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Final report

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An edited version of this report will be published by FAO and WHO in due course. The report as adopted by the workshop is reproduced here so that the information is disseminated quickly. This draft text will be subject to further editing. All working papers will be annexed in the printed edition.

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Acknowledgement

The workshop wishes to dedicate this report to the memory of Dr Eduardo Mendez for his vision and more than thirty years commitment to the principles and ideals of the Codex Alimentarius Commission, including his service as its first chairperson from a developing country.

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1. Executive Summary

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, 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.

In relation to analytical methodology, possible measures for addressing these concerns 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 MRL's 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.

2. Introduction

At the end of 2001 and during the first months of 2002 several control laboratories in member countries of the European Union detected trace amounts of chloramphenicol and nitrofurans in imported animal products (e.g. shrimps, chicken). These findings were triggered mainly by improvements of analytical methods which significantly lowered the levels of detection for residues of these drugs. Following the European Unions safeguard provisions for imports of animal products, some producers and producing countries were temporarily withdrawn from the list of approved exporters, while others were forced to rapidly implement drastic measures.

The *Joint FAO/WHO Technical Workshop on Residues of Veterinary Drugs without ADI/MRL in Foods* met in order to provide FAO, WHO and the Codex Alimentarius Commission with a first analysis of the disruptions in food trade that started in 2001/2002, identify the scientific, technical and regulatory problems related to them and discuss, if possible, any appropriate follow-up steps.

The experts who attended the meeting were selected by FAO and WHO according to their scientific and technical expertise on the topic, recent work on a national/international level on analytical methods for residues of veterinary drugs, experience in capacity building on control systems for veterinary drugs, or work in the risk assessment of veterinary drugs or the corresponding regulatory framework. In addition the selected panel as a whole should be balanced from a regional point of view, have sufficient expertise from developing countries (specifically from those countries who have been involved recently in these issues) and reflect current standard practice but also be open to new ideas and approaches and be able to provide independent scientific / technical advice.

All experts were asked to prepare working papers on specific issues; in addition input from other interested parties was invited. The working papers¹ and other material received by the Secretariat were distributed to the participants for consideration before the meeting.

At the meeting, the main issues identified in the working papers were presented in short summaries followed by discussions of two working groups which dealt with *Risk Assessments/Analytical Methodology* and *Regulatory Framework/Capacity Building*, respectively.

The workshop was opened by the Dr He Changhui, Assistant Director General and FAO Regional Representative for Asia and the Pacific and Mr Worwate Tamrongtanyalak, Secretary General of the National Bureau of Agricultural Commodity and Food Standards. Dr He thanked the government of Thailand for hosting the meeting and providing further support in its preparation and stressed that the subject of the meeting will further contribute to promoting and reinforcing policy and regulatory frameworks for food products and create sustainable increases in the supply and availability of food and other agricultural products. Mr Worwate underlined that the invitation is a signal of the country's commitment to improve the quality and safety of food in order to transform the food sector into a modern dynamic and competitive sector. As part of this effort Thailand had recently pursued a policy of "Clean and Safe Food for all in 2004", aiming at achieving and maintaining a high standard and quality of foods produced, consumed domestically and exported and meeting international food standards. Hence the country could possibly become the kitchen of the world.

The workshop appointed Dr Dieter Arnold, Germany, as Chairperson, and Dr Paul Brent, Australia, as rapporteur of the workshop, Dr Shoji Miyagawa, Japan, as Chairperson, and Dr Kevin Greenlees, USA, as rapporteur of the working group *Risk Assessments/Analytical Methodology*, and Dr Adriana Fernández Suárez, Argentina, as Chairperson, and Dr Glenn Kennedy, United Kingdom, as rapporteur of the working group *Regulatory Framework/Capacity Building*.

¹ All working papers will be annexed to the printed edition of the report.

3. Progress of analytical methods and impact on international trade

Description of status quo, state of the art

Problems arise when new methods or technologies with enhanced capabilities are introduced without due notification of other interested parties. While this may not be significant for substances with an MRL, it can have a profound impact when it involves reporting limits (action levels) for residues of veterinary drugs without a Maximum Residue Limits (MRL). Reporting limits are levels where the laboratory must report the presence of the analyte in the food matrix to the competent authority. For non approved compounds, the national regulatory authorities establish their action limits on the detection capability of the methods used in the laboratories responsible for the control of residues. The situation has worsened with the rapid acceptance of mass spectrometry (MS) and liquid chromatography – mass spectrometry (LC-MS) in those countries with resources to support the technology as the standard for analytical methods. Combined with changes in detector capabilities, this has resulted in a ten-fold increase in sensitivity since the early 1990s. There is no reason to believe that there won't be similar improvements in analytical method sensitivity in the future, resulting in a repetition of problems such as those encountered recently with residues of chloramphenicol and nitrofurans. These MS and LC-MS analytical methods have become the standard in major food importing countries. This has forced food exporting countries to work to match this technology to assure the acceptance of their exported food products.

Regulatory methods provided as part of registration packages are typically for the veterinary drug under consideration, while official regulatory laboratories typically use multi-analyte methods capable of detecting more than one drug. The best source multi-analyte drug residue methods are probably from counterpart regulatory laboratories in other countries. Therefore, transparency is a critical issue.

Analysis of gaps and identification of problems.

Official regulatory laboratories are obliged under the SPS Agreement to make their methods and validation reports available to counterpart laboratories in other countries on request to facilitate routine implementation and promote equivalency of test capabilities between laboratories in importing and exporting countries. This does not always happen. Downsizing and cost-saving steps have caused some national authorities to partially or fully privatize analytical laboratories. In some cases, this has led to the specifications of regulatory analytical methods being considered to be proprietary. These laboratories may be unwilling to share validation, performance, and procedural information about the analytical method.

Rather than reflecting the level of risk associated with exposure of consumers to residues of veterinary drugs without MRLs, the reporting limits only reflect the current analytical capabilities of analytical laboratories in that region of the world. Regional differences in the application of regulatory measures (e.g. analytical laboratory reporting limits, application of performance criteria for analytical methods, and other uncertainties) have created a profound impact on fair practice in the food trade.

Development of analytical methods does not consider the technical and resource limitations of developing countries frequently responsible for assuring the quality of exported food products derived from animals (including aquatic animals) treated with veterinary drugs. State of the art methodologies such as LC-MS are expensive to develop and maintain, particularly in the absence of the necessary technological infrastructure. As analytical method detection levels continue to improve there are increased cost associated with equipments and its maintenance, standards and consumables, staff training and retention, maintenance of quality assurance system and increased cost in avoiding cross contamination of the sample. The increased costs associated with increasingly sensitive analytical methods are incurred by both the importing and exporting countries.

Existing CODEX Volume 3 guidance on analytical method validation does not reflect the single laboratory validation approach but is currently being updated by the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF).

Changes in analytical methodologies and knowledge can lead to changes in marker residue and target tissue resulting in rapid change in control strategy of a national authority. The communication of the laboratory result to the risk manager could be the source of misunderstanding in the absence of a clear communication procedure.

The matrix tested should be representative of the raw material from animal origin and the presence of material from other origins has been shown to be a source of confounding results. The lack of availability of rapid, cheap and validated screening tests for residues of banned substances in tissues remains a problem.

4. Analysis and management of risk of low level residues

Description of status quo, state of the art.

There are a number of veterinary drugs for which Codex has not adopted an MRL. An ADI/MRL may not have been established because the veterinary drug may not have been evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) or in the JECFA evaluation, the toxicological data did not support an ADI, the residue data were insufficient, a suitably validated analytical method was not identified, or good agricultural practices would result in exceeding the MRL. JECFA is an expert scientific committee independent of Codex which provides risk assessment advice to Codex and member countries.

In the absence of ADI/MRL, national authorities commonly resort to zero tolerance regulatory approaches (where no detectable residue of the veterinary drug in the food is acceptable), with the prevalence of residues of concern potentially changing as analytical method detection capabilities improve. Additional tools are needed to evaluate risk when the existing approach of establishing an ADI and MRL cannot be applied.

The change in technology, for example LC-diode array to LC-MS has resulted in an improvement in detection capability so that a residue that was previously non-detectable now becomes reportable. The change in reported levels is independent of any toxicological risk posed by the food product.

Analysis of gaps, identification of problems.

An MRL cannot be established if the toxicological data do not support the derivation of an ADI, nor can an MRL be established if no data are provided for evaluation, as is the case for an unapproved use of a veterinary drug.

Low level residues of veterinary drugs without ADIs or MRLs may be present at concentrations approaching those of environmental contaminants. Considering that there may be environmental sources of the drug substance (that may differ regionally), it is not clear when residues of a banned veterinary drug should be evaluated as a contaminant. While the toxicological evaluations in the risk assessments would be the same, other considerations may be different.

Identification of the data requirements for evaluation by JECFA can be a problem for some national authorities. Similarly, the collection of sufficient data for an evaluation of veterinary drugs by the JECFA has been a problem for some compounds.

5. Risk assessments by JECFA

Description of status quo

There are currently several possible mechanisms for placing a substance used as veterinary drug on the agenda of JECFA. However, in the past the typical mechanism included prioritisation by

CCRVDF on the basis of a firm commitment of a private sponsor to provide the data necessary to perform a risk assessment and to elaborate proposed Maximum Residue Limits for Veterinary Drugs (MRL). As a result, only a relatively small fraction of the existing substances which are currently used in veterinary medicine and would require international MRLs have been evaluated by the Committee. There is currently no backlog in JECFA for veterinary drug review.

For the majority of substances evaluated by JECFA the data had been generated in order to primarily support major uses in developed countries. Only in a very few cases was it possible to obtain the data to evaluate substances which were of special interest to certain specific regions, for example in the cases of diminazene and of isometamidium which are both veterinary drugs with a long history of use for the treatment of animal trypanosomiasis in tropical countries, and in the case of oxytetracycline for use in shrimp culture where the government of Thailand generated the data.

In order to facilitate the evaluation of substances with a long history of use JECFA has adopted an approach implying that for the assessment of such substances and on a case by case basis certain studies not meeting modern criteria could be used in the light of other equivalent information, presented for example, in the form of literature reviews conducted by sponsors and/or evaluation reports drafted by experts in the field, provided that the safety of these products can be assured to an extent equivalent to that achieved for newer products supported by a contemporary data base.

Analysis of gaps and identification of problems

The consequences of the above described mechanisms are that many substances with the potential to leave residues in foods and to create problems in international trade have no ADI and no international MRLs, or their MRLs do not cover species and uses which were considered minor by the sponsors of the data. Some countries have a “minor use” policy that allows the extrapolation of data from approved uses in a “major use” species to use in “minor use” species. In those countries, minor use is typically defined as species not significantly consumed for food or species for which there is a very small market for pharmaceutical development. In these circumstances, the toxicological ADI is applied to the “minor use” species. The metabolism and residue evaluation data, up to and including the MRL, are extrapolated to the “minor use” species as is scientifically appropriate. This approach may be useful in increasing the number of species treated with the veterinary drug for which an MRL may be developed and may be particularly useful in aquaculture. The resulting problem for animal health, food safety and trade in food can be significant if minor uses in some regions represent major uses in other regions or if certain methods of production of animal-derived foods, for example aquaculture, grow rapidly in some parts of the world and only insufficient numbers of drugs with established specific good practices and international MRLs are available.

Inventories of substances currently needed in different regions of the world and the indications for which they are being used do not exist. Therefore it is currently not possible to develop concepts on how assessments by JECFA could be enabled. CCRVDF and JECFA have, up to now, not yet finalised the discussion of the risk assessment policy aspects and of the scientific criteria for extrapolating kinetic and residue data from species to species.

It is well known that for a significant number of substances state of the art risk assessments have been conducted by national authorities or international bodies. However, there is presently no mechanism to make the underlying data available to the JECFA/Codex system with the objective to promote the elaboration of international standards. In other cases at least parts of the data required for a JECFA evaluation are in the hands of national institutions, e.g. information on national good practices in the use of veterinary drugs and residue data.

6. Regulatory framework at the national and regional level

Introduction

The workshop noted that one responsibility of a national government is to provide for appropriate public and animal health protection by approving safe and effective veterinary drugs for use in food producing animals and enforcing other provisions regarding food safety. Incumbent in this regulatory framework is the responsibility of managing veterinary drugs without an ADI or MRLs to protect consumers and minimise disruption of international trade.

The workshop identified seven elements that were appropriate for either developed or developing country regulatory frameworks. Overlying the development of a regulatory system should begin with an appropriate definition of a government's policy regarding its public health objectives (e.g., its appropriate level of protection) applying appropriate science-based measures. Secondly, legislation, regulations and guidance documents should be provided on how to put the regulatory framework in place. The third essential element is to establish and maintain adequate technical resources for conducting food safety assessments and developing national regulatory standards for residues of veterinary drugs in food. To determine compliance with MRLs and provide assurance to consumers of the safety of food animal products, risk based residue control programmes are required. In addition, regulatory authorities need to have effective surveillance and compliance programs for pharmacovigilance and enforcement of national and/or international residue limits. To facilitate residue control programmes for food of animal origin, effective analytical methods are required. Finally, adequate data and information systems are critical for the assimilation and dissemination of information regarding national and international standards for residues of veterinary drugs.

Status quo

The workshop noted that the regulatory framework differs significantly between countries. Whilst some countries have a fully developed system, in others the use of veterinary drugs without an ADI/MRL is not adequately controlled and there is a very poorly developed food safety infrastructure with little experience in the effective control of veterinary drugs throughout the food production chain. Some countries may lack effective legislation (on the registration, distribution, use, etc, of veterinary medicines) and/or the means of implementing their legislation as a result of insufficient resources, knowledge & technical expertise. Other countries have a rapidly developing infrastructure and have most of the basic systems identified above, but lack specific technical expertise, for example, on analytical method validation.

Generally, developing countries seek assistance for their regulatory frameworks by looking to Codex to incorporate food safety standards into their regulatory framework, including national legislation

Regulatory framework weaknesses

The workshop was aware that several factors may exist that could result in some deficiencies among member countries contributing to the absence of one or more elements of a comprehensive regulatory framework, particularly in developing countries. Contributory factors include:

- Lack of priority for a government commitment to national policy
- Some countries give a low priority to implementation of their food safety measures
- Inadequate resources to formulate and implement national food safety programs
- Lack of co-ordination amongst relevant stakeholders
- Stakeholders are not always involved in the formulation and implementation of food safety programs

- Insufficient numbers of veterinary drugs have Codex MRLs that could be adopted by governments as national MRLs
- There is inadequate enforcement of measures to ensure the prudent use of veterinary drugs, especially at farm level.

The workshop was able to identify measures and actions to facilitate improvements in national regulatory programmes. These include:

- Increasing awareness and commitment of policy makers at national level to improve public health protection and promote international trade.
- Designing capacity building to meet specific national needs.
- Encouraging stakeholder involvement in the formulation and implementation of the food safety programs by national governments.
- Improving co-ordination and communication amongst competent authorities with responsibilities on food safety programs.
- Implementation of mentoring programs with countries having comprehensive food safety programs.
- Improving control on the use of veterinary drugs especially at the farm level.

Factors for improvement in food safety programs, particularly in developing countries

The workshop considered that there are promising factors that may facilitate improvements in food safety programmes, particularly in developing countries. These include the following:

- Market access and economic factors
- Consumer demand for safer food
- Export market access has increased the demand/need to produce safer and higher quality food
- The need to end disruption in international trade/markets
- The willingness to pay attention to substances without an ADI or MRL
- Paying attention to their obligation to review and update their food safety regulations to be science-based to comply with the WTO/SPS Agreement. Measures indicated above will facilitate meeting their commitments to the WTO/SPS agreement.
- Developing countries are not receiving full benefit of the provisions of the SPS Agreement regarding technical assistance².

² Article 9 "Technical Assistance" - 1) Members agree to facilitate the provision of technical assistance to other Members, especially developing country Members, either bilaterally or through the appropriate international organizations. Such assistance may be, *inter alia*, in the areas of processing technologies, research and infrastructure, including in the establishment of national regulatory bodies, and may take the form of advice, credits, donations and grants, including for the purpose of seeking technical expertise, training and equipment to allow such countries to adjust to, and comply with, sanitary or phytosanitary measures necessary to achieve the appropriate level of sanitary or phytosanitary protection in their export markets. 2) Where substantial investments are required in order for an exporting developing country Member to fulfil the sanitary or phytosanitary requirements of an importing Member, the latter shall consider providing such technical assistance as will permit the developing country Member to maintain and expand its market access opportunities for the product involved.

7. International regulatory framework provided by Codex and WTO

Characterisation of the currently applied framework

WTO: The applicable international framework is provided by the SPS Agreement, which addresses sanitary and phytosanitary measures that may affect international trade. Countries have also the right to implement separate measures, which provide appropriate levels of protection for their own population. Since such measures potentially hinder trade, the SPS agreement encourages international harmonisation of health related food standards. It recognises the Codex Alimentarius as the main source and reference for such harmonisation and correspondingly WTO promotes participation of developing countries in this work.

The SPS agreement also lays down a notification procedure to be followed if a country develops a new measure, which allows other members to comment and to prepare for the implementation of its own measures to meet these requirements.

Codex Alimentarius: The Codex Alimentarius Commission has the objective of protecting the health of the consumers and ensuring fair practices in the food trade by developing food standards and other texts related to food safety and quality. With respect to veterinary drugs residues, the Commission recognized that “the occurrence and safety of residues of veterinary drugs in foods of animal origin was of significance to public health and consumer concern”. In 1985 it established the Codex Committee on Residues of Veterinary Drugs in Foods, which was tasked to:

- determine priorities for the consideration of residues of veterinary drugs in foods;
- recommend maximum limits of such substances;
- develop codes of practice as may be required;
- consider methods of sampling and analysis for the determination of veterinary drug residues in foods.

MRLs are developed and adopted as Codex MRLs (i.e. international standards) if the risk assessment performed by JECFA results in the establishment of an ADI; and the recommended MRLs are achievable under good veterinary practices (GVPs), and the availability of a suitable analytical method. The evaluation process depends on the commitment of a sponsor to provide the data and to submit a dossier. Over two decades Codex has adopted MRLs for residues of approximately 50 veterinary drugs.

Codex Alimentarius contains general guidance to member countries on the exchange of information between countries on rejection of imported foods³. This guideline describes many elements that are essential for a rapid and transparent communication between administrations and laboratories if residues are detected in food.

Main problems and gaps

Applicable international standards do not exist: A closer examination of the definitions, guidance texts and procedures developed by the CCRVDF reveals that the Codex Alimentarius does not address residues of substances without an ADI/MRL. In cases where JECFA has decided not to establish an ADI or to propose an MRL (for various reasons), such substances are abandoned and disappear from the adoption procedure. In consequence, the Commission does not consider risk management measures for such substances. Since JECFA has evaluated only less than a third of the active compounds used in food animals, the majority of veterinary drugs used have not been considered and MRLs have not been adopted for their residues by Codex. CCRVDF has not fully complied with its initial mandate to evaluate, as a priority, those veterinary drug residues which pose a significant threat to human health and risk to international trade. In stark contrast to the

³ CAC/GL-1997 “Guidelines for the Exchange of Information between Countries on Rejections of Imported Foods”.

progress made by national and regional authorities, Codex has adopted comparatively few MRLs for veterinary drugs.

The absence of international standards creates significant trade problems since some member countries may ban, and others may tolerate the use of certain drugs. A ban often involves a zero-tolerance approach, which in practice means that the detection capability of the analytical method applied by the control laboratories of a country determines what levels of residue are tolerated. Debate also arises about what analytical methods should be employed and the residue levels at which a food is considered to be unsafe and should be destroyed. It is noted that these activities often do not involve formal risk consideration steps. Routine arbitration procedures do not exist and their development would be helpful. FAO and WHO shall study the feasibility to develop such procedures and to implement a corresponding system.

Other substances without a Codex MRL: A complication exists with substances which have not yet been evaluated by JECFA, or for which JECFA did not have sufficient information to complete the assessment, but which have been approved by national authorities. They have no Codex MRL but many of them are recognised to be safe and are used widely.

It is also recognised that, in some countries, many drugs are used in animal species for which neither JECFA nor national authorities have established MRL as a result of a lack of data.

Weakness of Codex: In summary, the Codex Alimentarius does not contain a comprehensive set of standards that could be implemented by countries to control the use of safe as well as unapproved drugs. In this area Codex has failed to promote harmonisation at an international level which results in a patchwork of national solutions. This failure is the major factor for the issues and problems that were reviewed and analysed by this workshop.

On the other hand, it was noted that guidance from the Codex Alimentarius on the exchange of information between countries on rejections of imported foods (CAC/GL 25), is not considered and implemented by member countries in the case of residues.

Weakness of the SPS notification system: The notification procedure of SPS that should be followed if national measures are developed seems to be inadequate and does not assure a consultation and involvement of exporting countries during the development and implementation of new methods. Language problems (documents may not be available in English), insufficient technical information, the short period of 60 days, the lack of capacity and co-ordination to comment in a rapid fashion are issues that weaken the system. New analytical methods are rarely communicated by this route.

8. Capacity building.

Status quo & state of the art

The capacity of a country to produce food that is acceptable for the national and international market is governed by a number of factors. These include the existence of national legislation and its implementation through registration, inspection & testing agencies, and communication of the principles of good manufacturing practices (GMP), GVPs and good agriculture practices (GAP) to stakeholders. Capacity building, focussing on quality control along the food chain, is required in a country when the activities of national government and/or the demand from international trade do not ensure the existence of effective enforcement of regulations and the integrity of the food chain or sufficient resources are not available to deliver an effective production control programme.

Building national capacity for the effective control of veterinary drug residues in food is frequently driven by the growth of consumer demand for safer food (either in the local market or the international market). Ensuring adequate national capacity in the production and control of food is to the advantage of consumers not only in the developing countries, but also in the developed world.

Currently there is a wide diversity in the capacity of developing countries (and economies in transition) to produce food of the standard required for local and international markets, as noted in Chapter 6.

Analysis of gaps & identification of problems

Effective capacity building requires a global vision and commitment at the highest political level to improving the quality of life for the global population. Capacity building may be provided by a number of bodies. These include international agencies and bilateral country agreements at national level. However, there is limited global co-ordination in the provision of capacity building.

The ability of developed countries to provide technical expertise to developing countries (and economies in transition) is limited by the availability of financial support by the host institution and the willingness of national governments to provide technical experts to visit developing countries. In addition, there is a perception, in some areas, that the provision of technical expertise can be viewed as “building up the ability of competitors to compete” for a share of the home market. There may also be a similar perception between countries within the same region that are competing for the same export markets.

It is important that capacity building is approached in a holistic manner. For example, technology transfer to developing countries, through the provision of technical expertise, will not necessarily address gaps in the legislative framework in the recipient country. It is necessary to ensure that all aspects of a nation’s capacity are enhanced by capacity building – and not just the laboratory infrastructure.

To achieve effective use of limited funds, it is essential that capacity building is directed to the most appropriate sector in the recipient countries. Most international agencies provide capacity building solely to government agencies. However, it is common practice in some developing countries for private sector laboratories to play a major role in the delivery of laboratory services in support of National Residue Control Plans. In order to ensure that the competent authority has the knowledge and expertise effectively to audit the work of the private sector it is important that the capacity of the state sector is fit-for-purpose. The state sector can then, if desired, transfer the technology to the private sector. Technology transfer from the private to the public sector is likely to pose problems of commercial confidentiality and is less likely to work effectively.

A major impediment to the capacity development in some countries is a basic lack of awareness of the roles and responsibilities of international agencies (e.g. Codex). The lack of a political will to understand and benefit from the activities of Codex, coupled with a lack of support for Codex contact officials in national administrations, reduces the ability of developing countries to benefit fully from their membership of these agencies. Similarly, the lack of a fully-developed national position regarding Codex policy hinders the effective flow of information from Codex to national authorities and vice versa.

Understanding the exact requirements of major trading blocks in matters concerning the quality and safety of food of animal origin poses a major difficulty for developing countries. Although many country’s requirements are publicly available on the Internet, much of the material is not in a form that is readily understandable. For example, understanding the recent changes in EU performance criteria required for analytical methods have caused considerable difficulties for developing countries.

Generation of revenue in many developing countries involves the exploitation of natural resources to produce food, in excess of national requirements, for the purposes of export. This has frequently been done in a non-sustainable way. It is important to ensure that future developments are carried out in a more sustainable manner. It is also important to ensure that primary producers are adequately educated to ensure that they use licensed alternatives to the drugs (e.g. nitrofurans, chloramphenicol) that have caused the recent major problems in international trade.

9. Conclusions and recommendations

Progress of analytical methods and impact on international trade

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.

The analytical laboratory has to develop adequate sample preparation procedures in cases of analysis of processed foods to ensure appropriate analysis of matrices of animal origin.

To facilitate transparency and the sharing of scientific analytical methods for the control of residues, it is recommended that FAO, in cooperation with other international agencies, develop an international network among official residue control laboratories.

Analysis and management of risk of low level residues

Mathematical tools such as the Benchmark Dose approach, low dose extrapolation and others can make better use of dose-response information so that it is possible for the risk manager to use the estimate of the risk to the human consumer at different exposure levels to manage the risk. It is recommended that the CCRVDF request that the JECFA use tools such as these to provide risk estimates when there is no ADI or MRL.

For compounds with extensive human use, clinical, non-clinical, and epidemiological data may be used to provide information on the dose-response characteristics of the drug. These data may be evaluated using mathematical extrapolation techniques such as the Benchmark Dose approach to estimate the concentration of veterinary drug with no appreciable risk in food or to estimate the risk of a given concentration of the drug in food.

CCRVDF and the JECFA for Veterinary Drugs should work with the Joint FAO/WHO Project to Update the Principles and Methods for the Assessment Chemicals in Food to evaluate additional tools to assess the risk of veterinary drug residues, particularly in those instances where an ADI may not be established. Closer interaction between risk managers and risk assessors should result in the development of different approaches to the risk analysis of low level residues.

The JECFA meetings evaluating food additives and contaminants, and some national/regional authorities (FDAs Center for Food Safety and Applied Nutrition, European Commission) have validated the approach of a threshold of toxicological concern for low level exposure to certain classes of compounds (examples include flavouring agents and food contact materials as indirect food additives). It is recommended that Codex work in conjunction with JECFA to consider margin of exposure and threshold of toxicological concern approaches being considered by Australia and Japan, respectively, as discussed in the working papers of this workshop. Approaches being considered by international activities (link with other ongoing activities) such as Joint FAO/WHO Project to Update the Principles and Methods for the Assessment Chemicals in Food should also be addressed.

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 low level exposure of consumers to the residues of the veterinary drug. Such risk estimates would be useful for management of risks associated with the residues.

Risk assessments by JECFA

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.

Regulatory framework at the national and regional level

Governments should develop and implement food safety regulatory frameworks with the participation of all stakeholders to ensure sustainability of safer food animal products.

Governments should focus on preventive measures for residue control to ensure compliance with science-based national food safety standards (e.g., MRLs) through good veterinary practice in accordance with Codex Guidelines on the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods (CAC/GL 16-1993).

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.

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

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.

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

International regulatory framework provided by Codex and WTO

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 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.
 - i. 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.
 - ii. 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 only and MRL should then 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 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.

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

Capacity building

When Codex documents are updated or developed, this should be done in a way that the texts are easily understandable and readily implementable.

Some developing countries require specific advice and technical assistance on:

- Legislation pertaining to the responsible use of veterinary medicines and on the control of production, importation, registration and distribution of veterinary medicines. Individual countries should make a formal request to OIE and FAO for assistance.
- Risk analysis of drugs without ADI/MRL. Individual countries must specify their exact needs to FAO and WHO.
- Organisation of forums and formulation of training modules to promote the responsible use of veterinary medicines at farm level, explaining the possible economic & public health consequences of misuse/abuse of veterinary medicines. This should be addressed by FAO.
- The theory and practice concerning the application of appropriate analytical methods. This may be directed towards screening technologies and/or towards more sophisticated confirmatory technologies, as dictated by the needs of the individual country. This should be addressed, to the Joint FAO/IAEA Division at IAEA.
- Best practice on analytical method validation and assessment of Measurement Uncertainty according to international guidelines. This may be addressed by seeking technical assistance from international funding agencies.

International bodies and governments that fund international research projects should give preference to those project applications that incorporate developing countries as end-users of the developed technologies and processes. This would enhance the funding body's capacity building efforts and would ensure that developing countries have an opportunity to be associated with state-of-the-art international research.

International agencies should work more closely together to ensure the efficient use of the funds available for capacity building at a global level. This may be facilitated by interaction with the Standards and Trade Development Facility (STDF). This facility is managed by FAO, WHO, World Bank, WTO and OIE.