

CODEX ALIMENTARIUS COMMISSION



Food and Agriculture
Organization of the
United Nations



World Health
Organization

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Agenda Item 5

CRD5

ORIGINAL LANGUAGE ONLY

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

AD HOC CODEX INTERGOVERNMENTAL TASK FORCE ON ANTIMICROBIAL RESISTANCE

Sixth Session

Comments of European Union

Mixed Competence

European Union Vote

The European Union and its Member States (EUMS) would like to commend the United States, Chile, China, Kenya and the United Kingdom for leading the work on the revision of CXC 61-2005. The EUMS would like make the following comments on the draft text.

General comments

The EUMS believe that in accordance with the One Health approach efforts should be directed to add value to Codex members' actions with a view to combat antimicrobial resistance and preserve effective treatments of microbial infections.

The revised Code should expand its scope to the whole food chain, including plants/crops production and environment. This is confirmed by the summary conclusions of the FAO/WHO expert meeting of 11-15 June 2018.

Responsible and prudent use of antimicrobials in all sectors is of the utmost importance to preserve the effectiveness of existing antimicrobials and to secure the effectiveness of future ones. At the same time, infection prevention and control and biosecurity measures together with good production and good farming and management practices are critical in the management of infectious diseases as they reduce the need for antimicrobials and consequently the opportunity for microorganisms to develop and spread resistance. Equally, effective actions require the involvement of all stakeholders in the prevention of AMR.

It is important that the revised Code of Practice is consistent with other relevant international guidance, in particular the OIE Terrestrial Animal Health Code. For example, a number of provisions in the current draft text are limited to medically important antimicrobials while according to the corresponding OIE guidance they should apply to all antimicrobials. These discrepancies are addressed in the specific comments.

Points for further comments and discussion at TFAMR6

Definition of plants/crops

The EUMS agree with the current draft definition for plants/crops.

Plant/crop health professional

The EUMS support using the term "plant/crop health professional" instead of "plant/crop advisor or consultant".

Antimicrobials vs. antibacterials

The EUMS support using the term "antimicrobial" with the explanation in paragraph 6.

Medically important antimicrobials

Most provisions which now refer to medically important antimicrobials should cover all antimicrobials. Specific comments are made to this end.

General Principles

General principles should be concise and contain language, which convenes principles instead of giving guidance.

Stepwise approach

The text as currently drafted sufficiently addresses the concerns in relation to the stepwise approach.

Surveillance and monitoring programmes

Since there will be a separate guidance on surveillance and monitoring, there is no need to introduce detailed recommendations in the CoP. The current paragraph 21 is probably sufficient.

Alternatives to antimicrobials

The current text in principle 2 without the footnote sufficiently addresses the issue of alternatives to antimicrobials.

Practices during production, processing, storage, transport, retail and distribution of food

These practices are extensively covered by the codes of hygienic practices. Therefore, there is no need to elaborate them further in this CoP. The current paragraphs 60bis and 60ter could be transferred under the "Responsibilities of food producers".

Specific comments on the proposed draft revised CoP

1. Introduction

Modify the first sentence of **paragraph 2** as follows:

This Code of Practice addresses the responsible and prudent use of antimicrobial agents by participants in the food chain, including the role of ~~regulatory~~ **competent** authorities, pharmaceutical industry, animal health professionals and plant/crop advisors or consultants, and food producers, ~~and processors,~~ **wholesalers and retailers**.

Rationale: It would be consistent with Codex terminology to use the term "competent authority" instead of "regulatory authority" throughout the document. Wholesalers and retailers should be added to cover the entire food chain.

Modify the first sentence of **paragraph 3** as follows

This Code of Practice ~~is an integral part of~~ **complements** risk analysis focusing on risk management...

Rationale: The measures recommended in the code of practice are a result of the risk analysis process rather than being integral part of it.

Paragraph 3bis seems to repeat what is already said in other paragraphs of the introduction. It could therefore be deleted. If retained, then the word "judicious" on the first line should be replaced with "prudent" to ensure consistent terminology.

Paragraph 6 explains that the CoP recommendations will focus on antibacterials, while some recommendations may also be applicable to antiviral, antiparasitic, antiprotozoal and antifungal agents. The EUMS have two remarks: a) if any of the recommendations listed would only be applicable to antibacterials (and not transposable to the other types of antimicrobials), it should be specified in the text to avoid any confusion; and b) it would then be appropriate to move paragraph 6 under the scope as paragraph 7bis.

2. Scope

Modify **paragraph 8** as follows:

This **Code of Practice provides** ~~document includes~~ guidance for all interested parties involved in the authorization, manufacture, sale and supply, prescription and use of antimicrobial agents along the food chain together with those involved in the handling, preparation, ~~food~~ processing, distribution and consumption of food who have a role to play in **ensuring responsible and prudent** ~~optimizing the~~ use of antimicrobial agents and/or who have a role with limiting the development and spread of foodborne antimicrobial resistant microorganisms and resistance determinants.

Rationale: Consistent terminology should be used.

3. Definitions

Delete definitions for "antibiotic" and "antibiotic resistance".

Rationale: the term "antibiotic" is used only twice in the text, and should be replaced by "antimicrobial".

Replace the definition for "medically important antimicrobials" with the following:

Antimicrobial classes used in human medicine, and therefore listed on the WHO CIA List where they are categorized according to specified criteria, as "important", "highly important" or "critically important" for human medicine, or national lists, where available.

Rationale: To be consistent with WHO.

Insert the following definition for pharmacovigilance:

Pharmacovigilance: the science and activities relating to the detection, assessment, understanding and prevention of suspected adverse events or any other problem related to a medicinal product.

Replace the term “therapeutic use” with “**veterinary medical use**”

Rationale: The Codex guidance should be consistent with the corresponding OIE guidance. The term “veterinary medical use” is used and defined in Article 6.9.2. of the OIE Terrestrial Animal Health Code.

Principle 2

Modify principle 2 as follows:

Biosecurity, appropriate nutrition, vaccination, animal and plant/crop best management practices, and **other** alternatives tools ~~to antimicrobial agents~~ where appropriate, and that have been proven to be efficacious and safe, should be considered to reduce the need for use of antimicrobial agents.

Rationale: There are currently no alternatives to antimicrobial agents that have been scientifically proven to be effective in treating diseased animals.

Principle 5

Principle 5 should be revised to read as follows:

Antimicrobial agents should not be granted regulatory approval for growth promotion and their use for growth promotion should be phased out. In particular, use for growth promotion purposes of those antibiotics that are listed by the WHO as Highest Priority Critically Important Antibiotics for human medicine should be restricted immediately.

Rationale: There is a growing international consensus that the use of antimicrobials for growth promotion should be phased out as recently confirmed at the 2nd OIE Global Conference on AMR in Marrakech, Morocco, on 29-31 October 2018¹. In the EU, the use of antibiotics for growth promotion as feed additives has been banned since 2006. The ban is re-enforced in the forthcoming EU Regulation on veterinary medicinal products (to be adopted by the end of 2018) which provides that antimicrobial agents shall not be used in animals for the purpose of promoting growth nor to increase yield.

Principle 6

Principle 6 should be modified as follows:

~~Medically important a~~Antimicrobial agents should only be used for therapeutic **veterinary medical** purposes (treatment, control/metaphylaxis or prevention/prophylaxis of disease); or in certain circumstances for research and conservation:

Rationale: To be consistent with the revised principle 5 and to align with the OIE Terrestrial Animal Health Code.

Principle 7

Principle 7 should be modified as follows:

~~Medically important a~~Antimicrobial agents should only be used in well-defined **and exceptional** circumstances for the prevention/prophylaxis of a specific disease risk, **based on epidemiological and clinical knowledge** and follow appropriate professional oversight, dose, and duration. **This use should not be systematic, nor routine, nor applied to compensate for poor hygiene or inadequate animal husbandry practices.**

Rationale: A clear principle is necessary to enshrine the conditions for preventive/prophylactic use of antimicrobials.

Add new principle 7bis

A new principle 7bis should be introduced:

Antimicrobial agents should only be used for the control of disease/metaphylaxis on the basis of

¹ http://www.oie.int/en/for-the-media/press-releases/detail/article/agriculture-ministers-join-forces-to-tackle-antimicrobial-resistance-in-farming/?utm_source=Press+Releases&utm_campaign=ac78d1d05a-EMAIL_CAMPAIGN_2018_10_29_04_14_COPY_01&utm_medium=email&utm_term=0_718fbd8136-ac78d1d05a-63139731

epidemiological and clinical knowledge and a diagnosis of a specific disease and follow appropriate professional oversight, dose, and duration. This use should not be systematic, nor routine, nor applied to compensate for poor hygiene or inadequate animal husbandry practices.

Rationale: A new principle is necessary to enshrine the conditions for disease control/metaphylactic use of antimicrobials.

Principle 10

Principle 10 could be deleted as it contains guidance, which is covered elsewhere in document.

Principle 12

Principle 12 should be modified as follows:

~~Medically important a~~Antimicrobials should be administered, prescribed, or applied only by, or under the direction of, veterinarians, plant/crop advisors or consultants or other suitably trained persons authorized in accordance with national legislation.

Rationale: The Codex guidance should be consistent with the corresponding OIE guidance. According to Article 6.10.3.(9) of the OIE Terrestrial Animal Health Code, all antimicrobial agents should be prescribed by a veterinarian or other suitably trained person in accordance with national legislation.

Principle 14

Principle 14 should be modified and a new sentence added as follows:

Administration of antimicrobial agents should be based on sound clinical judgement, experience, ~~and~~ treatment efficacy **and knowledge regarding side effects**. Where feasible and appropriate the results of bacterial cultures and antimicrobial susceptibility testing and integrated resistance surveillance and monitoring ~~can~~ **should** also be considered. **Relevant professional guidelines regarding the preferred choice of antimicrobial agents should be taken into account if available.**

Rationale: The knowledge of possible side effects is also an important consideration in the administration of antimicrobial agents. The preferred choice of an antimicrobial agent can be part of a (national) AMR strategy and should therefore play an important role in the final decision on which agent is administered.

Paragraph 17

Paragraph 17 should be modified as follows:

The regulatory authority should assess the potential of ~~medically important~~ antimicrobial agents to select for resistant microorganisms taking into account *Guidelines for risk analysis of foodborne antimicrobial resistance*, the *WHO list of critically important antimicrobials*, the *OIE list of antimicrobials of veterinary importance*, ~~or~~ **and** national lists **of prioritised antimicrobials**, where available.

Rationale: The Codex guidance should be consistent with the corresponding OIE guidance. According to Article 6.10.3.(4) of the OIE Terrestrial Animal Health Code, the potential of all antimicrobial agents to select for resistance should be assessed. To clarify which national lists are referred to and to bring the terminology in line with the draft guidelines on integrated surveillance of AMR which contain a definition for “prioritised antimicrobial agents”.

Paragraph 20

Paragraph 20 should be modified as follows:

The information in the summary of product characteristics ~~can~~ **should** be utilized in labelling and as a package insert

Paragraph 22

Paragraph 22 should be deleted as it repeats what is in the guidelines for surveillance and monitoring of AMR.

Paragraph 22bis

The 2nd sentence of paragraph 22bis should be modified as follows:

The information collected through the pharmacovigilance program should form part of the comprehensive strategy to minimize **antimicrobial** resistance

Paragraph 23

Paragraph 23 should be modified as follows:

Regulatory authorities, to the extent possible, should make sure antimicrobial agents are distributed through **licensed or authorised** appropriate distribution systems **and prescribed** in accordance with national legislation ~~and medically important antimicrobials are distributed to appropriately~~ **by** credentialed/registered veterinarians, plant/crop advisors or consultants, or other suitably trained persons authorized in accordance with national legislation.

Rationale: The Codex guidance should be consistent with the corresponding OIE guidance. According to Article 6.10.3.(9) of the OIE Terrestrial Animal Health Code, the relevant authorities should ensure that all antimicrobial agents are supplied only through licensed or authorised distribution systems and all antimicrobial agents should be prescribed by a veterinarian or other suitably trained person in accordance with national legislation.

Paragraph 24

Paragraph 24 should be modified as follows:

Distribution should be regularly controlled by the regulatory authorities, and monitoring of sales of antimicrobial agents ~~could~~ **should** be undertaken and information ~~could~~ **should** be analyzed with appropriate context to identify areas of concern and potential follow up

Paragraph 27

Paragraph 27 should be modified as follows:

All advertising of ~~medically important~~ antimicrobial agents should be controlled by the relevant authorities.

Rationale: To bring the text in line with the current version of CAC/RCP 61-2005.

Paragraph 28

The bullets of paragraph 28 should be modified as follows:

- **AMR consequences on public health;**
- information on disease prevention and management strategies to reduce the need to use antimicrobial agents;
- relevant information to enable the veterinarian and plant/crop advisors or consultants to use or prescribe antimicrobial agents responsibly and prudently;
- ~~training in new methodologies for molecular analysis of resistance~~ **understanding methods and results for susceptibility testing of antimicrobials;**
- the ability of antimicrobial agents to select for resistant microorganisms **or resistance determinants** that may contribute to animal, plant/crop, ~~or~~ human health **or environmental** problems; and
- the need to observe responsible and prudent use recommendations and using antimicrobial agents in production settings in agreement with the provisions of the marketing authorizations and professional advice.

Rationale: It is important that all stakeholders understand AMR consequences to public health. New methodologies for molecular analysis are not be relevant for the majority of stakeholders, understanding methods and results for susceptibility testing would be more relevant. Furthermore, the understanding of the selection process should also cover resistance determinants, as these could be located on different microorganisms, including commensal bacteria, and future metagenomics approaches might not specifically address any microorganisms but the resistance determinant. Finally, also environmental problems need to be covered by training.

Paragraph 30

Paragraph 30 should be modified as follows:

Research should be conducted, as resources permit, on antimicrobials, their metabolites, and risks of foodborne resistant microorganisms and resistance determinants in the primary production environment, and if feasible, factors affecting and the magnitude of resistance determinant transfer among microorganisms in the environment leading to ~~foodborne~~ AMR risk **for human health.**

Rationale: The use of antimicrobials can also lead to human health risks, not transferred by food. Research should cover all relevant aspects of the use of antimicrobials in the food chain.

Paragraph 33

The 1st bullet of paragraph 33 should be modified as follows:

Only antimicrobial agents meeting the quality standards of the importing country should be exported ~~from a country in which the products were produced.~~

Rationale: To take into account triangular trade.

Paragraph 35

Paragraph 35 should be modified as follows:

It is the responsibility of the marketing authorization holders to only advertise antimicrobial agents in accordance with the provisions of paragraphs 25-27 on the Responsibilities of the Regulatory Authorities, Control of Advertising and to not advertise ~~medically important~~ antimicrobials to farmers or producers.

Rationale: The Codex guidance should be consistent with the corresponding OIE guidance. According to Article 6.10.4.(3) of the OIE Terrestrial Animal Health Code, the industry should not advertise any antimicrobial agent directly to the food animal producer. The term 'producer' is not defined. In paragraph 28, the term 'other approved users such as farmers and producers' is used.

Paragraph 36

The second sentence of paragraph 36 should be modified as follows:

Promotional campaigns involving economic or material benefits for prescribers or suppliers of antimicrobials should be ~~discouraged~~ **avoided**.

Paragraph 40

Paragraph 40 should be modified as follows:

Wholesalers and retailers distributing ~~medically important~~ antimicrobial agents should only do so on the prescription of a veterinarian or other suitably trained person authorized in accordance with national legislation and all products should be appropriately labelled.

Rationale: The Codex guidance should be consistent with the corresponding OIE guidance. According to Article 6.10.5.(1) of the OIE Terrestrial Animal Health Code, distributors of all antimicrobial agents should do so on the prescription of a veterinarian or other suitably trained person authorized in accordance with national legislation.

Paragraph 41

Paragraph 41 should be modified as follows:

Distributors should encourage compliance with the national guidelines on the responsible **and prudent** use of ~~medically important~~ antimicrobial agents and should keep records of all antimicrobials supplied according to the national regulations including, for example:

Rationale: There is no justification to limit this provision only to medically important antimicrobial agents.

Paragraph 47

The 1st bullet of paragraph 47 should be modified as follows:

A prescription or order for application for ~~medically important~~ antimicrobial agents should indicate the dose, the dosage intervals, the duration of the administration, the withdrawal period, when appropriate, and the amount of antimicrobial agent to be delivered depending on the dosage and the characteristics of the individual or population to be treated.

The 3rd bullet of paragraph 47 should be modified as follows:

All ~~medically important~~ antimicrobial agents should be prescribed or applied and used according to label directions and the conditions stipulated in the national legislation.

Rationale: To bring the text in line with the current version of CAC/RCP 61-2005. There is no justification to limit these provisions only to medically important antimicrobial agents.

Paragraph 48

The 1st sentence of paragraph 48 should be modified as follows:

For food-producing animals, the appropriate use of ~~medically important~~ antimicrobial agents in practice is a clinical decision that should be based on the experience and local expertise of the prescribing veterinarian, and the accurate diagnosis, based on adequate diagnostic procedures

Rationale: To bring the text in line with the current version of CAC/RCP 61-2005. There is no justification to limit this provision only to medically important antimicrobial agents.

Paragraph 49

It is very important to develop a paragraph on the treatment of plants with antimicrobials as in these treatments antimicrobials are sprayed directly to environment and therefore risk of the development and spread of antimicrobial resistance is exceptionally high. Countries authorising such treatments should be invited to provide the necessary information on how the AMR risks can be managed.

Paragraph 50

The sub bullets of paragraph 50 should be modified as follows:

1st sub bullet:

the **expertise and** experience of the veterinarian, plant/crop health professional or suitably trained and authorized person

Rationale: The choice of an antimicrobial by a veterinarian should be first based on his/her expertise and then on his/her experience.

Add a new sub bullet:

treatment guidelines

Rationale: The expected efficacy of the administration should also be based on treatment guidelines.

Paragraph 51

The last sentence of paragraph 51 should be modified as follows:

Off-label use of ~~medically important~~ antimicrobial agents should not be permitted for growth promotion

Rationale: Off-label use of all antimicrobials for growth promotion should be prohibited.

Paragraph 52

Paragraph 52 should be modified as follows:

~~Human health risk~~ **Adverse health effects** related to foodborne antimicrobial resistance should be an important factor when considering the off-label use of veterinary antimicrobial agents.

Rationale: The defined term 'adverse health effect' should be used instead of 'human health risk'

Paragraph 58

The 4th bullet point of paragraph 58 should be modified as follows:

to isolate sick animals and dispose of dead or dying animals or **and contain contaminated** plants/crops promptly under conditions approved by relevant authorities

Rationale: To introduce appropriate measures to mitigate the risk of spreading AMR from contaminated plants/crops.

Paragraph 59

The second sentence of paragraph 59 should be modified as follows:

Efforts should aim to improve health, thereby reducing the need for ~~antibiotics~~ **antimicrobial agents**.

Rationale: For consistency.

The 3rd and 4th sentence of paragraph 59 should be modified as follows:

Disease prevention through the use of vaccines, integrated pest management, and other measures that have been clinically proven to be safe and efficacious, ~~such as probiotics (beneficial bacteria found in various foods), prebiotics (non-digestible foods that help probiotic bacteria grow and flourish) or competitive exclusion products (intestinal bacterial flora that limit the colonization of some bacterial pathogens)~~ may be considered and applied wherever appropriate and available. Disease prevention through the use of vaccines and other appropriate measures aimed at supporting animal health (such as adequate nutrition and whenever available feed additives ~~such as prebiotics, probiotics~~) should be considered.

Rationale: The use of probiotics, prebiotics and competitive exclusion has not generally been proven to be effective.

Paragraph 60bis

The last sentence of paragraph 60bis should be modified as follows:

This adaptation is sometimes associated with an increase in resistance to different ~~antibiotics~~ **antimicrobial agents**.

Rationale: For consistency.

Paragraph 63

The first sentence of paragraph 63 should be modified as follows:

The best way for consumers to prevent ~~cross-contamination by~~ foodborne AMR is through proper food handling **and personal hygiene**.