codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 7 **CX/RVDF 03/6 – Add. 1**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Fourteenth Session

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PROPOSED DRAFT CODE OF PRACTICE TO MINIMIZE AND CONTAIN ANTIMICROBIAL RESISTANCE

COMMENTS

Comments have been received from Australia, Costa Rica, France, European Community

AUSTRALIA

The document is now comprehensive and Australia supports it with a few minor changes as detailed below.

1. It contains some editorial artifacts that are hangovers from earlier drafts and need correct cross-referencing.

- Para 33, 5th dot point - "Part E4" does not exist
- Para 42 - "B10"
- Para 43 - "B11"
- Para 44 - third line "E4"
- Para 55 - "B10"

2. The term "non-therapeutic" is inappropriate as it is used in this document. Australia puts forward the definitions used in the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) report for consideration for use in the Draft Code. These 3 terms recognise that antibiotics can be used in animals in one of three ways:

Therapeutic use - The use of antibiotics for the purposes of inhibiting a pathogen which already infects the host; that is, initiating treatment because there is a disease condition.

Prophylactic use - The use of antibiotics (by any route of administration) to prevent infection with a pathogen(s) that is anticipated to challenge the host during the treatment period; that is initiating treatment in advance of an actual infection or disease condition because such a condition is expected to occur if treatment is withheld. The term **Metaphalyxis** refers to prophylactic mass medication of a whole group of animals.

Growth promotion - The use of substances to increase the rate of weight gain and/or the efficiency of feed utilization in animals by other than purely nutritional means. The term does NOT apply to the use of antibiotics used for the primary purpose of inhibiting specific pathogens even when an incidental growth response may be obtained.

If this terminology is accepted by the drafting group, Australia suggests that the text of the document be changed:

at Para 6: 5th dot point; Para 7 third last line and Para 52 last sentence, to reflect the following principles:

- when used for prophylaxis, should be undertaken for as short a treatment period as is necessary to control and prevent infection or disease.
- should avoid the use, for growth promotant purposes, of antimicrobials that have been shown to cause cross resistance to classes of antimicrobial agents used for therapy or prophylaxis in humans or animals.

3. Para 11, footnote 3 refers to the term "antimicrobials that are important to human medicine" and the need to define this term. Australia suggests that this term does not need definition in this document. Rather the document should put the onus of defining the term and providing a specific list of such antimicrobials on the regulatory authorities or other expert groups in each country, taking into account the availability and use patterns of antibiotics in their human and animal populations.

4. Para 41, second dot point, Since these products are important and their use should always be under veterinary control, this document should make it clear that no direct-to-consumer advertising should take place. Therefore “inappropriately” should be deleted.

5. Para 48, 8th (the last) dot point - it is again not clear what this is intended to mean, but based on dot 5 of para 58 it may be supposed to mean that only diseased animals should be treated. If that is the case it could better read “Antimicrobial agents should be administered only to diseased animals, or those requiring therapeutic treatment, not unaffected cohorts”.

6. Para 52, last sentence - given the concern about non-therapeutic uses, this sentence should be much more strongly worded to say “Off-label, non-therapeutic use of antimicrobials, should not be permitted in food animal species”.

Typographical/Grammar Comments

Para 1 line 6, add **s** to **antimicrobial** (also para 7, line 6, second line page 13, para 61 line 3)

Para 10 line suggest re-write "to administer these products on a prescription only basis , individuals should refer to .." as "to **authorise/supply** these products on a prescription only basis, **users** should **be referred to** ..."

Para 31, dot point 2, delete **s** from **prescriptions**

Para 34, dot point three should be cross-referenced to para 41 which refers to direct-to-consumer advertising

Para 37, **out-dated** should be **out-of-date** (as in para 27).

Para 40, first line - **only** should be **Only**

Para 40 dot two - rewrite to **The information necessary to evaluate the amount of antimicrobial agents marketed should be provided to the national regulatory authority.**

Para 48, dot 3, dash 7 – delete all words after **prognosis** as they are not required and confuse the point

Para 48, dot 6, add **n** to **regime**

Para 57 - why is this not just reworded and included as a dot point in 58?

Para 60 line 3 - replace **therein** with **herein** or **in this document.**

COSTA RICA

The Inter-Institutional Commission formed to address the issue of Antimicrobial Resistance analyzed the document and made the following comments:

- Replace the term "bacterial" with "antimicrobial"

- Include the problems of antimicrobial residues in animal fecal matter.
- Include the issue of the study of residues in plants for export.
- Stress the importance of the environment, referenced in point 29 on page 9. An oversight program is mentioned for evaluating the development of resistance in both animal and food pathogens. It is fundamental to conduct research on how antimicrobial resistance is found in environmental microorganisms, including those that are both pathogenic and non-pathogenic for humans and animals, since this would allow for the expansion of knowledge on the dissemination of resistant microorganisms.
- Include aquifer protection.
- Reconsideration of traditional methodologies for epidemiological oversight in each country.
- Each regulatory body could be considered as an agent for the notification and disclosure of information, thus establishing a flow of information to support the development of strategies, policies and programs and intervention measures in the oversight and/or proper use of antimicrobial agents in animals.
- Section 48 addresses the possibilities of Veterinarians with respect to the selection of an antimicrobial agent. It mentions that if the first antimicrobial line fails, or there is a recurrence of the disease, the second line should be used, based on an antibiogram. It would be advisable for the technical managers of veterinary pharmacies selling, for example, Fluoroquinolones, to have clear instructions that these should only be sold and used if an antibiogram has shown that the isolated microorganism is multiresistant and that Fluoroquinolones are the only alternative.

FRANCE

The French authorities may grant their general approval in principle on this document which is practically a complete reproduction of OIE guideline No. 2 "*Prudent and responsible use of anti-microbial agents in veterinary medicine*."

The French authorities consider it very important that prescriptions of antibiotics be issued by veterinarians or authorized professionals.

Furthermore, it is appropriate to point out two errors: one in paragraph 42 where "*defined in B.10*" should be replaced with "*defined in paragraph 35*" and the other in paragraph 43, replacing "*defined in B.11*" with "*defined in paragraph 36*."

In addition, the French authorities request that paragraph 58 (item 11) be completed with the addition of*: "name of the prescribing veterinary or authorized professionals."*

Finally, the French authorities insist that this document be addressed jointly with the OIE. The reasons for this are as follows:

- antimicrobial resistance is an essential issue in both animal and public health, and therefore within the scope of both the OIE and the Codex;
- the agreement between the Codex Alimentarius Commission and the OIE, signed in 2001, respectively, by the President and Director General of both organizations, specifically identified the issue of resistance to anti-microbial agents as an issue that should be subject to close collaboration;
- the OIE's new working group on food safety has targeted anti-microbial resistance as a future working issue;
- the report on the evaluation of the Codex, to be considered in a special meeting of the Executive Committee and then by the Commission in February, also recommends better coordination and collaboration between the two organizations for all subjects for which they have shared competence.

The French authorities propose that work begin under the auspices of the CCRVDF, it being understood that a reexamination of this issue should be undertaken once the Codex Commission rules on the appropriateness of increased coordination with the OIE and the potential methods for sharing duties or launching joint projects.

EUROPEAN COMMUNITY

The European Community would like to thank the United States of America and the drafting group for the preparation of this draft Code of Practice to minimise and contain antimicrobial resistance. The efforts undertaken by the United States of America to achieve consensus on the text in the drafting group is highly appreciated.

The European Community is generally in agreement with the drafting document and its scope, although there are concerns related to animal and consumer safety with respect to the wording of the paragraphs on requirements for prescriptions for antibiotic veterinary medicinal products and the phasing out of antimicrobials for non-therapeutic use.

Furthermore, the decision of the drafting group to refer the matters of definitions of non-therapeutic and therapeutic use as well as criteria to be applied for the definition of a critical human disease and drugs of importance to human medicinal therapy to CCRVDF is supported. The European Community notes that a definition for a veterinary medicinal product has already been adopted at the first session of CCRVDF, which include therapeutic, prophylactic or diagnostic use or use with a view to modify physiological functions of behaviour. Thus, non-therapeutic use could be defined by exception of therapeutic use from this definition. The European Community proposes the following definition for discussion in the plenary session: *"non-therapeutic use of antimicrobial means any use of these substances which is not intended to treat or prevent a specific diagnosed disease. It includes for example the use of antimicrobials as growth promoter*."

The European Community finds that a definition of critical human diseases and drugs of importance to human medicinal therapy should not be pursued due to regional variations and evolution in the disease patterns. It is nevertheless considered that such a general reference could be useful for national governments in their consideration of risk management measures.

As regards the other issues for consideration by CCRVDF, namely environmental concerns and specific guidance on pharmacokinetic studies, the European Community considers these areas outside the scope of both the drafting group and CCRVDF. Development of protocols for scientific studies does not fall within the terms of reference of CCRVDF.

A number of technical comments on the text are provided below.

- In paragraph 10 we find that the text should be revised to restrict the use of antimicrobials to therapeutic use and therefore should in principle only be available on prescription. The reference to the draft guideline published by OIE is questionable as long as it has not been adopted as an OIE standard. Furthermore, there are numerous guidelines on prudent use of antibiotics, which advocate use of antimicrobials on a prescription only basis. The last sentence of paragraph 10 should therefore be deleted. The word food animals in the second sentence should be changed to food producing animals.
- In Paragraph 12 it is assumed that the country in which a veterinary medicinal product is produced automatically also authorises the use of the substance in its own constituency. This is however not the case. A country without the necessary resources to implement an efficient authorisation procedure whose supply mostly depends on import should therefore *"seek information on authorisations valid in other country/countries."* (second bullet point).
- As the scope of the Code is antimicrobial resistance, this should be fully reflected in the document by replacing bacteria with micro-organisms in paragraphs 18 (1st bullet point), 21 (2nd bullet point), 48 (4th bullet point 2nd indent and 5th bullet point 2nd indent). The word antibacterials should be replaced by antimicrobials in paragraph 48 (5th bullet point, 1st and 2nd indent). In paragraph 59, 'bacterial diseases' should be changed to 'infectious diseases'.

- In paragraph 23, 4th line the word '*controls*' is better replaced by '*posology*'.
- In paragraph 26, reference could be made to international guidelines in the area elaborated in the framework of the international co-operation on harmonisation of technical requirements for registration of veterinary medicinal products (VICH) and adopted by some regions.
- In paragraph 30, it is stated that surveillance programmes should be established from the results of a risk analysis. Although the results of risk analyses are very useful in this context, in most cases such results are not readily available. Therefore, the results of risk analyses should not be understood as a precondition for establishing surveillance programmes. Instead the second sentence of paragraph 30 should start as follows "*The relevant authorities should implement a surveillance programme based on their national pattern of use of antimicrobials."*
- In paragraph 34, the 2nd bullet point should read as follows: "*is restricted to authorised professionals and in compliance with each country's legislation. This is considered to be important for the overall restrictions in use of antimicrobials"*.
- Paragraph 40 should read: "*only officially licensed/**authorised** products*….."
- In the title preceding paragraph 46 reference should also be made to the *"other suitably and authorised persons*" mentioned on paragraph 10. Moreover the necessary adaptations should be made in the following paragraphs where reference is made to veterinarians.
- In paragraph 48, 3rd bullet point last indent, the words '*what time*' are better replaced by '*a specified*', and in the 7th bullet point the word '*manufacturer*'s' is better replaced by '*approved*'. The last paragraph of 48 should read "*In circumstances where recourse to accurate diagnosis and microbial susceptibility testing is impossible, but where it is very likely that animals have been exposed to pathogenic bacteria, it may be justified to treat animals nevertheless with antimicrobials in order to prevent the development of clinical disease and for reasons of animal welfare*".
- In paragraph 52, the last sentence does not provide sufficient safeguards for the consumer. In paragraph 7, it is stated that non-therapeutic use should be terminated or phased out in the absence of risk-based evaluations. It is therefore not conceivable that veterinarians have no responsibility in the control of such measures. The last sentence should preferably be modified as follows: "*Non-therapeutic use of antimicrobials should not be allowed, in the absence of risk based evaluations"*.
- In paragraph 58, 6th bullet point, the words "*provisions of the leaflet and package insert*' should be changed to '*approved product labelling"*.