
WHO GUIDELINES ON USE OF MEDICALLY IMPORTANT ANTIMICROBIALS IN FOOD-PRODUCING ANIMALS

**Policy brief
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WHY IS WHO ISSUING THE GUIDELINES ?

Overuse and misuse of antibiotics in animals and humans is contributing to the rising threat of antibiotic resistance. Some types of bacteria that cause serious infections in humans have already developed resistance to most or all of the available treatments, and there are very few promising options in the research pipeline (1).

If no action is taken today, by 2050, almost all current antibiotics will be ineffective in preventing and treating human disease,

and the costs of losing these drugs will exceed US\$ 100 trillion in terms of national productivity (2,3). This underscores the slogan of the World Health Day on antimicrobial resistance launched by World Health Organization (WHO) in 2011, “No action today, no cure tomorrow” (4).

Scientific evidence clearly demonstrates that overuse of antibiotics in animals can contribute to the emergence of antibiotic resistance (5).

The control of antibiotics in food animal production is an important factor in combating antimicrobial resistance worldwide, because (i) antibiotics widely used in food-producing animals are identical to, or use a similar mechanism, to antibiotics used to treat bacterial infections in humans; (ii) the volume of animal antibiotic use, including for growth promotion, is increasing globally with the rise in demand for animal proteins (6); and (iii) foodborne diseases, including bacterial infections, are a major cause of death and illness in humans, particularly in children (7). Furthermore, antibiotic use in food production, especially for growth promotion, is also associated with multi-drug resistant pathogens due to the prolonged use of multiple drugs at sub-therapeutic doses (low doses that allow resistance to develop more easily).

Humans are exposed to the resistant bacteria originating from animal production through multiple pathways, including consumption of contaminated food products, direct animal-to-human contact on farms and in slaughterhouses, as well as indirectly through the environment.

In accordance with WHO's mandate to protect public health, WHO has developed these guidelines to help preserve the effectiveness of antibiotics important for human medicine by reducing their unnecessary use in animals.

They were developed following a stringent WHO process and based on sound scientific evidence to support recommendations that are appropriate for all countries, including high- and low-income countries, and for all scales of food animal production.

WHERE DO THESE GUIDELINES FIT IN?

These guidelines build on decades of expert reports and evaluations of the role of agricultural antibiotic use in the increasing threat of antibiotic resistance; they are one of the most direct and tangible responses of the WHO to the global action plan on antimicrobial resistance adopted by the Sixty-eighth World Health Assembly in May 2015 (8) and to the political declaration of the high level meeting of the United Nations General Assembly in September 2016 (9).

These documents recognize the global nature of antibiotic resistance and the rapid spread of resistant organisms and genetic determinants

of resistance across continents. They also recognize that all uses of antibiotics – both in humans and animals – contribute to the development of resistance in bacteria.

These guidelines are consistent with the work by a WHO expert group that has issued reports on the importance of evaluating agricultural uses for the purpose of protecting the efficacy of clinically important antibiotics for preventing and treating infectious disease in humans (10). This approach is also consistent with the multilateral approach (so-called “One Health” approach) to managing health risks at the animal-human-ecosystems interfaces (11).

WHAT ARE THE RECOMMENDATIONS IN THESE GUIDELINES?

These guidelines include recommendations based on evidence derived from systematic reviews and narrative literature reviews, and best practice statements based on expert experience. The recommendations address the use of antibiotics in animals for different purposes, namely growth promotion, disease prevention in the absence of disease, as well as

treatment and control of diagnosed disease. The recommendations use WHO's list of critically important antimicrobials for human medicine (WHO CIA list) (10) which groups all antibiotics currently used in humans and animals into three categories – "important", "highly important" and "critically important" – based on their importance to human medicine (see Annex).

Recommendations

1. WHO recommends an overall reduction in use of all classes of medically important antimicrobials in food-producing animals.
2. WHO recommends complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion.
3. WHO recommends complete restriction of use of all classes of medically important antimicrobials in food-producing animals for prevention of infectious disease that have not yet been clinically diagnosed.*
4. WHO suggests that antimicrobials classified as critically important for human medicine should not be used for control of the dissemination of a clinically diagnosed infectious disease identified within a group of food-producing animals. WHO

suggests that antimicrobials classified as highest priority critically important for human medicine should not be used for treatment of food-producing animals with a clinically diagnosed infectious disease**.

Specific considerations:

**Based upon the advice of a veterinary professional familiar with the disease history in the herd, these uses may be permitted if there is a high risk of contraction of a particular infectious disease.*

***Based upon the advice of a qualified veterinarian, these uses may be permitted if no other drug is available to treat infected animals or to prevent dissemination of diagnosed disease within groups of animals.*

Best practice statements

1. Any new class of antibiotics or new antimicrobial combination developed for use in humans will be considered critically important for human medicine unless categorized otherwise by WHO.
2. Medically important antimicrobials that are not currently used in food production should not be used in the future in food production including in food-producing animals or plants.

WHO DEVELOPED THE RECOMMENDATIONS?

The recommendations in these guidelines were drafted by the Guideline Development Group (GDG) consisting of 13 external experts from five WHO regions, under the overall guidance of a WHO Steering Group. GDG was a diverse group of qualified individuals with expertise in human medicine, veterinary medicine, microbiology, antimicrobial resistance, agricultural economics, veterinary ethics and a representative from an organization representing consumers. One member of the GDG was a Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologist. The GDG members were nominated and selected to achieve a balance in geographic representation and gender. Public comments were solicited on the proposed membership of the GDG before confirmation. Declared interests were managed according to the WHO policy. Potential conflicts of interest of members were assessed by the WHO secretariat and all were deemed not significant. The whole process was supervised by the WHO Guidelines Review Committee, which approved the final guidelines.

These guidelines were developed through translating evidence from systematic reviews and selected literature reviews into recommendations, following the required methodologies of WHO including use of GRADE (12) to evaluate the reliability of the evidence for each recommendation. The systematic reviews

assessed the reliability of scientific evidence for associations between use of antibiotics in food-producing animals and risks of human exposure to and infection by drug-resistant pathogens from food animal production. The narrative literature reviews evaluated the literature on illustrative examples of transfer of antimicrobial resistance determinants from food-producing animals to humans; unintended adverse impacts of restricting current uses of antibiotics in agriculture; and mechanistic information supporting the biological plausibility of observed associations between agricultural use of antibiotics and increased risks of health outcomes in humans.

The guidelines also took into account prior and on-going work by WHO on the identification of antibiotics that are critically important for human medicine. This work is done in collaboration with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE). This context provided a structure for prioritizing specific drugs in the recommendations stated in the guidelines. In 2005, WHO organized the first expert committee to develop and implement criteria for defining and prioritizing those antibiotics that are critically important for human medicine (13). These criteria have been used to establish and periodically update a WHO CIA list. The 2016 WHO CIA list (10) provides a basis for the recommendations in the current guidelines.

HOW CAN THESE GUIDELINES BE IMPLEMENTED?

The recommendations and best practice statements in these guidelines are not legally binding on WHO Member States. It is up to countries and other stakeholders, including the FAO/WHO Codex Alimentarius Commission, to take them into account when developing national or international standards or guidance.

Implementing the recommendations in these guidelines may require significant changes in current practices in food animal production. Although the benefits of implementing these recommendations are considered to greatly outweigh costs, the availability of resources of expertise and technical support vary among regions and countries. These resources are likely to be least available in those regions where the health and economic impacts of antibiotic resistance are the greatest in terms of burdens of human illnesses.

In order to reach the overall goal of reducing all uses of antibiotics in agriculture, there is a need to identify options to replace some current uses of antibiotics in food-producing animals for disease prevention in animals. Improved hygiene, improved biosecurity and better use of vaccines have been shown to be effective alternatives in some cases to ensure productivity and animal health in the absence of the use of antibiotics for growth promotion and disease prevention. Experience that has been gained by countries that prohibit antimicrobial growth promoters should be made widely available in other regions especially in developing regions with implementation, taking small holders into account.

International support for technical resources for microbiology and drug-resistance testing as well as increased resources in veterinary medicine are important for the successful implementation of these guidelines. The ability to collect specific data on antibiotic use is also needed in many countries. In addition to the WHO projects now underway to strengthen laboratory and other technical capacity in countries, international organizations such as FAO and OIE have valuable experience in assisting countries with many aspects of implementation including tools for veterinary oversight of antimicrobial use and enhanced biosecurity for farms.

Access to veterinary professionals is important in reaching decisions on the use of antibiotics for treatment and prevention of disease within groups of animals. The guidelines state that use of antimicrobials classified as critically important in human medicine should be justified on the basis of veterinary expertise when laboratory results indicate that a critically important antimicrobial is the only treatment option. This option is dependent on access to culture and sensitivity testing, which may not be available.

Furthermore, WHO encourages countries to establish national surveillance programmes to generate information on the extent of antibiotic use in agriculture and the presence of antibiotic resistance in food animals, consumer food products, human populations and the environment using the integrated One Health approach, to evaluate the effect of implementation of adopting the guidelines.

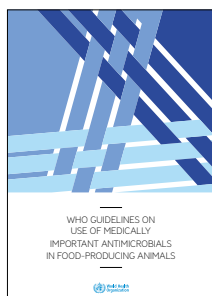
WHEN WILL THESE GUIDELINES BE REVIEWED IN THE FUTURE?

There will be an on-going evaluation process by the WHO Department of Food Safety and Zoonoses to assess the uptake of these WHO guidelines. This will be integrated into the monitoring and evaluation efforts by Member States of the WHO Global Action Plan on Antimicrobial Resistance. Furthermore, WHO will utilize the Advisory Group on Integrated Surveillance of Antimicrobial Resistance

(AGISAR) to assist in the evaluation process on the uptake of the WHO guidelines.

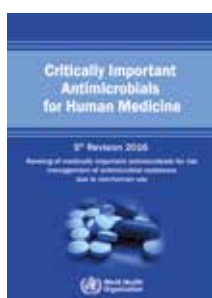
WHO will follow research development associated with use of antimicrobials in food-producing animals and review and updates these recommendations five years after publication of the guidelines, unless significant new evidence emerges, necessitating earlier revision.

NEED TO KNOW MORE?



WHO guidelines on use of medically important antimicrobials in food-producing animals :

http://who.int/foodsafety/publications/cia_guidelines/en/index.html



WHO List of Critically Important Antimicrobials for Human Medicine (WHO CIA list):

http://who.int/foodsafety/areas_work/antimicrobial-resistance/cia/en/

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ANNEX

AT A GLANCE: Recommendations in the WHO guidelines on use of medically important antimicrobials in food-producing animals

WHO classification and prioritization of medically important antimicrobials		Recommendation 1				
		Reduce overall use				
		Recommendation 2	Recommendation 3	Recommendation(s) 4		
		Growth Promotion use	Prevention use † (In absence of disease)	a. Control use (In presence of disease)	b. Treatment use (In presence of disease)	
Medically Important Antimicrobials	Critically Important	Highest Priority				
	High Priority					
	Highly Important					
	Important					



Complete restriction.



Responsible and prudent use.



The use may be permitted if a veterinary professional familiar with the disease history in the herd judges that a high risk of contraction of a particular infectious disease exists. The antimicrobials used should start with those of least importance for human medicine.



The use may be permitted if no other drug from lower categories is available to treat infected animals or to prevent dissemination of diagnosed disease within groups of animals.