
The World Veterinary Association (WVA), representing the global veterinary profession, wishes to commend the WHO on the development of its Guidelines on the Use of Medically Important Antimicrobials in Food-Producing Animals. The WVA Working Group on Pharmaceutical Stewardship is pleased to have the opportunity to give feedback on these guidelines and wishes to offer the following comments:

Introduction

The continuing global effort to preserve the lifesaving activity of antimicrobials represents a critical struggle for the health of animals and humans. The World Health Organization has been a global leader pressing for change in this area; however, by ‘medically important’, the WHO means to indicate medically important only to humans. A One Health approach to antimicrobial resistance (AMR), which the WVA has traditionally supported, recognizes the inter-dependence of different users and emphasizes the need for an enhanced focus on reduction of use by all groups and on the need for stewardship measures globally. Antimicrobial resistance is an issue that affects the future of life as we know it on the earth. The WHO Guidelines [1] provide suggestions for risk management to reduce the impact of AMR on human health, but these are exclusively focused on the mission of the WHO, which is to promote high standards of human health around the world.

Unfortunately, the Executive Summary of the WHO Guidelines on the Use of Medically Important Antimicrobials in Food-Producing Animals is unnuanced and incomplete on its own, with no context provided, but this brief section may be the only portion of the document read by an audience unfamiliar with antimicrobials and their use. For example, there is no acknowledgment of the potential adverse animal welfare impact of some of the recommendations listed. Further, the summary states that the recommendations are evidence-based, but the preamble fails to identify that the quality of the evidence underlying these recommendations is either low or very low. The summary fails to note that recommendation 4 is a conditional recommendation and, as stated in the WHO document, merely a ‘suggestion’. There is no acknowledgment in the document that most AMR found in human pathogens is the result of misuse of
antimicrobials in human medicine, such that the Guidelines may create a distorted perspective for regulators and policy makers or others unfamiliar with the topic. As noted in the Guidelines, there is no consensus as to what proportion of AMR found in bacteria isolated from humans is caused by use of antimicrobials in food-producing animals. This is a complex topic for which much of the evidence is weak and contradictory and based on a limited number of studies. Alternatively, use of a “One Health” approach would acknowledge this uncertainty especially in consideration of the WHO list of priority pathogens, few of which have any possible link to livestock conditions. ([http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/](http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/)).

Recommendation 1, Overall reduction of antimicrobial use in food-producing animals.
The WVA fully supports this recommendation as an approach to reduce AMR in both animals and in humans. Globally, this is already occurring with more oversight of antimicrobial drugs in food-producing animals, an increased focus on optimal use of antimicrobials in animals, and interest in discovering alternatives to antimicrobial drugs, through regulation, stewardship and other approaches. The focus should be not only on reduction of antimicrobials used but also on increased quality of use, where the benefits can be shown to be both clear and substantial. “Benchmarking” human medical or veterinary use and response to use is an increasingly valuable practice to evaluate use and reduce overuse. Bringing all use of medically-important antimicrobials under veterinary oversight in which veterinarians have a genuine and well-established veterinary-client-patient relationship (VCPR) is an important element in improving the use of antimicrobial drugs in food animals, as well as promoting adoption of alternatives (biosecurity and hygiene, management practices, vaccination, etc) to these therapeutics. Veterinarians play a vital role in antimicrobial stewardship, but no mention is made this in the document. Addressing AMR will require a systematic stewardship approach adapted to the particular characteristics of each country (as recommended by WHO), rather than blanket broad-ranging recommendations that are blunt and unfocused and that disregard the diversity of global antimicrobial use (for example, even amongst the EU member states there is a 100-fold difference in use identified by ESVAC [2], and national regulatory environments. As in human medicine, veterinary antimicrobial stewardship is an evolving and growing concept. It has multiple elements, all of which are designed to reduce and improve the use of antimicrobials in animals. These practices include not using antimicrobial drugs, best practice guidelines, categorization of therapeutics into use of “first line”, “second line” and “third line”, recommendations around culture and sensitivity testing, infection prevention and control, education of veterinarians and clients, and numerous other approaches. Recognition of the importance of different antimicrobials to human medicine is a part of veterinary antimicrobial stewardship. Regrettably, the WHO Working Group had no member versed in international veterinary efforts to improve antimicrobial use in animals.

Recommendation 2, complete restriction of antimicrobial use for growth promotion in food-producing animals.
The WVA fully supports the recommendation for complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion. This has been a repeated theme of the WHO that we believe is generally accepted by veterinarians. However, there are medically-unimportant antibiotics (designated ‘Important’ by WHO), such as bacitracin, which have growth promotion claims, when their benefit is actually for disease

prophylaxis (for example, necrotic enteritis in broilers). Such contextual nuances aren’t present within the document and are consequently misleading.

**Recommendation 3, complete restriction of medically important antimicrobials in food- producing animals for disease prophylaxis**
The WVA believes that this recommendation should be more nuanced, as acknowledged in the implementation considerations, by omitting the word ‘complete’.
Medically-important antibiotics have been used at subtherapeutic levels in animals for preventive purposes, in which the disease prevention benefits are dubious, and, in many cases, with minimal veterinary oversight. The WVA agrees that in many cases, this is an unjustified practice that needs to be abandoned. However, if a veterinarian is involved, there is an element of professional judgement in disease prophylaxis that is important. If there is a significant risk of acute disease in animals, then this needs to be weighed against the risks to human health of treating as well as to animal welfare of not treating. Use in such a case should only be implemented when the benefits are clear and substantial, and based on sound evidence. Use should be based on laboratory testing, wherever possible and appropriate. Risk-based prophylaxis as described, is defensible for supporting animal health and welfare if animals are judged by well-informed veterinarians to be at risk.

**Recommendation 4a, Antimicrobials deemed critically important for human medicine should not be used to control confirmed disease in food-producing animals.**
This recommendation has very important adverse health and welfare impacts for food-producing animals and is unlikely to be adopted by veterinarians. The WHO Critically Important Antimicrobials (CIA) list [3] continues to be problematic to veterinarians, since it includes most first-line antibiotics of value in veterinary medicine - in particular, penicillin, aminopenicillins, and aminoglycosides. These therapeutics are included on the OIE list of veterinary critically important antimicrobials. The use of antimicrobials to control and treat disease in an outbreak is an appropriate use of these therapeutics. This should only be by veterinary prescription based on laboratory sensitivity and should involve a “cascade” approach of using lower before higher importance drugs. Such veterinary practice needs to be documented and defensible.

**Recommendation 4b, Antimicrobials classified as highest priority critically important for human medicine should never be used for treatment of food-producing animals with clinically diagnosed infectious disease.**
The WVA’s comments are essentially the same as those listed under 4a, above. Such use should only be by veterinary prescription and supervision and should involve a “cascade” approach of using lower before higher importance drugs. Treatment of clinical illness in food animals with highest priority critically important antimicrobials can be an appropriate use of these drugs, with important animal welfare considerations, subject to appropriate veterinary judgement.

**Best Practice Statement I, Any new class of antimicrobial developed for use in humans will be deemed critically important.**
The WVA fully supports this statement.

**Best Practice Statement 2, Medically important antimicrobials not currently used in food production should never be used in the future in food-producing animals or plants.**

This Best Practice Statement precludes the possibility of the development of “food-animal only” antimicrobial classes, which could be short-sighted. If such drugs were developed, in the absence of any evidence for co-selection of antimicrobial resistance genes, they might have value in reducing the use of medically-important antimicrobials in food-producing animals.

Finally, although the Summary identifies the lack of availability of culture and sensitivity testing in many countries around the world, a far greater problem is total lack of any control of antimicrobial quality, distribution and use in humans and animals. Surveillance and monitoring of resistance and use are critical for implementation of the guidelines. Lack of such data globally is an issue that needs to be addressed to make rational, science-based decisions.

The World Veterinary Association has a long-standing interest in promoting responsible antimicrobial use in animals. The WVA position paper on this subject is available at: http://www.worldvet.org/uploads/docs/wva_position_on_the_use_of_antimicrobials.pdf.

On behalf of the WVA, I would like to thank you for taking in consideration the WVA’s input on the WHO guidelines.

With sincere regards,

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