Antimicrobial resistance and the activities of the Codex Alimentarius Commission

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Summary
The Codex Alimentarius Commission has been working on the subject of antimicrobial resistance, mainly through the activities of the Committee on Residues of Veterinary Drugs in Foods and the ad hoc Intergovernmental Task Force on Antimicrobial Resistance. Principal texts developed by Codex include the ‘Code of Practice to Minimize and Contain Antimicrobial Resistance’ (CAC/RCP 61-2005) and ‘Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance’ (CAC/GL 77-2011). The successful containment of antimicrobial resistance requires the collaboration of a wide range of stakeholders, working together to protect consumer health by ensuring the safety of food products of animal origin.

Keywords

Introduction
The Codex Alimentarius Commission was created in the early 1960s by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO), to develop international food standards, guidelines and recommendations to protect the health of consumers and to ensure fair practices in the food trade. The Codex Alimentarius Commission met for the first time in Rome in June 1963. The constituency of the Codex Alimentarius Commission comprises 184 Member Countries and one Member Organisation (the European Union), as of 31 January 2012.

Codex standards, guidelines and other recommendations are based on the principle of sound scientific analysis and evidence. In its work, the Codex Alimentarius Commission makes use of the scientific support provided by the Joint FAO/WHO Expert Committee on Food Additives, the Joint FAO/WHO Meeting on Pesticide Residues, the Joint FAO/WHO Expert Meeting on Microbiological Risk Assessment and ad hoc FAO/WHO Expert Consultations.

Codex standards are used by the policy-makers and regulators of a country to construct a sound national food control system to provide safe food and to protect the health of consumers at the national level. Codex standards, guidelines and other recommendations are not mandatory in nature and there is no obligation for governments to accept or apply these texts. However, the importance of Codex standards has been emphasised since the establishment of the World Trade Organization (WTO) which, through its Agreement on the Application of Sanitary and Phytosanitary Measures (the ‘SPS Agreement’), identifies Codex texts as the benchmark for food safety.

The relationship between the use of antimicrobials in food-producing animals and the emergence of resistant microorganisms in the food chain is a serious concern and has been the subject of numerous national and
international consultations. The extent to which the use of antimicrobial agents in food animals (including fish in aquaculture), horticulture or humans contributes to antimicrobial-resistant microorganisms in humans varies among different microorganisms and regions. When humans ingest antimicrobial-resistant microorganisms in food, some species of these microorganisms may cause illness. These and other species of microorganisms may also serve as a source of transferable resistance determinants for other microorganisms, including human pathogens.

Codex, while recognising the importance of an holistic approach to antimicrobial resistance and acknowledging the work carried out by other international organisations – such as WHO for aspects of the clinical and non-clinical use of antimicrobials and human health, and the World Organisation for Animal Health (OIE) for aspects of animal health – affirmed that its work on antimicrobial resistance should stay in the remit of the Commission’s mandate; should be based on sound science and follow risk analysis principles; and should take full account of the work of other organisations to avoid duplicating research (4). To ensure consistency with OIE texts, Codex documents include specific references to these OIE texts, where appropriate.

**Codex Alimentarius Commission and antimicrobial resistance**

Within Codex itself, there are a number of groups that have considered the public health implications of using antimicrobials in food-producing animals, including the Codex Committees on Residues of Veterinary Drugs in Foods (CCRVDF) and on Food Hygiene (CCFH), the ad hoc Codex Intergovernmental Task Force on Animal Feeding (TFAF) and, to a lesser extent, the Codex Committees on Pesticide Residues and on Fish and Fishery Products. Each of these groups has tended to approach the public health significance of antimicrobial resistance from the point of view of its own discipline, i.e. the safety of veterinary drug residues in CCRVDF, microbiological risk profiles in CCFH and feeding practices and the manufacture of animal feeds in TFAF.

The problem of sub-therapeutic use of antimicrobials in animals and its effects on public health was considered in the early 1980s by a Joint FAO/WHO Expert Consultation on Residues of Veterinary Drugs in Foods (13). This meeting of experts was convened by FAO and WHO to address the issue, raised in Codex, of residues from chemicals used in the mass medication of animals and of drugs used in veterinary medicine. The Consultation concluded that the occurrence and safety of veterinary drug residues in foods of animal origin was a significant public health issue and posed potential problems to international trade, and recommended the establishment of a new Codex Committee (CCRVDF) to deal with these problems. The Consultation clearly recognised that the risk to humans caused by the sub-therapeutic use of antimicrobials in animals and the development of resistant organisms in these animals should not be confused with the threat associated with the ingestion of veterinary drug residues. The Consultation also pointed out that this particular issue, although unrelated to drug residues, may require further action by FAO, WHO and other international organisations, with possible further implications for the Codex.

Codex again raised the issue of antimicrobial resistance in the early 2000s with a request to FAO and WHO, in collaboration with the OIE, to give advice on non-human antimicrobial use and antimicrobial resistance (2). In response to this request, FAO and WHO organised two separate workshops, to ensure the division between risk assessment and risk management issues, and to address the need for a multidisciplinary approach to coordinate the work of all organisations involved. The aim was to carry out a comprehensive risk analysis specifically based on the Codex ‘Working Principles for Risk Analysis’ (11). The first workshop (14), attended by independent scientists, conducted a preliminary scientific assessment considering all non-human uses of antimicrobials in animals (including aquaculture) and plants, and their role in antimicrobial resistance. The second (15), attended by all major stakeholder groups (e.g. the pharmaceutical industry, farmers, food processors, consumers and regulatory agencies), discussed the broad range of possible risk management options.

Codex considered the outcomes of these joint Consultations, which highlighted the multi-dimensional nature of antimicrobial resistance and the need for a coordinated approach among all the relevant international organisations to develop effective, science-based, risk assessment policies. In recognising the need for a more general and multidisciplinary response to dealing with antimicrobial issues, in 2006 the Codex Alimentarius Commission established an ad hoc Intergovernmental Task Force on Antimicrobial Resistance. Its purpose was to develop science-based guidelines to assess the risks to human health associated with the presence of antimicrobial-resistant microorganisms in food and feed (including aquaculture) and the transmission of antimicrobial resistance genes through food and feed, and to develop appropriate risk management strategies (5). The Task Force, hosted by the Republic of Korea, completed its work on the ‘Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance’ at its fourth and last session in October 2010. These Guidelines were adopted by the 34th Session of the Codex Alimentarius Commission in July 2011.
Codex texts on antimicrobial resistance

Specific texts developed by Codex on antimicrobial resistance include the ‘Code of Practice to Minimize and Contain Antimicrobial Resistance’ (CAC/RCP 61-2005) and the ‘Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance’ (CAC/GL 77-2011). Antimicrobial resistance is also addressed in other Codex texts, such as the ‘Code of Practice on Good Animal Feeding’ (CAC/RCP 54-2004), the ‘Code of Hygienic Practice for Eggs and Egg Products’ (CAC/RCP 15-1979) and the ‘Code of Practice for Fish and Fishery Products’ (CAC/RCP 52-2003).

Code of practice to minimize and contain antimicrobial resistance

This document (3) provides guidance for the responsible and prudent use of antimicrobials in food-producing animals and should be read in conjunction with the ‘Guidelines for the Design and Implementation of National Regulatory Food Safety Assurance Programmes Associated with the Use of Veterinary Drugs in Food Producing Animals’ (CAC/GL 71-2009) (9). The objectives of the Code are to reduce, as far as possible, any potential adverse effects on public health caused by using antimicrobials in food-producing animals. In particular, the Code aims to minimise the development of antimicrobial resistance, and to enable the safe and effective use of antimicrobials in veterinary medicine.

The Code focuses on the use of antimicrobials in food-producing animals and, although it recognises that antimicrobial resistance is also an ecological problem, does not address the persistence of resistant microorganisms in the environment. The Code recognises the importance of veterinary antimicrobials for controlling a great number of infectious diseases and stresses that appropriate systems should be established to ensure that veterinary antimicrobials are manufactured, marketed, distributed, prescribed and used responsibly.

According to the Code, the use of veterinary antimicrobials should be controlled by veterinary professionals or other parties with the required expertise. The responsible use of veterinary antimicrobials should not include the use, for growth promotion, of those veterinary drugs that belong to, or are able to cause cross-resistance to, classes of antimicrobial agents used in humans, without a thorough risk analysis. In addition, the use of veterinary antimicrobials should be limited to their approved and intended purposes and should be based on the results of surveillance and monitoring.

The Code highlights the responsibilities of those involved in the authorisation, production, sale and supply, prescription and use of antimicrobials in food-producing animals to limit the spread of resistant microorganisms. In particular, it defines the specific responsibilities of each of these groups:

- national regulatory authorities
- the veterinary pharmaceutical industry
- veterinarians
- distributors and producers of food-producing animals.

Regulatory authorities

National regulatory authorities should ensure that veterinary antimicrobials are prescribed only by veterinarians (or suitably trained individuals) and used according to their authorised purpose. Regulatory authorities should also ensure the quality and efficacy of veterinary antimicrobials and actively combat the illegal use of veterinary drugs. A pro-active approach should be developed in cooperation with animal and public health professionals to promote only the prudent use of antimicrobials in food-producing animals. This is an important element of a national strategy to contain antimicrobial resistance. Competent authorities should develop a structured approach to the investigation and reporting of the incidence and prevalence of antimicrobial resistance.

Veterinary pharmaceutical industry

The pharmaceutical industry should supply national authorities with all the information required to establish the quality, safety and efficacy of veterinary antimicrobials and should market/export only officially authorised veterinary antimicrobials. Advertising of veterinary antimicrobials should be in accordance with prudent use and national legislation.

Veterinarians

Veterinarians should identify recurrent disease problems and develop alternative strategies to prevent or treat infectious disease, including changes in husbandry conditions and vaccination programmes, where vaccines are available. They should ensure that veterinary antimicrobials are used only when necessary and in an appropriate manner, to minimise adverse effects. The importance of recording information about the use of veterinary drugs is also emphasised.

Distributors

Distributors should distribute veterinary antimicrobial drugs only on the prescription of a veterinarian and should encourage compliance with national guidelines on the responsible use of these drugs. In addition, they should keep records of all antimicrobials supplied.
Livestock producers

Farmers and livestock producers should prevent disease outbreaks, implement health and welfare programmes and use veterinary antimicrobials only when necessary, and in accordance with their approved use. They should also keep adequate records of their use and keep their veterinarian informed.

Guidelines for risk analysis of foodborne antimicrobial resistance

The purpose of these Guidelines (12) is to provide science-based guidance on processes and methodology for risk analysis of foodborne antimicrobial resistance. The Guidelines provide a structured risk analysis framework to address the risk to human health associated with the presence in food and animal feed (including aquaculture), and the transmission through food and animal feed, of antimicrobial-resistant microorganisms and resistance determinants linked to the non-human use of antimicrobial agents.

The Guidelines do not address such as residues of antimicrobial agents in food; antimicrobial resistance marker genes in recombinant-DNA plants and recombinant-DNA microorganisms, non-genetically modified microorganisms (for example, starter cultures), which are intentionally added to food for a technological purpose; and certain food ingredients which could potentially carry antimicrobial resistance genes, such as probiotics. These issues are covered in other existing Codex and/or internationally recognised guidelines.

The document provides general principles and describes the various components of risk analysis of foodborne antimicrobial resistance in a chronological sequence of events: from preliminary risk assessment to risk assessment and risk management activities. Foodborne antimicrobial risk communication and surveillance of antimicrobial use are presented in separate chapters, since these tasks are integral to each step of the entire risk analysis process.

The general principles define the purpose of the risk analysis and the elements to be considered when setting priorities for risk assessment/risk management activities. The principles also recognise that risk analysis of foodborne antimicrobial resistance should build on the Codex principles and guidelines for the conduct of microbiological risk assessment and risk management (1, 8). Such analysis should further consider the antimicrobial susceptibility of the microorganisms, as well as the potential consequences of exposure to these antimicrobial-resistant microorganisms for the treatment of human diseases.

Risk analysis of foodborne antimicrobial resistance should focus on clearly defined combinations of the food commodity, the antimicrobial resistance microorganism and the determinants and antimicrobial agents to which resistance is expressed. The principles highlight the importance of the monitoring and surveillance of antimicrobial use, and the need, where appropriate, to evaluate animal health aspects relevant to food safety.

The preliminary risk assessment activities, initiated by the risk managers, determine the scope and size of the food safety issue and, where necessary, lead to the decision to manage the identified risk and establish a risk assessment policy. An important aspect of this phase is the development of a foodborne antimicrobial risk profile, which describes the current state of knowledge about the food safety issue, the control measures in place and the potential risk management options. The main elements of a foodborne antimicrobial resistance risk profile are provided in an Appendix to the Guidelines.

The risk assessment activities identify and assess the chain of events that affect the frequency and numbers of antimicrobial-resistant microorganisms to which humans may be exposed through food, and describe the magnitude and severity of the adverse health effects from that exposure. The Guidelines describe the four components of the risk assessment process:

- hazard identification, which describes the foodborne antimicrobial-resistant hazard of concern
- exposure assessment, which estimates the level of exposure to the foodborne antimicrobial-resistant hazard
- hazard characterisation, which considers the characteristics of the hazard, the food and the host, to determine the probability of disease occurring in humans after exposure to the hazard
- risk characterisation, which considers the findings from the hazard identification, exposure assessment and hazard characterisation to estimate the actual risk.

The section on risk management advises risk managers on how to deal with the risk of foodborne antimicrobial microorganisms, including examples of both regulatory and non-regulatory measures. This section stresses that risk management decisions should be proportionate to the level of risk, and highlights the importance of evaluating, monitoring and reviewing the measures chosen. The Guidelines also emphasise that Good Veterinary and Good Hygienic Practices should be in place along the food production chain, from ‘farm to fork’, to ensure that antimicrobial resistance is properly managed.

Risk communication should be an open process, aimed at ensuring that the food safety issue is clearly identified and communicated by the risk managers to the risk assessors,
as well as to the affected consumers and industry. It should help to ensure a well-understood and common perception of risks and risk management approaches among all the parties involved.

Other texts

Antimicrobial resistance is also addressed in other Codex publications, in particular, the following:

a) The ‘Code of Practice on Good Animal Feeding’ (CAC/RCP 54-2004) (7). Section 4.5.1, ‘Feed additives and veterinary drugs used in medicated feed’, states that: ‘Antibiotics should not be used in feed for growth-promoting purposes in the absence of a public health safety assessment’ and makes reference to the WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food. The Code defines medicated feed and provides for the feed additives and veterinary drugs used in medicated feed to be assessed for safety and used under their stated conditions of use, as pre-approved by the competent authorities.

b) The ‘Code of Hygienic Practice for Eggs and Egg Products’ (CAC/RCP 15-1979) (6). Section 3.2.1, ‘Flock management and animal health’, considers that flock management is crucial in reducing the risk of human illness from egg consumption and that good husbandry practices should be used to reduce the likelihood of pathogens and thus reduce the use of veterinary drugs. It recognises that, where drug treatment occurs, its use should be appropriate and should take possible antimicrobial resistance into account.

c) The ‘Code of Practice for Fish and Fishery Products’ (CAC/RCP 54-2004) (10). Section 6, ‘Aquaculture production’, recognises that resistance may be promoted by uncontrolled and unlimited use of medicinal products that lead to the accumulation of undesirable residues in the treated fish and in the environment. It also highlights the responsibility of the veterinarian or other authorised professional to draw up programmes of preventive medicine for the fish farmer and to stress the importance of sound management and good husbandry in reducing the likelihood of fish diseases. Moreover, it emphasises that every effort must be made to use only those drugs known to be effective in treating the specific disease.

Conclusion

The successful containment of antimicrobial resistance requires the collaboration of a wide range of stakeholders, working together to protect consumer health by ensuring the safety of food products of animal origin. This task can only be achieved by preventing or reducing the spread of antimicrobial microorganisms or resistance determinants in animal populations; preventing the contamination of products of animal origin with antimicrobial residues; and complying with ethical obligations and the economic need to maintain animal health.

Codex texts on antimicrobial resistance go some way to providing guidance to countries attempting to reduce the risk of antimicrobial resistance. However, much work is still needed to assist countries to implement the ‘Code of Practice to Contain and Minimize Antimicrobial Resistance’ and carry out risk analyses in accordance with the ‘Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance’. Before risk analysis can be carried out, countries must first identify any problems associated with foodborne antimicrobial resistance by setting up surveillance programmes. For this purpose, bilateral assistance between countries when implementing the Guidelines, as well as assistance from other international organisations, such as the OIE, FAO and WHO, would be more than useful.

In future, the experience and ability gained by countries in carrying out risk analysis of antimicrobial resistance should be taken into account by the Guidelines to improve their applicability. Moreover, where necessary, international risk assessments should be undertaken for specific antimicrobial/antimicrobial-resistant pathogens/commodity combinations, and international standards developed to address these risks.
Actividades de la Comisión del Codex Alimentarius en relación con la resistencia a los antimicrobianos

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Resumen
La Comisión del Codex Alimentarius viene trabajando sobre el tema de la resistencia a los antimicrobianos principalmente a través del Comité sobre Residuos de Medicamentos Veterinarios en los Alimentos y del Grupo de Acción Intergubernamental Especial del Codex sobre la Resistencia a los Antimicrobianos. Entre los textos más importantes elaborados por el Codex en esta materia están el Código de prácticas para reducir al mínimo y contener la resistencia a los antimicrobianos (CAC/RCP 61-2005) y las Directrices para el análisis de riesgos de resistencia a los antimicrobianos transmitida por los alimentos (CAC/GL 77-2011). Para contener eficazmente la resistencia a los antimicrobianos es indispensable que muchos y muy diversos interlocutores colaboren entre sí y trabajen de consuno para proteger la salud del consumidor garantizando la inocuidad de los productos alimentarios de origen animal.

Palabras clave
References


