
Resolution on Antimicrobials in Animals Raised for Food

Introduction

The World Health Organization has indicated that overuse of antimicrobials is leading the world toward a post-antibiotic era in which important medicines used to treat or prevent human infections will no longer be effective. Common infections will become more difficult to treat, and routine surgeries will carry significantly greater risk. A review of neonatal and infant sepsis in developing countries found that the causal *Escherichia coli* (*E. coli*) bacteria were resistant to both the recommended first-line and alternative cephalosporin treatment regimens.¹ Reports and publications globally have consistently shown high rates of *E. coli* resistance to the last generation drugs commonly used to treat serious infections.² The global burden of antimicrobial resistance will lead to longer duration of illness and higher mortality in patients, increasing costs of treatment, and inability to perform procedures that rely on antibiotics to prevent infections.³

In many countries, antimicrobials are given daily to animals raised for food at low levels via daily feed and water rations. Much of this use is for production and efficiency purposes in intensive systems, rather than the protection of animal health. Many of the antibiotics routinely given to food animals are important to human medicine, including penicillin, tetracyclines, erythromycins, and bacitracin. Of the 86 drugs listed in the U.S. Food and Drug Administration's (FDA) "Ranking of antimicrobial drugs according to their importance in human medicine," part of the agency's guidance for evaluating the safety of new antimicrobial animal drugs, 78 percent are categorized as "highly" or "critically" important.⁴

The U.S. Centers for Disease Control and Prevention (CDC) and the U.S. National Academy of Sciences have stated that routine antimicrobial use in food animals contributes to rising drug-resistant infections in humans. In 2015 a joint report published by the three European Commission's agencies working on antimicrobial resistance confirmed that associations have been observed between antimicrobial consumption and resistance prevalence from animals to humans.⁵ Increasing concerns for the future efficacy of antimicrobials have led some countries to commit to policies that reduce the use of antimicrobials in animals raised for food. In November 2015, EU Member States proposed an article on Antimicrobial Resistance for inclusion in the Transatlantic Trade and Investment Partnership (TTIP).

TACD offers an update to its June 2011 "Resolution on Antimicrobials in Animal and Food Production," and the antimicrobial resistance section of its October 2013 "Resolution on the approach to food and

¹ World Health Organization. (2014). *Antimicrobial Resistance: Global Report on Surveillance*. France: WHO Press.

² World Health Organization. (2014). *Antimicrobial Resistance: Global Report on Surveillance*. France: WHO Press.

³ R. Laxminarayan, et al. (2013). "Antibiotic resistance—the need for global solutions," *The Lancet Infectious Disease Commission*. Published online 17 November, available at: [http://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/8996/CarsEtAl_AntibioticResistance-TheNeedforGlobalSolutions_LancetInfectiousDiseases_2013\[1\].pdf?sequence=1](http://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/8996/CarsEtAl_AntibioticResistance-TheNeedforGlobalSolutions_LancetInfectiousDiseases_2013[1].pdf?sequence=1).

⁴ U.S. FDA. (2003) *Guidance for Industry #152: Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern*. Center for Veterinary Medicine, U.S. Department of Health and Human Services Food and Drug Administration (23 October).

⁵ ECDC/EFSA/EMA first joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals (2015).

nutrition related issues in Transatlantic Trade and Investment Partnership.” Since 2011, governments and international organizations have made commitments regarding the need to stem the rise of antibiotic-resistant infections and promote greater stewardship of antimicrobial usage in the human health industry. However, policies and actions aimed at reducing the use of antimicrobials in animals raised for food and ending their routine, non-therapeutic use for growth promotion, disease prevention, and disease control are lacking. Many national and regional strategies, as well as international collaborative efforts such as the Trans-Atlantic Task Force on Antimicrobial Resistance (TATFAR), lack strong language on dealing with drivers of antimicrobial resistance in food animal production.

Recommendations

- TACD urges a complete ban on the uses of antimicrobials in animal and food production for growth promotion and feed efficiency, and a ban on the routine prophylactic (disease prevention) and metaphylactic (disease control) use of antimicrobials. This prohibition should not prevent prophylactic use in an individual animal following an operation or a difficult birth. Use of antimicrobials for metaphylaxis is permissible where disease has been identified in an animal or within a group of animals and such use is narrowly prescribed. As the Antibiotic Resistance Coalition’s *Declaration on Antibiotic Resistance* states, “Antibiotics should only be used for treating animals when indicated by a genuine therapeutic need and based on antibiotic therapeutic guidelines.”⁶
- TACD recommends that governments restrict the therapeutic and metaphylactic use of antimicrobials identified as highly or critically important to human medicine in food producing animals, especially fluorquinolones and third- and fourth-generation cephalosporins. The use of non-medically important antimicrobials for metaphylaxis is acceptable as it can prevent disease spreading from infected animals to others in the group. However, governments must take steps to ensure that regular metaphylactic use is not allowed and is replaced by disease prevention through improved husbandry, housing, and hygiene, and reduction of group sizes.
- TACD calls on governments to establish and fund comprehensive monitoring systems for surveying, quantifying, and qualifying on-farm antimicrobial usage in animals raised for food. These surveillance systems must report the amounts, durations, administration route, and indications for all antimicrobial agents administered to animals raised for food.
- TACD emphasizes the need for governments to require all antimicrobial use in animals raised for food to be subject to veterinary prescription. Governments must also provide technical and financial assistance or guidance for animal producers in remote areas or areas without local veterinarians to access veterinary services for therapeutic antimicrobials needs when they arise. Veterinarians must have no financial interest in the drugs that they prescribe.
- TACD asserts the need for improvements in animal production and management practices that reduce the need for antimicrobials. Improved livestock housing, biosecurity measures, hygiene, health management, stock management, and nutrition strategies should be developed, as well as further research on alternative production methods.
- TACD urges governments to phase in a ban over three years on the use of antimicrobials in plant/crop protection.

⁶ Antibiotic Resistance Coalition. (2014) *Declaration on Antibiotic Resistance* (22 May).

- TACD recommends international harmonisation of standards and practices that prohibit routine, non-therapeutic uses of antimicrobials and establish permissible, therapeutic uses of antibiotics that maximize the health of consumers and animals. E.U. Member States have proposed an article for inclusion in the TTIP on addressing antimicrobial resistance, setting a goal of international collaboration to harmonise surveillance, best practices, and quality assurance programs. In addition to this goal, the U.S. and E.U. Member States must provide leadership through international efforts, such as the World Organization on Animal Health (OIE) and the Codex Alimentarius Commission (Codex), to expedite strong agreements on measures that states must take to prohibit and prevent non-therapeutic uses of antibiotics in animal production. The E.U. and U.S. must also provide financial assistance for implementation of such agreements in OIE member countries that lack technical and financial capacity.

Background

Animal nutrition studies in the 1940s and 50s demonstrated that including antimicrobials in animal feeds promotes faster growth and improves feed conversion. Antimicrobials are thought to promote animal growth through their effects on gut microflora, suppressing microbes that would otherwise compete with the host for nutrients.⁷ Today, it is estimated that the annual consumption of antimicrobials per kilogram of animal produced is 45 milligrams/kilogram (mg/kg) for cattle, 148 mg/kg for chicken, and 172 mg/kg for pigs, globally.⁸ And, according to the Organisation for Economic Co-operation and Development (OECD) in 2015, consumption of antimicrobials in the animal sector is projected to increase by 67 percent by 2030.⁹ A 2014 analysis of farms in nine E.U. member states found that the use of one type of antimicrobial does not exclude the use of additional, unrelated antimicrobials,¹⁰ suggesting that producers use multiple antimicrobials simultaneously.

The U.S. Department of Agriculture (USDA) outlines four main purposes for antimicrobial use in food animal production:¹¹

- Disease treatment: the control of a diagnosed illness in animals that are symptomatic.
- Disease control (metaphylactic): preventing illness in healthy animals when diseased animals are present in the herd or flock to prevent the diagnosed illness from spreading.
- Disease prevention (prophylactic): preventing disease in healthy animals when no animals display signs of clinical disease.
- Growth promotion or feed efficiency: providing antimicrobials for their role in faster animal growth and improved conversion of feed to weight gain.

Only the disease treatment of a diagnosed illness should be allowed in the future. All further efforts must be oriented to that aim.

⁷ S. Sneeringer, J. MacDonald, N. Key, W. McBride, & K. Matthews. (2015) *Economics of Antibiotic Use in U.S. Livestock Production*, Washington, D.C.: USDA Economic Research Service (November).

⁸ T.P. Van Boeckel et al. (2015). "Global trends in antimicrobial use in food animals," *Proceedings of the National Academy of Sciences of the United States of America*, 112(18) (5 May): 5649-5654.

⁹ Organisation for Economic Co-operation and Development. (2015) *Global Antimicrobial Use in the Livestock Sector*. TAD/CA/APM/WP(2014)34/FINAL. Trade and Agriculture Directorate Committee for Agriculture (26 February).

¹⁰ L. Garcia-Migura, R.S. Hendriksen, L. Fraile, & F.M. Aarestrup. (2014). "Antimicrobial resistance of zoonotic and commensal bacteria in Europe: The missing link between consumption and resistance in veterinary medicine," *Veterinary Microbiology*, 170: pp. 1-9.

¹¹ S. Sneeringer, et al. (2015).

A substantial body of evidence indicates the overuse of antimicrobials in intensive animal production contributes significantly to antimicrobial resistance. Routine administration of antimicrobials drives resistance among target and non-target pathogens, many of which pose a direct health threat to humans. This is particularly relevant as in the E.U. 91 percent of antimicrobial sales are for group treatment and only 9 percent for individual treatment.¹² Despite difficulty, some studies have demonstrated strong connections linking antimicrobial use in animals raised for food to drug-resistant human infections. A study from the National Food Institute in Denmark found a strong correlation between resistant *E. coli* isolates in human blood stream infections and isolates from poultry, swine, and cattle. The correlation between drug-resistant *E. coli* isolates in human blood stream infections and usage of antimicrobials in humans was less strong.¹³ The zoonotic bacteria *Salmonella*, *Campylobacter*, and *E. coli* pose a particular threat to human health. The latest European Food Safety Agency (EFSA) report on *Salmonella* and *Campylobacter* confirmed that these bacteria show significant levels of resistance to common antimicrobials in humans and animals.¹⁴

A current survey in Germany shows “that the transferrable gene *mcr-1* which was first detected in China and which causes resistance to the antibiotic colistin is also widespread in intestinal bacteria in farm animals in Germany. Most frequently, this colistin resistance is detected in *Escherichia coli* of fattening poultry. Transferrable resistance genes can be passed on from harmless intestinal bacteria, so-called commensal bacteria, to pathogens thus making these pathogens harder to treat. It was previously assumed that resistance to colistin could not be transferred between bacteria.”¹⁵ This example illustrates the complexity of antimicrobial resistance, the need for international research, and the importance of banning the use of antibiotics in animal farming that have applications to or shared characteristics with human medicines.

Drug-resistant organisms are carried off the farm by workers,¹⁶ wildlife,¹⁷ and insects,¹⁸ as well as on the meat and animal products.¹⁹ Antimicrobial resistance can transform easy-to-treat infections into severe illnesses that require prolonged or aggressive treatment, lengthy hospitalisations, or even death. In November 2015, research by the American Academy of Pediatrics demonstrated that the use of antibiotics in livestock for purposes other than treating illness contributes to the threat of resistant infections in humans through the food supply, and young children are especially vulnerable to resistant

¹² ECDC/EFSA/EMA first joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals (2015)

¹³ A.R. Vieira, P. Collignon, F.M. Aarestrup, S.A. McEwen, R.S. Hendriksen, T. Hald, and H.C. Wegener. (2011). “Association Between Antimicrobial Resistance in *Escherichia coli* Isolates from Food Animals and Blood Stream Isolates from Humans in Europe: An Ecological Study,” *Foodborne Pathogens and Disease*, 8(12) (December): 1295-1301; Harrison et al., 2013; Morley et al., 2011; Mather et al., 2013

¹⁴ ECDC/EFSA/EMA first joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals (2015)

¹⁵ Bundesinstitut für Risikobewertung. (2016) “Transferrable colistin resistance found in bacteria from German farm animals,” BfR Press Release (7 January), available at http://www.bfr.bund.de/en/press_information/2016/01/transferrable_colistin_resistance_found_in_bacteria_from_german_farm_animals-196150.html.

¹⁶ Center for Disease Dynamics, Economics & Policy. 2015. *State of the World's Antibiotics, 2015*. CDDEP: Washington, D.C.

¹⁷ N.T. Nhung, et al. (2015). “High Levels of Antimicrobial Resistance among *Escherichia coli* Isolates from Livestock Farms and Synanthropic Rats and Shrews in the Mekong Delta of Vietnam,” *Applied and Environmental Microbiology*, 81(3) (February): 812-820.

¹⁸ L. Zurek & A. Ghosh. (2014). “Insects Represent a Link between Food Animal Farms and the Urban Environment for Antibiotic Resistance Traits,” *Applied and Environmental Microbiology*, 80(12) (June): 3562-3567.

¹⁹ S. Sneeringer, et al. (2015).

food-borne infections.²⁰ Approximately 25,000 and 23,000 deaths each year are attributed to antibiotic-resistant infections in the E.U. and U.S., respectively.²¹

Strong policies and actions aimed at reducing use of antimicrobials in farming must form a central aspect of the strategy for combating antimicrobial resistance. The Center for Disease Dynamics, Economics & Policy's 2015 *State of the World's Antibiotics* suggests that antibiotics policies should focus more on preservation of current antibiotics and shift away from a dominant emphasis on developing new antimicrobial agents due to the potential for any new drugs to be misused.²² Additionally, countries with less restrictive policies—Czech Republic, France, and the Netherlands—tended to use larger amounts of multiple antimicrobial classes than those with more restrictive policies.²³ France raises Europe's largest population of beef cattle and the Netherlands exports three-quarters of the poultry, meat, and eggs it produces, illustrating how less restrictive antimicrobial policies in one country may pose significant public health risks for its trading partners. Restrictions on the use of antibiotics on food animals vary greatly globally. A survey by the World Organization on Animal Health (OIE) found that half of the 178 surveyed countries still allow the use of antimicrobials for growth promotion.²⁴ Further, few OIE member states have implemented systems for antibiotic use data collection.²⁵

In 1986, Sweden banned the use of antimicrobial feed additives, making the use of antimicrobials in animal feeds illegal without a veterinary prescription. In 1999, Denmark terminated the non-therapeutic use of antimicrobials. The Swedish and Danish bans demonstrated that it is possible to achieve competitive production results without the routine use of antimicrobials. Antimicrobial use in Denmark, the world's largest exporter of pork, has significantly declined, as have the incidences of antimicrobial resistance, despite its industrial scale meat production. In 2006, the E.U. banned the use of most antimicrobials as feed additives for growth promotion and in 2009 began collaboration with the U.S. called the Trans-Atlantic Task Force on Antimicrobial Resistance (TATFAR). TATFAR issued a list of 17 recommendations in 2011, but included little reference to stewardship or reduction of antimicrobial use in food-producing animals.

In 2014, the European Commission issued a proposal to update regulations on medicated feed and veterinary medicines. The medical feed proposal specifies that "[m]edicated feed containing antimicrobial veterinary medicinal products shall not be used to prevent diseases in food-producing animals or to enhance their performance."²⁶ However, the absence of a parallel provision in the veterinary medicines regulation, which covers antibiotics use as top-dressing (i.e. added on top of the feed) and in drinking water, results in an incomplete prohibition of routine administration of antimicrobial veterinary medicinal products. Members of the European Parliament are now proposing to align both texts and ban the prophylactic use of antibiotics. A few defined exemptions will be included to allow prophylaxis in some limited cases such as surgery or when an individual animal is injured. The

²⁰ Paulson J.A., et al. (2015). "Nontherapeutic use of antimicrobial agents in animal agriculture: Implications for pediatrics" *Pediatrics*.

²¹ European Commission. (2015). *EU proposal to include an article on Anti-Microbial Resistance within the SPS Chapter of TTIP*. Brussels (6 November).

²² Center for Disease Dynamics, Economics & Policy. (2015). *State of the World's Antibiotics, 2015*. CDDEP: Washington, D.C.

²³ L. Garcia-Migura, et al. (2014).

²⁴ A.D. So, T.A. Shah, S. Roach, Y.L. Chee, and K.E. Nachman. (2015). "International Agreement to Address the Contribution of Animal Agriculture to Antibiotic Resistance: A One Health Approach," *Journal of Law, Medicine & Ethics*, 43(2) (Summer): pp. 38-45.

²⁵ A.D. So, et al. (2015)..

²⁶ European Commission. (2014). Article 16.2

Commission also wants to set a new database to mandatorily collect information on consumption of antimicrobials in food-producing animals.²⁷ In addition the European Commission proposes that feed containing antimicrobial veterinary medicinal products may only be supplied in quantities sufficient for two weeks of treatment and that feed businesses must keep records for five years. The European Parliament and the Council of Ministers are now discussing the proposals and the final texts are not likely to be adopted before 2017.

Regulations that narrowly emphasize feed-based antimicrobial uses in food animals are insufficient. They not only fail to address other routes of administration, such as daily water rations, for terrestrial animals, but also the primary route of administration for farmed aquatic animals. As the WHO *Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food* states, a food producing animal is any animal raised for the purpose of providing food for humans,²⁸ and therefore is not limited to terrestrial livestock. The most common route of administration in aquaculture is medicating the water the fish and shellfish inhabit.²⁹ Currently, data on the quantities of antimicrobial agents used in aquaculture are unavailable in most countries, and “An important proportion of the aquatic animals produced within the global aquaculture industry are raised in countries with insufficient regulation and limited enforcement of the authorised use of antimicrobial agents in animals.”³⁰ It is critical that efforts to reduce the use of antimicrobials in food animals directly address their uses in aquaculture production and that states commit to implementing surveillance strategies for their aquaculture industries.

In 2015, the U.S. White House published a National Action Plan for Combatting Antibiotic-Resistant Bacteria (CARB). Regarding antimicrobial use in animal agriculture, the CARB Action Plan relies exclusively on implementation of voluntary guidance on “judicious use” of medically-important antimicrobials issued by the U.S. Food and Drug Administration (FDA) in 2012 and 2013.³¹ FDA considers “judicious use” to be limiting the use of medically important antimicrobial drugs to uses considered necessary for assuring animal health, and requiring veterinary oversight or consultation for all uses of medically important antimicrobials.³² The use of medically important antimicrobials for prevention (prophylactic) purposes when approved by a veterinarian for a specific bacterial disease is considered “judicious use.” The FDA guidance documents and the CARB Action Plan continue to allow the routine use of antimicrobials for prophylaxis and metaphylaxis. Beginning in 2016, all feed containing medically-important antimicrobials will require a veterinarian prescription. However, no U.S. regulation currently

²⁷ European Commission, (2014) *Proposal for a Regulation of the European Parliament and of the Council on veterinary medicinal products*, Article 54

²⁸ World Health Organization. (2000). *Global Principles for the containment of antimicrobial resistance in animals intended for food*. Report of a WHO consultation with the participation of the Food and Agriculture Organization of the United Nations and the Office International des Epizooties, 5-9 June, Geneva, WHO.

²⁹ Y.H. Park, et al. (2012) “Use of antimicrobial agents in aquaculture,” *Rev. sci. tech. Off. int. epiz.*, 31(1): pp. 189-197.

³⁰ Y.H. Park, et al. (2012) “Use of antimicrobial agents in aquaculture,” *Rev. sci. tech. Off. int. epiz.*, 31(1): pp. 189-197, at 195.

³¹ U.S. Food & Drug Administration. (2012). *Guidance for Industry #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*. Washington, DC: U.S. Department of Health & Human Services (13 April); U.S. Food & Drug Administration. (2013). *Guidance for Industry #213: New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209*. Washington, D.C.: U.S. Department of Health & Human Services.

³² U.S. Food & Drug Administration. (2012). *Guidance for Industry #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*. Washington, DC: U.S. Department of Health & Human Services (13 April)

exists that would prevent or restrict a veterinarian from owning their own animals or feed mill. In 2014, Canada implemented a voluntary strategy similar to that of the U.S.³³

In 2015, E.U. Member States proposed the addition of an Article on AMR within the Sanitary and Phytosanitary (SPS) chapter of the TTIP. The article calls for the creation of a Technical Working Group of experts to facilitate the exchange of information on AMR and animal production and spur the development of a harmonized surveillance system, guidelines for veterinarians and producers on best practices, and quality assurance programmes for assessing stewardship.³⁴ The article rightly sets out that the goal of international collaboration on antibiotics in animal production must be reduced use. However, the focus on surveillance mechanisms and guidelines for best practices rather than commitments from Parties to implement bans, restrictions, and regulatory oversight regarding antimicrobial use in animals raised for food will not provide consumers with an appropriate level of sanitary and phytosanitary protection. The request that Parties shall “follow existing and future guidelines, standards, recommendations and actions...aiming to promote reduced use of antibiotics and relating to animal production and veterinary practices,” is the strongest language encouraging Parties to directly address antimicrobial use.

Additionally, the Commission’s proposed article states that AMR work under TTIP “would be seen as complementary to and facilitating” the work of TATFAR.³⁵ As stated above, TATFAR’s work to date has made little reference to addressing antimicrobial use in food-producing animals, particularly the need to achieve significant reductions in use. As such, facilitating the activities of TATFAR will not adequately address the issue of antimicrobial resistance as it relates to use in animals raised for food. Any reference to TATFAR in the proposed article must seek to augment the collaborative effort by holding member states accountable for reducing the use of antimicrobials in agriculture.

Resolution

Because the risk of cross-border spread of antimicrobial-resistant pathogens is a shared one, the TACD calls on governments to develop a common and cooperative approach to addressing antimicrobial use in animals raised for food. Specifically, TACD requests that countries institute bans on the non-therapeutic and routine (performance (growth promotion and feed efficiency), prophylactic (disease prevention), and metaphylactic (disease control) use of antimicrobials in animals raised for food. TACD also requests countries establish restrictions on the therapeutic use (disease treatment and non-routine metaphylaxis) of medically-important antimicrobials. The use of modern cephalosporins in poultry is already banned in the E.U. since 2012 while the U.S. banned fluroquinolones in poultry in 2005. Further, TACD emphasizes that the use of any antimicrobials in animals raised for food must only be allowed with a prescription from a licensed veterinarian and after physical examination of the animals. To preclude any economic incentive to overprescribe, veterinarians should not profit from the sale of antimicrobials, and in particular antibiotics. Better data collection systems are key to identify current practices and set future directions. Countries should join forces and develop a global monitoring system with similar indicators to allow direct comparisons. Consumption data should at the very least provide information by species and production types.

³³ Center for Disease Dynamics, Economics & Policy. (2015).

³⁴ European Commission. (2015). *EU proposal to include an article on Anti-Microbial Resistance within the SPS Chapter of TTIP*. Brussels (6 November).

³⁵ European Commission. (2015). *EU proposal to include an article on Anti-Microbial Resistance within the SPS Chapter of TTIP*. Brussels (6 November).