 96).

4. Priority List of Veterinary Drugs Requiring Evaluation - ALINORM 89/31A, Appendix VII

The Committee agreed to request Governments and international organizations to submit any request for including veterinary drugs in the priority list along with supporting information according to the selection criteria.

Governments and international organizations wishing to submit comments and information on the above subject matter are invited to do so no later than 15 May 1989 and as directed below:

For points C1 - C2 above:

Dr. Gerald Guest
Director, HFV-1
Center for Veterinary Medicine
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857, U.S.A.
(Telex No. 898488 PHS PKLN ROV, Telefax No. 301.443.1719)

For point C3 above:

Dr. Richard Ellis
Director, Chemistry Division
Food Safety and Inspection Service
U.S. Department of Agriculture
Room 302, Annex Building
300 12th Street, S.W.
Washington, D.C., U.S.A.
(Telex No. 89491, Telefax No. 202.447.2257)

For point C4 above:

Mr. G.N. Hooper
Pesticides Coordinator
Bureau of Rural Resources
Department of Primary Industries and Energy
Barton, Canberra, ACT 2600
Australia
(Telex No. AA62188)

In addition, please forward a copy of the comments to:

Chief
Joint FAO/WHO Food Standards Programme
Food and Agriculture Organization of the United Nations
Via delle Terme di Caracalla
00100 Rome, Italy
(Telex No. 610181 FAO I, Telefax No. 6799563)

Summary and Conclusions

The Third Session of the Codex Committee on Residues of Veterinary Drugs in Foods reached the following conclusions during its deliberations:

- Advanced the Proposed Draft **Maximum Residue Levels for Chloramphenicol, Estradiol-17 beta, Progesterone, Testosterone and Zeranol** to Step 5 (Paras. 69,74 and 80).

- Retained the Proposed Draft **Maximum Residue Level for Trenbolone Acetate** at Step 4 in order to allow for JECFA re-evaluation (Para.77)

- Agreed to request **JECFA to review use of the term "unnecessary"** when establishing MRLs, in view of possible negative implications (Para. 71).

- Adopted revised definitions for **"Maximum Residue Level"** and **"Good Practices in the Use of Veterinary Drugs"**, and agreed to forward the draft definitions to the Codex Committee on General Principles for endorsement and to the Commission for adoption (Paras. 55 and 58).

- Agreed to forward proposed procedures for the **Elaboration of Codex Maximum Residue Levels, Elaboration of Codex Maximum Levels - Introduction** and **Acceptance of Codex Maximum Residue Levels** to the Codex Committee on General Principles for endorsement and to the Commission for adoption (Paras. 62, 63, 65).

- Agreed that Canada, with the assistance of an informal working group, would revise and circulate the proposed **Glossary of Terms and Definitions** for comments and discussion at the next Committee session (Para. 86).

- Agreed that the United Kingdom should revise and circulate the draft **Code of Practice for Control of the Use of Veterinary Drugs** for comment and discussion at the next Committee session. In addition, the Committee reconfirmed that this Code should not include discussions concerning the **marketing and registration of veterinary drugs** (Paras. 90-91).

- Agreed that the United States of America should revise and circulate the proposed **Guidelines for the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods** for comment and eventual discussion at the next Committee session (Para. 120).

- Agreed to continue revision of the **Priority List of Veterinary Drugs Requiring Evaluation** through the use of a questionnaire, government comments and the **Working Group on Priorities** for discussion at the next Committee session (Para. 114).

- Agreed to continue revision of the working papers regarding **Methods of Analysis and Sampling** through government comments and the **Working Group on Methods of Analysis and Sampling** for discussion at the next Committee session (Para. 97).

Summary and Conclusions (Cont'd)

- Agreed that the revision of the **Compendium of Veterinary Drugs** continue through government comments for eventual discussion at the next Committee session (Para. 41).

- Agreed that the **Survey on Intake Studies** should continue through government comments for discussion at the next Committee session (Para. 87).

- Requested the Codex Secretariat to keep the Committee informed as to activities of the FAO Fishery Industries Division and the Codex Committee on Fish and Fishery Products in relation to the proposed **Code of Practice for Aquaculture** and the **Report of the Working Party on Withdrawal Period for Drugs - Therapeutics Used in Fish Production** (Paras. 14 and 22).

- Requested the Codex Secretariat to keep the Committee informed as to activities of the **FAO Animal Production and Health Division** (Para. 24).

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APPENDICES

INTRODUCTION

1. The Third Session of the Codex Committee on Residues of Veterinary Drugs in Foods was held from 31 October to 4 November 1988 in Washington, D.C., by courtesy of the Government of the United States of America. The Session was chaired by Dr. Gerald B. Guest, Director, Center for Veterinary Medicine, Food and Drug Administration. Representatives and observers from 34 countries and 8 international organizations were present.

2. The Session was preceded by the Second Meeting of an Ad Hoc Working Group on Methods of Analysis and Sampling under the chairmanship of Dr. Richard Ellis, Director, Chemistry Division, Food Safety and Inspection Service, United States Department of Agriculture. The report of the working group meeting was presented to the Plenary under Agenda Item 10.

3. A list of the participants at the Session, including officers of FAO and WHO, is attached as Appendix I to this report.

OPENING OF THE SESSION (Agenda Item 1)

4. The Session was opened by Dr. Lester M. Crawford, Administrator, Food Safety and Inspection Service, U.S. Department of Agriculture. Dr. Crawford highlighted the importance of developing an international consensus on animal drug trade and health issues which take the needs of all countries into account. He also stressed that this Committee was recognized as the international body concerning veterinary drug residue issues based on practical and scientifically sound principles.

5. Dr. Crawford also addressed the importance of this Committee's deliberations concerning the prevention of technical barriers to trade through the General Agreement on Tariffs and Trade (GATT). It was emphasized that the United States would continue to grant full support to Codex activities in the future. The full text of Dr. Crawford's remarks is attached as Appendix II to this Report.

APPOINTMENT OF RAPPORTEUR

6. The Committee appointed Dr. Dieter Arnold of the Federal Republic of Germany to serve as Rapporteur of the Session.

ADOPTION OF THE AGENDA (Agenda Item 2)

7. The Committee had before it the Provisional Agenda for the Session (CX/RVDF 88/1). The Chairman noted the similarity of Agenda Items 3e and 9, which addressed Good Practices for the Registration and the Marketing of Veterinary Drugs and a Code of Practice for the Control of the Use of Veterinary Drugs, respectively. The Committee agreed to combine these two items for discussion under Agenda Item 9. The Committee also agreed to reverse discussion of Agenda Items 5 and 6, which concern Proposed Draft MRLs for Veterinary Drugs in Foods and Procedures for the Elaboration and Acceptance of Codex Maximum Residue Levels, respectively.

8. At the suggestion of the delegation of the United States, the Committee agreed to establish an ad hoc Working Group on Priorities under the Chairmanship of Australia in order to organize a priority list of veterinary drugs requiring evaluation based on written and oral comments.

9. The provisional agenda was adopted as amended by the Committee.

MATTERS OF INTEREST ARISING FROM SESSIONS OF OTHER CODEX COMMITTEES (Agenda Item 3a)

10. The Committee had before it Working Paper CX/RVDF 88/2, which addressed matters of interest arising from the Codex Committee on Pesticide Residues and the Codex Committee on Fish and Fishery Products.

Codex Committee on Pesticide Residues (CCPR) - 20th Session (ALINORM 89/24)

11. The Committee noted that the Codex Committee on Pesticide Residues (CCPR) re-emphasized the importance of health considerations in setting pesticide maximum residue limits, and expressed concerns regarding the establishment of a definition for veterinary drug Maximum Residue Levels. The CCPR also agreed that the preparation of a document comparing the establishment of MRLs by CCPR and CCRVDF was premature at present.

12. The CCPR also noted that its list of Codex maximum limits for pesticide residues would include an annotation ("v") to indicate those pesticides which may also accommodate veterinary drug uses, and that these compounds would be referred to CCRVDF by the Codex Secretariat for consideration.

Codex Committee on Fish and Fishery Products (CCFFP) - 18th Session (ALINORM 89/18)

13. The Committee noted that the CCFFP considered a background paper concerning a proposed Code of Practice for Aquaculture as developed by the FAO Fisheries Department. The CCFFP recommended that efforts to elaborate such a Code should continue, and that information concerning the scope and content of the proposed Code should be sought from member governments through a comprehensive questionnaire.

14. The Committee requested the Codex Secretariat to keep it informed of future developments concerning the proposed Code.

MATTERS ARISING FROM FAO AND WHO ACTIVITIES (Agenda Item 3b)

15. The Committee had before it Working Paper CX/RVDF 88/3 (Conference Room Document 2) which summarized activities of interest to this Committee arising from FAO, WHO, and joint FAO/WHO activities.

JOINT FAO/WHO ACTIVITIES

Joint FAO/WHO Expert Committee on Food Additives (JECFA)

16. The Committee noted that the 32nd JECFA report (June 1987) was published by WHO as Technical Report Series No. 763. The residue studies and methods of analysis for the substances evaluated are summarized in FAO Food and Nutrition Paper No. 41, "Residues of Some Veterinary Drugs in Animals and Foods". The toxicological monographs for chloramphenicol, trenbolone acetate, and zeranol will be published by the Cambridge University Press as WHO Food Additives Series, No. 23.

17. The delegation of Norway emphasized the importance of the expeditious dissemination of toxicological monographs to Codex Contact Points. The WHO representative indicated that it was the intention of FAO and WHO to do so, and that future efforts will concentrate on their distribution as quickly as possible.

18. The Committee noted that the 34th meeting of JECFA, scheduled to be held from 30 January - 8 February 1989, will also be devoted to the evaluation of veterinary drug residues. Data had been received for most of the compounds scheduled for evaluation, as requested in CL 1988/7-RVDF, and were presently being reviewed and summarized by WHO Temporary Advisers and FAO Consultants. A summary report of the meeting should be available for consideration by the Fourth Session of CCRVDF.

FAO ACTIVITIES

Fishery Industries Division

19. The Committee noted that the Fish Utilization and Marketing Service of the FAO Fishery Industries Division had provided the Codex Secretariat with a paper entitled "Report of the Working Party on Withdrawal Period for Drugs - Therapeutics Used in Fish Production - Pharmacokinetics, Residues, Withdrawal Periods", (EIFAC/XV/88/INF. 13, March 1988). The paper was presented for discussion at the 15th Session of the European Inland Fisheries Advisory Commission (EIFAC). The report summary and EIFAC recommendations were presented to the Committee for information.

20. The report contains information and recommendations concerning pharmacokinetics, drug concentration in tissues, and withdrawal periods for therapeutics used in the prevention and treatment of infectious diseases in fish. The report concludes that the uptake, distribution and elimination of therapeutics in fish are greatly influenced by factors relating to the fish species, the therapeutics used and the environment. The report also concludes that additional pharmacokinetic data concerning drug use in fish, guidelines for the use of chemicals and therapeutics in fish farming, withdrawal periods and rules to protect the environment are other important issues.

21. The Committee also noted that the EIFAC recommended additional work to improve the report's recommendations, and to enhance collaboration with other groups interested in this subject, such as the CCFFP and the CCRVDF.

22. It was agreed that the Codex Secretariat would keep CCRVDF informed of developments concerning these issues.

Animal Production and Health Division

23. The Animal Health Service of the FAO Animal Production and Health Division provided the Committee with written information through the Codex Secretariat concerning foods of biotechnological origin, the creation of an international network of specialized collaborating research centers to facilitate the monitoring and evaluation of veterinary drug residues and the desire for this Committee to evaluate acaricides as part of its future work.

24. The Codex Secretariat assured the Committee that it would continue to be provided with information concerning future developments in these areas.

WHO ACTIVITIES

International Exchange of Information on Veterinary Drugs

25. The WHO representative reported on activities of the WHO Pharmaceuticals Unit regarding two publications designed for information exchange. The WHO Pharmaceuticals Newsletter, a publication with limited regulatory authority distribution, contains information concerning regulatory human drug actions, pharmaceuticals used in veterinary practice, medical devices, and short summaries of recently-reported adverse drug reactions and newly-approved drugs. WHO Drug Information is an official WHO publication that is available by paid subscription. It contains commentaries on regulatory matters and developments and prescribes information on essential drugs. It was indicated that WHO is dependent upon the submission of information from regulatory authorities for effective exchanges, and that information for inclusion in these publications should be forwarded to the WHO Pharmaceutical Unit.

Activities in the Region of the Americas (Pan-American Health Organization, PAHO)

26. The Observer from PAHO outlined WHO veterinary public health activities in the Region of the Americas related to residues of veterinary drugs in foods. A number of meetings, workshops, and training courses have been held regarding these issues. The PAHO Regional Office has also been actively working with the Unified Laboratory for the Control of Food and Drugs in Argentina, where a technical person is stationed to analyze anabolics, pesticides, and heavy metals in food. A major activity of this group is the creation of an international reference laboratory at the Pan American Zoonoses Centre in Argentina. This laboratory provides training, consultative services, methods, and reference testing in support of residue analysis activities by countries in the region.

MATTERS ARISING FROM THE ACTIVITIES OF OTHER INTERNATIONAL ORGANIZATIONS (Agenda Item 3c)

27. The Committee was orally informed of activities in a number of international organizations which relate to residues of veterinary drugs in foods.

International Dairy Federation (IDF)

28. The Observer from IDF outlined the work of two expert groups, namely, Group A 4 dealing with residues and contaminants in milk and milk products, and Group E 47 concerning the "Detection of Inhibitors".

29. Group A 4 is preparing a monograph entitled "Residues and Contaminants in Milk and Milk Products". Veterinary drugs are addressed in Chapter 4 and include information concerning antibiotics, sulfa drugs, parasiticides, and hormones. The monographs will contain general information addressing the toxicological evaluation, significance and principles of analysis for these compounds. The monograph should be available by the end of 1989, and will update IDF Monograph 113 (1979).

30. Group E 47 has prepared a compendium on methods for the detection of antibiotics, IDF Bulletin 220 (1987), available from the IDF Secretariat in Brussels. At present the group is preparing a documentation on chemical - physical methods for detecting antibiotics and sulfa drugs. These methods should facilitate a "two step procedure" for the screening and confirmation/identification of antibiotics. Other topics of the Group's work include the selection of more sensitive test microorganisms for screening purposes for antibiotics, especially in the case where pencillinase may have been used on the farm to destroy beta-lactams.

European Economic Community (EEC)

31. The Observer from the EEC highlighted recent EEC legislative developments related to veterinary drugs.

32. On 1 January 1988, Council Directive 87/153/EEC, which established Guidelines for the Evaluation of Additives in Animal Feedingstuffs, came into effect. This directive describes residue studies required when applying to market a new additive within the Community. The legislation is related to animal feedingstuff additives and includes a number of substances of interest to this Committee, such as certain anti-microbial compounds and coccidiostats, which are used at low doses for nutritional or prophylactic purposes.

33. Following its annulment due to procedural reasons by the Court of Justice of the European Communities on 7 March 1988, the Council reenacted a directive (88/146/EEC) prohibiting the use of certain hormonal substances as growth promoters in livestock farming. In order to ensure the rational marketing of meat obtained from animals which had previously been lawfully treated with these substances, the Council decided to extend certain transitional arrangements to 31 December 1988 (87/561/EEC). A further Council Directive of 17 May 1988 (88/299/EEC) provides for trade in animals intended for reproductive purposes and reproductive animals at the end of their career which have been treated with these substances for therapeutic purposes, for the synchronisation of the estrous cycle, the termination of unwanted pregnancy, the improvement of fertility or the preparation of donors and recipients for the implantation of embryos.

34. Following the promulgation of Council Directive 86/469/EEC concerning the examination of animals and fresh meat for the presence of residues, Member states were required to submit their national plans for the supervision of hormonal residues before 31 May 1987. These plans were approved by the Commission on 18 February 1988. In addition, Member states were required to submit their national plans for the surveillance of other veterinary medicinal product residues before 31 May 1988. These plans are currently under consideration by the Commission. A Commission decision of 14 July 1987 establishes methods to be used for detecting residues of substances having a hormonal or thyrostatic action.

35. The working party on the safety of residues of the Committee for Veterinary Medicinal Products has continued its activities in providing the Commission with scientific and technical assistance for the determination of tolerances (maximum residue levels). The Group has agreed to recommendations concerning trimethoprim and dapsone and is completing consideration of the benzimadazole group. The group is currently considering nitroimidazoles, ivermectine, beta-lactam antibiotics and macrolides. The priorities selected for future review include other antibiotics and anthelmintics, together with tranquillisers used in slaughter pigs.

Consultation Mondiale des Industries de Santé Animale (COMISA)

36. The Committee was informed of the establishment of COMISA, a body representing the global animal health industry. Its principle objective is to establish and develop

formal relations between the animal health industry and international bodies dealing with animal health affairs. Other objectives of the organization include (1) developing common policy agreements in cooperation with both governmental and non-governmental public organizations; (2) encouraging the acceptance of common, objective and scientific criteria by national and international regulatory bodies relating to the licensing and registration of animal health products and (3) liaising with international allied associations, such as GIFAP. COMISA is striving to enhance its relationship and communications with this Committee and JECFA. Founding members of COMISA include animal health industry associations of ten western European nations, five South American countries, the U.S.A., Japan, Canada, Australia and New Zealand.

International Technical Consultation on Veterinary Drug Registration (ITCVDR) and International Office of Epizooties (OIE)

37. The head of the delegation of France informed the Committee of the Fourth ITCVDR Meeting held from 10-13 May 1988 in Adelaide, Australia. The main topics of discussion concerned activities of international organizations in the veterinary drug field, undesirable side effects of veterinary drugs, public health residue issues, veterinary drug use in aquaculture, problems specific to developing countries in the registration of veterinary drugs and biotechnology products. The Consultation adopted a number of resolutions, which includes support for the role of CCRVDF as the appropriate structure for the establishment of maximum residue levels, support for the OIE Seminar on the Registration of Veterinary Drugs in Africa, to be held in January 1989 in Arusha, Tanzania, and for establishing a working group on the use of veterinary drugs in aquaculture. A draft constitution was adopted which defined the objectives, structure and procedures of the Consultation.

38. The head of the delegation of France also informed the Committee of activities of the Office International des Epizooties (OIE). The OIE is devoted to facilitating the exchange of information on registration of veterinary drugs and other matters of interest. Its activities include (a) the publication of two annual issues of the Veterinary Drug Registration Newsletter; (b) preparation of a code of good practices for the registration and marketing of veterinary drugs; (c) elaboration of a questionnaire about the undesirable effects of veterinary drugs; (d) organization of a seminar on registration problems in Africa, 19-20 January 1989 in Arusha, Tanzania; (e) a project on the minimal registration requirements for developing countries who lack adequate regulatory veterinary infrastructures.

PROGRESS REPORT ON COMPENDIUM OF VETERINARY DRUGS (Agenda Item 3d)

39. The Committee had before it Working Paper CX/RVDF 88/4 - Part I (Conference Room Document 3) "Progress Report on the Compendium of Veterinary Drugs", as prepared by the United States of America.

40. The United States of America, as outlined in CL 1988/6 RVDF, had requested comments and data through a questionnaire concerning the registration of veterinary drugs in the member countries of Codex. Replies to the circular letter were received from Botswana, Canada, Cuba, Egypt, Federal Republic of Germany, Finland, France, Ghana, Guatemala, Ireland, Japan, Korea, Malaysia, Mexico, Netherlands, New Zealand, Norway, Philippines, Poland, Sweden, Thailand, the United Kingdom, the United States of America, and Zambia. The delegation thanked those countries who commented, and noted that all replies except those recently received from Botswana and the Federal Republic of Germany were included in the working paper.

41. The delegation of the United States of America noted that the Inter-American Compendium was available on compact disc for distribution to interested parties. The Committee agreed to accept the proposal of the United States of America to continue the survey for an additional year, and requested governments who have not provided information to do so. The delegation of Norway noted errors of interpretation in that country, and also noted that information from different countries varied considerably in detail. The Committee requested countries to review data summarized in the Draft Compendium, and to submit corrections, data and comments to the United States of America.

DEFINITION OF "MAXIMUM RESIDUE LEVEL" AND "GOOD PRACTICES IN THE USE OF VETERINARY DRUGS" (Agenda Item 4)

42. The Committee had before it working paper CX/RVDF 88/5 and Conference Room Document 8, which included the comments of Australia, Cuba, Federal Republic of Germany, Mexico, New Zealand, Norway, Poland, and the United States of America. The Chairman recalled the Committee's earlier decision to treat these definitions separately from the glossary of terms, with a view towards their inclusion in the Codex Procedural Manual.

43. The U.S. Secretariat introduced document CX/RVDF 88/5 and read the definitions adopted at the second CCRVDF session as outlined in Appendix III of ALINORM 89/31.

Maximum Residue Level (MRL)

44. The United States of America, Australia and the Observer from COMISA expressed the view that the references in paragraph 4 to "allergenic potential" and "promotion of resistance" were inappropriate for the MRL definition and proposed that this paragraph of the text be removed. The delegation of France stressed that difficulties in establishing allergenic potential were also encountered at the EEC level, but that allergenic reactions should be considered in cases where significant evidence was present. The delegation of Canada agreed with the definition, in principle, but also supported the proposal to remove paragraph 4. The Committee agreed to remove paragraph 4 of the definition.

45. The delegation of Australia proposed an MRL definition based in concept and structure on the definition for pesticide maximum residue limits. It also argued that harmonization should be sought between this and other definitions already established by various Codex Committees. The Secretariat pointed out that the two situations were not identical, and that different approaches were applied in the elaboration of MRLs for pesticide and veterinary drug residues.

46. Several delegations, including France and Australia, discussed presenting a simplified, limited and flexible definition of only one paragraph for MRL. This would be accompanied by various footnotes and/or notes of explanation. The delegation of the Netherlands and Federal Republic of Germany recommended that footnotes not be used because they would not always be taken into consideration when the definition of MRL was applied in practice.

47. The delegation of the United States of America expressed its support to the removal of paragraph 4, but also stressed that the expression allowing the reduction of MRLs in accordance with good practices in the use of veterinary drugs was not appropriate, since developments in good husbandry and good veterinary practice may lead to changes in residue levels. More flexibility should be left for national tolerances as long as they remain below scientifically based MRLs.

48. The Committee requested the Secretariat to revise the draft definitions on the basis of the above discussion, and the revised draft definitions were subsequently distributed as Conference Room Document 13.

49. The delegation of the United States of America questioned the use of the expression "direct or indirect" when referring to toxicological hazards for human health. The delegation of France felt that this expression would include resistance promotion and allergenicity potential and must be taken into account. The delegation of Norway stated that the definition should not be based entirely on toxicological hazards but should be broader, and take into account other relevant risks as well as the "toxicological risks" referred to in paragraph 2. It proposed the addition of a statement reading, "It also takes into account other relevant public health risks as well as food technological aspects". This would have the effect of controlling other aspects, such as the inhibitory effect of antibiotic residues in milk intended for the production of cheese or other cultured dairy products. The delegations of Denmark and the United Kingdom both supported the delegations of France and Norway. They both suggested reinstating a reference to allergenicity and resistance effects as mentioned in paragraph 4 of the original draft definition. The Committee agreed to make reference to technological aspects in the definition, and to revise paragraph 2 as follows:

"It is based on the type and amount of residue considered to be without any toxicological hazard for human health as expressed by the Acceptable Daily Intake (ADI), or on the basis of a Temporary ADI that utilizes an additional safety factor. It also takes into account other relevant public health risks as well as food technological aspects."

50. The delegation of the United States of America, supported by the delegation of Sweden, requested the deletion of the reference in paragraph 3, reducing the MRL from the toxicologically derived level to a level consistent with good veterinary practice in the use of veterinary drugs. It stated that a maximum residue level should be arrived at through toxicological evaluation only, and that individual national MRLs could be established provided that they did not exceed the MRL and provided that countries would agree not to impede trade in foods with higher residue levels, as long as they were in compliance with the Codex MRLs. The delegation of Australia supported this concept in principle, but did not wish to delete the last sentence in paragraph 3 because MRLs should reflect the amount of residues which would be present following drug use in accordance with good veterinary practice.

51. The delegation of the Netherlands proposed not to delete the sentence. It stated that for the purpose of international trade there should be one MRL for a drug as opposed to various levels. It felt that it was necessary for all countries to reach common agreement in this matter. This proposal was supported by both the delegations of Denmark and France.

52. The delegation of the United Kingdom stated that the definition did not indicate, with sufficient clarity, that MRLs would normally be lowered from a level set on a toxicological basis to a level which was consistent with good practice in the use of veterinary drugs, and proposed that this fact should be stated more precisely.

53. The WHO Representative explained that the evaluation of residue data and use patterns, which would be required for the revision of an MRL, could be examined within a year of a request for re-evaluation and could be carried out independently of a toxicological re-evaluation. The Secretariat stated that JMPR procedures for pesticide MRLs could be used as an example for MRL re-evaluation within the space of one year. A procedure for re-evaluating an MRL individually was available and should not pose any hinderance.

54. The delegation of the United States of America stated that if this Committee and the JECFA would be able to re-evaluate MRLs on this basis, it would not object to paragraph 3, provided the words "may be" were used in relation to reducing the MRL below the toxicologically derived level.

55. The Committee adopted a revised definition of "Maximum Residue Level", and agreed to forward it to the Committee on General Principles for endorsement and to the Commission for adoption and inclusion in the Procedural Manual. The newly revised draft definition for "Maximum Residue Level" is given in Appendix III of this report.

Good Practices in the Use of Veterinary Drugs (GPVD)

56. The Committee considered the proposed revised definition for "Good Practices in the Use of Veterinary Drugs".

"Good Practices in the Use of Veterinary Drugs (GPVD) is the official recommended or authorized usage including withdrawal periods, approved by national authorities, of veterinary drugs under practical conditions, which is designed to leave toxicologically acceptable residues of the smallest amount practicable."

57. The delegation of the Netherlands, supported by those of the Federal Republic of Germany, United States of America, Canada and the United Kingdom, stated that the definition would be acceptable provided that reference would not be made to the nature and amount of the residue which, it believed, was covered in the definition of MRL.

58. The Committee accepted this proposal and agreed to forward the draft definition to the Committee on General Principles for endorsement and to the Commission for adoption

and inclusion in the Procedural Manual. The newly revised draft definition for "Good Practices in the Use of Veterinary Drugs" is included in Appendix III of the present report.

CONSIDERATION OF PROCEDURES FOR THE ELABORATION AND ACCEPTANCE OF CODEX MAXIMUM RESIDUE LEVELS (MRLS) FOR VETERINARY DRUGS IN FOODS (Agenda Item 6)

59. The Committee had before it working papers CX/RVDF 88/7, CX/RVDF 88/7 Addendum 1 (Conference Room Document 4) and Conference Room Document 8. The documents in question provided background information and included government comments on procedures for the elaboration and acceptance of MRLs proposed for veterinary drug residues.

Elaboration Procedures

60. The Committee noted that at its last session it was decided to circulate two proposed elaboration procedures for comments as contained in Appendix IV A and IV B of ALINORM 89/31. Comments were received from Australia, Cuba, Federal Republic of Germany, Mexico, New Zealand, Norway, Poland, Sweden, and the United States of America.

61. The Codex Secretariat indicated that the proposed elaboration procedure in Appendix IV A provided for the omission of Steps 6 and 7 in a manner similar to the current elaboration procedures for Codex maximum limits for pesticide residues. However, it was indicated further that the general introduction to the elaboration section would need revision so as to expedite procedures specific to the elaboration of MRLs for veterinary drug residues.

62. The Committee agreed to forward the proposed elaboration procedure in Appendix IV A of ALINORM 89/31 through the Codex Committee on General Principles to the Commission for adoption with the understanding that Steps 6 and 7 may be omitted on the basis of a two-thirds majority of votes cast in the Commission. The Procedure for the Elaboration of Codex Recommendations for Maximum Residue Levels of Veterinary Drugs is attached to this report as Appendix IV A.

63. As discussed in paragraph 61 above, the Committee also agreed to forward the revised elaboration introductory section through the Codex Committee on General Principles to the Commission for adoption to insure the possibility of the elimination of Steps 6 and 7 when warranted by a majority vote of two-thirds of the Commission. The revised introductory elaboration section is attached as Appendix IV B to this report.

Acceptance Procedures

64. The Committee noted that at its last Session it was decided to circulate the proposed acceptance procedure for comments as contained in Appendix V of ALINORM 89/31. Comments were received from Australia, Cuba, Federal Republic of Germany, Norway, Poland the United States of America.

65. The Committee noted that the comments received supported the proposal agreed to by the Committee's Second Session, and decided to forward the proposed acceptance procedure as contained in Appendix V of ALINORM 89/31 to the Codex Committee on General Principles for endorsement and to the Commission for adoption.

CONSIDERATION OF PROPOSED DRAFT MRLS FOR VETERINARY DRUG RESIDUES IN FOODS AT STEP 5 (Agenda Item 5)

66. The Committee had for its consideration proposed draft MRLs as contained in ALINORM 89/31, Appendix VI, which had been circulated to governments for comments following the decision of the Committee at its Second Session (see ALINORM 89/31, paragraph 96). Comments in response to Codex Circular Letter 1988/8-RVDF had been received from Cuba, Federal Republic of Germany, Mexico, New Zealand, Poland, Sweden, the United States of America, the European Economic Community (CX/RVDF 88/6), and Australia (Conference Room Document No. 8).

CHLORAMPHENICOL

67. The Observer from the EEC drew attention to its written comments included in document CX/RVDF 88/6. The Committee was informed that chloramphenicol had been considered by the EEC Committee for Veterinary Medicinal Products, and that, in 1985, it had agreed that chloramphenicol played an important role in veterinary therapy, particularly in the treatment of younger animals when long withdrawal periods could realistically be observed. On the other hand, the EEC Committee had recommended that on the basis of the information available, chloramphenicol should not be used in laying birds or lactating animals. In those cases where chloramphenicol was deemed to be indispensable in other animals, its use should be limited to the extent absolutely necessary. In these latter cases, the use of an analytical procedure for monitoring the observance of appropriate withdrawal times sensitive to at least 10 ppb (µg/kg) was recommended. This recommendation had been implemented by the EEC Member States.

68. The Chairman of the Ad Hoc Working Group on Methods of Analysis and Sampling, Dr. R. Ellis (U.S.A.), noted that the Working Group had asked for further information on available methods of detection of residues of chloramphenicol. Several changes in the situation with regard to available methods had occurred since discussions leading to the level of 10 µg/g referenced in the 32nd JECFA report. He stated that methods were now available for detection of chloramphenicol at, or below, 1 µg/g, (see also Para. 93).

Status of the MRL for Chloramphenicol

69. The Committee agreed to advance the MRL "not allocated" for chloramphenicol to Step 5 of the Procedure.

ESTRADIOL 17-BETA; PROGESTERONE; TESTOSTERONE

70. The delegation of Norway stated that the use of the expression "unnecessary" was unfortunate and requested that this term and its implications be reconsidered by JECFA. The delegations of Canada, Jamaica, and the United States of America supported this view. The representative of WHO stated that the closest approximation in terminology used by JECFA in other areas was "not specified", but that the 32nd Session of JECFA had declined to use this term.

71. The Committee agreed to request JECFA to review the terminology used in such cases, and also agreed to incorporate into the summary statement of MRLs a footnote explaining why the term had been used.

72. The Observer from the EEC, as well as the delegation of Spain, which spoke on behalf of the Member states of the EEC present at the session, stated that the proposed draft MRLs of these substances related exclusively to their use as growth promoters. The Community had specific legislation regarding the use of hormones. The European consumer was opposed to the use of hormones for fattening and demanded meat from animals which have not been so treated. The response of the Community to consumer demands regarding the food they eat and the enforcement they expect had been to prohibit the use of these potent hormones for fattening purposes. This prohibition included the use of any substances having an oestrogenic, androgenic or gestagenic action or thyreostatic substances.

73. In consequence, the Member states of the Community did not find it appropriate to examine further in the Codex system recommendations for proposed draft Codex MRLs for residues resulting from the use of these substances for fattening purposes, and reserved their position in relation to the advancement of these MRLs to Step 5 of the Procedure, (see Para. 79).

Status of the MRLs for Estradiol 17-beta; Progesterone and Testosterone

74. The Committee, noting the position of the EEC Member States, but also recognizing the use of these substances in other countries who are members of the Codex Alimentarius Commission, advanced the Proposed Draft MRLs for Estradiol 17-beta, Progesterone and Testosterone for consideration by the Commission at Step 5 of the Procedure.

75. The delegation of Norway, while not opposing the advancement of the MRLs to Step 5, reiterated its position that it was opposed to the use of these substances as growth promoters.

TRENBOLONE ACETATE

76. The delegation of Norway drew attention to the need to carefully define the relationship between the nature of the residue and the tissue affected by stating that it may be necessary to define the terms "tissue", "muscle", and other terms so as to avoid confusion. The Committee agreed and requested Canada to address this issue when preparing the glossary of terms.

77. The Committee noted that this substance would be re-evaluated by JECFA at its 34th session in January 1989. It agreed to retain the MRL at Step 4 of the Procedure so as to consider it at its next session in light of the JECFA re-evaluation.

Status of the MRLs for Trenbolone Acetate

Retained at Step 4.

ZERANOL

78. The Committee noted that the acceptable residue level as established by JECFA had been based on the maximum residue levels occuring after use of the substance in accordance with Good Practice in the Use of Veterinary Drugs and was well below the level which would be of any toxicological significance. In the case of bovine muscle, the MRL was the lowest level consistent with current reliable analytical methodology.

Status of the MRLs for Zeranol

79. The delegation of Spain, speaking on behalf of the Member states of the EEC present at the Session, reiterated the opinion of the EEC that it was not appropriate to examine further in the Codex system recommendations for the proposed draft MRLs for hormones being advanced to Step 5. (See Paras. 72-73).

80. The Committee, noting the position of the EEC member countries, but also recognizing the use of this substance in other member countries of the Codex Alimentarius, advanced the Proposed Draft MRLs for zeranol for consideration by the Commission at Step 5 of the Procedure.

81. A summary of the proposed draft MRLs is included in Appendix V to the present report.

PROGRESS REPORT ON THE ELABORATION OF A GLOSSARY OF TERMS AND DEFINITIONS (Agenda Item 7)

82. The Committee had before it Working Papers CX/RVDF 88/8, CX/RVDF 88/8 - Addendum 1 (Conference Room Document 7) and Conference Room Document 8, which addressed the Proposed Glossary of Terms for Consideration by the Codex Committee on Residues of Veterinary Drugs in Foods as prepared by the Delegation of Canada. In introducing the item, the Delegation of Canada stated the the Committee in its previous sessions had not given a time frame for the completion of this document.

83. The delegation of Norway suggested that the Committee should take full advantage of and use currently established Codex definitions. It also suggested that the Glossary should be shortened to encompass only items essential to its work. The delegation of Canada agreed that if there were current definitions, they should be used, and stated that they had referenced definitions from other Committees that they knew existed.

84. The delegation of Spain requested that there be an indication of definitions from other Codex Committees through the use of an asterisk. The Committee noted that such definitions had been identified through the use of reference listings, but recommended that future versions of the Glossary should also be marked with asterisks, as requested.

85. The delegation of France proposed the establishment of a small working group to address existing problems with the translation of some definitions into other languages. The Committee decided to establish a working group to be chaired by Canada which would coordinate all activities concerning the glossary before the next Committee meeting in 1989. The delegations of Australia, France, Mexico, Spain, Switzerland, the United Kingdom and the United States of America agreed to participate in the working group deliberations.

86. It was agreed to send all comments concerning the glossary directly to Canada, with a copy of the comments to be sent to the Joint FAO/WHO Office in Rome.

SURVEY ON INTAKE STUDIES (Agenda Item 8)

87. The Committee had before it Working Papers CX/RVDF 88/9 (Conference Room Document 5) and Conference Room Document 11 concerning comments to the survey on intake studies as requested in CL 1988/5-RVDF. The delegation of the United States introduced the document and pointed out that it was based on comments from Canada, Cuba, Federal Republic of Germany, Finland, Korea, Norway, the Philippines and the United Kingdom. The delegates were aware of the preliminary character of the collated data and, considering the importance of dietary intake information agreed (a) to have the United States of America continue conducting the survey for an additional year, (b) to redistribute the questionnaire to all member countries of the Codex Alimentarius, (c) that the data should be analyzed and reported back to the 4th Session of the CCRVDF, (d) the Committee urged all member countries to submit the information outlined in the questionnaire. Special emphasis should be given to those studies which provide information useful to the determination of maximum residue levels, based upon the ADI. The delegation of the United States of America agreed to provide these data to JECFA for this purpose.

CONSIDERATION OF DRAFT CODE OF PRACTICE FOR THE CONTROL OF THE USE OF VETERINARY DRUGS (Agenda Item 9)

88. The Committee had before it Working Papers CX/RVDF 88/10 (Conference Room Document 6), Conference Room Document 1 and Conference Room Document 15. As outlined under Agenda Item 2, the Committee noted its decision to include discussions concerning "Good Practices for the Registration and Marketing of Veterinary Drugs" (Agenda Item 3e) under this agenda item.

89. The delegation of the United Kingdom presented a background and summary of the proposed code, and indicated that considerable input was derived from a previous code prepared by the Netherlands (CX/RVDF 87/9). The Committee also noted that the delegation of Peru had forwarded a proposed code (CRD 1) in its written comments.

90. The Committee recalled its decision at its last session concerning the elaboration of a code concerning "Good Practices for the Registration and Marketing of Veterinary Drugs" (para. 88, ALINORM 89/31), whereby this subject was considered outside its terms of reference. The Committee reconfirmed this decision, and decided that the draft code for the control of the use of veterinary drugs should not include discussions concerning the marketing and registration of veterinary drugs. It was further agreed to leave matters of registration and marketing to the competent international authority, the Office International des Epizooties.

91. The Committee thanked the delegation of the United Kingdom for its efforts, and concluded that the elaboration of this document should continue under the direction of the United Kingdom along with input from Peru and the Netherlands. The Committee agreed further that the proposed code would be circulated for comment and eventual discussion at its next session.

CONSIDERATION OF METHODS OF ANALYSIS AND SAMPLING BASED ON THE REPORT OF AN AD HOC WORKING GROUP ON METHODS OF ANALYSIS AND SAMPLING (Agenda Item 10)

92. The Committee had before it Working Papers CX/RVDF 88/15 Addenda I, II and III (CL 1988/42-RVDF) as prepared by the United States and Conference Room Document 12 "Report to the Plenary Session of the Second Meeting of the Ad Hoc Working Group Methods of Analysis and Sampling". The Chairman of the Working Group, Dr. R. Ellis (U.S.A.) introduced the

report of the meeting which took place on 28 October 1988. Delegates and observers from Australia, Botswana, Canada, Denmark, France, Federal Republic of Germany, New Zealand, Netherlands, Poland, Sweden, the United Kingdom, the United States of America, and the European Economic Community, FAO and WHO were present. The Working Group had reviewed and discussed three working papers, namely, "General Considerations of Analytical Methods for Regulatory Control", "Attributes of Analytical Methods" and "Sampling for the Control of Veterinary Drugs in Foods".

93. The Working Group exchanged information on existing methods for chloramphenicol, but due to the lack of analytical performance data, was unable to make a selection or recommendation. It was suggested to request these data for the next session of CCRVDF, (see also Para. 68).

94. The Group decided to use established Codex format procedures for the presentation and publication of analytical methods.

95. Deliberations also focused on the development of simpler methods accessible to developing countries as well as to the international validation of methods. Regional validation was proposed as a means to minimize possible problems related to the shipment of biological samples across borders.

96. The Committee agreed to adopt the following working group recommendations:

a) That the Joint FAO/WHO Secretariat prepare a Circular Letter to request information concerning cross border shipments of biological samples used for international validation of methods for veterinary drugs. The Circular Letter should also request that methods of analysis be submitted to the chairman of the working group for compounds scheduled for evaluation at the 34th JECFA meeting in February 1989. The Circular Letter should indicate that (i) the methods should be applicable to edible animal tissues and products used as commodities in international trade, as methods for other biological tissues and fluids used in residue studies are not necessarily applicable to trade commodities; (ii) the methods should apply to MRL regulatory control and enforcement; (iii) that only validated methods, or methods with data on analytical performance should be submitted; (iv) that more information be requested concerning the development of statistical sampling plans for residue control programmes of veterinary drugs in foods for consideration within the framework of the working paper on "Sampling for the Determination of Residues of Veterinary Drugs in Foods."

b) That the definitions agreed upon by the Working Group be forwarded to the delegation of Canada for incorporation into the CCRVDF glossary of terms.

97. The Committee decided:

a) To circulate the three working group documents for comments at Step 3 and eventual discussion at the next CCRVDF session (please see Appendix VI).

b) To extend the mandate of the Ad Hoc Working Group on Methods of Analysis and Sampling under the Chairmanship of the delegation of the United States of America.

PRIORITY LIST OF VETERINARY DRUGS REQUIRING EVALUATION (Agenda Item 11)

98. The Committee had before it Working Paper CX/RVDF 88/11 (Conference Room Document 9) concerning priority list comments submitted in response to CL 1988/34-RVDF, and Conference Room Document 14, the Report of the Ad Hoc Working Group on Priority Drugs.

99. The Chairman of the Working Group, Mr. G. Hooper (Australia), introduced the Working Group report and recommendations. The delegations of Australia, Brazil, Canada, Federal Republic of Germany, France, Italy, Mali, Mexico, the Netherlands, New Zealand, Spain, Sweden, the United Kingdom, the United States of America and representatives of FAO, WHO, FEDESA and COMISA participated in the working group session.

100. The Group had considered drugs prioritized at the previous RVDF session (ALINORM 89/31, Appendix VIII), government comments (CX/RVDF 88/11) and nominations submitted by delegations at the present meeting. A draft priority list (Appendix B, Conference Room Document 14) had been prepared and presented for consideration by the Committee, and included an indication of the availability of toxicity and residue data. The Group agreed to submit a number of future work suggestions for approval by the Committee, namely; (a) development of a questionnaire to compile information on compound identity, conditions of use, and availability of residue and toxicological data; (b) to continue priority list updating between the Committee sessions; and (c) to collect data for older compounds.

101. Support for the development of the questionnaire was expressed by the delegations of France and the United Kingdom. The delegation of France also suggested that the Group consider a questionnaire prepared for similar purposes by the EEC Working Group on the "Safety of Residues".

102. In opening discussions on the priority list the Chairman indicated that nitrofurans and quinoxalines were prioritized at the Second RVDF Session and should remain on the list, as they were not currently scheduled for evaluation at the 34th JECFA meeting. The delegation of Poland supported the inclusion of nitrofurans in the priority list.

103. The delegation of Belgium, with other delegate support, pointed out that benzimidazoles (febantel-fenbendazol-oxfendazol) were closely inter-related in action and metabolism and, therefore, should be considered by JECFA as a group. The delegation of the United Kingdom stressed that other important benzimidazoles were all closely inter-related in metabolism, and the delegation of the Federal Republic of Germany suggested that benzimidazoles be evaluated as a group to determine the applicability of extrapolation of data for various representatives of the group. The delegation of Australia agreed that there was considerable interest in benzimidazoles, and proposed verification by questionnnaire for their evaluation at a later date.

104. The delegation of the United States of America stated that the information on febantel might not be readily available and therefore, the compound should be removed from the priority list. The delegation of France stated that it might be difficult to predict the availability of future data and indicated that this should not prejudice the priority list decisions, as for example, in the case of the benzimidazoles.

105. The Committee agreed to include the two nitrofurans and quinoxalines for the next, possibly 1990, JECFA meeting and to assign second priority to benzimadazoles as a group, tentatively for a later JECFA meeting.

106. The delegation of Belgium proposed and the Committee agreed to the inclusion of the antihelmintic ivermectin in the priority list. The delegation of Australia also nominated the antihelmintic closantel for evaluation, and stated that Australia would provide data for consideration at the 1990 JECFA meeting. Similarly, the Committee agreed to the inclusion of levamisole on the priority list at the suggestion of the delegation of the United Kingdom.

107. The delegation of the United States of America proposed the inclusion of bovine and porcine somatotropins in the priority list, although it noted that these substances did not meet all criteria for the selection of priority compounds. Nevertheless, the delegation was of the opinion that an early scientific evaluation could prevent misunderstandings as to the safety of foods containing residues of these substances. This approach was supported by the delegation of Poland, but several other delegations stated that studies, particularly in Europe, were still at a very early experimental stage. The Committee agreed to place bovine and porcine somatotropins on the list of second priority substances, for evaluation at a later JECFA meeting.

108. The delegation of France, supported by the delegations of Canada, Norway and the United Kingdom, proposed the inclusion of oxytetracycline for priority consideration. This substance, widely used in aquaculture, would be an excellent model for consideration of resistance phenomena for which sufficient data from published studies were available. The Committee agreed with this proposal.

109. The delegations of France and the Netherlands proposed priority listing for benzyl penicillin because in addition to presenting some public health problems, it would also be the ideal model for JECFA evaluation of a compound with a manifested allergenic potential. This proposal was accepted by the Committee.

110. The delegations of Norway and the Netherlands supported the evaluation of sulfonamides as a priority group, but the Committee was of the opinion that these should be evaluated at a later date, pending the availability of additional data. The representative of COMISA stated that they would determine the availability of data on sulfonamides and other older compounds through appropriate contacts with member companies for forwarding to the Secretariat.

111. The delegation of France proposed that a group evaluation of compounds be considered, and that a circular letter be distributed to request information on government interest and applications. The delegation also pointed out that while availability of data is undoubtedly an important factor, it should not limit the consideration of decisive public health factors. A balance should be maintained between new compounds and older drugs.

112. The delegation of the Federal Republic of Germany proposed the inclusion of phenothiazine tranquillizers for prioritization, however, the delegation of Norway stated that the pre-slaughter use of such drugs was considered not to be good veterinary practice in Norway.

113. The Committee reached agreement on the priority list as presented in Appendix VII. The list includes drugs that should be considered by the next JECFA session and a number of other compounds for later JECFA evaluation.

114. The Committee decided to extend for one year the mandate of the working group under the Chairmanship of the delegation of Australia.

GUIDELINES FOR THE ESTABLISHMENT OF A REGULATORY PROGRAMME FOR CONTROL OF VETERINARY DRUG RESIDUES IN FOODS (Agenda Item 12)

115. The Committee had before it Working Paper CX/RVDF 88/12 (Conference Room Document 10).

116. The Committee recalled discussions at its last session concerning these guidelines, whereby a working paper was introduced by the delegation of the United States. At that session, the Committee agreed that the document in question should be simplified and revised for presentation at this session of the Committee.

117. The delegation of the United States of America indicated that it reviewed the FAO/WHO/UNEP Guidelines for the Development of Effective National Food Control Systems as well as the Report of the Group of Developing Countries in Asia Concerning Pesticide Residues Problems (Appendix III of ALINORM 87/15) when revising these guidelines. The delegation of the United States concluded that problems facing developing countries for pesticide residues and veterinary drug residue control were similar, and that coordination between these committees was desirable.

118. The United States of America recommended that the guidelines describe the establishment of a regulatory system which utilizes multi-residue screening methods to assure authorities that imported animal products do not contain excessive levels of residues. As a second step, the guidelines could describe the criteria required for establishing a more sophisticated monitoring programme.

119. The delegation of France, on behalf of OIE, suggested that the proposed guidelines be presented to the next OIE sponsored meeting of the Regional Commission for Africa in Tanzania next year. Several delegations, including countries of the African region, supported this suggestion. The Codex Secretariat also encouraged delegations to confer with their Regional Representatives concerning these issues, especially in relation to the upcoming sessions of the Regional Coordinating Committees for Africa and Latin America and the Caribbean. The delegation of the United States offered its support and technical advice concerning this subject through their attendance at these meetings.

120. The Committee thanked the United States for its efforts and recommended that deliberations concerning the proposed Code should continue, while taking into account the above suggestions. The Committee agreed that the proposed Code should be revised as soon as possible to allow for input from other meetings as discussed above.

OTHER BUSINESS AND FUTURE WORK (Agenda Item 13)

121. The Committee concluded and agreed that the Agenda for its next session should include the following items:

- Progress report on the Compendium of Veterinary Drugs for the Americas.
- Draft MRLs for Residues of Veterinary Drugs in Foods, Step 7 (if approved by the Commission).
- Proposed Draft MRLs for Residues of Veterinary Drugs in Foods at Step 4.
- Elaboration of the Glossary of Terms and Definitions.
- Survey on Intake Studies.
- Draft Code of Practice for the Control of the Use of Veterinary Drugs.
- Methods of Analysis and Sampling.
- Review of Priority List of Veterinary Drugs Requiring Evaluation.
- Guidelines for the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods.

DATE AND PLACE OF NEXT SESSION (Agenda Item 14)

122. The Committee was informed that the Government of the United States of America offered to host the Fourth Session of CCRVDF from 23-27 October 1989, with the understanding that the Working Group Sessions (i.e. Methods of Analysis and Sampling, Priorities) would be held on Monday 23 October, and the general Plenary session would commence on Tuesday 24 October.

123. The Committee agreed to this proposal.

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Summary Status of Work

Code/Guideline/Maximum Residue Level	Step	For Action by:	Document Reference
Definitions for "Maximum Residue Level" (MRL) and "Good Practices in the Use of Veterinary Drugs" (GPVD)	--	9th CCGP 18th CAC	ALINORM 89/31A, Appendix III
Procedures for the Elaboration of Codex Maximum Residue Levels for Veterinary Drugs in Foods	--	9th CCGP 18th CAC	ALINORM 89/31A, Appendix IVA
Procedure for the Elaboration of Codex Maximum Residue Levels for Veterinary Drugs in Foods - Introduction	--	9th CCGP 18th CAC	ALINORM 89/31A, Appendix IVB
Procedure for the Acceptance of Codex Maximum Residue Levels for Veterinary Drugs in Foods	--	9th CCGP 18th CAC	ALINORM 89/31A, Para.65
Proposed Draft MRLs for Veterinary Drugs in Foods	5	18th CAC	ALINORM 89/31A, Appendix V
Proposed Draft MRLs for Veterinary Drugs in Foods	4	34th JECFA 4th CCRVDF	ALINORM 89/31A, Appendix V
Glossary of Terms and Definitions	--	Canada with Australia, France, Mexico, Spain, Switzerland, U.K. and U.S.A. 4th CCRVDF	ALINORM 89/31A, Paras. 82-86
Code of Practice for Control of the Use of Veterinary Drugs	2	U.K. with Netherlands, and Peru 4th CCRVDF	ALINORM 89/31A, Paras. 88-91
Guidelines for the Establishment of a Regulatory Control Programme	2	U.S.A. 4th CCRVDF	ALINORM 89/31A, Paras. 115-120
Priority List of Veterinary Drugs Requiring Evaluation	--	Governments 4th CCRVDF	ALINORM 89/31A, Appendix VII
Methods of Analysis and Sampling	--	Governments 4th CCRVDF	ALINORM 89/31A, Appendix VI

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CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Summary Status of Work (Cont'd)

Code/Guideline/Maximum Residue Level	Step	For Action by:	Document Reference
Compendium of Veterinary Drugs	--	Governments 4th CCRVDF	ALINORM 89/31A, Paras. 39-41
Survey on Intake Studies	--	Governments 4th CCRVDF	ALINORM 89/31A, Para. 87
Amendment to Terms of Reference (Clause d - Methods of Analysis and Sampling)	--	No further action required.	ALINORM 89/31, Para. 19
Definitions for "Veterinary Drug" and "Residue of Veterinary Drug"	--	No further action required.	ALINORM 87/31, Paras. 93 and 101
Criteria for the Selection of Veterinary Drugs for the Establishment of Maximum Residue Levels (MRLs)	--	No further action required.	ALINORM 89/31, Appendix VIII - Part I
Format for the Presentation of Codex MRLs for Veterinary Drugs	--	No further action required	ALINORM 89/31, Appendix IV - Part A

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CODEX: KEEPING THE PROMISE

Many of you have traveled very far to work very hard for the next five days. When you leave on Friday, though, I believe you will leave feeling invigorated, rather than drained. That is because you are participating in one of the most energetic and successful forums we have for reaching international scientific consensus on the animal drug trade issues that are also public health issues.

I am especially pleased to see, once again, an impressive representation of nations from the continent of Africa. I am aware, colleagues, of the special regional concerns that region brings to this body, and, in particular, your requisite as regards trypanocides. I would like to formally encourage our distinguished Chairman and the U.S. Delegate to pay particular attention to the African position.

As U.S. Coordinator, I am especially happy to be here today. In 1985, as U.S. Delegate, I supported the historic decision to form this committee, and in 1986 and 1987, I had the honor of chairing it. Because of this involvement, I am personally pleased at recent U.S. decisions, in terms of financial support for the parent organizations of Codex.

We need Codex. I firmly believe that some of the trade disputes now facing countries -- and certainly the hormone issue is one of the most divisive -- could have been avoided if this committee had existed only a few years ago. A disagreement between professionals can be settled quickly and politely, on the basis of objective information. Resolving a trade disagreement between countries at diplomatic levels is time-consuming, painful, and potentially damaging to all the mutual relationship.

In a few minutes, I will formally relinquish the committee chairmanship to my distinguished colleague and friend, Dr. Gerald Guest. Frankly, I am delighted to do so. Dr. Guest is very much a founding father of the committee, and under his leadership the committee can be expected to continue its exceptional progress.

A Model

But first, I would like to make a few observations from my new vantage point as U.S. Coordinator.

As you begin your work today, you can all be proud of the example this committee has set for other Codex committees. The Food Hygiene Committee, for example, has taken note of the expert contributions provided by observers from the veterinary drug and affiliated industries. Consequently, that committee has strengthened its own complement of industry observers. It has found their involvement and commitment invaluable in defining subjects for committee consideration; and the Committee on Food Hygiene expects the industry perspective to be formally important in shaping its resolutions and recommendations.

A vital mix of regulatory and industry expertise is necessary if international food standards are to be workable in facilitating trade in the real world. Today, the real world includes many multinational corporations. To disregard that perspective would be illogical and self-defeating, for effective international standards must be practical as well as scientifically sound.

Food Safety is Public Health

Of course, much more than fair trade is at stake here. Codex standards provide consumers around the world with the same high standard of protection. This does not mean providing irrefutable evidence of absolute protection from all possible risks in the food supply, no matter how negligible. That is not humanly possible, even if it were fiscally feasible. It is a promise that cannot be kept, and it should not be made.

Rather, our international goal is protecting consumers from significant risks in the food supply. How can this be accomplished? First, countries must recognize food safety as a public health issue. It is not an aesthetic issue. It is not a proper tool for political manipulation. It is not only an issue of sanitation or veterinary medicine. Food safety must be framed in public health terms.

If nations could agree on this fundamental point, they would incorporate food safety into all programs for public health promotion and disease prevention, including nutrition. The logical consequence of this action would be regulatory systems whose primary objective is to prevent problems rather than merely detect them. A prevention-based program is most

effective when industry acknowledges and fulfills its equal responsiblity for safe food, and when countries use objective measures to verify industry accountability.

I contend that the countries which embrace food safety as a public health issue are those represented here today, and in other codex committees. Those nations send representatives of all their significant food regulatory agencies to codex meetings, for they believe that scientific consensus is the only way to develop practical, enforceable standards founded in the best scientific evidence available. Such standards represent honest food safety: A promise that can be kept.

Public health policies that are not based on science are doomed to failure. It may take some time, but eventually it becomes apparent that requirements are based on no core of reasonable evidence. When that occurs, such requirements may be openly ignored or easily circumvented by the unscrupulous. Enforcement becomes a near impossibility, and citizens may actually receive less protection than they would have with no standards at all.

There is no danger of that outcome here. This Committee's process and progress show that it is indeed possible to develop international food safety standards that offer a high measure of protection and are practical and enforceable.

Retrospective

In just two short years, the Committee has achieved much. You have selected several compounds for expert safety review to determine maximum residue levels for proposed codex adoption. That accomplishment is perhaps of most interest to the consuming public, so concerned and confused about residues.

Recommendations for some priority compounds have already been received from the joint expert committee on food additives (JEFCA), allowing the Committee to develop proposed maximum residue levels on which several countries have commented. Early in 1989, the joint expert committee on food additives (JEFCA) will examine available data on the list of priority compounds agreed upon at last year's committee session.

Less visible to the public are the accomplishments that lay the groundwork for more effective international regulation of veterinary drugs. Certainly the development of draft codes of practice or guidelines for veterinary drug registration, marketing, and residue enforcement fall into this category, as does the veterinary drug compedium. The work on surveying dietary intake of residues is also critically important.

Methods. The Committee's accomplishments in developing draft criteria for classifying and evaluating methods of analysis and sampling have brought us much closer to international consensus on a critical aspect of residue control.

To the general public, perhaps a test is a test is a test. However, scientists recognize that methods fall on a continuum, in terms of use, practicality, precision, and validation.

At one end of the continuum are methods suitable primarily for exploratory use, to determine whether or not a residue problem exists. The intensity of the problem must then be determined by more precise analysis. Exploratory methods may not be ideal; they may require highly specialized instrumentation; and they may not have been subjected to interlaboratory study. Nevertheless, they serve a legitimate and useful purpose in problem identification. Developed nations with more technological resources may be more likely to develop methods for exploratory use, but developing nations will also benefit from the results of exploratory studies.

At the other end of the continuum are methods appropriate for routine use in enforcement of maximum (allowable) residue levels. That is, they detect analytes at or below the limit set by law, regulation, or written policy. Such methods may identify or quantify residues, but in either case they must be rugged and they may have been subjected to extensive multilaboratory analysis, because they may have to support legal action. The United States has developed rapid methods that fall into this category, and is pursuing the development of others.

A tool, not an answer. I do not think it is possible to overestimate the importance of sound methodology. Even so, a cautionary note is in order.

We in the field recognize the complexity of methods development, as well as the eternal vigilance necessary to assure quality results from good methodology. We also realize that the challenging work of methods development never ends. Months or years of intense effort may produce a method that is beautiful in its simplicity; however, a better method is always just around the corner. Finally, we recognize sound methodology as only one of many tools for assuring food safety from the residues that are most harmful to health and most likely to be present in the environment and the food we eat.

Some consumers, however, appear to believe that "more tests" are all we need. They may wish for a complete arsenal of perfect methods that would instantaneously and unambiguously

detect, identify, and quantify all potential chemical residues in all food before sale. They do not understand the assurance provided by random statistical sampling. If such methods could be developed and implemented for all foods, this would be as astronomically expensive. Even so, the results would not provide the absolute proof of zero risk that many citizens seem to demand from their governments. For the possibility of human error will always be present.

A sign of this demand is the interest some americans have in range-fed chicken and other "natural" meat and poultry. In his 1986 speech to this committee, the late Dr. Donald Houston noted that this trend "presents great opportunities for the unscrupulous."

Interestingly, in the past year the U.S. Department of Agriculture has found it necessary to request some meat and poultry companies to verify animal production claims in point-of-purchase labeling, which -- unlike advertising -- falls under our jurisdiction. Such claims might include: "raised without antibiotics" or "raised without food exposed to pesticides." While most companies have completed, a few have chosen to stop making the claims rather than verify them.

Risk Perception and Regulatory Action

Why do some consumers willingly accept extravagant advertising claims at face value, yet expect their governments to provide absolute proof of absolute safety?

I believe that mixed perceptions of science provide part of the answer. One side of the coin shows a godlike scientist, but the other side shows a made scientist.

In the twentieth century, science has produced dazzling achievements that have dramatically improved our lives and their quality. Consumers in developed nations have come to take scientific miracles almost for granted without necessarily understanding how the "miracles" work. Scientists may enjoy the pedestal on which this perception places them, but I suspect many do not enjoy the price -- public misunderstanding of the scientific process and its limits.

This century has also shown the painful human consequences of policy decisions based in part on inadequate science, as with thalidomide and diethylstilbestrol. Such events have left their own residue of distrust for science and government, as well as they safety assurances we can provide.

In this milieu, regulators must acknowledge the multidimensional nature of food safety issues. There are few that can be characterized as "simple problems". And scientists must step down from the pedestal and communicate more clearly about the place of science in food safety assurance. There are few simple solutions.

Above all, we must not make regulatory promises on the basis of public risk perception, for we cannot keep them. The promise we can keep is to protect food consumers from significant actual health risks associated with food. In the residue arena, this means regulators must continue working for "fail-safe" residue control systems with sound methodology as an essential component.

At the domestic level, that is every food regulatory agency's mission. At the international level, it is the mission of this committee, and codex is general. Your work in codifying international scientific consensus on the important aspects of veterinary drug residues is invaluable in that mission.

Harmonization

In addition to codex, two other international organizations play harmonizing roles for animal health and plant health standards respectively. They are the international office of epizootics (OIE) and the International Plant Protection Convention (IPPC).

These three organizations -- Codex, the OIE, and the IPPC -- were founded in efforts to facilitate fair trade. They have helped, particularly for those organizations and industries which have chosen to take active roles. However, the organizations share one weakness; No true enforcement mechanism for the harmonized codes and standards developed.

The United States supports codex, OIE, and IPPC; lock, stock, and barrel; that means we firmly believe that the harmonized standards these organizations develop should be enforced. There is a way to assure enforcement among the 94 signatory countries of the general agreement on tariffs and trade (GATT).

GATT has two dispute mechanisms, Article XXB and the Tokyo Round Agreement on Technical Barriers to trade (the standards code). The advancement of free trade for agricultural products is one of the key goals of the current Uruguay Round of Multilateral Trade discussions. The United States believes that free trade would be geratly facilitated by linking Codex,

OIE, and IPPS with GATT dispute mechanisms. This would mean that when a member country brought a trade dispute to GATT, GATT would turn to Codex, OIE, and IPPC codes for resolution of questions about the health or sanitary basis for a country's trade policy. Codex would be an arbiter, not merely a reference, as it is now.

We believe that this action would eliminate many time-consuming and ultimately pointless efforts to cloak nontariff trade barriers in the guide of health and sanitary regulations. It would also enhance the effectiveness of the GATT, which established seven new arbitration panels in the past year to deal with an increasing number of trade disputes. And it would enable us to harmonize health and sanitary regulations by the year 2000.

The United States hopes to see universal acceptance of the principle of harmonization in the near future, perhaps at the midterm review of the Uruguay Round of Multilateral discussions, to be held in Montreal in December. Whether or not the U.S. proposal to the GATT is accepted in total, though, I think the impetus for harmonization is undeniable.

The work of this vital committee has brought us a few steps closer to harmonization 2000. You have shaped the initial framework for more consistent international regulation of veterinary drug use and residues, infusing both scientific and practical considerations to assure fair trade and public health protection. That is the promise of codex, and you are showing that the promise can be kept.

Thank you.

DRAFT DEFINITIONS OF "MAXIMUM RESIDUE LEVEL" and "GOOD PRACTICE IN THE USE OF THE VETERINARY DRUGS"

For the Purpose of Codex Alimentarius

"Maximum Residue Level (MRL) is the maximum concentration of residue resulting from the use of a veterinary drug (expressed in mg/kg or µg/kg on a fresh weight basis) that is recommended by the Codex Alimentarius Commission to be legally permitted or recognized as acceptable in or on a food.

It is based on the type and amount of residue considered to be without any toxicological hazard for human health as expressed by the Acceptable Daily Intake (ADI), or on the basis of a temporary ADI that utilizes an additional safety factor. It also takes into account other relevant public health risks as well as food technological aspects.

When establishing an MRL, consideration is also given to residues that occur in food of plant origin and/or the environment. Furthermore, the MRL may be reduced to be consistent with good practices in the use of veterinary drugs and to the extent that practical analytical methods are available.

"Good Practice in the Use of Veterinary Drugs (GPVD) is the official recommended or authorized usage including withdrawal periods, approved by national authorities, of veterinary drugs under practical conditions."

PART 5

PROCEDURE FOR THE ELABORATION OF CODEX MAXIMUM RESIDUE LEVELS FOR VETERINARY DRUGS

STEPS 1, 2 and 3:

The Secretariat distributes the draft recommendations for MRLs for veterinary drug residues, based on JECFA evaluations, and requests comments from governments and interested international organizations on all aspects, including possible implications of the draft recommendations for maximum levels of veterinary drug residues on their economic interests.

STEP 4:

The Codex Committee on Residues of Veterinary Drugs in Foods examines the recommendations for maximum levels for veterinary drug residues in the light of comments. The Codex Committee, when formulating its recommendations for proposed draft Codex maximum levels, takes all appropriate matters into consideration including the need for urgency, the government comments at Step 3 and the likelihood of new evidence becoming available in the immediate future and, on the basis of such considerations, indicates to the Commission those proposed draft maximum levels which, in its view, need to be passed through the full Procedure and those for which there might be an omission of Steps 6 and 7, it being understood that any MRL at Step 5, for which it has been recommended that Steps 6 and 7 could be omitted or any MRL at Step 8 shall be dealt with by the Commission in accordance with the Guide to Consideration of Standards at Step 8 of the Procedure for the Elaboration of Codex Standards.

STEPS 5-8:

As for the Procedure for the Elaboration of World-wide Codex Standards, Codex Alimentarius Procedural Manual, Sixth Edition, (pages 39 to 41).

PROCEDURE FOR THE ELABORATION OF CODEX STANDARDS AND CODES OF PRATICES, CODEX MAXIMUM LIMITS FOR PESTICIDE RESIDUES, CODEX ADVISORY SPECIFICATIONS FOR THE IDENTITY AND PURITY OF FOOD ADDITIVES AND CODEX MAXIMUM LEVELS FOR VETERINARY DRUG RESIDUES

INTRODUCTION

1. The procedure for the elaboration of Codex standards is as follows. The Commission decides, taking into account the "Criteria for the Establishment of Work Priorities and for the Establishment of Subsidiary Bodies", that a standard should be elaborated and also which subsidiary body or other body should undertake the work. Decisions to elaborate standards may also be taken by subsidiary bodies of the Commission in accordance with the above-mentioned criteria subject to subsequent approval by the Commission or its Executive Committee at the earliest possible opportunity. The Secretariat arranges for the preparation of a "proposed draft standard" which is circulated to governments for comments and is then considered in the light of these by the subsidiary body concerned which may present the text to the Commission as a "draft standard". If the Commission adopts the "draft standard" it is sent to governments for further comments and in the light of these and after further consideration by the subsidiary body concerned, the Commission reconsiders the draft and may adopt it as a "Codex standard". The Codex standard is published and is sent to governments for acceptance. Details of Government acceptances are published periodically by the Commission's Secretariat.

2. Except for provisions relating to acceptance, the provisions set out in Parts 1 and 2 of this document apply, mutatis mutandis, to the elaboration of codes of practice, and, as determined by the Commission, to other texts of a non-mandatory nature.

3. The Commission or the subsidiary body or other body concerned may decide that the draft be returned for further work at any appropriate previous Step in the Procedure. The Commission may also decide that the draft be held at Step 8. The Commission may authorize the omission of Steps 6 and 7 if it considers, without dissent, that the completion of the standard is a matter of exceptional urgency or if it notes that

the standard is uncontroversial and it has already proved to be generally acceptable to Members of the Commission. The Commission may authorize, on the basis if a two-thirds majority of the votes cast, the omission of Steps 6 and 7 of the Procedure in Parts 3 and Part 5 of this document in respect of maximum limits for pesticide residues and maximum levels for veterinary drug residues, respectively, where such an omission is recommended by the Codex Committee on Pesticide Residues or by the Codex Committee on Residues of Veterinary Drugs in Foods.

4. The Commission may at any stage in the elaboration of a standard entrust any of the remaining Steps to a Codex Committee or other body different from that to which it was previously entrusted.

5. It will be for the Commission itself to keep under review the revision of "Codex standards". The procedure for revision should, mutatis mutandis, be that laid down for the elaboration of Codex standards, except that the Commission may decide to omit any other step or steps of that Procedure where, in its opinion, an amendment proposed by a Codex Committee is either of an editorial nature or of a substantive nature but consequential to provisions in similar standards adopted by the Commission at Step 8.

6. The provisions set out in Part 2 apply, mutatis mutandis, to the elaboration of Codex standards for groups of countries specifically designated by the Commission.

7. The provisions set out in Part 3 of this document apply to the elaboration of Codex maximum limits for pesticide residues in accordance with paragraph 3 above.

8. The provisions set out in Part 4 of this document apply to the elaboration of Codex specifications for the identity and purity of food additives.

9. The provisions set out in Part 5 of this document apply to the elaboration of Codex maximum levels for veterinary drug residues in accordance with paragraph 3 above.

PROPOSED DRAFT MRLS AT STEP 5 OF THE PROCEDURE

NOTE: Section 5 - Reference to JECFA Reports - contains reference to the reports of meetings of the Joint FAO/WHO Expert Committee on Food Additives, as published in the WHO Technical Report Series. Relevant toxicological monographs are published in the WHO Food Additives Series and specifications of the substances concerned, are published in the FAO Food and Nutrition Paper Series.

1.	Substance: Chloramphenicol	
2.	Acceptable Daily Intake (ADI) as established by JECFA	No ADI Allocated
3.	(a) Commodity	(a) Foods of animal origin
	(b) MRL	(b) Not allocated
	(c) Definition of Residue on which MRL was set	(c) Chloramphenicol
4.	References to Recommended Methods of Analysis	(To be elaborated)
		WHO TRS 430 (1969)
5.	References to JECFA reports	WHO TRS 763 (1988) FAO FNP 41 (1988) WHO FAS 23 (1988)
6.	References to previous Codex Publications	None

1.	Substance: Estradiol-17B	
2.	Acceptable Daily Intake (ADI) as established by JECFA	Unnecessary*
3.	(a) Commodity	(a) Foods of bovine origin
	(b) MRL	(b) Unnecessary
	(c) Definition of Residue on which MRL was set	(c) Estradiol-17B
4.	References to Recommended Method(s) of Analysis	
5.	References to JECFA reports	WHO TRS 669 (1981) WHO TRS 763 (1988) FAO FNP 41 (1988)
6.	References to previous Codex Publications	None

1.	Substance: Progesterone	
2.	Acceptable Daily Intake (ADI) as established by JECFA	Unnecessary*
3.	(a) Commodity (b) MRL (c) Definition of Residue on which MRL was set	(a) Foods of bovine origin (b) Unnecessary (c) Progesterone
4.	References to Recommended Methods(s) of Analysis	
5.	References to JECFA reports	WHO TRS 669 (1981) WHO TRS 763 (1988) FAO FNP 41 (1988)
6.	References to previous Codex Publications	None

1.	Substance: Testosterone	
2.	Accepable Daily Intake (ADI) as established by JECFA	Unnecessary*
3.	(a) Commodity (b) MRLK (c) Definition of Residue on which MRL was set	(a) Foods of Bovine origin (b) Unnecessary (c) Testosterone
4.	References to Recommended Method(s) of Analysis*	
5.	References to JECFA Reports	WHO TRS 669 (1981) WHO TRS 763 (1988) FAO FNP 41 (1988)
6.	References to previous Codex Publications	None

* Establishing an ADI and an Acceptable Residue Level for a hormone that is produced endogenously at variable levels in human beings was considered unnecessary by the Committee. Residues resulting from the use of this substance as a growth promoter in accordance with good animal husbandry practice are unlikely to pose a hazard to human health.

1.	Substance: Zeranol	
2.	Acceptable Daily Intake (ADI) as established by JECFA	0 - 0.5 ug/kg body weight
3.1 (a)	Comodity	(a) Bovine liver
(b)	MRL	(b) 10 ug/kg
(c)	Definition of Residue on which MRL was set	(c) Zeranol
3.2 (a)	Comodity	(a) Bovine muscle
(b)	MRL	(b) 2 ug/kg
(c)	Definition of Residue on which MRL was set	(c) Zeranol
4.	References to Recommended Method(s) of Analysis	(To be elaborated)
5.	References to JECFA reports	WHO TRS 683 (1982) WHO TRS 696 (1983) WHO TRS 763 (1988) FAO FNP 41 (1988) WHO FAS 23 (1988)
6.	References to previous Codex Publications	None

Proposed Draft MRLS at step 4 of the Procedure

1.	Substance: Trenbolone acetate	
2.	Acceptable Daily Intake (ADI) as established by JECFA	0-0.1 ug/kg body weight (temporary)
3.1 (a)	Comodity	(a) Bovine tissue
(b)	MRL	(b) 1.4 ug/kg
(c)	Definition of Residue on which MRL was set	(c) beta-trenbolone
3.2 (a)	Comodity	(a) Bovine liver & kidney
(b)	MRL	(b) 14 ug/kg
(c)	Definition of Residue on which MRL was set	(c) alpha-trenbolone
4.	References to Recommended Method(s) of Analysis	(To be elaborated)
5.	References to JECFA reports	WHO TRS 683 (1982) WHO TRS 696 (1983) WHO TRS 763 (1988) FAO FNP 41 (1988) WHO FAS 23 (1988)
6.	References to previous Codex Publications	None

GENERAL CONSIDERATIONS OF ANALYTICAL METHODS FOR REGULATORY CONTROL

Paper prepared by Richard L. Ellis (Chairman), Michael K. Hoffman, and David L. Soderberg, U. S. Department of Agriculture, Food Safety and Inspection Service, Washington, D.C. 20250.

It would be ideal to have analytical methods available for regulatory purposes that are effective and practical for detection, quantification, and identification, at the appropriate levels of interest, of all residues of pesticides and drugs that may be present in meat and poultry. These methods could then be routinely used to detect, reliably quantify, and unambiguously identify all residues which may be present in meat, poultry and their processed products at levels above, at and below their established safe residue limits, the maximum (allowable) residue limit (MRL), to determine whether a product is adulterated.

Because of the extensive number of potential residues which may find their way into the food chain, methods with the above characteristics are not available for many compounds of interest. To optimize their ability to test for the presence of residues, regulatory programs should use available methodology to assure a safe and wholesome food supply and, as necessary, take appropriate regulatory action against adulterated products, consistent with the reliability of the analytical data. Therefore it is necessary to define the types of methods and a general set of attributes which regulatory programs may utilize in carrying out their missions.

The principal attributes of analytical methods are specificity, precision, accuracy (systematic error and recovery), and sensitivity. To ensure analytical reliability, the performance of these principal attributes in a method must be determined by multi-laboratory evaluation. These and additional attributes will be presented in a subsequent section of this paper in more detail.

TYPES OF ANALYTICAL METHODS

Several types of methods may be used by regulatory agencies and programs to conduct analyses depending on the suitability of these methods. Decisions on the use of analytical methods depend on the intended objectives of the regulatory program and the analytical performance characteristics of methods.

Methods which are suitable for routine enforcement of MRL's are, commonly, those which have been subjected to an extensive and successful multi-laboratory study for defined tissue and species combinations. These methods provide results for either quantitation or identification that are appropriate to report and/or takeregulatory action without the need for additional analyses. These methods may, in some cases, be considered reference methods, but reference methods frequently are not routine.

Many methods currently used in regulatory control programs meet these requirements. Validated and collaborative study methods generally satisfy these analytical requirements. Validated methods are those subjected to a properly designed interlaboratory study in three or more laboratories. Collaborated methods have been successfully studied in six or more laboratories in a statistically designed study. Some regulatory methods have demonstrated their usefulness for enforcement of MRL's that have an historical origin. These methods were considered to be the best available at the time of initial regulatory use and have continued in use over an extended period of time in the absence of more effective validated methods.

With additional properly designed laboratory studies, collaborated or validated methods may be extended to additional tissues, species, products, or combinations thereof not included in the original multi-laboratory study. On a case by case basis, results from such method extensions may require additional analysis and/or review before reporting results or taking regulatory action.

Methods which have not been validated by traditional interlaboratory study, but have demonstrated results which may be correlated and/or compared with data obtained from a collaborated or validated method, may serve a regulatory purpose. The validated and non-validated methods must be compared using a portion of the same (homogeneous) samples used for this comparison, and the data should be reviewed by a peer group of regulatory scientists before action is taken by a regulatory control program.

There are some non-routine methods suitable for enforcement of MRL's. These methods may not have been subjected to an interlaboratory study because they need specialized expertise or equipment. Data obtained from these methods should be reviewed by a peer group before regulatory action is taken, and may require analysis by another method to corroborate the initial experimental findings.

Occasionally, a method, either because of its design or the analyte of interest has an MRL at a very low concentration, is suitable for enforcement only at residue levels above the defined MRL. Methods for analytes that do not have an established MRL, such as chloramphenicol, would fit this category. Some methods in this category will include those presented above which are not sufficiently sensitive to quantitate and/or identify analyte(s) at or below the MRL. Such methods also may not meet other performance factors stated above.

There are some methods for which additional analysis is required to support regulatory action. This category may include methods that do not provide adequate information of structure or concentration. Analytical methods which may have been subjected to

ruggedness testing[1] , but not successfully to a multi-laboratory study to evaluate method performance, may have limited usefulness in a regulatory program. However, these methods may be used in non-recurring or infrequent analyses, but commonly require use of a rigorous protocol for sample analysis. Results from such methods should be considered only as estimates of analyte concentration or identification without additional supporting analytical information. Results from these methods can be useful for gathering residue information and determining whether there is a need to develop a more definitive method. These methods should not be used alone on official samples, or for taking regulatory action, without additional information (such as identification of the sample from an injection site, for example).

Certain methods may only be suitable for determining whether or not a residue problem exists. Methods in this category are used for information gathering, or exploratory studies, to determine whether a particular problem exists. Exploratory studies may also be undertaken using methods which have not been subjected to interlaboratory study. These non-routine methods may be complex, or require highly specialized instrumentation, and may have been developed to be performed in only a single laboratory. Results should not be used independently in taking regulatory action, but may be used to determine the need for additional testing and/or the development of a method suitable for routine enforcement of MRLs.

Methods designed to rapidly analyze large numbers of samples may be used to determine the presence or absence of one or more compounds in a quantitative or semi-quantitative manner, at or above a specified concentration. Results at or above the MRL, while accounting for its standard deviation, require further analysis using a method with acceptable performance characteristics before taking regulatory action. If results can be obtained below the MRL, but above a level of reliable measurement of a more definitive method, this data may be useful in determining exposure patterns.

PERFORMANCE ATTRIBUTES OF METHODS

Developing an analytical method requires analysts, laboratory space, equipment, and financial support. To optimize the benefit of these resources, it is important to provide introductory and background information to establish a perspective for planning an analytical method development project, and for evaluating the performance of the analytical method.

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[1] Ruggedness is defined in W. J. Youden and E. H. Steiner, Statistical Manual of the AOAC, Association of Official Analytical Chemists, 1111 N. 19th St., Suite 210, Arlington, VA 22209, 1975, p. 33-36. Ruggedness testing of a method involves the identification of critical steps within that method, and analysis of the effect of deliberate and specified variations within those steps as the method is performed.

Regulatory programs should use available methodology to assure a safe and wholesome food supply. Necessary and appropriate regulatory action should be taken against adulterated products, consistent with the reliability of the analytical data. One should consider the intended use and need for a method in a regulatory program before initiating methods development activities. Other considerations include the compound or class of compounds of interest (and interferences), the measurement system and its properties, the pertinent physical and chemical properties that may influence method performance, the specificity of the testing system and how it was determined, stability data and purity of reagents, the acceptable operating conditions for meeting method performance factors, sample preparation guidelines, method environmental factors, safety items, and any other specific information influencing method performance.

Specificity is the ability of a method to distinguish between the analyte being measured and other substances which may be present in the sample being analyzed. A residue control method must provide for the unambiguous identification of the compound being measured. A key consideration of specificity is that it must be able to quantitatively differentiate the analyte from homologues, analogues, or metabolic products under the experimental conditions employed.

Precision is the closeness of agreement between mutually independent test results obtained under the stipulated conditions of use. Analytical variability between different laboratories is defined as reproducibility, and the variability from repeated analyses within a laboratory is defined as repeatability. Precision is usually expressed as standard deviation. Another useful term is relative standard deviation, or coefficient of variation. This is defined as the standard deviation, divided by the absolute value of the arithmetic mean. It may be reported as a percentage by multiplying by one hundred.

The variability achieved in the developing laboratory, after considerable experience with a method, is usually less than what is achieved by other laboratories that may later also use the method. For this reason, the final version of a method should be statistically analyzed by procedures described by Youden and Steiner (ref: Statistical Manual of the AOAC, Association of Official Analytical Chemists, 1975). If a method cannot achieve a suitable level of performance in the developing laboratory, it cannot be expected to do any better in other laboratories.

Accuracy is closely related to systematic error and recovery. Accuracy refers to the closeness of agreement between the true value and the mean result, which would by obtained by applying the experimental procedure a very large number of times to a set of homogeneous samples. The accuracy requirements of different types of methods will vary depending upon the use being made of the results. Generally the accuracy at and below the level of interest must be equal to or greater than the accuracy above the level of interest.

Systematic error is analytical method bias, the difference of the measured value from the mean of other measured values.

The percent recovery of analyte added to a blank tissue matrix is a related measurement that compares the amount found by analysis

with the amount added to the sample. In interpreting recoveries, it is necessary to recognize that analyte added to a sample may not behave in the same manner as the same biologically incurred analyte.At relatively high concentrations, analytical recoveries are expected to approach one hundred percent. At lower concentrations and, particularly with methods involving a number of steps including extraction, isolation, purification, and concentration, recoveries may be lower. Regardless of what average recoveries are observed, recovery with low variability is desirable.

The sensitivity of a method is a measure of the ability of a method to detect the presence of an analyte and to discriminate between small differences in analyte content. Sensitivity also requires the ability to distinguish between analyte and background interferences. For analytical instruments, sensitivity is determined by two factors: instrumental response to an analyte and background interference, or instrument noise. Response is measured by the slope of the calibration curve with known standards at the level of interest. An ideal situation would be afforded by a linear curve. Instrument noise is the ordinary variability in signal produced by an instrument with no analyte added.

Beyond these principle method attributes are a number of collateral attributes suitable for analytical methods for regulatory control programs. Methods should be rugged or robust, cost effective, relatively uncomplicated, portable, and capable of simultaneously handling a set of samples in a time effective manner. Ruggedness of a method refers to its capability to be relatively unaffected by small deviations from the established values in the use of reagents, quantities of reagents used, and time factors for extractions or reactions or temperature. This does not, however, provide latitude for carelessness or haphazard techniques. Cost-effectiveness refers to use of relatively common reagents, instruments, or equipment customarily available in a laboratory devoted to trace environmental analyses. An uncomplicated method refers to use of simple, straightforward mechanical or operational procedures throughout the method.

Portability is the characteristic of the method that enables it to be transferred from one location to another without loss of established performance characteristics.

The capability to simultaneously analyze a set of samples aids in method efficiency by allowing sets or batches of samples to be analyzed at the same time. This attribute reduces the analytical time requirements of sample analysis. It provides, for example, the capability of completing four or more analyses in a normal working day. This is particularly important when large numbers of samples must be analyzed in short or fixed time frames.

The importance of establishing method performance attributes cannot be overemphasized. They provide the necessary information to allow public health agencies to develop and manage their programs of public health responsibilities. Performance attributes for analytical methods also provide a basis for good management decisions in future planning, evaluation, and product disposition. For the animal health care industry, it provides a guideline for knowing exactly what performance must be achieved in developing analytical procedures. All will benefit by having well defined analytical method performance factors.

INTEGRATING ANALYTICAL METHODS FOR REGULATORY PURPOSES

Regulatory control and standard setting organizations have different terminologies to describe analytical methods. Methods for the analysis of veterinary drug residues in foods must ultimately be able to reliably detect the presence of an analyte of interest, and to correctly identify that analyte at and above an established maximum (allowable) concentration or residue limit (MRL), for regulatory enforcement actions to be taken. Such methods would be classified as confirmatory methods. These confirmatory methods may or may not have a quantitative or semi-quantitative component.

Other types of methods which may be used within regulatory programs and which can strengthen such a program may be classified into two additional categories. Quantitative methods provide precise information concerning the amount of an analyte that may be present, but may only provide indirect information about the structural identity of the analyte. Screening methods quickly determine the presence of one or more compounds, based upon one or more common characteristics of a class of veterinary drugs in a quantitative or semi-quantitative manner at a specified level, or that an analyte is below the limit of detection of the screening method.

To a great degree these three categories of methods, confirmatory, quantitative, and screening, share a common set of performance characteristics described above. The relationship between the three categories is vital in the development and operation of a balanced regulatory program. Screening methods are useful because they provide greater efficiency, i.e. a greater number of analyses may be performed in a shorter time-frame than determinative (quantitative) and/or confirmatory methods. In many circumstances screening methods could be performed in non-laboratory environments. Using screening methods that are capable of being used in non-laboratory environments could prove to be less expensive for regulatory control programs than conducting all testing within a laboratory setting. The use of these screening tests would mean that laboratory analyses would become more efficient by focusing on samples which test positive by such screening tests and are more likely to contain residues at, or above, levels of regulatory interest.

Screening tests may also be efficiently utilized within a laboratory setting because of their ability to analyze more samples in a shorter time frame. The cost savings will not be as great as use in non-laboratory environments because the costs associated with the handling and shipping of samples must still be incurred. Results obtained from laboratory screening methods should not be used independently in taking regulatory action. Data obtained from such methods may be used to determine the need for additional testing and/or the development of a method suitable for routine enforcement of MRLs.

METHOD DEVELOPMENT AND VALIDATION CONSIDERATIONS FOR REGULATORY METHODS

In addition to developing the analytical method itself and optimizing its performance, the multi-laboratory validation study is the most important factor in providing analytical data to define method performance characteristics.

In developing a regulatory method, whenever possible, data should be collected from three types of samples. Control tissue from non-treated animals provides information about background interferences from the tissue. Fortified tissue, containing known amounts of the analyte added to the control tissue, yields information about the method's ability to recover the analyte from tissue. Dosed or biologically incurred tissue, from animals that have been treated with the drug, provide additional information about biological or other interactions that may occur when analyzing regulatory control samples.

Residue methods should be designed with as much simplicity as possible to minimize the variety, size, and type of glassware and equipment needed, to minimize the potential for analytical error, and to reduce costs. Reagents and standards must be readily available. Instrumentation should be emphasized based on its performance characteristics rather than manufacturer.

Residue methods are sometimes designed using internal standards. A properly used internal standard will compensate for much of the variability of an analysis, improving precision. However, an improperly used internal standard may obscure variables that are an important part of the measurement. If an internal standard is used, it should be added to a sample as early as possible in the extraction procedure. Caution must be taken in the choice of internal standards to ensure that they do not change the percent recovery or interfere with the measurement. It is essential to know exactly, the extent and predictability of the effects of the internal standard. Internal standards can greatly enhance a method when used properly.

Subjecting methods to widely variable residue testing environments may place some additional requirements on methods, but improve method ruggedness. Warmer environments may require reagents to be more thermally stable, solvents to be less volatile, and tissue sample considerations to be more tolerant. Cooler environments may require reagents and solvents to have physical properties, such as lower freezing point and greater solvating properties, to ensure effective extraction of an analyte. Environmental temperatures may also influence the time required to perform an analysis, as well as such phenomena as influencing reaction rates for gravitational separation and color development. These considerations may strain efforts to standardize methods for use in broadly differing environments because of the need to adapt methods to compensate for these factors.

An analytical method developed and used in only one laboratory is of limited use. The reliability of reported values may be a concern even though strong quality control procedures may have been employed. As a minimum, three laboratories expected to use such methods should be able to successfully conduct the analytical procedure and obtain statistically acceptable agreement on the same samples divided among the testing laboratories. Methods with higher reliability for residue testing should be able to successfully undergo a collaborative study involving at least six different laboratories (ref: Use of Statistics to Develop and Evaluate Analytical Methods by G.T. Wernimont and W. Spendley, for the Association of Official Analytical Chemists; Compound Evaluation and Analytical Capability National Residue Program Plan 1987, section 5, USDA, Food Safety and Inspection Service).

The principles for conducting either a validation or collaborative study of a method are the same. Samples for evaluating method performance should be unknown to the analyst. Samples should contain the residue near the MRL as well as samples with the analyte above and below the level of interest, and tissue blanks. All study samples should be analyzed over a limited number of days, with replicate analysis, to improve statistical evaluation of method performance. It should be noted that these are only minimal requirements. Duplicate analyses in only six laboratories with one or two animal species and tissues would yield limited quality estimates for repeatability and reproducibility.

All these principles are essential for quality assurance in regulatory control programs. Quality control and quality assurance are essential components of residue analysis. They provide the basis for ensuring optimum method performance for all methods, regardless of their attributes, whenever they are used. Quality control monitors those factors associated with the analysis of a sample by a testor, while quality assurance provides the oversight by an independent reviewer to ensure that the analytical program is performing in an acceptable manner. These programs are invaluable in supporting decision-making for regulatory control agencies, and improving the integrity of analytical results. Their value cannot be overemphasized. We must provide confidence to consumers, producers, and law making bodies for ensuring a safe and wholesome food supply.

WORKING GROUP PAPER FOR CC/RVDF - ATTRIBUTES OF ANALYTICAL METHODS

Paper prepared by Richard L. Ellis (Chairman) and Michael K. Hoffman, U.S. Department of Agriculture, Food Safety and Inspection Service, Washington, D.C. 20250.

To ensure reliability and enhance the credibility of regulatory programs, the performance characteristics of analytical methods must be defined and evaluated. The accompanying paper General Considerations of Analytical Methods for Regulatory Control presents a discussion of general types or categories of regulatory methods, and provides a scheme based upon the intended purpose of an analytical method within a regulatory framework. In the discussion below, attributes regarded as common to three categories of methods referred to as level I, level II and level III methods will be presented first, followed by additional attributes which are applicable to only one or two of the types of methods.

GENERAL CRITERIA FOR ATTRIBUTES

(Note: This section contains numerous definitions. The ad hoc working group on Methods of Analysis and Sampling for CC/RVDF has attempted to harmonize these definitions with those provided in the Codex Alimentarius Commission Procedural Manual. However, the Canadian Delegation to the CC/RVDF has been assigned to develop suitable definitions. When appropriate, these definitions have been incorporated.

All methods are characterized by a set of attributes that determine its usefulness: specificity - what is being measured; precision - the variability of the measurement; and systematic error or bias - measured as analytical recovery. Another attribute, accuracy, usually refers to the closeness of agreement between the true value and the mean value obtained by analyzing a large number of samples of the test material. Accuracy may also be defined for semi-quantitative methods and screening methods as a measure of false negative and false positive readings. The limit of detection, method sensitivity, practicality of use, tissue/species applicability, limit of detection, and limit of quantitation are additional attributes which will have varying relevance to different method types, depending upon the use for the analytical results.

Methods may be classified according to performance attributes rather than the usual approach of classification by intent of use or purpose. This alternative approach defines methods by the level of analytical detail provided concerning the amount and nature of the analyte(s) of interest. Level I methods are the most definitive. Level III methods generally provide only broad information about the presence of a functional group and semi-quantitative information about the amount of material present.

Level I methods quantify the amount of a specific analyte or class of analytes and positively identify the analyte in a single analytical procedure. These are assays with the highest level of credibility and provide unequivocal identification at the level of interest. They may be single procedures that determine both the concentration and identity of the analyte. Or they may be combinations of methods for determining and confirming a residue for definitive identification. A good example of the latter is a chromatographic technique combined with mass spectrometry. Although Level I methods are generally instrumental procedures, observation of a pathology or other morphological change which is pathognomonic for exposure to a class of veterinary drugs could potentially be a Level I method, given sufficient sensitivity and precision. Level I methods may be limited to those analytes with appropriate physical and chemical properties amenable to chromatographic and other instrumental methods of analysis. For example, at the present time, there are very few antibiotic drugs that have mass spectrometric procedures useful to regulatory analysis because of their relatively low volatility and stability to chemical techniques for mass spectral analysis Level I methods are often refered to as confirmatory and reference methods.

Level II methods are those which do not provide unequivocal identification, but are used to determine the concentration of an analyte at the level of interest and to provide structural information. These methods may use structure, functional group, or immunological properties as the basis for the analytical scheme. With these methods it is common to use a first level II method as the determinative assay and a second level II method as the positive identification procedure. These methods may be used to verify the presence of a compound or class of compounds. Two Level II methods may provide information suitable for a Level I attribute method. The majority of analytical methods presently available and used by regulatory programs are Level II laboratory methods. Level II methods are usually quantitative methods used for the more routine laboratory regulatory analysis.

Level III methods are those that generate imperfect but useful information. These testing procedures generally detect the presence or determine the absence of a compound or class of compounds at some designated level of interest. They are often based on non-instrumental techniques for analytical determination. For these reasons, Level III methods are commonly refered to as screening or semi-quantitative methods. Results on a given sample are not as reliable as Level I or II methods and need corroborating information. For example, Level III methods may provide reasonably good quantitative information, but poor identification. Or they may provide strong or unequivocal identification with very little quantitative information. Level III methods are not poorly described or sloppy methods. They must have well-defined operating characteristics and performance. Many of the microbiological assay procedures and immunoassay card-based systems are in this category. They are used because of greater sample capacity, portability, convenience and potential suitability to non-laboratory environments. The limitation of Level III type methods is that action based on individual positive results requires verification using Level I or II methods. Individual results may be verified by epidemiological information. These methods may offer substantial advantages to a regulatory control program. Those advantages include analytical speed, sample efficiency through batch analysis, portability to non-laboratory environments, sensitivity, or the ability to detect classes of compounds. Even though a Level III method may not detect a specific compound at a regulatory limit on every sample, it may be better than relying on Level I and II methods due to the ability to test more samples.

The decision to use Level III methods should be determined in part by performance characteristics, as well as the need to test large numbers of samples within a given time frame. Two key characteristics are the percent false positives and percent false negatives, as measured against a validated quantitative assay in a statistically designed protocol. The percent false negatives must be quite low at the levels of interest, while slightly more flexibility may be acceptable for false positives. A working range for residue detection can be described based on these two parameters.

Specificity is the ability of a method to distinguish between the analyte being measured and other substances which may be present in the extract being analyzed. This characteristic is predominately a function of the measuring principle used. The proposed method must provide the required specificity for identification of the compound being measured and discriminate between other structurally similar substances. Certain instrumental techniques such as Fourier transform infrared spectroscopy or mass spectrometry may be sufficiently specific by themselves to provide unambiguous identification. These are known as confirmatory methods. Confirmatory methods are considered necessary before an adverse action is taken if an analytical method is not sufficiently specific for regulatory purposes. Confirmatory methods may be considered Level I methods if they have two components: a determinative portion to quantify and perhaps tentatively identify a given analyte, and a confirmatory procedure which verifies the identity of the analyte of interest. They may be combined in one method if the confirmatory method uses an internal standard.

Other techniques, if they are used in combination, may be capable of achieving a comparable degree of specificity as confirmatory techniques. For example, specificity may be verified by combinations of methods such as thin layer chromatography, element-specific gas-liquid chromatography, formation of characteristic derivatives followed by additional chromatography, or determining characteristic relative retention times using several chromatographic systems of differing polarity. Such procedures must be applicable at the designated maximum residue level (MRL) of the analyte.

The specificity of a screening method normally is not expected to be as great as that of a determinative method, because screening methods frequently take advantage of a structural feature common to a group or class of drugs. Such a method generally falls into the Level III category. Techniques based on biological assays, immunoassays, or chromogenic responses are not expected to be as specific as those techniques which unequivocally identify a single compound.

Specificity of a screening method may be increased by the use of chromatography or other separation techniques.

If non-specific responses or some ambiguity in results are still obtained (i.e. cross-reactivity with components of the matrix other than that for which the analysis was designed), studies will be required to identify the compounds that also respond to the detection system to approximate the concentration of the non-specific response of the analytical method. If the method is not sufficiently specific, then a confirmatory or identification procedure will be needed to further characterize the analyte of interest.

Precision is an important performance characteristic of methods. This attribute will be common to all methods, and as noted below, acceptable precision is not a function of the type of method, but of the concentration of the analyte in the original sample. There are several types of precision. Inter-laboratory precision, or reproducibility, is the closeness of agreement between test results obtained with the same method on identical test material in different laboratories. The variation in replicate analyses of a test material within a laboratory when performed by one analyst is repeatability. The intra-laboratory variability among analysts performing the same analysis is within-laboratory bias, and is due primarily to random error. Precision is usually expressed as a standard deviation, (an absolute value determined experimentally). More useful is the relative standard deviation or coefficient of variation. This parameter, axpressed as percent variability, exhibits less variation over a considerable concentration range than does the standard deviation. Acceptable precision for analytical methods, as a function of concentration, is presented below, taking into account the wide variety of methods, analytes, matrices, and species encountered in a broad-based regulatory control program.

Concentration	Coefficient of Variability (CV) Repeatability
$\leq$ 1 ug/kg	35%
$\geq$ 1 ug/kg $\leq$ 10 ug/kg	30%
$\geq$ 10 ug/kg	20%
$\geq$ 100 ug/kg	15%

The variability finally achieved in the laboratory of the developer of a method after considerable experience is usually smaller than that attained by less experienced laboratories which may later use the method. The final version of the method should be optimized by such procedures as ruggedness testing to identify its critical control points and ensure its performance will not be adversely affected by small changes in the analytical procedure. If a method cannot achieve an acceptable degree of repeatability in the sponsor's laboratory, it cannot reasonably be expected to perform any better in other laboratories. When developing analytical data to be used to define expected method variability and other performance characteristics, methods should be performed by an analyst who has not been directly involved in the development of the method. This procedure will also verify the adequacy of the method's description and help identify critical parameters which affect method performance.

The within laboratory coefficient of variation should be $\leq$15 percent when the designated concentration of the analyte is greater than or equal to 100 ug/kg. When the designated concentration of the analyte is 10 ug - 100 ug/kg, the within laboratory coefficient of variation should be $\leq$20 percent. When the concentration is below 10 ug/kg, a coefficient of variation of $\leq$30 percent may be acceptable.

A semi-quantitative and/or screening (Level III) method should be capable of identifying samples that contain a residue concentration at the level of interest. If a sample is found to contain a residue that exceeds the MRL using a semi-quantitative (screening) method and if the regulatory action to be taken requires a precise quantitation, it will still be necessary to subject the sample to a determinative method in addition to a confirmatory method. A useful attribute for semi-quantitative and or screening methods is precision at and just below the MRL. Precision may be somewhat less important above the MRL.

Systematic error, or method bias, is the difference between the experimentally determined (measured) value and the mean result that would be obtained by applying the experimental procedure a very large number of times to the test material. This value is generally expressed as the percent recovery of the analyte of interest. It is obtained experimentally by adding known quantities of the analyte directly to separate portions of the same test sample and comparing the amount recovered with the amount added. The percent recovery of an analyte added directly to the sample matrix is generally a higher value than is obtained experimentally when isolating the same biologically incurred (endogenous) analyte from the same type of sample matrix. At relatively high analyte concentrations, recoveries are expected to approach 100 percent. At lower concentrations or with multi-step methods that require extractions, solvent transfers, concentration steps, and absorption chromatography, recoveries will be lower. Variability of recoveries is usually as important as the percent recovery itself and should be small.

If an analytical method can be performed with acceptable precision, then average recoveries of 80 to 110 percent should be obtained when the designated MRL for the analyte is 100 ug/kg or greater. Acceptable recoveries at lower MRLs are 60 to 110 percent when the MRL of the analyte is 10 ug/kg to 100 ug/kg, and 40 to 110 percent when the MRL is less than 10 ug/kg. These recovery ranges are

reasonable when viewed within the context of the wide variety of residues, methods, matrices, and species normally found in a broad-based regulatory control program. Variability in recovery should be small regardless of the percent recovery.

Correction factors for more or less than 100 percent recovery may be appropriate if based upon an integral and scientifically rational part of the analytic procedure, i.e. when isotope dilution procedures or appropriate internal reference standards are used.

The accuracy requirements of different types of methods will vary with the use for the results. In general, methods will require the same or greater accuracy at or below the MRL as above the MRL. The quantitative accuracy requirements of confirmatory methods need not be as great, because under traditional regulatory programs these methods are only performed after a residue concentration greater than the MRL has been determined by a quantitative method. Most confirmatory methods have a quantitative aspect built into them which serves as an additional check on the previously performed quantitative method. Suggested accuracy for methods is given below, and are based upon the previously stated considerations of a broad-based regulatory control program.

Concentration	Acceptable Range
$\leq$ 1 ug/kg	-50 to +20%
$\geq$ 1 ug/kg $\leq$ 10 ug/kg	-30 to +10%
$\geq$ 10 ug/kg	-20 to +10%

Non-Quantitative and/or screening methods may be used under several scenarios. For example, these types of methods may be used in situations where no MRL can be established or where one does not otherwise exist, and an adverse regulatory action may be taken if any amount of the residue is found. Non-quantitative methods may also be used when the MRL or the level of interest is a stated quantitative value less than the level of detection of the screening method. In both cases, it is necessary to evaluate methods to determine the lowest concentration at which an analyte can be detected and to determine the method accuracy in terms of false negatives, (i.e., a negative analytical result is obtained when the analyte is in fact present above the level of interest), and false positives, (i.e.,a positive result is obtained when the analyte is not present at, or above, the MRL or level of interest).

If non-quantitative and/or screening methods involve a manufactured test kit, the accuracy and lowest detection limit data should be provided by the manufacturer of the test kit. The users should verify the validity of this data through their own study and monitor performance by quality control checks. The lowest detectable concentration of a method should represent the smallest amount of an individual analyte that can be reliably observed or found in the test sample The method accuracy, expressed in terms of false negatives and false positives, should be determined by a statistically valid, scientifically correct study with appropriate controls.

In general, non-quantitative methods should produce less than 5% false negatives and less than 10% false positives when analysis is performed in the test sample. These values may vary depending on the type of action that will be taken as a result of the test results. Conservative values should be chosen appropriate to regulatory control needs.

The limit of detection is the smallest measured concentraton of an analyte from which it is possible to deduce the presence of the analyte in edible animal products with acceptable certainty. This determination should consider matrix-related interferences with a signal to instrumental noise (S/N) ratio greater than 5:1 or the concentration determined by 3 standard deviations above uncontaminated, blank tissue, whichever is less.

Sensitivity is a measure of the ability of a method to detect the presence of an analyte and to discriminate between small differences in analyte content. This may be determined by the slope of the standard curve at the concentration range of interest.

COLLATERAL PARAMETERS FOR METHODS SUITABLE FOR ROUTINE USE FOR ENFORCEMENT OF MAXIMUM RESIDUE LIMITS

For efficiency the method should ideally require no more than about 2 hours of analytical time per sample. This does not mean results for a set of analytical samples must be completed within 2 hours. Methods may require several hours to prepare a set of extracts or complete a microbiological incubation. Methods should be designed to analyze several samples simultaneously, normally in groups of four or more during a normal work period.

The limit of decision is related to the purpose for which the analytical data are used and not an inherent attribute of the analytical method which produced the data. For this reason it is not considered relevant to the description of method performance characteristics.

The applicability of a method refers to the tissue matrices and animal species to which a particular method has demonstrated acceptable method performance.

The limit of quantitation corresponds to the smallest measured concentration of residue from endogenously incurred animal tissue above which a determination of the analyte can be made with a specified degree of accuracy and precision.

Whenever possible, the method should require only instrumentation generally available in a laboratory devoted to trace environmental analyses in animal tissue.

The method should have written protocols which include extensive quality assurance and quality control components. These quality assurance plans should also include analyst training needs.

The method should be capable of analyzing analytes at or below the established MRL.[1]

Whenever applicable, the method should be subjected to an interlaboratory study using some test samples with biologically incurred analyte. This generally better defines the performance characteristics of the method.

Regulatory methods should utilize commercially available reagents. Methods become impractical and potentially unreliable if new or unusual reagents are not readily available. New or unusual reagents and/or standards must be supplied by the sponsor of an analytical drug method upon request.

Regulatory methods should be able to be performed at their described performance characteristics by reasonably experienced analysts who have received training and have successfully demonstrated completion of that training.

Regulatory methods should be able to be completed within reasonable time periods (within two working days) and analyzed in sets of samples consistent with regulatory objectives.

Regulatory methods should not use large quantities of solvents, reagents, and supplies which would render the method economically impractical or unsafe. Regulatory control methods should be designed to be performed safely by trained analysts.

Several other indicators of satisfactory performance may be helpful in determining whether or not a method is acceptable for regulatory purposes. These include: a) calibration (standard) and analytical (recovery) curves; b) information concerning the effectiveness of extraction in removing specific potential interferences; c) adequate method sensitivity (slope of the calibration curve) and resolution; d) sufficiently low and reproducibly consistent blanks; and e) stability studies performed on the matrix, the analyte within the matrix, and reagents used within the procedure. The analytical response of the blank should be no more

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[1]Some compounds may be regulated with a zero MRL. Methods used to detect and/or identify zero MRL compounds are suitable for regulatory use if they meet the suitability parameters listed above and are capable of analyzing analytes at or below the operational definition of zero defined by the regulatory body.

than 10% of the analyte response at the MRL, whenever an MRL is established. Critical control points within the analytical procedure, those steps where extreme care must be taken to insure optimum method performance, and stopping points within the method need to be identified.

SPECIFIC DATA NEEDED

The developer of a method needs to provide all information and supporting data necessary to familiarize the intended users with a satisfactory methods performance level. This necessary information should include the following:

For regulatory control methods, the developer of a method should collect and provide to regulatory agencies data from three types of samples: a)control tissue samples from animals which are known to have not been treated with the analyte; b) tissue samples which are fortified or spiked by the addition of known amounts of the analyte to uncontaminated control tissue; and c) dosed or incurred tissue samples obtained from animals treated with the veterinary drug to the desired concentration of the analyte of interest.

Developer provided methods and test kits should only be approved for use by a regulatory program after it can be demonstrated that the method will meet established performance characteristics or provide an improvement over presently used regulatory methods and will provide for regulatory decision making and regulatory consistency.

The developer of the method must determine the response obtained when the matrix is known to be free from chemical interferences, the method variability, and the lowest concentration at which the amount of analyte present can be detected with reasonable statistical certainty. The developer should demonstrate that the proposed method can satisfactorily recover and identify known amounts of the analyte which have been added to the matrix of interest, the target tissue. Finally, the developer should demonstrate that the proposed method can satisfactorily recover the analyte from the target tissue matrix in which it has been biologically bound or incurred. The recovery must be demonstrated to be free from substances which interfere or adversely affect the reliability of the analysis.

The method must perform acceptably in both controlled laboratory environments and in field trials which represent anticipated operating conditions, if that is the intended use of the method. The results must be verified by appropriate quality assurance and quality control procedures, including the analysis of known negative samples. Analysis of sufficient numbers of both positive and negative samples to establish false positive and negative rates must be performed, with a statistically appropriate number of these samples having been analyzed by a separate within laboratory method to verify the results. This will enable the test to predict both false positive and false negative results with an improved degree of accuracy.

The developer of a method must provide a complete description of the method which includes scientific principles upon which the

method is based, sampling information, preparation of analytical samples, appropriate target tissue samples, shelf life and storage conditions for the analyte both in solution and in the target tissue matrix, reagent shelf life and stability, standards, instrumentation, and identification of critical steps and stopping places. Test limitations as well as appropriate and inappropriate uses of the test must be described. Critical test components and reagents must be identified and specifications described. The developer must provide evidence of consistency of test kit performance from batch to batch within the manufacturing process, as well as guarantee long-term availability of all components necessary to successfully perform the test.

The quality control criteria needed to verify and maintain method performance and to determine that a test kit is operating properly must be provided. Information to verify proper test data interpretation associated with the quality control criteria must be specified.

A standard curve prepared from the analyte of known purity must be provided. A typical analytical curve prepared by fortifying uncontaminated blank tissues with the analyte must be provided.

Data derived from uncontaminated, fortified, and dosed tissue must be provided to show that the method meets the specificity, precision, systematic error, and accuracy attributes. Samples should be fortified at 0.5 (where practical), 1, and 2 times the MRL or level of interest. Additional samples encompassing this range may be included.

Properly labeled worksheets, calculations, statistical analyses, spectrograms, chromatograms, and all other relevant information from control, fortified, and dosed tissue must be provided to permit evaluation of the method.

An interlaboratory study report should be provided. The method should be tested in three or more laboratories. Each laboratory should analyze samples fortified as stated previously and should test biologically incurred samples which contain the analyte at the same concentrations.

Test kits should utilize simplified procedures. The analytical procedures which are designed into test kits to be used by field personnel should be successfully evaluated by at least six trained individuals in a properly designed study before being placed into general use. The study environment must be similar to that expected for routine use of the test. The design should provide for determination of a statistical description of false positive and false negatives. It must be sufficiently detailed to allow determination of the analytical range (limits) of the test. Participants should include not only those individuals who have been trained by the developer of the test, but also persons trained by those who received training from the developer, to determine that training procedures are sufficient to provide trained testers.

STANDARD REFERENCE MATERIALS FOR VETERINARY DRUGS

At the present time it is not practical to develop standard reference materials for determination of residues of veterinary drugs in animal tissues. There are specific difficulties in developing standard reference materials for international use:

Some drugs are not stable in animal tissues at ordinary freezer temperatures. Veterinary drug residue concentration commonly depletes with time at ordinary freezer temperatures. These tissues must be stored and shipped at ultracold temperatures or lyophilized, irradiated, or otherwise treated to reduce enzymatic activity and loss of analyte. The relevant studies have not been published at this time, so it is not known whether these treatments will affect the extent to which the drugs of interest are bound to the tissues, whether drug residues remain stable in tissues, or whether they might chemically alter the trace residues.

Recognized standard reference materials are generally very expensive and, considering their other limitations, are not cost effective for regulatory analysis. Commercial reference standards for veterinary drugs are virtually unavailable at the present time. Because of these and other limitations, such as analytical variability of a method versus the concentration of the analyte (i.e. low mg/kg to ug/kg), standard reference materials are generally inappropriate.

SAMPLING FOR THE CONTROL OF VETERINARY DRUGS IN FOODS

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I. Introduction

The Joint FAO/WHO Food Standards Programme describes recommended sampling procedures for inspection of food commodities in the Codex Committee on Methods of Analysis and Sampling - Instructions on Codex Sampling Procedures. The Guide to Codex Recommendations Concerning Pesticide Residues Part 5 - CAC/PR 5-1984 describes sampling procedures recommended by the Codex Alimentarius Commission for inspection of lots of food commodities and to collect the "final sample" which is representative of the lot to determine its average pesticide residue content. Because of the difficulties in obtaining a representative sample from bulk shipments of meat and poultry products, another sampling system for veterinary drug residues and for pesticides is desirable for these products. The Codex Committee on Pesticide Residues (CCPR) has proposed alternative methods for sampling of meat and poultry products for the determination of pesticide residues at Step 3 in CL 1988/33 - PR. In the interest of harmonizing recommendations and policies between closely related committees dealing with meat and poultry contaminants, these recommendations for sampling for veterinary drug residues are consistent with the guidelines for sampling set forth by the CCPR. Sampling of eggs, milk, and fish for veterinary drug residues are also included in these recommendations and are consistent with CCPR.

The economic costs and damage done when sampling bulk lots of meat and poultry products are significant considerations when sampling is done according to commodity type sampling. This guideline is designed to apply maximum residue limits (MRLs) to sampling of a variety of meat and poultry products (i.e., shipments of live animals for slaughter, frozen or fresh/chilled carcasses, sides, or quarters, or large containers of bulk frozen, fresh/chilled, or processed products for retail marketing). The meat and poultry sampling guideline, presented in Annex A and Appendix A, is based on the principle that, unlike other commodity sampling, primary samples taken from a lot should be analyzed individually and the Codex maximum residue limit (MRL) should be applied to the residue concentration in the primary sample. A primary sample is defined as "a quantity of material taken from a single place in the lot."

Sampling of lots of eggs, milk, and fish products is recommended to be done under the commodity bulk sampling guidelines as presented in Annex B and Appendix B. Because of the bulk nature of these commodities it is more appropriate to sample them following final sample guidelines. Randomly collected primary samples are combined and mixed to constitute a bulk sample. One or more bulk samples may be combined to provide the final sample, which may then be subsampled. Precautions must be taken for a subsample or final sample to be representative of the primary samples.

This guideline is intended to satisfy criteria developed to meet Codex recommended standards for control programs used in member countries, but not to supersede or replace the residue program of any particular country. The primary Codex interest is in the control of imported products. But it is desirable that Codex recommendations be consistent in principle and appropriate for use by countries in the examination of products in domestic control and international trade programs.

The principles recommended in these papers are consistent with the European Council Directive (86/469/EEC) concerning the examination of animals and fresh meat for the presence of residues.

II. DISCUSSION

A. Sampling principle and design

Sampling for control must be consistent with principles used in setting an MRL. Sampling must also be practical for the examination of the commodity in commerce.

MRLs are developed from experimental data obtained from field trials in which food commodities are treated or exposed to chemicals or drugs in accordance with good agricultural practices (GAP), or good veterinary practices (GVP), and within legally permitted dosage. For most commodities a bulk sample is collected that consists of a number of primary samples. These are combined in a final sample which is analyzed as a representative sample of the lot. But in the experiments with meat and poultry commodities, tissue from each animal is analyzed separately,

except when combining of tissue from more than one animal is required to obtain an adequate sample size for analysis (e.g., for poultry organs). Codex Maximum Residue Limits for zeranol and trenbolone acetate were developed by 32nd Joint Expert Committee on Food Additives. Future sessions of the JECFA will establish MRLs for other veterinary drugs. For pesticides, this data has been evaluated by the Joint Meeting for Pesticide Residues (JMPR). JMPR makes recommendations for MRLs that are consistent with national GAPs and are not expected to be exceeded in any animal when marketed for human food. The principle of applying an MRL to primary or final samples should be equally applicable to control of veterinary drug residues.

B. Compatibility with National Residue Control Programs

Codex primary interest is in products in international trade, (i.e., sampling by an importing country for enforcement purposes). But it is desirable for Codex recommendations to also be consistent with and appropriate for use by countries in domestic control programs, since some countries legislate that the same standards apply to both domestic and imported products.

Many effective control programs for residues are based on testing of primary samples collected at slaughter. In some programs when violative residues are found, methods used include animal traceback to the producer source or quarantine to prevent further marketing of animals until the identified problem has been corrected. Applying the Codex MRL to the primary sample in meat and poultry products will achieve uniformity with these programs. This is especially important for countries that acceptimported meat products based in part on an evaluation of the effectiveness of the residue control and testing programs conducted by the exporting country. Other effective control programs for residues are based on testing of bulk or final samples from other commodities, such as milk and eggs.

C. Practical considerations

While CAC/PR 5-1984 recommendations are useful for bulk products, such as eggs and milk, it is not practical for application to meat and poultry products in international trade. Sampling of such products to obtain a representative sample can be difficult and time consuming, and can cause substantial costs in disfiguring product. For example, a lot of frozen beef typically weighs 18,000 kilograms or more, and is packed as bulk frozen product containing 25 to 30 kilograms in each carton. To collect 15 primary samples from the lot, as recommended in CAC/PR 5-1984, the sampling official would have to collect a representative sample from 15 cartons of product, disfiguring about 400 kilograms of product. The guideline for meat and poultry products presented as Appendix A to this paper attempts to minimize these costs of collecting a representative sample. The guideline for milk, eggs, and fish products presented as Appendix B follows sampling recommendations for bulk commodities. They provide a practical framework for applying the MRL to primary or final (bulk) samples collected from a variety of commodities.

D. Application of the sampling principle to meat and poultry products

A lot is defined as "an identifiable quantity of goods delivered at one time, having, or presumed by the sampling officer to have, common properties or uniform characteristics, such as the same origin, the same variety, the same consignor, the same packer, the same type of packing, or the same mark." The sampling officer must determine from available information what quantity of product constitutes a lot. In the absence of producer codes or other relevant information, a consignment is often treated as a lot, although it may consist of product from animals raised under different conditions of exposure to veterinary drugs.

As recommended in the sampling guideline Appendix A for meat and poultry products, a lot complies with the MRL if none of the primary samples analyzed contains a residue above the MRL. If some, but not all, of the primary samples comply with the MRL, these results indicate some units in the lot have been exposed to veterinary drugs under conditions that do not comply with GVP or GAP. It may be possible to separate the unadulterated product in the lot that comply with the MRL, but an importing country should not be required to assume this burden.

1. Sampling design

The sampling guideline includes separate approaches to the sampling level to be used for lots when there is reason to believe that the product may be adulterated (suspect lots) from that to be used for lots with no reason to believe that the product is adulterated (non-suspect lots). For example, a lot may be suspected to be adulterated if it originates from a source with a history of non-compliance with MRLs, when inspection of live animals imported for slaughter reveals signs of disease, or when other relevant information is available to the inspection official.

2. Sampling of non-suspect lots

A statistically-based random sampling program is recommended for non-suspect lots, typically collecting primary samples from many lots, with a minimum of sampling from any one lot. Recommended sampling may include stratified random sampling, systematic sampling, or biased, worst case sampling. Some sampling designs may allow extrapolation of the extent to which imported products as a whole comply with Codex MRLs. Table 1 provides information relevant to deciding the number of samples to select, which will allow for systematic testing of compliance with Codex MRLs. Table 1 is not included as part of the proposed guideline.

3. Sampling of suspect lots

The guideline recommends that at least 6 and usually no more than 30 primary samples be analyzed from a suspect lot. For example, the smaller number of samples would be appropriate when the suspected adulteration is likely to occur throughout the lot or when the location of suspected adulterated is readily identified.

TABLE 1. Number of samples required to detect at least one violation with predefined probabilities (i.e., 90, 95, and 99 percent) in a population having a known violation incidence rate.

Violation Incidence (%) in a Population	Minimum number of samples required to detect a violation with a confidence level of:		
	90%	95%	99%
35	6	7	11
30	7	9	13
25	9	11	17
20	11	14	21
15	15	19	29
10	22	29	44
5	45	59	90
1	230	299	459
.5	460	598	919
.1	2302	2995	4603

The number of primary samples is independent of population size, except when the number of samples shown in Table 1 is greater than about 10% of the population size. The following formula can be used to adjust the table values for the minimum number of primary samples (n_o) and to compute the required minimum number of primary samples (n) for a given lot size (N):[1]

$$n = \frac{n_o}{1 + (n_o - 1)/N}$$

The larger the number of samples collected, the greater the assurance that product not in compliance will be detected.

E. Application of the sampling principle to eggs, milk, and aquatic animal products

A bulk sample is defined as a combined total of all the primary samples taken from the same lot. A final sample is

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[1] Cochran, William G., Sampling Techniques, 2nd ed., 1963, pp.74-75, John Wiley and Sons, Inc.

defined as the bulk sample or a representative portion of the bulk sample to be used for control purposes. The sampling officer must determine from available information what quantity of product constitutes a lot and collect appropriate samples for laboratory analysis.

As recommended in the sampling guideline Appendix B for eggs, milk, and aquatic animal products, a lot complies with the MRL if the final sample when analyzed does not contain a residue above the MRL.

Recommended Sampling Schedule

Lot Size	Number of Subsamples
12 or less	5
13 to 18	6
19 to 30	7
31 to 56	8
57 to 190	9
over 190	10

F. What commodities as defined in CAC/PR 4-1988 should be included?

1. Class B Primary Food Commodities of Animal Origin

Included in Annex A are mammalian products (Type 06) and poultry products (Type 07), except for eggs and milk products. Included in Annex B are mammalian products (Type 06) milk, poultry products (Type 07) eggs, and aquatic animal products (Type 08-including freshwater fish (No. 040), diadromous fish (No. 041), fish roe and edible offal of fish (No. 043), and crustaceans (No. 045)), amphibians and reptiles (Type 09), and invertebrate animals (Type 10). These commodities are commercially produced and may be exposed to veterinary drugs during production. These commodities are marketed as fresh/chilled or fresh/frozen products without further processing and are listed by their group number as primary food commodities.

2. Class E Processed Foods of Animal Origin

Only Class E Processed Foods of Animal Origin that are derived from the selected Class B commodities were considered for the proposed guideline. Further evaluation was done to determine if a commodity retains its identity with a single animal source, the size and economic value of the units of the commodity to be sampled, and the form of a unit as it is usually shipped. Taking these characteristics of a commodity into consideration, this guideline proposes appropriate procedures for sampling based on accepted Codex sampling procedures.

ANNEX A

SAMPLING FOR THE CONTROL OF VETERINARY DRUG RESIDUES IN MEAT AND POULTRY PRODUCTS

1. Objective

To provide instructions for sampling a lot of meat or poultry products, to determine compliance with Codex maximum residue limits (MRL) for veterinary drugs (to be developed) to control adulteration in the meat supply.

2. Definitions

2.1 Lot

An identifiable quantity of food delivered for slaughter or distribution at one time, determined to have common characteristics, such as origin, variety, type of packing, packer or consignor, or markings, by the sampling official. Several lots may make up a consignment.

2.2 Consignment

A quantity of food as described on a particular contractor's shipping document. Lots in a consignment may have different origins or be delivered at different times.

2.3 Primary Sample

A quantity of food taken from a single animal or from one place in the lot. If this quantity is inadequate for the analysis for the residue, then samples from more than one animal or location in the sample can be combined for the primary sample (such as poultry organs).

2.4 Laboratory Sample

The sample intended for laboratory analysis. A whole primary sample may be used for analysis or the sample may be subdivided into representative portions, if required by national legislation.

3. Commodities to which the guideline applies

3.1 Selected Class B: Primary Food Commodities of Animal Origin

Type 06 Mammalian Products

No. 030 Meat (Mammalian)

No. 031 Fat (Mammalian)

No. 032 Edible Offal (Mammalian)

Type 07 Poultry Products

No. 036 Poultry Meats

No. 037 Poultry Fats

No. 038 Poultry, Edible Offal of

3.2 Selected Class E: Processed Products of Animal Origin made from only Primary Foods Nos. 030, 032, 036, and 038

Type 16 - Secondary Products

Type 18 - Manufactured (single ingredient) products of a minimum of one kilogram container or unit size

Type 19 - Manufactured (multiple ingredient) products of a minimum of one kilogram container or unit size

4. Principle adopted

For purposes of control, the maximum residue level (MRL) is applied to the residue concentration found in each primary sample taken from a lot. Lot compliance with a Codex MRL is achieved when none of the primary samples contains a residue level greater than the MRL.

5. Employment of authorized sampling officials

Samples must be collected by officials authorized for this purpose.

6. Sampling procedures

6.1 Product to Sample

Each lot to be examined must be sampled separately.

6.2 Precautions to take

During collection and processing, contamination or other changes in the samples which would alter the residue or affect the analytical determination must be prevented.

6.3 Collection of a Primary Sample

Detailed instructions for collection of a primary sample of various products are provided in Appendix I. Quantities to collect are dependent on the analytical method requirements. Minimum quantity requirements are included in Appendix I. The following are general instructions.

a. Each primary sample should be taken from a single animal or unit in a lot, and, when possible, be selected randomly.

b. When multiple animals are required for adequate sample size of the primary sample (i.e., poultry organs), the samples should be collected consecutively after random selection of the starting point.

c. Canned or packaged product should not be opened for sampling unless the unit size is at least twice the amount required for the primary laboratory sample, and should contain a representative portion of juices surrounding the product. Such a sample should then be frozen as described in paragraph 6.5.

d. Frozen product should not be thawed before sampling.

e. Large, bone-containing units of product (i.e., prime cuts) should be sampled by collecting edible product only as the primary sample.

6.4 The Number of Primary Samples to Collect from a Lot

The number of primary samples collected will vary depending on the status of the lot. If adulteration is suspected by origin from a source with a past history of residue violations of the MRLs, by evidence of contamination during transport, by signs of toxicosis observed during ante- or post-mortem inspection, or by the availability of other relevant information to the inspection official, the lot is designated a suspect lot. If there is no reason to suspect adulteration, the lot is designated a non-suspect lot.

6.41 Sampling Suspect Lots

A minimum of six to a maximum of thirty primary samples should be collected from a suspect lot. When the suspected adulteration is expected to occur throughout the lot or is readily identifiable within the lot, the smaller number of samples is sufficient.

6.42 Sampling Non-Suspect Lots

A statistically-based, random sampling program is recommended for non-suspect lots. Any of the following types of sampling can be used.

a. Stratified random sampling

In a complex system where commodities must be sampled at many locations over extended time periods, it is very difficult to apply simple random criteria in the design of a sampling program. A useful alternative sampling design is stratified random sampling which separates population elements into non-overlapping groups, called strata. Then samples are selected within each stratum by a simple random design. Homogeneity within each stratum is better than in the whole population. Countries or geographic regions are natural strata because of uniformity in agricultural practices. Time strata (e.g., month, quarter) are commonly used for convenience, efficiency, and detection of seasonal variability. Random number tables or other objective techniques should be used to ensure that all elements of a population have an equal and independent chance of being included in the sample.

b. Systematic sampling

Systematic sampling is a method of selecting a sample from every 'K' quantity of product to be sampled, and then sampling every 'K' unit thereafter. Systematic sampling is quicker, easier, and less costly than random sampling, when there is reliable information on product volumes to be used to determine the sampling interval that will provide the desired number of samples over time. If the sampling system is too predictable, it may be abused. It is advisable to build some randomness around the sampling point within the sampling interval.

c. Biased or estimated worst case sampling

In biased or estimated worst case sampling, the investigator uses his own judgment and experience regarding the population, lot, or sampling frame to decide which samples to select. As a non-random technique, no inferences should be made about the population sampled, based on data collected. But the population group anticipated to be at greatest risk can be identified.

Since some exporting countries conduct a comprehensive residue testing program and provide results to importing countries, an importing country may exempt that country's products from further testing or reduce the level of testing from that normally applied to non-suspect products from countries which do not provide residue testing results showing MRL compliance.

6.5 Packaging and Transmission of Primary Samples

a. Each primary sample should be placed in a clean, chemically inert container to protect the sample from contamination and from being damaged in shipping.

b. The container should be sealed so that unauthorized opening is detectable.

c. The container should be sent to the laboratory as soon as possible, after taking precautions against leakage and spoilage.

d. For shipping, all perishable samples should be frozen to minus $20^{o}C$, immediately after collection, and packed in a suitable container that retards thawing. If possible, the shipping container should be placed in a freezer for 24 hours prior to packing and shipping the frozen sample.

7. Records

Each primary sample should be correctly identified by a record with the type of sample, origin of the sample (e.g., country, state, or town), location of collection of the sample, date of sampling, and additional information useful to the analyst or to regulatory officials for follow-up action if necessary.

8. Departure from recommended sampling procedure

If there is a departure from recommended sampling procedure, records accompanying the sample should fully detail procedures actually followed.

ANNEX B

SAMPLING FOR THE CONTROL OF VETERINARY DRUG RESIDUES IN FISH, MILK, AND EGG PRODUCTS

1. Objective

To provide instructions for sampling a lot of eggs, milk, or aquatic animal products, to determine compliance with Codex maximum residue limits (MRL) for veterinary drugs to control adulteration in the meat supply.

2. Definitions

2.1 Lot

An identifiable quantity of food delivered for slaughter or distribution at one time, determined to have common characteristics, such as origin, variety, type of packing, packer or consignor, or markings, by the sampling official. Several lots may make up a consignment.

2.2 Consignment

A quantity of food as described on a particular contractor's shipping document. Lots in a consignment may have different origins or be delivered at different times.

2.3 Primary Sample

A quantity of food taken from a single animal or from one place in the lot, unless this quantity is inadequate for the analysis for the residue. When the quantity is inadequate, samples from more than location in the container can be combined for the primary sample.

2.4 Bulk Sample

The combined total of all the primary samples taken from the same lot.

2.5 Final Sample

The bulk sample or a representative portion of the bulk sample to be used for control purposes.

2.6 Laboratory Sample

The sample intended for laboratory analysis. A whole primary sample may be used for analysis or the sample may be subdivided into representative portions, if required by national legislation.

3. Commodities to which the guideline applies

3.1 Selected Class B: Primary Food Commodities of Animal Origin

Type 06 Mammalian Products

No. 033 Milks

Type 07 Poultry Products

No. 039 Eggs

Type 08 Aquatic Animal Products

No. 040 Freshwater Fish

No. 041 Diadromous Fish

No. 043 Fish Roe and Edible Offal of Fish

No. 045 Crustaceans

Type 09 Amphibians and Reptiles

No. 048 Frogs, Lizards, Snakes and Turtles

Type 10 Invertebrate Animals

No. 049 Molluscs and Other Invertebrate Animals

3.2 Selected Class E: Processed Products of Animal Origin made from only Primary Foods Nos. 033, 039, 040, 041, 043, 045, 048, and 049

Type 16 - Secondary Products

Type 17 - Derived Edible Products of Aquatic Animal Origin

Type 18 - Manufactured (single ingredient) products of a minimum of one kilogram container or unit size

Type 19 - Manufactured (multiple ingredient) products of a minimum of one kilogram container or unit size

4. Principle adopted

For purposes of control, the maximum residue level (MRL) is applied to the residue concentration found in each bulk or final sample taken from a lot. Lot compliance with a Codex MRL is achieved when this final sample does not contain a residue level greater than the MRL.

5. Employment of authorized sampling officials

Samples must be collected by officials authorized for this purpose.

6. Sampling procedures

6.1 Product to Sample

Each lot to be examined must be sampled separately.

6.2 Precautions to take

During collection and processing, contamination or other changes in the samples must be prevented which would alter the residue, affect the analytical determination, or make the laboratory sample not representative of the bulk or final sample.

6.3 Collection of a Primary Sample

Quantities to collect are dependent on the analytical method requirements. Minimum quantity requirements are included in Appendix B. The following are general instructions.

a. Each primary sample should be taken from a single unit in a lot, and, when possible, be selected randomly.

b. Canned or packaged product should not be opened for sampling unless the unit size is at least twice the amount required for the primary laboratory sample, and should contain a representative portion of juices surrounding the product. Such a sample should then be frozen as described in paragraph 6.5.

c. Frozen product should not be thawed before sampling.

6.4 The Number of Primary Samples to Collect from a Lot

The number of primary samples collected will vary depending on the status of the lot. If adulteration is suspected by origin from a source with a past history of residue violations of the MRLs, by evidence of contamination during transport or by the availability of other relevant information to the inspection official, the lot is designated a suspect lot. If there is no reason to suspect adulteration, the lot is designated a non-suspect lot.

6.41 Sampling Suspect Lots

A minimum of six to a maximum of thirty primary samples should be collected from a suspect lot. When the suspected adulteration is expected to occur throughout the lot or is readily identifiable within the lot, the smaller number of samples is sufficient.

6.42 Sampling Non-Suspect Lots

A statistically-based, random sampling program is recommended for non-suspect lots. Any of the following types of sampling can be used.

a. Stratified random sampling

In a complex system where commodities must be sampled at many locations over extended time periods, it is very difficult to apply simple random criteria in the design of a sampling program. A useful alternative sampling design is stratified random sampling which separates population elements into non-overlapping groups, called strata. Then samples are selected within each stratum by a simple random design. Homogeneity within each stratum is better than in the

whole population. Countries or geographic regions are natural strata because of uniformity in agricultural practices. Time strata (e.g., month, quarter) are commonly used for convenience, efficiency, and detection of seasonal variability. Random number tables or other objective techniques should be used to ensure that all elements of a population have an equal and independent chance of being included in the sample.

b. Systematic sampling

Systematic sampling is a method of selecting a sample from every 'K' quantity of product to be sampled, and then sampling every 'K' unit thereafter. Systematic sampling is quicker, easier, and less costly than random sampling, when there is reliable information on product volumes to be used to determine the sampling interval that will provide the desired number of samples over time. If the sampling system is too predictable, it may be abused. It is advisable to build some randomness around the sampling point within the sampling interval.

c. Biased or estimated worst case sampling

In biased or estimated worst case sampling, the investigator uses his own judgment and experience regarding the population, lot, or sampling frame to decide which samples to select. As a non-random technique, no inferences should be made about the population sampled, based on data collected. But the population group anticipated to be at greatest risk can be identified.

Since some exporting countries conduct a comprehensive residue testing program and provide results to importing countries, an importing country may exempt that country's products from further testing or reduce the level of testing from that normally applied to non-suspect products from countries which do not provide residue testing results showing MRL compliance.

6.5 Preparation of the Bulk Sample

The bulk sample is prepared by combining and mixing the primary samples.

6.6 Preparation of the Final Sample

The bulk sample should, if possible, constitute the final sample. If the bulk sample is too large, the final sample may be prepared from it by a suitable method of reduction.

6.7 Preparation of the Laboratory Sample

The final sample should be submitted to the laboratory for analysis. If the final sample is too large to be submitted to the laboratory, a representative subsample should be prepared. Some National legislation may require the final sample be subdivided into two or more portions for separate analysis. Each portion should be representative of the final sample. Precautions in paragraph 6.2 should be observed.

6.8 Packaging and Transmission of Final Samples

a. Each final sample or subsample should be placed in a clean, chemically inert container to protect the sample from contamination and from being damaged in shipping.

b. The container should be sealed so that unauthorized opening is detectable.

c. The container should be sent to the laboratory as soon as possible, after taking precautions against leakage and spoilage.

d. For shipping, all perishable samples should be frozen to minus 20°C, immediately after collection, and packed in a suitable container that retards thawing. If possible, the shipping container should be placed in a freezer for 24 hours prior to packing and shipping the frozen sample.

7. Records

Each sample must be correctly identified by a record with the type of sample, origin of the sample (e.g., country, state, or town), location of collection of the sample, date of sampling, and additional information useful to the analyst or to regulatory officials for follow-up action if necessary.

8. Departure from recommended sampling procedure

If there is a departure from recommended sampling procedure, records accompanying the sample should fully detail procedures actually followed.

APPENDIX A

MEAT AND POULTRY PRODUCTS

COMMODITY	INSTRUCTIONS FOR COLLECTING A PRIMARY SAMPLE	MINIMUM QUANTITY REQUIRED
I. Group 030 (Mammalian Meats)		
A. Whole carcass or side, unit weight normally 10 kg or more	Collect diaphragm muscle, supplement with cervical muscle, if necessary, from one animal.	0.5 kg
B. Small carcass (e.g., rabbit)	Collect hind quarter or whole carcass from one or more animals.	0.5 kg after removal of s and bone
C. Fresh/chilled parts 1. Unit minimum weight of 0.5 kg, excluding bone, (e.g., quarters, shoulders, roasts)	Collect muscle from one unit.	0.5kg
2. Unit weighing less than 0.5 kg, (e.g., chops, fillets)	Collect the number of units from selected container to meet laboratory sample size requirements.	0.5 kg after removal of b
D. Bulk frozen parts	Collect a frozen cross-section from selected container, or take muscle from one large part.	0.5 kg
E. Retail packaged frozen/chilled parts, or individually wrapped units for wholesale	For large cuts, collect muscle from one unit or take sample from number of units to meet laboratory sample size requirements.	0.5 kg after removal of b
Ia. Group 030 (Mammalian Meats where MRL is found in carcass fat)		
A. Animals sampled at slaughter	See instructions under II. Group 031.	
B. Other meat parts	Collect 0.5 kg of visible fat, or sufficient product to yield 50-100 g of fat for analysis. (Normally 1.5-2.0 kg of product is required for cuts without	Sufficient t yield 50-100 of fat

COMMODITY	INSTRUCTIONS FOR COLLECTING A PRIMARY SAMPLE	MINIMUM QUANTITY REQUIRED
II. Group 031 (Mammalian fat)		
A. Large animals sampled at slaughter, usually weighing at least 10 kg	Collect kidney, abdominal, or subcutaneous fat from one animal.	0.5 kg
B. Small animals sampled at slaughter[1]	Collect abdominal and subcutaneous fat from one or more animals.	0.5 kg
C. Bulk fat tissue	Collect equal size portions from 3 locations in container.	0.5 kg
III. Group 032 (Mammalian Edible Offal)		
A. Liver	Collect whole liver(s) or portion sufficient to meet laboratory sample size requirements.	0.4 - 0.5 kg
B. Kidney	Collect one or both kidneys, or kidneys from more than one animal, sufficient to meet laboratory sample size requirement. Do not collect from more than one animal if size meets the low range for sample size.	0.25 - 0.5 k
C. Heart	Collect whole heart or ventricle portion sufficient to meet laboratory sample size requirement.	0.4 - 0.5 kg
D. Other fresh/chilled or frozen, edible offal product	Collect portion derived from one animal unless product from more than one animal is required to meet laboratory sample size requirement. A cross-section can be taken from bulk frozen product.	0.5 kg

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[1]When adhering fat is insufficient to provide a suitable sample, the whole commodity, without bone, is analyzed and the MRL will apply to the

COMMODITY	INSTRUCTIONS FOR COLLECTING A PRIMARY SAMPLE	MINIMUM QUANTITY REQUIRED
V. Group 036 (Poultry Meats)		
A. Whole carcass of large bird, typically weighing 2-3 kg or more (e.g., turkey, mature chicken, goose, duck)	Collect thigh, leg, and other dark meat from one bird.	0.5 kg after removal of s and bone
B. Whole carcass of bird typically weighing between 0.5-2.0 kg (e.g., young chicken, duckling, guinea fowl)	Collect thigh, legs, and other dark meat from 3-6 birds, depending on size.	0.5 kg after removal of s and bone
C. Whole carcasses of very small birds typically weighing less than 0.5 kg (e.g., quail, pigeon)	Collect at least 6 whole carcasses.	0.25 - 0.5 k muscle tissu
D. Fresh/chilled or frozen parts		
1. Wholesale packaged a. Large parts	Collect an interior unit from selected container.	0.5 kg after removal of s and bone
b. Small parts	Collect sufficient parts from a selected layer in the container.	
2. Retail packaged	Collect a number of units from selected container to meet laboratory sample size requirement.	0.5 kg after removal of s and bone
Va. Group 036 (Poultry Meats where MRL is expressed in carcass fat)		
A. Birds sampled at slaughter	See instructions under VI. Group 037	
B. Other poultry meat	Collect 0.5 kg of fat or sufficient product to yield	0.5 kg of fa tissue

COMMODITY	INSTRUCTIONS FOR COLLECTING A PRIMARY SAMPLE	MINIMUM QUANTITY REQUIRED
VI. Group 037 (Poultry Fats)		
A. Birds sampled at slaughter	Collect abdominal fat from 3-6 birds, depending on size.	Sufficient t yield 50-100 of fat
B. Bulk fat tissue	Collect equal size portions from 3 locations in container.	0.5 kg
VII. Group 038 (Poultry Edible Offal)		
A. Liver	Collect 6 whole livers.	0.25 - 0.5 k
B. Other fresh/chilled or frozen edible offal product	Collect appropriate parts from 6 birds. If bulk frozen, take a cross-section from container.	0.25 - 0.5 k
IX. Class E - Type 16 (Secondary Meat and Poultry Products)		
A. Fresh/chilled or frozen comminuted product of single species origin	Collect a representative fresh or frozen cross-section from selected container or packaged unit.	0.5 kg
B. Group 080 (Dried Meat Products)	Collect a number of packaged units in a selected container sufficient to meet laboratory sample size requirements.	0.5 kg, unle fat content less than 5% MRL is expre on a fat bas then 1.5-2.0 is required
XII. Class E-Type 18 [2] (Manufactured, single ingredient product of animal origin)		

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[2] For unit size less than 1 kg, apply the sampling described in CAC/PR-1984.

COMMODITY	INSTRUCTIONS FOR COLLECTING A PRIMARY SAMPLE	MINIMUM QUANTITY REQUIRED
A. Canned product, (e.g., ham, beef, chicken) unit size of 1 kg or more	Collect one can from a lot. When unit size is large (greater than 2 kg), a representative sample including juices may be taken.	0.5 kg unles fat content less than 5% MRL is expre on a fat bas Then 1.5-2.0 is required.
B. Cured, smoked, or cooked product (e.g., bacon slab, ham, turkey, cooked beef) unit size of at least 1 kg	Collect portion from a large unit (greater than 2 kg), or take whole unit, depending on size.	0.5 kg unles fat content less than 5% MRL is expre on a fat bas Then 1.5-2.0 is required.
XIII. Class E - Type 19[3] (Manufactured, multiple ingredient, product of animal origin)		
A. Sausage and luncheon meat rolls with a unit size of at least 1 kg	Collect cross-section portion from a large unit (greater than 2 kg), or whole unit, depending on size.	0.5 kg

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[3]For unit size less than 1 kg, apply sampling as described in CAC/PR-1984.

APPENDIX B

MILK, EGGS, AND AQUATIC ANIMAL PRODUCTS

COMMODITY	INSTRUCTIONS FOR COLLECTING A FINAL SAMPLE	MINIMUM QUANTITY REQUIRED
I. Group 033 (Mammalian Products - Milks)		
A. Fluid Milk Products		
1. Retail containers	Randomly collect subsamples according to sampling schedule. Subsample size will be 1 retail unit. When the retail unit is less than 16 ozs. then collect 2 units per subsample.	0.5 kg
2. Bulk tank trucks	Agitate product in truck then collect 2 quarts from each bulk tank.	0.5 kg
B. Manufactured Dairy Products		
1. Concentrated liquid milk products	Randomly collect subsamples according to sampling schedule. Subsample size will be 1 retail unit, except when the retail unit container size is less than 16 ozs., then collect 2 retail units per subsample.	0.5 kg
2. Dried milk products, cheese, ice cream, and related dairy products	Use sampling schedule to determine sample size. For containers of 16 ozs. or less or 1 pint or less collect a minimum of 2 units per subsamples. For containers of 1 to 24 pounds select 1 unit per subsample. For containers of 25 lbs. or more collect 2 lbs. from each unit sampled.	0.5 kg

COMMODITY	INSTRUCTIONS FOR COLLECTING A FINAL SAMPLE	MINIMUM QUANTITY REQUIRED
II. Group 039 (Eggs and egg products)		
A. Liquid and frozen eggs	Use sample schedule. Subsample size will be 1 pt. liquid or 1 qt. packed shavings from aseptic drillings into containers.	0.5 kg
B. Dried egg products	Use sample schedule. Use same subsample sizes as 1.b. Dried milk products. Collect with aseptic technique.	0.5 kg
C. Shell eggs		
1. Retail packages	Use sample schedule. Subsample size is 1 dozen.	0.5 kg or 10 whole eggs
2. Commercial cases	For 15 cases or less collect 1 dozen from each case, minimum of 2 dozen eggs. For 16 or more cases collect 1 dozen from 15 random cases.	0.5 or 10 whole eggs
III. Class B - Type 08 (Aquatic Animal Products)		
A. Packaged fish, fresh, frozen, smoked, cured, or shellfish (except oysters)	Collect 12 subsamples randomly. Mimimum subsample size is 1 kg.	1.0 kg
B. Bulk fish - 1-3 lb/fish	Collect 12 subsamples randomly. Each subsample should total 1 lb. of edible fish.	1.0 kg
C. Bulk shellfish (except oysters)	Collect 12 - 2 lb. subsamples.	1.0 kg
D. Other fish and shellfish products (including oysters)	Collect 12 - 1 pt. subsamples.	1.0 kg

	COMMODITY	INSTRUCTIONS FOR COLLECTING A FINAL SAMPLE	MINIMUM QUANTITY REQUIRED
IV.	Class E - Type 17 (Derived Edible Products of Aquatic Animal Origin)		
	A. Canned fish and shellfish products (except oysters)	Collect 12 subsamples of 5 cans per subsample.	1.0 kg
	B. Other fish and shellfish products - fish flour and meal	Use sample schedule. Collect 2 lbs. per subsample.	1.0 kg

PRIORITY LIST OF VETERINARY DRUGS REQUIRING EVALUATION

A) Substances proposed to be considered for evaluation at the next JECFA meeting devoted to veterinary drug residues.

Nitrofurans

- Furazolidone
- Nitrofurazone

Quinoxalines

- Carbadox
- Olaquindox

Benzyl Penicillin

Closantel

Ivermectin

Levamisole

Oxytetracycline

B) Substances to be considered for evaluation at a later date.

Benzimidazoles (febantel, fenbendazole, oxfendazole)

Bovine Somatotropin

Porcine Somatotropin

Sulfonamides (sulfaquinoxaline, sulfadimethoxine)

C) Other substances recommended for consideration in the priority list.

Trimethoprim (antimicrobial)

Dapsone (antimicrobial)

Tylosin (macrolide antibiotic)

Spiramycin

Chlortetracycline (antibiotic)

Tetracycline (antibiotic)

Avoparcin (antibiotic)

Carazolol (beta-blocker)

Phenothiazines (tranquillizer)

- Chloropromazine
- Propionylpromazine
- Acetylpromazine
- Promazine

Azaperone (tranquillizer)