codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 7 **CX/RVDF 04/15/5**
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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

PROPOSED DRAFT CODE OF PRACTICE TO MINIMIZE AND CONTAIN ANTIMICROBIAL RESISTANCE

COMMENTS AT STEP 3

Comments submitted by Canada, Colombia, Ecuador, Egypt, Finland, Japan, Malaysia, Consumers International, IFAH and OIE in response to CL 2003/40-RVDF

GENERAL COMMENTS

CANADA

Canada would like to compliment the US delegation for taking the lead in re-drafting the Code of Practice, in which Canada participated.

This version of the draft provides a comprehensive approach to minimizing and containing antimicrobial resistance.

Canada recommends further revision of this draft in line with the comments provided below.

COLOMBIA

Colombia would like to thank the United States of America and the drafting group the efforts to prepare and update this version of the draft Code of Practice to minimize and contain antimicrobial resistance.

Colombia is generally in agreement with the drafting document and its scope, but we would like to make the following observations:

EGYPT

We have the pleasure to address the following comments:

1. It's appreciated to keep with Codex mission to consider the ecological factors when dealing with persistence of resistant microorganisms.

2. We have to consider the role of control authorities in the activities concerned with the control of spreading resistant microorganisms.
3. The prescription of veterinary drugs has to be practices according to the national regulations.

FINLAND

Finland would like to thank the working group on the revised proposed draft code of practise to minimize and contain antimicrobial resistance. It is clearly a step forward in having effective antimicrobials available also in future.

However, Finland wants to point out that according to our experience, antimicrobials are not needed as feed additives for production animals. Currently there is a voluntary agreement in Finland not to use antimicrobial growth promoters as feed additives. We believe that this will decrease the general selection pressure on pathogens and keep antimicrobials effective for the treatment of diseases.

We would like to recall that FAO/WHO/OIE have conducted recently two expert meetings on non-human antimicrobial usage and antimicrobial resistance and that the Codex Food Hygiene Committee (CCFH) at its 36th session 29 March - 3 April 2004 supported the establishment of a Codex/OIE Task Force to develop broad risk management options. Finland is of the opinion that the establishment of the Task Force should be taken into account when further considering the development of this document.

JAPAN

Japan supports the development of a Code to minimize the potential adverse effect of antimicrobials on public health through their responsible and prudent use. We are glad to have an opportunity to provide following comments for consideration.

MALAYSIA

Malaysia would like to support Australia's comments with regards to replace the term "non-therapeutic use" with the term "prophylactic use" and agrees to the definition proposed by Australia.

Malaysia agrees that the drafting group establishes criteria and/or definition for a critical human disease(s) and drugs of importance to human medical therapy.

CONSUMERS INTERNATIONAL

CI welcomes this opportunity to provide further comments on the CCRVDF Revised Proposed Draft Code of Practice to Minimize and Contain Antimicrobial Resistance (RPDC). CI has participated in the drafting process at earlier stages, including participating in the drafting group that worked on the document now under consideration. CI is concerned that through the drafting process the goal of the draft code " to minimize the potential adverse impact on public health resulting from the use of antimicrobial in food producing animals, in particular the development of antimicrobial resistance" has not always been kept in focus. We are submitting these comments in the hopes that they may help to refocus the document towards its stated goal of protecting public health.

If the RPDC is to actually lead to reduced antimicrobial resistance, it must include recommendations that lead to reduced antimicrobial use. The RPDC does this for antimicrobials used for growth promotion stating that antimicrobials should not be used as growth promoters in the absence of a risk based evaluation. While we strongly support this step, growth promotion is not the only area where antimicrobials are overused. Evidence from Europe where antimicrobial use data is available shows that animal drug use varies drastically between countries independently of animal health needs. This clearly indicates that much work needs to be done to reduce the overuse of these important animal drugs. CI believes strongly that medically important antimicrobials should be used only for disease treatment except in rare situations where needed for control of outbreaks despite use of good husbandry practices. Whenever possible non-antimicrobial methods should be used to prevent disease. Unfortunately, the current draft does not sufficiently emphasize the need to reduce overall antimicrobial use.

CI is also concerned about attempts to introduce a risk/benefit analysis into the evaluation of the risks associated with antimicrobial use. The purpose of the RPDC is to address the risks to public health from antimicrobial resistance (AMR). Thus, it is not appropriate to take into account benefits *other than* public health benefits of antimicrobial use for drugs that are, or may become, important in human medicine. Moreover, given the inevitability of resistance developing whenever antimicrobials are used, the claimed public-health benefits of antimicrobial use animals should be viewed with caution, and non-antimicrobial methods for reducing foodborne disease should be pursued.

IFAH

IFAH, the International Federation for Animal Health, is the federation representing manufacturers of veterinary medicines, vaccines and other animal health products in both developed and developing countries across five continents. As such, IFAH has considerable interest and participates in the work of Codex.

IFAH appreciates the opportunity to comment on the Revised Proposed Draft Code of Practice to Minimize and Contain Antimicrobial Resistance that has been developed by a Working Group of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF). Comments were requested by Codex Alimentarius in CL 2003/40-RVDF. Our comments will be grouped as general, specific or editorial. The numbering of our comments will correspond to the paragraph number in the Code.

The CCRVDF should give careful consideration to the impact the recent recommendation to create a Codex Task Force on Antimicrobial Resistance will have on the development of this Code of Practice. This Code of Practice will not even be a Step 3 document at the October meeting of CCRVDF. As CCRVDF only meets every eighteen months, a new Task Force on Antimicrobial Resistance may require that this Code be put on “hold” until the work of the Task Force is completed.

The term “veterinary medicinal products” is used throughout the Code of Practice. As antimicrobials are not limited to use in medicinal products, the term “antimicrobial veterinary drug” should be used in the document. Codex provides a definition of a veterinary drug.

Anticoccidials are only mentioned in the Glossary and Definitions of Terms section of the Code. The inclusion of anticoccidials as antimicrobials is technically correct. However, within the text of the document, the general term antimicrobial is used, which by default includes anticoccidials. For many anticoccidial products, such as polyether ionophores, there are no genetic mechanisms of resistance and no human use. Therefore, there is no issue with respect to minimizing and containing antimicrobial resistance. The introduction and glossary should be amended to note this fact.

The document provides general guidance to a variety of groups such as regulatory authorities, drug sponsors, veterinarians and allied organizations with the goal of minimizing and containing antibiotic resistance. The focus is solely on the approval and use of antimicrobial products; there is no consideration given to other interventions within the food chain that could effectively minimize transfer of antimicrobial resistant foodborne bacteria to humans. For example, significant contributions to minimizing antimicrobial resistance can be made by prevention of cross-contamination of animals pre-slaughter and prevention of contamination of carcasses with faeces. These aspects should be addressed in these recommendations.

The stated objectives of the Code are "to minimize the potential adverse impact on public health," "to protect the health of consumers," and "Protect consumer health by ensuring the safety of food of animal origin intended for human consumption." The Code focuses on the "potential" to impact resistance to antimicrobials used in human medicine, yet does not acknowledge the demonstrated positive impacts of antimicrobials with respect to human health. Although antimicrobial resistance is a concern, the overall concern should be human health. If elimination of an antimicrobial because of resistance results in more harm to human health than benefit, the objective will not be met. Thus, all aspects of the risk/benefit of antimicrobial use must be taken into account. The present document does not recognize that antimicrobials can result in a safer food supply. Therefore, the following changes should be made throughout the document: "risk-based" to "risk/benefit-based" and "risks" to "risks and benefits."

IFAH appreciates this opportunity to provide comments and welcomes additional clarifications should they be needed.

OIE

The 12th Session of the Codex Committee on Residues of Veterinary Drugs in Foods reviewed the CX/RVDF 03/6 document. This document was overhauled by a Working Group on July 14th and 15th, leading to the revised document CL 2003/40-RVDF referred to in this letter.

The OIE hereby notes the outstanding work done to this day and underlines the importance of having access to internationally established good practices in regards to the use of antimicrobials, both for the sake of public health and animal health.

This paper also underlines the importance of regularly reviewing existing documents, especially since the project amended during the July 14th-15th 2003 Session draws on the official OIE guidelines for a responsible and prudent use of antimicrobials in veterinary medicine (international standard adopted in 2003 by member countries of the OIE and integrated into the *Sanitation Code for Land Animals*).

However, the ongoing Codex procedure leads to the duplication of some works resulting in a waste of resources, without eliminating the risk of eventual discrepancies and inconsistencies among the various texts.

Furthermore, in the wake of works and results of the tripartite FAO/WHO/OIE meeting, held in Oslo from March 15th to March 18th, I suggest that this item be discussed within the OIE Codex Task Force on Antimicrobial Resistance, to be implemented soon. It would allow for defining the methodology to be developed in order to update and promote existing OIE standards while avoiding the aforementioned redundancies.

As far as I am concerned, I would recommend that the emphasis be put on improving existing standards, within the jurisdiction of Codex and OIE, rather than drafting new reference documents duplicating existing ones.

Thus, I suggest that current works relating to this paper be continued based on future recommendations of the aforementioned Codex/OIE Task Force.

SPECIFIC COMMENTS

INTRODUCTION (paras 1-5)

CANADA

Page 2, paragraph 3: "A number of codes of practice relating to the use of antimicrobials and the conditions there of have been developed by different organisations." It would be helpful to provide an appendix listing and detailing these Codes of Practice.

ECUADOR

Under INTRODUCTION, item 4. The document should make clear that the Code of Practice should be used not only with respect to food-producing animals and companion animals, but also with respect to any animal species used, kept or feed by humans. We consider that animals grown for other purposes that food such us pelts, draft, etc. or kept for research and zoos should be included too. Perhaps the concept should be extended to any animal who may be treated with antibiotics by humans.

JAPAN

The last sentence of paragraph 1 should be modified as follows:

> This document defines the respective responsibilities of authorities and groups involved in the authorization**, control**, production~~, control~~, distribution and use of veterinary antimicrobials such as the national regulatory authorities, the veterinary pharmaceutical industry**, pharmacists**, veterinarians~~,~~ ~~pharmacists~~ and producers of food-producing animals.

Rationale:

To make the wording coincide with the order of contents of the Code.

AIMS AND OBJECTIVES (paras 5-8)

CANADA

Page 3, item # 8, bullet # 5: Restricting the use of growth promoters that belong to or are able to cause cross resistance to classes of antimicrobial agents used in humans, whereas in paragraph 9 (last sentence) states the use of growth promoters that belong to classes of antimicrobial agents used in humans and animals should be terminated. For consistency in wording, both paragraphs could state the following: “The use of antimicrobial agents in food-producing animals should be restricted if they are also used in humans. Any decisions on the restricted use of products should be based on a scientific risk analysis”.

JAPAN

The third item in paragraph 6, "Prevent the contamination of animal derived food with antimicrobial residues which exceed the established MRL", should be deleted.

Rationale:

> This item cannot be an aim or an objective of the "recommendations intended to prevent or reduce the selection of antimicrobial resistant microorganisms". The necessity of preventing contamination which exceeds the established MRL is not specific to antimicrobials.

CONSUMERS INTERNATIONAL

Paragraph 7

Add a third bullet: “Regulatory authorities should also assess the transfers of both antimicrobials and resistance determinants via disposal of wastes from food animals, particularly those raised in confined animal feeding operations”

Paragraph 8

Paragraph 8 in general does not include the public health community among those professionals who are to be involved in assuring responsible use of antimicrobials. Public health professionals are responsible for developing and maintaining surveillance of AMR and for investigating human cases of AMR infections. Exclusion of these professionals runs counter to the often-expressed commitment of FAO/WHO/OIE to coordinate and communicate among their professional communities. Because of the multiple pathways by which AMR is transferred from food animal production to human it is essential for public health professionals to be involved in the assessments, evaluations, and control measures.

3rd Bullet Add the following sentence at the end of the third bullet point. "Other therapeutic options should be considered prior to antimicrobial therapy when available."

5th bullet This bullet restricts the use of antimicrobials for growth promotion "in the absence of a risk-based evaluation" but fails to include a standard for what such an evaluation should show. It is important to add "showing that such use does not contribute to resistance affecting humans." Because available data indicate that it is extremely unlikely that such a finding can be made for many antimicrobials, this document should avoid encouraging use of antimicrobials for growth promotion. Moreover, recent analyses in the EU and the U.S have demonstrated there is little economic justification for such uses. A strong statement in this regard is of great urgency, given the rapid spread of industrialized food animal production methods worldwide.

IFAH

Paragraph 7.

This paragraph should be deleted. Environmental concerns are outside the mandate of Codex. The second principle concerning the role of science in the Codex decision-making process states "When elaborating and deciding upon food standards Codex Alimentarius will have regard, where appropriate, to other legitimate factors relevant for the health protection of consumers and for the promotion of fair practices in food trade." However, the Criteria for the Consideration of the Other Factors Referred to in the Second Statement of Principle states "only those other factors which can be accepted on a world-wide basis, or on a regional basis in the case of regional standards and related texts, should be taken into account in the framework of Codex.

Paragraph 8.

The fifth bullet states that "The responsible use of antimicrobials in food-producing animals: does not include the use for growth promotion of antimicrobials that belong to or are able to cause cross resistance to classes of antimicrobial agents used (or submitted for approval) in humans in the absence of a risk-based evaluation." However, the third bullet of paragraph 51 conflicts with this statement by limiting the use of antimicrobials to diseased animals or animals requiring therapeutic treatment. The third bullet in paragraph 51 should be deleted.

Also in the fifth bullet is the statement "focus on the potential to impact resistance to antimicrobials used in human medicine." This should be changed to "focus on the impact to adversely affect human health, including the potential negative impact of antimicrobial resistance and positive impact of a healthier food supply."

RESPONSIBILITIES OF THE REGULATORY AUTHORITIES (paras 9-16)

CANADA

Page 3, item # 9: Responsibilities of the regulatory authorities: This section should also include the following statement: "Strategic policies relating to prudent and judicious use of antimicrobials are needed and their development and application depend on research, surveillance, education, infection prevention and control efforts".

COLOMBIA

In paragraph 9 we find that the text should be reference to the “Good Practice on Animal Feeding” specifically to restrict the use of antimicrobials to therapeutic use and therefore should in principle only be available on prescription.

In paragraph 11 the sentence should preferably be modified as follows: “The use of antimicrobials agents in food-producing animals, under anything form and route of administration, requires a marketing authorization, granted by the competent authorities, only if safety, quality and efficacy are met”.

JAPAN

Paragraphs 13 and 34 should be modified as follows:

> 13. The relevant authorities should make sure that all the antimicrobial agents used in food-producing animals are prescribed by a veterinarian or other suitably trained person authorized in accordance with national legislation **or used under conditions stipulated in the national legislation**. (See OIE Guidance on Antimicrobial Resistance: Responsible and Prudent Use of Antimicrobial Agents in Veterinary Medicine http://www.oie.int/eng/ publicat/rt/2003/Anthony.pdf.)
>
> 34. The relevant authorities should make sure that all the antimicrobial agents used in food-producing animals are, to the extent possible:
>
> - prescribed by a veterinarian or other suitably trained person authorized in accordance with national legislation **or used under conditions stipulated in the national legislation**;

Rationale:

Systems for regulations of antimicrobial agents used in food-producing animals vary among countries reflecting different purposes and methods of use. The prescription by a veterinarian or other suitably trained person is not the only practical way to secure the food safety. In such countries where prescriptions are not obligatory, the conditions of use should be determined and written in the national legislation on the basis of risk assessment.

The words "antimicrobials", "antimicrobial agents", "veterinary antimicrobials", "veterinary medicinal products" and other similar terms seem to be used without clear distinction. The word "antimicrobials" should be applied for substances and the word “veterinary medicinal products” should be applied for commercial products.

CONSUMERS INTERNATIONAL

Paragraph 12

CI supports the intent of this paragraph, but we strongly disagree with the last sentence, which proscribes examinations that are “generalized to the class of antimicrobials to which the particular active principle belongs.” The whole issue of AMR is mechanism-based, not product-based: bacteria develop resistance to, for example, the class of fluoroquinolones, not to enrofloxacin, ciprofloxacin, etc. For that reason, it is essential for this issue (the contribution of agricultural antimicrobial use to AMR) that all examinations and assessment MUST be mechanism-, not product-based, and use of class-based approaches should be endorsed rather than criticized. We consider that Paragraph 14 has similar problems.

Paragraph 13

To clarify the scope of this recommendation, insert after “food-producing animals” the following “(including additions to feed for growth promotion)”.

Paragraph 14

The second sentence is out of place in this paragraph since it is not clear simply why expediting market approval processes for new antimicrobial-containing formulations will "have the potential to make an important contribution in the control of antimicrobial resistance". Recent history indicates that without specific attention to AMR, new approvals only create new resistant strains, or amplify existing resistance determinants through cross-resistance mechanisms. Sentence three in paragraph 14 should be modified to indicate that restrictions should be placed on off-label use of antimicrobials that are important for human medicine. The final sentence should indicate that national authorities should require specific conditions for off label use. Paragraph 14 would then read as follows: "No antimicrobial should be administered to animals unless it has been evaluated and authorized for such use by the relevant authorities or the use is allowed through off-label guidance or legislation. Off-label use should not be allowed for antimicrobials that are important for human medicine. For other antimicrobials, if off-label use is allowed it should only be authorized under a valid veterinarian/client/patient relationship, it should only be used for disease treatment, and it should not result in a violative food residue."

Paragraph 15

Responsibility for prudent use of veterinary medicinal products should be shared among countries, particularly since many of these products will be exported by manufacturers headquartered in industrialized nations to those countries lacking the resources described in this paragraph. We suggest an additional bullet: "International efforts should be made to assist in the development of competence in managing these products in developing agricultural sectors, including technology transfer for monitoring AMR in humans, food animals, food, and the environment, as well as sharing experience to avoid repetition of national experiences with development of AMR after drugs are registered for agricultural use, particularly on a herd-wide, flock-wide, or school-wide basis. International assistance should also be provided to assist developing agricultural sectors to avoid the use of antimicrobials for growth promotion, through prudent animal husbandry. Manufacturers should ensure full transfer of information and adequate training to national marketers and end users." We note that this additional bullet is consistent with CCRVDF's endorsements of international cooperation among countries in developing technology related to residue analysis.

Paragraph 16

Focus should not be limited to illegal and counterfeit products, but also include combating inappropriate marketing, advertising, and other promotion of pharmaceutical products for uses not in accord with these guidelines.

IFAH

Paragraph 11.

The first bullet states "The examination of dossiers/drug applications must include an assessment of the risks to both animals and humans resulting from the use of antimicrobial agents in food-producing animals." IFAH strongly endorses the concept that the assessment should include risks and benefits to both animals and humans. Of particular importance are those benefits to animals that result in increased human safety. The words "only if" should be replaced with the word "when."

Paragraph 14.

Listing of antimicrobials that are of "critical importance for human medicine" needs better definition. The Oslo meeting has this as an Action Item so perhaps this phrase should be deleted for now or until a generally agreed definition can be provided. By default, the Consequence section of a sponsor driven risk assessment will actually describe the clinical consequences of antimicrobial resistance in humans, so the need for such a list is not clear. In order to develop such a list, a risk assessment actually needs to be done.

QUALITY CONTROL OF ANTIMICROBIAL AGENTS (paras 17)

No comments received

ASSESSMENT OF EFFICACY (paras 18-23)

No comments received

ASSESSMENT OF THE POTENTIAL OF ANTIMICROBIALS TO SELECT FOR RESISTANT MICROORGANISMS (paras 24-25)

CANADA

Page 5-6, item # 25, bullet 1 and 4, Please add:

Bullet 1: the route and level of human exposure to food-borne or other resistant organisms.

Bullet 4: The concentration of active compounds in the gut of the animal (enabling the derivation of microbiological ADI) at the defined dosage level.

IFAH

Paragraph 24.

The likelihood of getting much information from clinical trials as an "add-on" by taking samples during the live-phase is low.

ESTABLISHMENT OF ADIS (ACCEPTABLE DAILY INTAKE). MRLS (MAXIMUM RESIDUE LIMIT), AND WITHDRAWAL PERIODS FOR ANTIMICROBIAL COMPOUNDS (paras 26-28)

CANADA

Page 6, item # 27: Please add the following statement: "The determination of withdrawal periods should also take into account microbiological considerations, including AMR".

ESTABLISHMENT OF A SUMMARY OF PRODUCT CHARACTERISTICS FOR EACH ANTIMICROBIAL FOR FOOD PRODUCING ANIMALS (para. 29)

CANADA

Page 6 item # 29 Please add:

- Class of antimicrobial

SURVEILLANCE PROGRAM (paras 30-33)

CANADA

Page 7, item 33: Please include: "Such re-evaluation should be based on a risk-analysis approach".

CONSUMERS INTERNATIONAL

Paragraphs 30-33

CI strongly supports the recommendations for the establishment of effective surveillance systems on the incidence and prevalence of AMR. These systems should be guided by two concepts: relevance to public health (i.e., early and reliable detection of AMR) as well as relevance to detection of problems in agricultural use of antimicrobials. Thus these programs require close interactions among relevant professionals, including public health authorities (see our comment on Paragraph 8).

IFAH

Paragraph 33.

It is implied that surveillance data from a government operated program will be used to require a re-evaluation of the conditions of use of an antimicrobial agent. This implies a threshold or bright-line standard will be set. This also was a recommendation of the Oslo consultation. As mentioned above, this Code may be premature.

DISTRIBUTION OF THE ANTIMICROBIAL AGENTS IN VETERINARY MEDICINE (para. 34)

JAPAN

(see comments on paragraph 13)

CONSUMERS INTERNATIONAL

Paragraph 34

In the first sentence, change "all the antimicrobial agents used" to "all uses of all antimicrobial agents". We believe this change clarifies that this opening sentence addresses all uses, including antibiotics used for growth promotion. The sentence would then read "The relevant authorities should make sure that ~~all the~~ all uses of all antimicrobial agents used in food-producing animals are, to the extent possible:"

CONTROL OF ADVERTISING (para. 35)

CONSUMERS INTERNATIONAL

Paragraph 35

Advertising, particularly to professionals involving in prescribing drugs, and to agricultural purchasers and users, should include information on the hazards of AMR from inappropriate or unauthorized uses. Our recommendation is in accord with codes of practice developed by the pesticide industry. We are aware of very misleading product promotions in certain countries by pharmaceutical sales personal, who also have printed documentation that explicitly encourages use of antimicrobials for growth promotion and encourages farmers to add antimicrobials to feed and water themselves.

IFAH

Paragraph 35.

This paragraph on "Control of advertising" should be deleted. There is no definition of advertising within Codex. Advertising by itself is not within the mandate of any Codex committee. Also, national legislation is not consistent among Codex member countries. Therefore, any statements about advertising within a Codex document would lead to inconsistent measures between member countries.

TRAINING OF ANTIMICROBIAL USERS (para. 36)

CONSUMERS INTERNATIONAL

Paragraph 36

Once again, public health professionals and health care givers need to be included in this training

DEVELOPMENT OF RESEARCH (para. 37)

CONSUMERS INTERNATIONAL

Paragraph 37

We support the need for further research but make the following recommendations.

3rd Bullet This bullet should be clarified to focus it on the selection and spread of antimicrobial resistant organisms and resistance determinants. We recommend changing this bullet to read as follows: " develop practical methods for applying the concept of risk analysis to assess the public health concerns associated with the selection and dispersal of resistant microorganisms and resistance determinants."

5th Bullet Modify to state "develop and encourage the use of non-antimicrobial methods to prevent infectious diseases."

COLLECTION AND DESTRUCTION OF UNUSED PRODUCTS AND CONTAINER (para. 38)

No comments received

RESPONSIBILITIES OF THE VETERINARY PHARMACEUTICAL INDUSTRY

MARKETING AUTHORISATION OF ANTIMICROBIALS FOR FOOD-PRODUCING ANIMALS (paras 39-40)

CONSUMERS INTERNATIONAL

Paragraph 39 (also 42)

We recommend addition of a bullet stipulating the responsibilities of the industry to ensure accurate advertising and product promotion that emphasizes the importance of controlling AMR, including sound management of animal wastes and avoidance of growth promoter use of antimicrobials in feed and water.

IFAH

Paragraph 40.

There is little incentive for sponsors to undertake product line extension research on "older" products because of all the new requirements such as those included in the Code. It is unlikely to be cost-effective to do so. Another issue that impacts this type of research is generic drugs. Even if a sponsor obtains exclusivity for a line extension, it is difficult for regulatory authorities to enforce.

MARKETING AND EXPORT OF VETERINARY MEDICAL PRODUCTS (para. 41)

ECUADOR

Under MARKETING AND EXPORT OF VETERINARY MEDICINAL PRODUCTS, item 41. The document suggests that veterinary medicinal products should meet quality standards of the country in which they were produced. Quality standards vary from country to country and only because a given country produces veterinary medical products does not necessarily mean that they comply with adequate quality standards. We suggest that in such case, that both importer and exporter countries should agree in using the most detailed and strict standards of either one. If the producer has the most detailed and strict standards, the user will be most benefited. On the contrary, if the most detailed and strict standards are held by the importer, it is for his best interest to have the product comply with his standards.

IFAH

Paragraph 41.

The first bullet should be changed to: "Only antimicrobial veterinary drugs meeting the quality standards of the importing country should be exported from a country in which the products were produced." The manufacturers of veterinary products have the primary responsibility of producing products that meet the quality standards of the country in which they are used.

ADVERTISING (para. 42)

IFAH

Paragraph 42.

For the reasons given above, this paragraph on advertising should be deleted.

TRAINING (para. 43)

No comments received

RESEARCH (para. 44)

No comments received

RESPONSIBILITIES OF PHARMACISTS AND/OR DISTRIBUTORS (paras 45-47)

CANADA

Page 9, item # 46: Please replace "Pharmacists" with "Prescribing and dispensing professionals" because in some jurisdictions, pharmacists are not the only ones dispensing antimicrobial drugs.

IFAH

Paragraph 45-47.

Pharmacists are not relevant sources in many countries, and where they do operate, there may not be many of them.

RESPONSIBILITIES OF VETERINARIANS(paras 48-55)

CANADA

Page 11, item # 54, bullet 4: Please change "a bad choice" to "an inappropriate choice".

ECUADOR

Under RESPONSIBILITIES OF VETERINARIANS, item 51. We recommend that an important issue that veterinarians should recommend is Withdrawal periods. Although the importance of a prescription for antimicrobial veterinary medicines is mentioned, prescriptions usually include drugs, dosages, and treatment periods, but often do not include withdrawal periods. A suggestion should be included in the document for the veterinarian to either include in the prescription or give separate detailed indications on withdrawal periods.

CONSUMERS INTERNATIONAL

Paragraphs 48-55

We strongly support the statements strengthening the responsibilities of veterinarians. It should be made unequivocally clear that these recommendations apply to all uses of antimicrobials.

Paragraph 51

CI strongly supports the recommendation in bullet three that antimicrobials be restricted to treating diseased animals. The following bullet point should be added to this paragraph. When other therapeutic options exist they should be used prior to antimicrobial therapy. If antimicrobial therapy is necessary, antimicrobials considered important in treating infections in human or veterinary medicine should be used in animals only after careful review and reasonable justification. Other antimicrobials should be considered for initial therapy.

Paragraph 53

The lead statement in the second set of bullets should be changes to clearly indicate that the potential to select for AMR must be considered when making choices about antimicrobial use. The lead statement to the second set of bullets in this paragraph should be changed to read " The need to minimize the adverse health impact from the development of antimicrobial resistance based on:"

IFAH

Paragraph 51.

Much of the information required on the prescription would be stated on the product label. This information should not have to be given in the prescription unless off-label use was proposed. The third bullet should be deleted.

Paragraph 54 Bullet 1.

Combinations of antimicrobials may be used because there is a need to medicate for different purposes that cannot be accomplished by the administration of a single product. For example, anticoccidial agents may be used "in combination" with an antibiotic; one is targeted to coccidia, the other for bacteria. This does not exactly "broaden the spectrum of activity." Suggest that a clarification for the rationale is needed.

Paragraph 54 Bullet 2.

Combination prohibitions are generally indicated on the label.

Paragraph 54 Bullet 4 and 5.

These are speculative outcomes that are case-specific and do not warrant separate bullet points. If the projected outcome of a "choice" were to be included in each paragraph of the document, it would become speculative and useless.

OFF-LABEL USE OF ANTIMICROBIAL VETERINARY MEDICINAL PRODUCTS (paras 56-57)

CANADA

Page 11, item # 56: The draft Code should indicate that: "The off-label uses of drugs related to critical human medicine should only be permitted in exceptional circumstances for therapeutic purposes".

CONSUMERS INTERNATIONAL

Paragraph 57

The last sentence should be rewritten for clarity as "Off label use of antimicrobial agents for growth promotion or for purposes other than disease treatment should not be permitted."

RECORDING (paras 58-59)

No comments received

TRAINING (para. 60)

No comments received

RESPONSIBILITIES OF PRODUCERS (paras 61-62)

CANADA

Page 12, item # 62, bullet # 3: Please indicate that: "The off-label use of antimicrobial by producers should be done under the context of a valid veterinarian/patient/client relationship (VPCR)".

Page12, item # 62, Please modify:

-Bullet 10: to maintain all clinical and laboratory records of microbiological and susceptibility tests if required by the national regulatory authority.

-Bullet 11, sub-bullet 6: quantity and duration of the antimicrobial agent administered.

COLOMBIA

In paragraph 61, perhaps the second sentence does not provide sufficient safeguards and should be modified as follows: "they may, call on the assistance of their veterinarian or other suitable trained person authorized in accordance with national legislation, but in certain situation related to suspect zoonotic or official control diseases, the producers have to call a veterinary or a person officially authorized".

In paragraph 62, third item, we suggest this redaction: "to isolate sick animals and dispose of dead or dying animals promptly. In any case could be necessary to practice the necropsy under veterinary assistance".

In paragraph 62, eleventh item; considering of potential consumer risk from antimicrobial drug residues remaining at injection sites, they identification should be including.

CONSUMERS INTERNATIONAL

Paragraph 62

CI also supports the statements stipulating the responsibilities of food animal producers, particularly the emphasis given to good management and farm hygiene in ensuring the health of food animals. We recommend addition of three bullets: "to ensure sound management of animal wastes and other materials to avoid dissemination of antimicrobial agents and resistance determinants into the environment", "to ensure the safety of all personnel and workers in the farm environment to prevent their contact with and transmission of resistant bacteria", and "to assist relevant authorities in surveillance programs related to antimicrobial resistance."

CONCLUSION (paras. 63-65)

EGYPT

Conclusions were comprehensive and reflected what have already been presented.

GLOSSARY AND DEFINITIONS OF TERMS

ECUADOR

Under GLOSSARY AND DEFINITIONS OF TERMS, Growth Promotion. There is no scientific evidence that antimicrobial products increase the rate of weight gain in animals. This is an indirect effect and not a direct effect. Growth promotion occurs when certain hormones and like compounds are used. Antimicrobial substances help controlling microbial growth and products of microbial origin (such us lactic acid) thus reducing the energy spent by the animal in responding the bacterial aggression (by means of immune system, maintaining tissue integrity in the gut and others). Codex should make every effort to keep users of "growth promoter antibiotics" focused in that they are still affecting microbial growth and thus should follow guidance accordingly.

EGYPT

In glossary and definitions of terms, it's advisable to add a third item to antibiotics and anticoccidials which is antimicrobials, not antibiotics including:

Sulphonamides, Quinolones – Nitrofurans as chemically and pharmacologically different from antibiotics.

EDITORIAL COMMENTS

IFAH

6. Change the third bullet to read "…which exceed the established MRLs."

8. Change "risk-based" to "risk/benefit-based."

9. Change "risk-based" to risk/benefit-base."

11. Change "risks" to "risks and benefits."

37. Change "risk" to "risk/benefit."