codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS
Fifteenth Session
Washington, DC (metro area), (United States of America), 26- 29 October 2004

MATTERS FROM FAO AND WHO

INTRODUCTION

1. This paper describes FAO/WHO activities in the area of Scientific Advice implemented since the 14th Session of the Codex Committee on Residues of Veterinary Drugs in Foods, which are complementary to the work of the Codex Alimentarius Commission.

A. PROGRESS REPORT ON THE FAO/WHO CONSULTATIVE PROCESS ON PROVISION OF SCIENTIFIC ADVICE TO CODEX AND MEMBER COUNTRIES

2. The review of the FAO/WHO programs providing scientific advice to Codex and member countries is ongoing, as requested by the Codex Alimentarius Commission[1] and in response to recommendations of the Codex Evaluation[2].

3. Progress to date includes the completion of the two of the three planned steps in the review process, namely an electronic forum[3] held in the second half of 2003, and an FAO/WHO Workshop on the Provision of Scientific Advice to Codex and Member Countries was held in Geneva, Switzerland, from 27-29 January, 2004[4].

4. The Workshop resulted in a set of recommendations on 1) essential principles, definitions and scope governing the provision of scientific advice, 2) management issues and 3) procedures and mechanisms. Due regard was given to enhancing the participation of developing countries in the provision of scientific advice.

5. The executive summary and the recommendations of the Workshop report were circulated through the Codex Contact Points to member countries and international observer organisations in March 2004 soliciting official comments to be submitted to FAO and WHO. Comments received and steps undertaken by FAO and WHO since the implementation of the Workshop were made available at the 27th Session of the Codex Alimentarius Commission (ref. CAC/27 INF 3A).

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1 24th Codex Alimentarius Commission, ALINORM 01/41, paras 58-62

2 Report of the Evaluation of the Codex Alimentarius and other FAO and WHO Food Standards Work, Rome, 2002

3 The report of the e-forum can be found on this FAO webpage: http://www.fao.org/es/ESN/proscad/forum_en.stm.

4 The report of the Workshop is available on the websites of FAO (http://www.fao.org/es/ESN/proscad/index_en.stm) and WHO (http://www.who.int/foodsafety/en/).

6. Activities prioritised by FAO/WHO to enable implementation of the workshop recommendations include the following:

- Elaborate a ***Procedural Guideline*** that would compile all written procedures followed by FAO and WHO in the provision of scientific advice;
- Establish an ***Internal FAO/WHO Task Force*** to review the management options for the provision of scientific advice and consider improved coordination;
- Prepare ***Review Papers*** to address procedures for the selection of experts, to consider factors associated with enhanced openness of meetings, and to improve procedures on use of data;
- Convene a ***Workshop*** (brain-storming session) to explore new approaches to enhance the participation of experts and use of data from developing countries in the international scientific advice activities.

7. In addition to the review process described above, specific projects are ongoing to strengthen the working procedures of certain aspects of scientific advice by FAO and WHO. Results and recommendations of these parallel review processes will be considered by FAO/WHO.

FAO/WHO worksharing activities with national governments and regional authorities for the evaluation of pesticide residues and toxicology

8. A pilot project on worksharing was initiated in response to the request from the CCPR on ways to improve the timeliness of the recommendations of the JMPR in establishing MRLs. One substance has been identified for this pilot project and will be evaluated at the 2004 JMPR, using national and regional evaluations as a basis. The 36th Session of the CCPR was advised that the purpose of this worksharing pilot project was to investigate the feasibility of using national and regional evaluations to expedite JMPR evaluations and make better use of the resources available, increase the transparency of the evaluation process, facilitate the international acceptance of JMPR evaluations by governments and facilitate the submission of dossiers by the industry. The results and experience of the worksharing pilot project will be summarised in an evaluation report and will be presented to the 37th Session of the CCPR.

Follow-up on the implementation of the York and Zoning reports

9. The 36th Session of the CCPR was informed that the JMPR had already been using the recommendations of the York and Zoning reports whenever possible but that JMPR needs further information from the national governments before their full utilization. The York workshop implemented in 1999 focussed on “Developing minimum data requirements for the estimation of MRLs and import tolerances”. The “Zoning meeting” (2001), concluded that the impact of climate on the behaviour of residues of some foliar applied pesticides on certain crops is negligible, and residue trials could be extrapolated from one place to another when good agriculture practices and agronomical factors were similar.

10. Recognizing that practical experience would be necessary to see how recommendations could be implemented, the JMPR agreed to pilot test the practical applicability of the principles with one pesticide scheduled for evaluation by JMPR in 2004. A survey on the issues raised at the York and Zoning meetings, on which consensus was not achieved at that time, have been considered in the survey and distributed to member governments of the CCPR and the OECD for comments by the end of May 2004. The results would be improved transparency of pesticide evaluation at national and international level.

B. FAO/WHO EXPERT MEETINGS AND CONSULTATIONS

Antimicrobial resistance resulting from non-human usage of antimicrobials

11. In response to a recommendation from the 48th Session of the Executive Committee, FAO, WHO and OIE organized a two-step multidisciplinary expert consultation process to advise the Commission on possible directions to be taken on the issue of antimicrobial resistance.

12. The first Workshop on Non-human Antimicrobial Usage, held in December 2003 in Geneva conducted a preliminary scientific assessment considering all non-human uses of antimicrobials in animals (including aquaculture) and plants, and their role in antimicrobial resistance, based on the available scientific information. Based on the outcome, the second Workshop in Oslo considered the broad range of possible risk management options and included the participation of all major stakeholder groups. In particular, it focused on potential directions of future Codex, FAO, OIE and WHO work in this area, in order to prevent and minimize antimicrobial resistance at the global level. The reports of both workshops were published by WHO and are available on the web pages of all three participating organisations (e.g.: http://www.who.int/foodsafety/publications/micro/en/).

13. The Executive Summary of the two Workshops are attached Appendix 1 and 2 to this document.

Residues of veterinary drugs without ADI/MRL

14. In July 2003, the 26th Session the Codex Alimentarius Commission discussed a request from Thailand to assess the issue of "Risk Analysis for Substances with No ADI and/or MRL" and took note of FAO's proposal to examine, at a technical consultation, the regulatory issues, including zero tolerance and *de minimis* limits and risks associated with substances at the limit of detection or *de minimis* levels. The Joint FAO/WHO Technical Workshop on Residues of Substances without ADI/MRL in Foods was held from 24-26 August 2004, Bangkok, Thailand.

15. The workshop identified the scientific, technical and regulatory problems as well as appropriate follow-up steps related to disruptions in food trade that occurred in 2001/2002, which were caused by the detection of trace amounts of chloramphenicol and nitrofurans in animal products. In relation to analytical methodology, possible measures have been considered and are recommended to the Codex Member Countries. Moreover, it was also recommended to Codex Member Countries, that work on international MRLs for veterinary drugs that have been evaluated by national governments and are currently in use is completed within the coming ten years. This could be achieved, with the assistance of the JECFA, by establishing a list of temporary MRL's based on national/regional evaluations, which after a certain time could be made permanent if, the original evaluations were not put in question or JECFA was able to establish an ADI and propose an MRL. Lastly it is recommended to international organisations like FAO and WHO to build international networks to facilitate transparency and sharing of scientific information in relation to methods of control of veterinary drug residues. This may require innovative approaches to capacity building.

16. The Workshop formulated the following recommendations on risk management to the Codex Committee on Residues of Veterinary Drugs in Foods:

A) Substances, whose residues are generally recognised as highly toxic and which should not be used as veterinary drugs have to be addressed by the Codex Alimentarius:

- CCRVDF should identify these substances and develop a policy that aims to ensure that they are not used in food animal production.
- There is also a need for an agreement on parameters for the analytical methods that are used to determine the residues of unsafe drugs. Specifically the requirements for the detection capability and performance of such methods should be discussed and harmonized, if possible.
- CCRVDF should establish harmonized criteria and rules for the evaluation of food consignments containing residues of these substances.
- All of the above should not condone the illegal use of these substances.

For veterinary drugs which, because of health concerns, JECFA cannot allocate an ADI and recommend an MRL, CCRVDF should request that JECFA perform and report, if possible, an estimate of the risks associated with the anticipated exposure of consumers to the residues of the veterinary drug. Such risk estimates would be useful for management of risks associated with the residues.

The Codex Alimentarius Commission should include consideration of cost-benefit and risk comparisons in its risk analysis policies.

The recommended performance level (RPL) for regulatory analytical methods should be established by the risk manager to reflect the toxicological risk of the veterinary drug residue and/or the control strategy chosen by the competent authority.

B) For substances which have been evaluated by national governments and are legally used in many countries but which have no Codex MRL, CCRVDF should develop a more comprehensive approach which would allow completion of the work on MRLs within the coming ten years.

Such an approach should aim to elaborate a comprehensive list of MRLs that cover all substances used in veterinary drugs. It is recognized that efforts are already being made to address this and that several options exist.

- One option would be to ask JECFA to perform risk assessments for all these substances. However, the considerable number of substances, the resources required for their evaluation, and the lack of sponsors make this option less attractive.
- Another option would, with the assistance of JECFA, be the creation of an initial list of temporary/operative MRLs which is based on national/regional MRLs and their accompanying assessment reports which have been adopted using a procedure that applies risk assessment principles. This initial list should be valid for a certain time period (to be determined by Codex) and the MRL should subsequently be made permanent if (a) no comments have been received that put the original risk assessment into question, or (b) JECFA was enabled to establish an ADI based on review of the underlying data and to propose an MRL. Substances which do not fulfil either of these conditions should be moved to a list of compounds not to be used in food animals.

In this context, CCRVDF should monitor the progress of the CCPR/JMPR pilot “Work sharing” project and consider the development of a policy and mechanisms (including cooperation of drug sponsors and national/regional veterinary drug approval authorities) for the use of national and regional risk assessments by JECFA in order to expedite review and avoid unnecessary duplications of effort. The JECFA would be a peer review forum with particular focus on the international considerations.

C) Drugs which are seen as important in developing countries should be assessed by a consultative process that may involve JECFA and subsequently be added into the temporary list of the abovementioned second option. It is noted that this approach still requires significant work and support from developing countries since the conditions of use (species, dosage regime, waiting periods) of these drugs are not known outside of the country. In order to facilitate this work, FAO and WHO should explore the development of more detailed procedures to develop MRLs for species where data do not exist by extrapolating from existing data. It is urgently required that the Joint FAO/WHO Project to Update the Principles and Methods for the Risk Assessment of Chemicals in Food develops guidance to JECFA that would allow extrapolation of the data from species to species. In parallel, CCVRDF should develop a corresponding risk assessment policy.

CCRVDF should amend its procedures in its ad hoc working group on priorities for selection of veterinary drugs for JECFA evaluation to facilitate development of MRLs for veterinary drugs routinely used by developing countries in their food animal production programmes and take other measures as appropriate to meet this critical need.

FAO and WHO should convene an expert workshop to consider the needs for veterinary drugs for aquaculture.

D) CCRVDF should expedite completion of its revised guidance for science-based residue (regulatory) control programmes and analytical method validation for residue control programmes.

E) CCRVDF should complete development of its risk management policy to provide assistance to governments, with particular attention to developing countries, for improving their science-based regulatory framework for control of residues of veterinary drugs in food, including those veterinary drugs without an ADI or MRLs.

17. The Executive Summary of the Workshop is attached Appendix 3 to this document.

C. JOINT FAO/WHO PROJECT ON HARMONIZATION JMPR/JECFA

The Conference on International Food Trade Beyond 2000: Science-based Decisions, Harmonization, Equivalence and Mutual Recognition held in Melbourne, Australia, in October 1999 recognized these developments and the fact that the evaluations performed by JECFA and JMPR serve as the scientific foundation for international food standards that are of increasing importance within the Codex Alimentarius Commission and the World Trade Organization. This Conference recommended that:

"WHO should consider updating and harmonizing between JECFA and JMPR all the common principles of the toxicological evaluation of food chemicals (e.g., natural constituents, additives, contaminants, residues of pesticides and residues of veterinary drugs) and publish this information in a single consolidated document."

In response to this need, FAO and WHO have initiated a project to update the General Principles and Methods for the Risk Assessment of Chemicals in Food.

The objectives of this project are to:

i. assure the continuation of transparent and sound expert evaluations of scientific data for risk assessments of chemicals in food;

ii. review principles and procedures used by JECFA and JMPR and reaffirm those that remain valid in view of current scientific knowledge;

iii. facilitate the incorporation of new scientific tools, approaches and knowledge in the implementation of risk assessment of food chemicals (e.g., regional diets, dose-response modelling, and biomarkers, including genomics, proteomics);

iv. harmonize, to the extent possible, risk assessment procedures for different classes of chemicals in food (e.g., additives, contaminants, pesticide residues, veterinary drug residues, and natural toxicants); and

v. harmonize, to the extent appropriate, approaches to risk assessment by JECFA and JMPR with those of other scientific groups (including national, regional, other public health and environmental).

The chapter topics are:

Chapter 1. Introduction

Chapter 2. Special Considerations

Chapter 3. Chemical Characterisation, Analytical Methods, and the Development of Specifications for Hazard Identification and Characterisation and for Risk Management

Chapter 4. Toxicological Tests and Evaluation for Hazard Identification and Characterisation:

Chapter 5. Human Data for Hazard Identification and Characterisation

Chapter 6. Dose-Response Assessment

Chapter 7. Intake Assessment

Chapter 8. Risk Characterisation

Chapter 9. Maximum Levels/Limits for Residues, Contaminants,and Constituents

Glossary

This will be a web-based, print on demand, document with stand-alone chapters. This will facilitate revisions, particularly by JECFA and JMPR, as risk assessment science advances.

Drafts of Chapters 1, 4 and 5 and the glossary have been completed. Work is in progress on chapters 2, 3, 6, 7, 8 and 9. The latter will include considerations for species extrapolations for MRLs. A workshop on intake assessment for chemicals in food is being planned for spring 2005. The draft chapters will be available on the internet for review and comment.

An International Programme on Chemical Safety workshop on dose-response modelling was carried out from 13-17 September 2004 in Geneva. This purpose of the workshop was to develop general guidance for the use of dose-response modelling in risk assessments. This includes approaches that can be used to provide risk estimates when there is no ADI or MRL. This guidance will be included in Chapter 6.

APPENDIX 1

***Executive Summary of the Joint WHO/FAO/OIE Expert Workshop on Non-human Antimicrobial Usage and Antimicrobial Resistance (*Geneva, 1 – 5 December 2003)**

Antimicrobial agents are essential drugs for human and animal health and welfare. Antimicrobial resistance is a global public health concern that is impacted by both human and non-human antimicrobial usage. Antimicrobial agents are used in food animals, including from aquaculture, companion animals and horticulture to treat or prevent disease. Antimicrobial agents are sometimes used in food animals to promote growth. The types of antimicrobials used are frequently the same as, or closely related to, antimicrobials used in humans.

Managing human health risks from non-human usage of antimicrobials and the resulting antimicrobial resistant bacteria requires national and international interdisciplinary cooperation. This consultation was convened by FAO, OIE and WHO to perform a scientific assessment of resistance risks arising from the usage of antimicrobials in animals (including aquaculture) and plants and to formulate recommendations and options for future risk management actions to be considered by the Codex Alimentarius Commission and OIE.

There is clear evidence of the human health consequences due to resistant organisms resulting from non-human usage of antimicrobials. These consequences include infections that would not have otherwise occurred, increased frequency of treatment failures (in some cases death) and increased severity of infections, as documented for instance by fluoroquinolones resistant human Salmonella infections. Evidence shows that the amount and pattern of non-human usage of antimicrobials impacts on resistant bacteria in animals and on food commodities and thereby human exposure to these resistant bacteria. The foodborne route is the major transmission pathway for resistant bacteria and resistance genes from food animals to humans, but other routes of transmission exist. There is much less data available on the public health impact of antimicrobial use in aquaculture, horticulture and companion animals.

The consequences of antimicrobial resistance are particularly severe when pathogens are resistant to antimicrobials critically important in humans. Therefore, the workshop recommends that an expert clinical medical group appointed by WHO define which antimicrobials are considered critically important in humans.

The expert workshop concluded that surveillance of non-human usage of antimicrobials and antimicrobial resistance in food and animals is important for the identification of resistance problems and as a basis for choosing interventions to limit the development and spread of resistance at all levels.

Several recent attempts to quantify the magnitude of related health impacts in the human population have been made. Estimates vary widely from small to large, depending on the organism and antimicrobial of interest, and are accompanied by considerable uncertainty.

The workshop concluded that residues of antimicrobials in foods, under present regulatory regimes, represents a significantly less important human health risk than the risk related to antimicrobial resistant bacteria in food.

Risk assessment approaches that adequately address the broad range of potential human health impacts need to be further developed with a view towards enabling efficient risk management of antimicrobial resistance in the international arena. OIE is invited to continue its work on risk analysis in coordination with FAO and WHO.

The Workshop recommended that the Codex Alimentarius Commission, where appropriate in collaboration with OIE, takes coordinated steps towards managing these risks focusing on the microbiological nature of the hazards.

APPENDIX 2

***Executive Summary of the Joint FAO/OIE/WHO 2nd Workshop on Non-human Antimicrobial Usage and Antimicrobial Resistance: Management Options* (Oslo, Norway, 15-18 March 2004)**

Antimicrobial agents are essential drugs for human and animal health and welfare. Antimicrobial resistance is a global public and animal health concern that is impacted by both human and non-human antimicrobial usage. The human, animal and plant sectors all have a shared responsibility and role in efforts to prevent and minimize antimicrobial resistance selection pressures for both human and non human use of antimicrobials. Antimicrobial agents are used in food animals, aquaculture, companion animals and horticulture to treat or prevent disease. Antimicrobial agents are sometimes used in food animals to promote growth. The types of antimicrobials used are frequently the same as, or closely related to, antimicrobials used in humans.

Managing human health risks from non-human usage of antimicrobials and the resulting antimicrobial resistant bacteria requires national and international interdisciplinary cooperation. The 1st Workshop on Non-human Antimicrobial Usage, December 2003 in Geneva, conducted a preliminary scientific assessment considering all non-human uses of antimicrobials in animals (including aquaculture) and plants, and their role in antimicrobial resistance, based on the available scientific information. Based on the outcome of the 1st Workshop in Geneva, as well as other relevant input (e.g. reports of previous WHO and OIE workshops), the 2nd Workshop in Oslo considered the broad range of possible risk management options for antimicrobial resistance from non-human usage of antimicrobials. In particular, it focused on potential directions of future Codex, FAO, OIE and WHO work in this area, in order to prevent and minimize antimicrobial resistance at the global level. To ensure that the conclusions of the 2nd Workshop reflected the perspectives of affected parties, the major stakeholder groups (e.g., pharmaceutical industry, farmers[5], food processors, consumers, regulatory agencies, and veterinarians) participated in the meeting.

The workshop process has resulted in suggestions for a way forward in this area, for Codex, as well as for OIE, WHO and FAO. Among the important conclusions were:

1. The risks associated with non-human antimicrobial use and antimicrobial resistance should be part of the human safety assessment. The concept of “thresholds of resistance” should be pursued as a tool for risk management. If these thresholds are exceeded, this should trigger a range of risk management actions.
2. The concept of “critically important” classes of antimicrobials for people should be developed by WHO with a view to enabling specific resistance preventive actions for such antimicrobials related to non-human use. A similar list of “critically important” classes of antimicrobials for animals should be pursued by OIE.
3. Through stringent implementation of good agricultural practices including good animal husbandry and good veterinary practices it is possible to reduce the necessity for antimicrobials.
4. The need for rapid implementation by governments and all stakeholders of the WHO Global Principles for the Containment of Antimicrobial Resistance in Animals intended for Food and the OIE Guidelines on Antimicrobial Resistance is emphasised.
5. There is need for capacity building, networking and co-ordination to facilitate implementation of surveillance programmes in various countries, in particular developing countries. FAO, WHO and OIE should take a leading role in this.
6. A Codex/OIE Task Force should be established to develop risk management options for antimicrobial resistance related to non-human use of antimicrobials. Risk communication and transparency are critical to achieve effective risk management. Moreover, the International Code of Practice, General Principles of Food Hygiene should be reviewed to take account of antimicrobial resistance issues.

The outcome of this consultative process will be discussed in detail at the Codex Alimentarius Commission meeting in June 2004 in Geneva, based on the full publication and distribution of both reports to all Member States. Furthermore the outcome will be discussed in relevant OIE fora and will support future WHO work in this area.

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[5] In the context of this report, farmers include individuals, groups and companies involved in primary food production.

APPENDIX 3

***Executive Summary of the FAO/WHO Technical Workshop on Residues of Veterinary Drugs Substances without ADI/MRL in Foods* (Bangkok, Thailand, 24-26 August 2004)**

The *Joint FAO/WHO Technical Workshop on Residues of Veterinary Drugs without ADI/MRL in Foods* met in Bangkok, Thailand from 24th to 26th August 2004, in order to provide FAO, WHO and Codex with a first analysis of disruptions in food trade that occurred in 2001/2002. The disruptions which were caused by the detection of trace amounts of chloramphenicol and nitrofurans in animal products. The experts were asked to identify the scientific, technical and regulatory problems related to these findings and to identify appropriate follow-up steps.

The rapid progress of analytical methods has resulted in large improvements in detection capabilities of low residue levels of veterinary drugs, and has exposed gaps in the current national and international regulatory systems, leading particularly to major impacts on international trade. Decisive and innovative action, which is both realistic and flexible, is needed to address these gaps.

The impact of analytical methodology was discussed in detail. Possible measures for addressing these concerns focussed on alternatives to using the limit of detection of the analytical method as the basis for regulatory actions. The alternatives include establishment of recommended performance levels (RPLs) that consider the toxicological risk of the veterinary drug residue or control strategy chosen by the competent authority, and thresholds of toxicological concern for residues of veterinary drugs without acceptable daily intakes (ADIs) or maximum residue limits (MRLs). The development of different and more useful approaches than the existing one may be achieved by closer interaction between risk managers and risk assessors. Such new approaches should not condone the illegal use of these substances.

Substances whose residues are generally recognised as highly toxic and which should not be used as veterinary drugs have to be addressed at an international level. The Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) should identify those compounds not to be used in food animals. It is also very important that work on international MRLs for veterinary drugs that have been evaluated by national governments and are currently in use is completed within the coming ten years. This could be achieved, with the assistance of the FAO/WHO Joint Expert Committee on Food Additives (JECFA), by establishing a list of temporary MRLs based on national/regional evaluations, which after a certain time period could be made permanent if, the original evaluations were not put into question or JECFA was able to establish an ADI and propose an MRL.

Drugs which are seen as important in developing countries and have a national approval should be assessed by a consultative process that may involve JECFA and subsequently be added to the abovementioned list of temporary MRLs. It was noted that this activity still requires significant work and support from developing countries since the conditions of use of these drugs are not known outside of the country.

With regard to regional/national frameworks, the workshop noted that the regulatory frameworks amongst countries can differ significantly in relation to the comprehensive nature of a regulatory control programme including its MRLs for veterinary drugs. Measures identified to overcome some of these problems should include improving coordination and communication amongst competent authorities with responsibilities for food safety programs, capacity building designed to meet specific country needs and development of programmes to focus on good veterinary and animal health practices at farm level, and controlling compliance with MRLs for foods of animal origin.

It will also be critical to continue the effort to build international networks to facilitate transparency and sharing of scientific information in relation to methods of control of veterinary drug residues. This may require innovative approaches to capacity building. Some possible measures and actions to address better coordination of capacity building activities include increasing the availability and quality of information on international standards and requirements of trading blocks for developing countries, support for the establishment of regional reference laboratories and/or laboratory networks, and creation of a network/platform and a mentorship approach to share experience, knowledge and data between experts and officials from developed and developing countries.