

# Containment of antimicrobial resistance due to use of antimicrobial agents in animals intended for food: WHO perspective

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## Summary

The use of antimicrobial agents in humans and food-producing animals has important consequences for human and animal health, as it can lead to the development of resistant bacteria (pathogens and/or commensals with resistance genes). Moreover, resistant bacteria in animals can be transferred to people – usually through the consumption of food, but also through direct contact with food-producing animals or through environmental spread. Ultimately, this can result in human infections with bacteria that are resistant to antimicrobial agents and that can therefore be difficult or impossible to cure. Of special concern is resistance to antimicrobial agents classified by the World Health Organization (WHO) as critically important for human medicine, such as fluoroquinolones, third- and fourth-generation cephalosporins, and macrolides. WHO encourages the agricultural, food, veterinary and health sectors to work together to eliminate the burden of antimicrobial resistance arising from the use of antimicrobial agents in food-producing animals. Joint efforts should be made to reduce the inappropriate use of antimicrobial agents (e.g. the use of antimicrobials as growth promoters) and limit the spread of bacteria resistant to antimicrobial agents. WHO will continue to address this issue in conjunction with the Food and Agriculture Organization of the United Nations, the World Organisation for Animal Health, the animal health/production industry and other important stakeholders. It will also continue to enhance the capacity of its Member States (through training courses and sentinel studies), particularly developing countries, to conduct integrated surveillance of antimicrobial use and resistance, to carry out risk assessments to support the selection of risk management options and to implement strategies for the containment of antimicrobial resistance.

## Keywords

Antimicrobial agent – Antimicrobial resistance – Containment – Food animal – Multisectoral – World Health Organization.

## Introduction

Large amounts of antimicrobial agents are used in modern food animal production. In addition to therapeutic use, large quantities of antimicrobial agents are used for other purposes, such as prophylaxis and growth promotion. As a result, healthy animals are routinely exposed to antimicrobial agents. This provides favourable conditions for the emergence, development, spread and persistence of

antimicrobial-resistant bacteria capable of causing infections in animals and humans. Resistant microorganisms that develop and are carried by food animals can spread to people, via consumption of food, direct contact with animals or by environmental spread. The genes coding for antimicrobial resistance can also be transferred to human pathogens.

This raises particular concern, since the same classes of antimicrobial agents are used both in humans and animals.

Moreover, few new antibiotics are being developed to replace those becoming ineffective through resistance. Food is generally considered to be the most important vector for spread of resistance between humans and animals.

Food animals and food of animal origin are traded worldwide. Therefore, when antimicrobial resistance affects the food supply of one country, it becomes a potential problem for other countries.

As far back as 1990, realising that modern livestock production and agriculture development throughout the world rely on antimicrobial substances, the World Health Organization (WHO) called for the sectors concerned to work together to eliminate the burden of antimicrobial resistance arising from the use of antimicrobials in food-producing animals. This was the first alert of an increase in antimicrobial resistance in zoonotic and foodborne pathogens and the first call for intersectoral collaboration and the harmonisation of monitoring and surveillance methods across sectors. An international working group was then established by WHO to develop guidelines for regular and systematic monitoring and surveillance of antimicrobial resistance susceptibility testing worldwide using a common method of testing (4).

In 1998, the World Health Assembly adopted a resolution (WHA51.17) on antimicrobial resistance urging Member States to encourage the reduced and rational use of antimicrobial agents in food animal production. This resolution was followed by the development of the WHO 'Global principles for the containment of antimicrobial resistance in animals intended for food' (6).

The publication of the Global Principles was followed by more than ten WHO expert consultations (some held jointly with the Food and Agriculture Organization of the United Nations [FAO] and the World Organisation for Animal Health [OIE]) to first assess the public health risk associated with the use of antimicrobial agents in animal husbandry (including aquaculture) and then to propose management options to address the identified risks. This consultative process has clearly demonstrated that antimicrobial use in food animals can select for antimicrobial-resistant bacteria in the animal gut and, subsequently, these resistant bacteria or their resistance determinants can be transferred to humans via the food chain. Consequently, this has led to two important WHO initiatives:

- the development of the WHO list of Critically Important Antimicrobials for Human Medicine
- the establishment of a WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance.

In this paper the authors will highlight key WHO initiatives which have contributed to raising awareness of

this major public health concern and/or have been major drivers behind other important initiatives at the international level in the area of containment of antimicrobial resistance arising from use of antimicrobial agents in food-producing animals.

## Major WHO initiatives addressing the public health impact of the use of antimicrobial agents in food-producing animals

### **Berlin 1997 – assessing the medical impact**

In 1997, WHO convened an expert meeting on 'The Medical Impact of the Use of Antimicrobials in Food Animals' in Berlin (5). The objective was to achieve an international consensus on priority medical problems arising from the use of antimicrobial agents in livestock production.

The meeting acknowledged that antimicrobial use can select resistant forms of bacteria in the ecosystem and resistant bacteria and resistance genes can be exchanged between human, animal and other ecosystems. The following adverse consequences of selecting resistant bacteria in animals were identified:

- transfer of resistant pathogens to humans via direct contact with animals or through the consumption of contaminated food or water
- transfer of resistance genes to human bacteria
- increased incidence of human infections caused by resistant pathogens
- potential therapeutic failures.

The meeting underlined the importance of monitoring antimicrobial resistance from farm to table, and the importance of prudent use of antimicrobial agents as a risk management tool at primary production level for the containment of antimicrobial resistance.

The meeting recommended that:

- the use of any antimicrobial agent as a growth promoter should be terminated if it is also used in human therapeutics or known to select for cross-resistance to antimicrobial agents used in human medicine
- no antimicrobial should be administered to a food animal unless it has been evaluated and authorised by competent national authorities

- a systematic approach to replacing growth-promoting antimicrobial agents with safer non-antimicrobial alternatives should be established
- national authorities should maintain records of export/import figures for bulk chemicals that have the potential to be used as antimicrobials, because such information is vital for quantitative assessments of the medical risks related to the use of antimicrobial agents in livestock production
- national authorities should continue to monitor and review levels of antimicrobial agent residues in food from animal sources and ensure compliance with national standards
- WHO/FAO should convene an expert consultation to develop a code of practice for prudent use of antimicrobial agents in food animal production (2).

In summary, the meeting in 1997 concluded that the use of antimicrobial agents in food animals is a public health issue and that guidelines on the prudent use of antimicrobials should be implemented. It also concluded that monitoring of both antimicrobial usage and antimicrobial resistance was warranted.

### **Geneva 2000 – an important milestone: the publication of the WHO Global Principles for containment of antimicrobial resistance in animals intended for food**

The development of the WHO Global Principles represented a logical continuation of WHO activities on the health implications of non-human use of antimicrobial agents. They strengthened and endorsed earlier WHO recommendations, such as the need to terminate the use of antimicrobial growth promoters pending comprehensive human health safety evaluations, and the need to establish surveillance systems on antimicrobial consumption.

They provided a framework of recommendations to reduce the overuse and misuse of antimicrobial agents in food animals for the protection of human health. The Global Principles are part of a comprehensive WHO Global Strategy for the Containment of Antimicrobial Resistance (7).

The process by which the WHO Global Principles were developed took into account the need for a broad partnership that included all stakeholders. From the start WHO consulted with a wide spectrum of interested groups. Collaboration has been vital in identifying complementary activities, avoiding duplication, and coordinating efforts towards successful development and implementation of the Global Principles.

The final step in the development of the Global Principles was a WHO Consultation held in Geneva from 5 to

9 June 2000. The participants of the Consultation included experts from the fields of human and veterinary medicine, communicable disease surveillance, food safety, registration of medical and veterinary pharmaceuticals, marketing and sales of veterinary antimicrobial agents, and food animal production. In addition to FAO and the OIE, 14 other governmental and non-governmental international organisations, federations and associations participated, including several representatives of COMISA (the World Federation of the Animal Health Industry, now known as the International Federation for Animal Health).

The Global Principles focused primarily on human health and included details of not only interventions to reduce overuse and misuse of antimicrobial agents on farms, but also of other important areas of intervention, such as registration, distribution/sales, advertising, surveillance and education/training.

The Global Principles were adopted consensually by participants and representatives of attending organisations and federations after a long and, at times, vigorous discussion. They include a set of recommendations which can be used by WHO Member States in their endeavours to minimise the public and human health risks from misuse of antimicrobial agents in animals intended for food.

National governments were advised to adopt a proactive approach and to develop a national strategy for the containment of antimicrobial resistance that included measures intended to:

- reduce the need for antimicrobial agents in animals (thereby limiting their contribution to antimicrobial resistance)
- ensure the prudent use of antimicrobial agents (including reducing overuse and misuse).

### **Tripartite WHO/FAO/OIE expert consultations**

Considering that antimicrobial usage and resistance is a multifactorial problem and thus requires a multidisciplinary approach, the Executive Committee of the Codex Alimentarius Commission (Codex), at its 53rd session, recommended that FAO, WHO and the OIE should give consideration to convening a multidisciplinary expert consultation. They stated that all issues surrounding the use of antimicrobial agents in agriculture and in the veterinary field (including aquaculture) should be considered and that the role played by antimicrobial agents as essential human and veterinary medicines should be taken into account. It was also agreed that the issues raised by several Codex Committees required a more general multidisciplinary and multi-agency response.

The three organisations decided to have two separate consultations to be consistent with the risk analysis framework recommended by Codex: a first workshop on risk assessment, followed by a second workshop on risk management.

### **First Workshop, December 2003, Geneva: scientific assessment of the risk**

This expert workshop was convened by FAO, WHO and the OIE to undertake a scientific assessment of the human health risks associated with the use of antimicrobial agents in animals intended for food, taking into account all available information (8).

Prior to the meeting, a group of experts was asked to prepare a background paper. This document covered the following:

- surveillance of non-human usage
- surveillance of antimicrobial resistance in animals and food
- surveillance of antimicrobial resistance in human pathogens
- factors contributing to the emergence and spread of resistance in food production
- evidence of associations between non-human use of antimicrobial agents and resistance in bacteria from humans, and the human health consequences of such resistance
- a review of risk assessment approaches for non-human use of antimicrobial agents
- the assessment procedures used by the Joint FAO/WHO Expert Committee on Food Additives and Contaminants in its consideration of the potential for antimicrobial resistance resulting from residues of veterinary drugs in food
- the economic impact (agricultural production, health care) and environmental consequences.

Based on the background paper the expert workshop convened four working groups. Each group reviewed one of the following issues:

- surveillance guidelines and drug-use monitoring (including standardisation)
- evidence of an association between use in food animals and resistance in humans
- evidence of adverse human health consequences (what types of resistant bacteria are of greatest importance)
- risk assessment approaches.

During the workshop the main scientific findings on the relationship between the use of antimicrobial agents in animals and antimicrobial resistance in human bacteria were presented and discussed.

The workshop concluded that there is clear evidence of an association between non-human usage of antimicrobial agents and antimicrobial resistance in humans.

Antimicrobial resistance emerges in primary food production in response to antimicrobial selective pressure. Movement of animals, animal manure and animal by-products facilitates the spread of resistance. Bacterial factors, such as fitness of the clone and its resistance to antimicrobial agents, can promote the spread of some clones over others in the food production chain. Some resistant bacteria that have emerged in food and animals can cause human infections, whereas others can pass their resistance determinants, by means of horizontal transmission, to human pathogenic bacteria. Resistance can spread from non-human sources to humans by a multitude of routes. However, the foodborne route is the most prominent route in the transmission from food-producing animals to humans.

### **Second Workshop, March 2004, Oslo: risk management options**

Based on the outcome of the First Workshop in Geneva, as well as other relevant input (e.g. reports of previous WHO and OIE workshops), the Second Workshop in Oslo considered the broad range of possible risk management options for antimicrobial resistance from non-human usage of antimicrobial agents (9). In particular, it focused on potential directions of future Codex, FAO, OIE and WHO work in this area, in order to prevent and minimise antimicrobial resistance at the global level. To ensure that the conclusions of the Second Workshop reflected the perspectives of affected parties, the major stakeholder groups (e.g. pharmaceutical industry, farmers [individuals, groups and companies involved in primary food production], food processors, consumers, regulatory agencies, and veterinarians) participated in the meeting.

The workshop process has resulted in suggestions for a way forward in this area, for Codex, as well as for the OIE, WHO and FAO. Among the important conclusions were:

- a) The risks associated with non-human antimicrobial use and antimicrobial resistance should be part of the human safety assessment.
- b) The concept of 'thresholds of resistance' should be pursued as a tool for risk management. If these thresholds are exceeded, this should trigger a range of risk management actions.
- c) The concept of 'critically important' antimicrobial agents for humans should be developed by WHO with a view to establishing measures to prevent resistance emerging as a result of non-human use of these antimicrobials. A similar list of 'critically important' classes of antimicrobial agents for animals should be developed by the OIE. Both lists should be reviewed on a regular basis.

d) Through stringent implementation of good agricultural practices, including good animal husbandry and good veterinary practices, it is possible to reduce the need for antimicrobial agents.

e) It is important that governments and all stakeholders rapidly implement the WHO Global Principles and the OIE Guidelines on Antimicrobial Resistance.

f) There is a need for capacity building, networking and coordination to facilitate implementation of surveillance programmes in various countries, in particular developing countries. FAO, WHO and the OIE should take a leading role in this.

g) A Codex/OIE Task Force should be established to develop risk management options for antimicrobial resistance related to non-human use of antimicrobial agents (3). Risk communication and transparency are critical to achieve effective risk management. Moreover, the Codex 'Recommended International Code of Practice: General Principles of Food Hygiene' (1) should be reviewed to take account of antimicrobial resistance issues.

### The WHO list of Critically Important Antimicrobials for Human Medicine

There are many serious infections in people (including enteric infections) for which there are few or no alternative antimicrobial agents that can be used if antimicrobial resistance develops. The antimicrobial classes that are currently irreplaceable are classified as 'critically important' (the terms 'essential', 'reserve' or 'last resort' are also used).

Antimicrobial classes are classified as critically important when they are the only available therapy or one of a limited number of drugs available to treat serious human disease or enteric pathogens that cause foodborne disease. The main bacteria to be considered are those that can be transferred from food production animals to humans as either zoonotic pathogens or commensal bacteria (i.e. *Escherichia coli*, *Salmonella* spp., *Campylobacter* spp. and *Enterococcus* spp.). However, this classification should also take into account other bacteria that could be potentially transferred via foods as commensal bacteria (e.g. *Pseudomonas aeruginosa*).

The WHO list of Critically Important Antimicrobials for Human Medicine was first developed at a working group consultation in Canberra in 2005 (10). This consultation was the first important attempt to classify antimicrobial agents based on their importance in human medicine. The list was subsequently re-examined and updated in 2007 (11), in 2009 (12) and in 2011 (publication in progress).

To develop the list, all antimicrobial agents used to treat bacterial infections in people were classified into three categories of importance. No antimicrobial or class of

antimicrobial agent used in human medicine was considered unimportant. The three categories were defined as follows: 'critically important', 'highly important' and 'important' antimicrobial agents. Each antimicrobial agent (or class) was assigned to one of the three categories on the basis of two criteria: 1) the antimicrobial was the sole therapy or one of few alternatives to treat serious human disease; and 2) the antimicrobial was used to treat diseases caused by organisms that may be transmitted via non-human sources or diseases caused by organisms that may acquire resistance genes from non-human sources. 'Critically important' antimicrobial agents are those which meet both criteria 1 and 2. 'Highly important' antimicrobial agents are those which meet criterion 1 or 2. 'Important' antimicrobial agents are those which meet neither criterion 1 nor 2.

In relation to criterion 1, it is self-evident that antimicrobial agents that are the sole therapy or one of only a few alternatives for treatment of serious infections in humans have an important place in human medicine. It is of prime importance that the effectiveness of such antimicrobial agents should be preserved, as loss of efficacy in these drugs due to emergence of resistance would have an important impact on human health. When drawing up the list, the working group consultation developed a table of antimicrobials that met criterion 1 and in it they included examples of the diseases for which the given antimicrobial (or class of selected agents within a class) was considered the sole treatment, or one of a limited number of therapies, for specific infection(s). This criterion does not consider the likelihood that such pathogens may transmit, or have been proven to transmit, from non-human sources to humans.

According to criterion 2, antimicrobial agents used to treat diseases caused by bacteria that may be transmitted to humans from non-human sources are considered of higher importance. In addition, commensal organisms from non-human sources may transmit resistance determinants to human pathogens and the commensals may themselves be pathogenic in the immunosuppressed. The evidence of the link between non-human sources and the potential to cause human disease appears greatest for certain bacteria (e.g. *Salmonella*, *Campylobacter*). In the table of antimicrobial agents that met criterion 2 the working group included examples of the bacterial genera or species of concern. The working group did not consider that transmission of such organisms or their genes must be proven, but only the potential for such transmission to occur. In most antimicrobial classes similar drugs are used in food animals, e.g. enrofloxacin as a fluoroquinolone, tylosin as a macrolide.

It is important to appreciate that if resistance develops to one chemical group of antimicrobial agents then, generally, all the other antimicrobial agents in that group are also

affected due to cross-resistance. The WHO classification should be considered to be the principal list of the most 'critical' antimicrobial agents globally; however, considerations such as cost and availability of antimicrobial agents in various geographic areas, as well as local resistance rates, could cause the list of critically important agents to be altered for regional use (e.g. an antimicrobial agent ranked 'highly important' may become 'critically important' in a particular region).

The WHO classification was conceived to guide decisions on risk management strategies for use of antimicrobial agents in food-producing animals. The list is updated regularly as new information becomes available, including data on resistance patterns, new and emerging diseases, and the development of new drugs. The history of the development of antimicrobial resistance shows that resistance may appear after a long period of usage. As an example, vancomycin resistance in *Enterococcus* was first detected after the drug had been in use for over 40 years. Conversely, however, it can also develop and disseminate rapidly, as was the case with the production of penicillinase in *Staphylococcus aureus*. Even if resistance has not developed to date in particular groups of bacteria it does not mean that it will not develop in the future.

The focus in the WHO list has been on the clinical importance of antibacterial drugs in human medicine and on the main bacterial pathogens for which resistance is a problem. However, it is important to note that the same principles apply for other agents, including anti-fungals. We need also to acknowledge that most research and studies have been on organisms that cause disease directly, neglecting important contributions by commensal bacteria which carry antimicrobial resistance genes. These bacteria infrequently cause disease, but can transfer antimicrobial resistance to pathogenic bacteria.

The WHO list should be used to support more comprehensive assessments of risk. Such assessments should include information on the potential development of resistance in pathogens in animals (release assessment) and the potential spread of resistant organisms or their genes from animals to humans (exposure assessment). The risk assessment can then be used to develop strategies to manage that risk.

Agents within the 'critically important' category were assessed in order to identify which agents were the highest priority in terms of managing the risks from antimicrobial resistance (and to allocate resources accordingly). Quinolones, third- and fourth-generation cephalosporins, and macrolides were identified as being in most urgent need of a comprehensive risk management strategy. However, the prioritisation of these three classes of drugs should not minimise the importance of other drugs categorised as critically important on the list.

### Management options for critically important antimicrobials for human medicine

The development of this list is part of a more comprehensive approach to the public health issue of antimicrobial resistance in both animals and humans. The first revision of the WHO list of Critically Important Antimicrobials (Copenhagen, 2007) emphasised that there should be a sense of urgency to the development of such risk management strategies, particularly for quinolones and third- and fourth-generation cephalosporins. For these antimicrobial classes, in addition to the management options for all antimicrobial agents, specific options include the following:

- not using the drugs at all
- using the drugs only in individual animals and only on the basis of culture results and when there is a lack of alternative agents
- using the drugs in groups of animals after risk assessment demonstrates an acceptable level of safety.

These options are listed in the order of their capacity to minimise selective pressure (greatest capacity first) and thereby minimise the development and spread of resistant bacteria in animals treated with these agents.

Contingency plans could be developed to control or eradicate *Salmonella* and other zoonotic pathogenic bacteria resistant to two or more critically important antimicrobial agents when they appear in food production animals or in the food supply. Options include:

- recalling associated foods
- restricting movement of infected or colonised animals
- processing that guarantees removal of all resistant bacteria
- destroying food items
- destroying groups of animals infected or colonised.

These options are listed in the order of their capacity (least capacity first) to minimise the spread and persistence of these multi-resistant bacteria and thus safeguard public and animal health.

### The WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance

The WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (WHO-AGISAR) ([www.agisar.org](http://www.agisar.org)) was established in December 2008 to support WHO efforts to minimise the public health impact of antimicrobial resistance associated with the use of antimicrobial agents in food animals. In particular, the Advisory Group assists WHO on matters related to the

integrated surveillance of antimicrobial resistance and the containment of food-related antimicrobial resistance. The terms of reference of WHO-AGISAR state that the aims of the group are to:

- develop harmonised schemes (including appropriate sampling) for monitoring antimicrobial resistance in zoonotic and enteric bacteria
- support WHO capacity-building activities for antimicrobial resistance monitoring in Member States (e.g. Global Foodborne Infections Network training courses and workshops [[www.who.int/gfn/training/en/index.html](http://www.who.int/gfn/training/en/index.html)])
- promote information sharing on antimicrobial resistance
- provide expert advice to WHO on containment of antimicrobial resistance, with a particular focus on human critically important antimicrobials
- support and advise WHO on the selection of sentinel sites and the design of pilot projects for conducting integrated surveillance of antimicrobial resistance
- support WHO capacity-building activities for antimicrobial usage monitoring in Member States.

The WHO-AGISAR comprises over 20 internationally renowned experts, in a broad range of disciplines relevant to antimicrobial resistance, who were appointed following a web-published call for advisers and a transparent selection process. The Advisory Group holds regular telephone conferences and annual face-to-face meetings. The first meeting was held in Copenhagen, Denmark. The second was held in Guelph, Canada, from 5 to 7 June 2010. The four AGISAR subcommittees (antimicrobial usage monitoring, antimicrobial resistance monitoring, capacity building and data management) are in the process of developing practical tools/guidelines/protocols to support WHO Member States in their efforts to implement a national programme for integrated surveillance of antimicrobial resistance.

## The way forward

The topic of World Health Day 2011 was antimicrobial resistance and this was an opportunity for WHO to identify the main challenges in the containment of antimicrobial resistance arising from the use of antimicrobial agents in food-producing animals and to determine the core actions needed to combat the problem.

### Main challenges

a) Data on the occurrence of resistance and information on the use of antimicrobial agents in animals are essential

for risk analysis and for assessing the effectiveness of interventions. However, very few countries have put in place monitoring systems for antimicrobial resistance and even fewer have systems for monitoring the use of antimicrobial agents.

b) The data collected are often difficult to interpret because methodologies are not sufficiently harmonised.

c) The lack of intersectoral collaboration for surveillance of antimicrobial resistance in bacteria from humans, food and animals makes it difficult to analyse the public health impact of antimicrobial use in food animals and to implement focused interventions.

d) Inadequate training on appropriate use of antimicrobial agents in food-producing animals and insufficient understanding of their effects on antimicrobial resistance in humans are common among farmers, veterinary prescribers and dispensers.

e) The use of antimicrobial agents is often unduly increased when antimicrobials are administered for non-therapeutic purposes, e.g. to promote growth in food animals. Antimicrobial use can also be increased by illegal trading and by financial incentives, such as increasing sales profits (some veterinarians that do not respect the ethics imposed by Veterinary Statutory Bodies may prescribe more antibiotics in an attempt to boost income).

f) Insufficient legislation to implement restrictions on the approved usage of licensed antimicrobial agents and inadequately enforced regulatory mechanisms on antimicrobial supply contribute to excessive drug use.

### Core actions

a) Provide national leadership and promote intersectoral collaboration:

- establish a formal mechanism of interaction between the Ministry of Health and other relevant Ministries and authorities to address the issue of antimicrobial resistance in the agricultural sector

- include agricultural authorities in the national intergovernmental steering committee on antimicrobial resistance.

b) Create and enforce an enabling regulatory framework:

- establish a regulatory framework for authorisation and control of the quality of veterinary medicines

- introduce pre-licensing safety evaluations of antimicrobial agents for veterinary use, with consideration of potential resistance to human drugs

- terminate non-therapeutic use of antimicrobial agents such as growth promotion

- restrict or eliminate use of antimicrobial agents identified as critically important in human medicine,

especially fluoroquinolones and third- and fourth-generation cephalosporins

- require prescriptions for all antimicrobial agents used for disease control in food animals.

c) Strengthen surveillance and monitoring:

- create national systems to monitor antimicrobial usage in food-producing animals

- develop national integrated surveillance programmes with quantitative susceptibility data for zoonotic pathogens and indicator bacteria to monitor current and emerging antimicrobial resistance patterns (surveillance should involve close collaboration between public health authorities, Veterinary Services and food laboratories)

- set up a multidisciplinary task force involving public health, veterinary medicine and food safety authorities to act on the surveillance data to identify trends, assess risk and implement focused interventions in a timely way

- develop common protocols to facilitate global harmonisation of surveillance of antimicrobial usage in humans and animals, and of antimicrobial resistance.

d) Promote education and training around antimicrobial use in food-producing animals:

- develop prudent use guidelines with multidisciplinary involvement to reduce overuse and misuse of antimicrobial agents in food animals, taking into consideration antimicrobial agents categorised as ‘critically important’ for human medicine and as ‘important’ for veterinary medicine

- provide training for both veterinarians and farmers on the use of guidelines and implement auditing and feedback to veterinarians and agricultural producers to improve compliance

- develop and implement education strategies which emphasise the importance and benefits of prudent use principles, and which provide relevant information on antimicrobial resistance to producers, stakeholders and the public

- facilitate implementation of Codex and OIE guidelines related to antimicrobial resistance.

e) Reduce the need for antimicrobial agents through better animal husbandry:

- introduce measures to improve animal health and reduce the need for antimicrobial treatment, including introduction of effective vaccines

- improve health management for food animal production by ensuring good hygiene practices and compliance with Good Farming Practices.

## Conclusion

WHO will work closely with partners at international, regional and national levels to ensure the implementation of the ‘Global principles for the containment of antimicrobial resistance in animals intended for food’. The organisation will focus particularly on enforcing the ban on antimicrobial growth promoters, promoting the rational prescription and use of veterinary drugs and restricting the use of human critically important antimicrobials in animal husbandry, in particular quinolones and third- and fourth-generation cephalosporins.

WHO will work with FAO, the OIE and powerful stakeholders, including industry, to achieve a reduction in the use of certain classes of antimicrobial agents in animals and to phase out the use of antimicrobial agents as growth promoters in animals intended for food.

WHO will enhance the capacity of its Member States (through training courses and sentinel studies), particularly developing countries, to conduct surveillance of antimicrobial use and resistance, to carry out risk assessments to support the selection of risk management options, and to implement strategies for the containment of antimicrobial resistance.



# Maîtrise de la résistance aux agents antimicrobiens imputable à l'utilisation de ces produits chez les animaux élevés pour l'alimentation humaine : le point de vue de l'OMS

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## Résumé

L'utilisation des agents antimicrobiens chez l'homme comme chez les animaux élevés pour l'alimentation humaine a des conséquences majeures sur la santé humaine et animale, car elle peut favoriser le développement de bactéries résistantes (pathogènes et/ou commensales porteuses de gènes codant pour la résistance). De plus, il existe un risque de transfert à l'homme des bactéries résistantes présentes chez les animaux, qui se produit généralement par voie alimentaire, mais peut également survenir par contact direct avec des animaux élevés pour l'alimentation humaine ou par propagation dans l'environnement. En fin de compte, il en résulte que certaines infections dues à des bactéries résistantes aux agents antimicrobiens deviennent difficiles, voire impossibles à traiter chez l'être humain. La résistance aux agents antimicrobiens considérés par l'Organisation mondiale de la santé (OMS) comme étant d'une importance critique en médecine humaine, en particulier les fluoroquinolones, les céphalosporines de troisième et de quatrième génération et les macrolides, évolue de manière particulièrement préoccupante. L'OMS encourage les secteurs de l'agriculture, de la production agroalimentaire, de la santé animale et de la santé publique à coopérer en vue d'éliminer le fardeau de la résistance aux agents antimicrobiens imputable à l'utilisation de ces agents chez les animaux destinés à l'alimentation humaine. Des efforts concertés doivent être déployés pour réduire l'utilisation inappropriée de ces agents (par exemple en tant que promoteurs de croissance) et pour limiter la propagation des bactéries résistantes. L'OMS entend poursuivre son combat dans ce domaine, en liaison avec l'Organisation des Nations Unies pour l'alimentation et l'agriculture, l'Organisation mondiale de la santé animale, les secteurs de la santé et de la production animales ainsi que d'autres parties prenantes influentes. L'OMS continuera également à renforcer les capacités de ses États membres, et plus particulièrement des pays en développement (au moyen de formations sur ce thème et d'enquêtes de surveillance sentinelle) afin que ces pays puissent exercer une surveillance intégrée de l'antibiorésistance et de l'utilisation des agents antimicrobiens, réaliser des évaluations du risque en appui des décisions de gestion du risque, et mettre en œuvre des stratégies appropriées pour maîtriser la résistance aux agents antimicrobiens.

## Mots-clés

Agent antimicrobien – Animaux élevés pour l'alimentation humaine – Antibiorésistance – Approche multisectorielle – Maîtrise – Organisation mondiale de la santé.



# Contención de la resistencia a los agentes antimicrobianos provocada por el uso de antibióticos en animales destinados al consumo humano desde el punto de vista de la OMS

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## Resumen

El empleo de antimicrobianos a la vez en personas y en animales destinados al consumo humano tiene importantes consecuencias para la salud humana y animal, pues puede llevar a la aparición de bacterias resistentes (patógenos y/o comensales con genes de resistencia). Además, las bacterias resistentes presentes en animales pueden transferirse al ser humano (en general por el consumo de alimentos, pero a veces también por contacto directo con animales destinados al consumo humano o por diseminación en el medio). A la postre ello puede provocar la infección de personas por bacterias resistentes a los antimicrobianos, generando patologías de muy difícil o imposible curación. Especial inquietud suscitan las resistencias a los agentes antimicrobianos que la Organización Mundial de la Salud (OMS) considera “de importancia crucial para la medicina humana”, como las fluoroquinolonas, las cefalosporinas de tercera y cuarta generación o los macrólidos. La OMS alienta a los sectores agrícola, alimentario, veterinario y médico a trabajar conjuntamente para eliminar la carga que suponen las resistencias a los antimicrobianos provocadas por el uso de antibióticos en animales destinados al consumo humano. Se impone un esfuerzo colectivo para reducir el uso inadecuado de antimicrobianos (por ejemplo como promotores del crecimiento) y contener la propagación de bacterias resistentes. La OMS seguirá trabajando sobre el tema junto con la Organización de las Naciones Unidas para la Alimentación y la Agricultura (FAO), la Organización Mundial de Sanidad Animal (OIE), la industria de producción y sanidad animales y otros importantes interlocutores. También seguirá mejorando los medios de acción de sus Estados Miembros (mediante cursos de formación y estudios centinelas), en particular de los países en desarrollo, para instaurar una vigilancia integrada del uso de antimicrobianos y la aparición de resistencias, realizar evaluaciones de riesgos para poder decidir con conocimiento de causa sobre distintas alternativas de gestión del riesgo y aplicar estrategias de contención de las resistencias a los antimicrobianos.

## Palabras clave

Agente antimicrobiano – Animal destinado al consumo humano – Contención – Multisectorial – Organización Mundial de la Salud – Resistencia a los antimicrobianos.



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