Reduce unintentional exposure and the need for antimicrobials, and optimize their use

IACG Discussion Paper

Disclaimer: This document reflects the discussions of IACG subgroup responsible for optimizing use of antimicrobials so far and will be subject to change as the discussions continue. It does not necessarily reflect the views of the IACG as a whole.

Key messages

- **Good guidance is available:** There is a wealth of good, relevant guidance that, if put into practice, would lead to a significant, rapid reduction in the inappropriate use of antimicrobials in humans, animals and plants.
- **AMR in the environment is a challenge:** There is a need to better understand resistance in the environment, the root causes and the means to prevent and mitigate the spread of resistance in the environment.
- **Implementation is key:** Ways must be found to increase the implementation of existing guidelines and facilitate good practices, with a focus on solutions and strategies suitable for settings with limited resources.
- **Infection prevention and control measures, supported by adequate water and sanitation infrastructure, will make a difference:** Significant WASH improvements and effective strategies to change practices are essential, combined with the application of biosecurity measures.
- **Balancing increased and sustainable food production will be a challenge:** Measures that address the need to phase out the inappropriate use of antimicrobials in food production must take into account the need to sustainably increase safe food production in accordance with the Sustainable Development Goals.
- **Effective measures to reduce the burden of food- and waterborne infections** will also reduce the need for antimicrobial therapy and prevent the spread of AMR.
- **Harmonized approaches to regulation are essential:** To ensure effective, science-based regulation on AMR, and to avoid trade friction elicited by different regulatory approaches to AMR, countries must be encouraged to take a harmonized approach based on international standards.

Introduction and scope

All use, including appropriate, inappropriate, over- and under-use of antimicrobial agents drives the development and spread of antimicrobial resistance (AMR). Strong selection pressures created by the extensive use of antimicrobials among humans, animals and plants over time has led to the development of resistance to many vital, life-saving therapies.

The Interagency Coordination Group (IACG) on AMR was established to provide practical guidance for approaches needed to ensure sustained effective global action to address AMR; and to report back to the UN Secretary-General in 2019. AMR is a global and multisectoral problem requiring a coherent response that bridges human, animal, plant and environmental health. In order to effectively address the broad AMR challenge, the IACG developed discussion papers to facilitate public consultation. Responses will help inform the deliberations for producing the IACG report to the United Nations Secretary-General in 2019.

Box 1 – Topic areas

1. **Prevention and control of human infection**
2. **Clean water, sanitation and hygiene**
3. **Optimizing use in animals and plants**
4. **Prevention and control of animal infection**
5. **Food safety and food production**
6. **Environmental contamination**
7. **Optimizing use in humans**

To cover the broad scope of the subject, this paper is structured according to seven topic areas (see box 1). It describes the challenges for each area, and current initiatives to meet those challenges. Several themes emerged across multiple areas. These include: ensuring that existing guidelines are used to promote good practices, and supporting and monitoring their use, increasing resources, promoting behaviour change, generating evidence, and regulating/legislating.

The discussion paper solicits input on a limited number of open questions based on convergence across the various topic areas.

We encourage all stakeholders to consider the questions posed at the end of this document and to submit their perspectives to the IACG at iacg-secretariat@who.int.

Topic areas, challenge and response

1. Prevention and control of human infection in the provision of health care

The challenge: Effective infection prevention and control (IPC) averts infections associated with health care, and protects both patients and health workers. IPC has a crucial role in the response to AMR, as it reduces the transmission of microbes, including antimicrobial-resistant organisms, thereby reducing the future need for antimicrobials.

Substandard IPC practices during ordinary health care delivery result in harm to hundreds of millions of patients worldwide every year. Several recent alerts, most notably during the epidemic of Ebola virus disease in West Africa, have raised awareness of this issue; yet adequate IPC is still a challenge in many countries. The global database[1] of country self-assessments of AMR shows that although

[1] https://extranet.who.int/sree/Reports?op=vs&path=%2FWHO_HQ_Reports/G45/PROD/EXT/amrcsat_Menu

86% of countries reported having a policy or plan for IPC, only 37% implemented it nationwide and monitored IPC measures in health facilities.[2]

Common barriers include competing political agendas, resource constraints, lack of expertise in IPC and lack of feasible implementation approaches for low-resource settings. Resistance to behaviour change among health workers may also be an issue. Other key gaps identified include a lack of sufficient financial and human resources dedicated to IPC programmes at the national and facility level, poor knowledge and implementation of IPC measures in healthcare settings, including poor compliance with hand hygiene, the lack of recognition of the role of IPC in reducing AMR spread and emergence, compared with the importance given to appropriate antibiotic use, the low level of integration of IPC plans and actions with other programmes/priorities such as WASH, health emergency preparedness and the International Health Regulations, and limited evidence about the effectiveness and cost-effectiveness of IPC interventions to improve patient outcomes as well as about local solutions for low-resource settings. There is also a need to confirm and support the role of the accreditation bodies in demanding that health care settings have IPC and antimicrobial stewardship programmes in place.

Current response: WHO and collaborating national and international organizations have undertaken numerous initiatives to strengthen understanding of IPC and national IPC systems and programme and to provide guidance on specific issues and country support for implementation. Two relevant documents have been recently published, in addition to previous guidelines and resources on hand hygiene and other precautions.[3] The Guidelines on core components of IPC programmes at the national and health care facility level[4] address the IPC component of AMR national action plans, while Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in health care[5] concern the emerging threat of carbapenem-resistant microorganisms. Validated implementation strategies and tools to translate these guidelines into practice are available and are continuously expanded.[3]

2. Clean water, sanitation and hygiene (WASH)

The challenge: Access to clean drinking water, safely managed sanitation and water and soap and water for hygiene (WASH) is far from universal. WHO and UNICEF estimated in 2015 that up to 61% of the world's population did not have access to safe sanitation and that in areas with large populations only 30-60% of piped sewage is treated.[6] In addition, 38% of health facilities did not have a source of water, nearly 19% had no toilets and 35% had no water and soap or alcohol-based hand rub for handwashing,[7] making IPC almost impossible. These conditions also tend to lead to high rates of prescriptive or prophylactic use of antibiotics, especially during childbirth.

In addition, the spread of pathogens through unsafe water results in a high burden of gastrointestinal disease, increasing even further the need for antibiotic treatment.

[2] http://www.who.int/antimicrobial-resistance/global-action-plan/database/en/
[3] http://www.who.int/infection-prevention/en/; http://www.who.int/infection-prevention/publications/hh_evidence/en/
[4] http://www.who.int/infection-prevention/publications/core-components/en/
[5] http://www.who.int/infection-prevention/publications/focus-amr/en/
[6] WHO/UNICEF 2017, 2017. Progress on drinking water, sanitation and hygiene: 2017 update and SDG baselines. http://www.who.int/mediacentre/news/releases/2017/launch-version-report-jmp-water-sanitation-hygiene.pdf
[7] WHO/UNICEF, 2015. Water, sanitation and hygiene in health care facilities: urgent needs and actions. Meeting Report. http://www.who.int/entity/water_sanitation_health/facilities/wash-in-hcf-geneva.pdf?ua=1

It is important to highlight that the link between AMR and WASH must be better acknowledged and communicated.

Current response: A WHO expert meeting in 2017 on the link between AMR and WASH concluded that:

- Existing WASH interventions in health facilities and communities offer significant co-benefits for combatting AMR, and investment should be increased, including through national action plans on AMR;
- Manufacturers of antimicrobials need to improve wastewater treatment to reduce the release of residues into the environment; and
- Additional research is needed on the relative impact of inadequate WASH on AMR infections, and on effective management strategies.

In 2015, WHO and UNICEF launched a global action plan on WASH in health facilities[8] to advance work on advocacy and policy, on monitoring (including under SDG 6[9]) and evidence, and on facility improvement. Over 40 partners are engaged, from both the WASH and health sectors, and work is under way to ensure that national action plans on AMR include concrete actions for WASH.

3. Optimizing use in animals and plants

The challenge: Food source animals and plants are both subject to infection. Animals that have – or are at risk of having – bacterial infection should be treated with antimicrobials of assured quality, prescribed by a veterinarian. The problem is twofold. While in some countries the use of antimicrobials in animal husbandry is estimated to be as high as, or even higher than in the human health sector, others (particularly low- and middle-income countries, LMICs) often experience difficulties in accessing effective antibiotics to treat their livestock. Similarly, plant diseases and production losses are often caused by bacteria and fungi, especially in LMICs, and climate change is predicted to further exacerbate the problem. Unfortunately, animal producers do not always adhere to optimal practices, relying on the availability of cheap antimicrobials to prevent and treat infections and, in some cases, to promote the growth of animals.

SDG 2[10] recognizes the need for a maintainable increase in animal and plant production to meet the demands of a growing world population and diets with more foods of animal origin. Balancing increased and sustainable food production will be a challenge. Antimicrobials are approved for use in treating plant diseases in at least 20 countries, not including European Union member states. In a number of countries, antimicrobial use in animal production has fallen as a result of coordinated action by international and national authorities, veterinarians and farmers. Intensification of animal production, however, is predicted to increase the use of antimicrobials in livestock by nearly 70% by 2030 if production methods do not become more sustainable.[11]

[8] WHO, 2017. Water, sanitation and hygiene (WASH) in health care facilities global action plan. http://www.who.int/water_sanitation_health/facilities/healthcare/wash-in-hc-facilities-action-plan-updated-20161005.pdf

[9] SDG 6: Ensure availability and sustainable management of water and sanitation for all. https://unstats.un.org/sdgs/report/2017/goal-06/

[10] SDG 2: End hunger, achieve food security and improved nutrition and promote sustainable agriculture. https://unstats.un.org/sdgs/report/2017/goal-02/

[11] Van Boeckel T, Brower C, Gilbert M et al. Global trends in antimicrobial use in food animals. Proceedings of the National Academy of Sciences May 2015, 112 (18) 5649-5654.

A significant proportion of animal producers in some countries follow less-than-optimal practices for a variety of reasons, including a lack of knowledge, tools or economic means, inadvertent use (for example in ingredients of supplements marketed as nutritional substances) without veterinary oversight, and the overt intention of promoting animal growth.

Current response: FAO, OIE and other international organizations are supporting animal producers by issuing guidance and standards for good practices, prevention and control of diseases, animal welfare and prudent use of antimicrobials. The OIE Terrestrial Code Chapter 6.9 and OIE Aquatic Code Chapter 6.2, outline standards for all relevant stakeholders in animal production.[12] OIE has also published its Strategy on AMR and the Prudent Use of Antimicrobials.[13] FAO has published good practice guides for various sectors,[14] conducted training and prepared a toolkit for biosecurity in swine and poultry operations on family farms. It is also identifying good regulatory and policy practices to reduce the inappropriate use of antimicrobials and the emergence and spread of AMR.

The Codex Alimentarius Commission has issued normative standards on AMR in the food chain.[15] The Commission re-established its ad hoc Task Force on AMR, which is tasked to revise an existing code of practice on responsible use and develop new guidelines on integrated surveillance, and requested FAO and WHO to establish a capacity-development programme to respond to the identified needs. FAO has developed an action plan to support the food and agriculture sectors in implementing the Global Action Plan on AMR to minimize the impact of antimicrobial resistance, as well as an International Code of Conduct on Pesticide Management. The organization is working closely with veterinarians, farmers and food safety professionals to support best animal health practices, which underpin the prudent use of antimicrobials.

4. Prevention and control of infection in animals

The challenge: Animal production is expected to increase in the coming years as a result of economic and population expansion, and it is expected that the use of antimicrobials will increase concomitantly. Applying optimal husbandry practices and good biosecurity measures, including vaccination, reduces the incidence of disease and the need for antimicrobials.

To apply good infection prevention and control measures, producers must have three things: knowledge about how to prevent disease, access to those preventive measures, and incentives to change their practices.

Current response: Multiple organizations are supporting animal producers by developing guidance and standards on good practices to prevent and control diseases, promote animal welfare and the prudent use of antimicrobials. In addition to documents and tools mentioned previously, FAO is working to identify regulatory and policy practices that could reduce the inappropriate use of antimicrobials and the emergence and spread of AMR. Section 4 of the OIE Terrestrial Code contains

[12] OIE, 2017. Terrestrial Animal Health Code, Chapter 6.9. (http://www.oie.int/fileadmin/Home/eng/Health_standards/tahc/current/chapitre_antibio_use.pdf); and OIE Aquatic Animal Health Code, Chapter 6.2. (http://www.oie.int/fileadmin/Home/eng/Health_standards/aahc/current/chapitre_antibio_resp_prudent_use.pdf).
[13] http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/PortailAMR/EN_OIE-AMRstrategy.pdf
[14] FAO Responsible use of antibiotics in aquaculture. FAO Fisheries technical paper. http://www.fao.org/3/a-a0282e.pdf
[15] FAO A Code of Practice to minimize and contain AMR (CAC/RCP 61-2005), Guidelines for risk analysis of food-borne AMR (CAC/GL 77-2011), http://www.fao.org/docrep/012/i1379e/i1379e06.pdf, http://www.mhlw.go.jp/english/topics/importedfoods/guideline/dl/04.pdf

relevant standards for Disease Prevention and Control.[16] To prioritize vaccine research needs, OIE has developed a list of priority diseases in chicken, swine and farmed fish where the development of vaccines would largely reduce the use of antibiotics. OIE is extending this work to other animals including cattle, sheep and goats, and has prepared disease-specific standards to avoid infection through trade.[17] OIE is also collecting data on global use of antimicrobials in animals to establish baseline information and enable countries to follow trends,[18] and have published a strategy on AMR and prudent use of antimicrobials.[19] The Organisation for Economic Co-operation and Development (OECD) has convened an expert steering group to estimate the benefits and costs of reducing antimicrobial use in food animal production.

5. Food safety and food production

Many of the challenges and responses described in previous sections are directly related to the area of food safety, particularly those concerning optimizing use in animals and plants, and prevention and control of infection in animals. The following are important additional issues related to the complexity of transmission and emergence of AMR along the food chain, from food primary production to consumption. The main issues concern reducing the burden of foodborne bacterial diseases and developing and implementing good practices in primary production and processing.

The challenge: Effective measures to reduce the burden of foodborne bacterial diseases could also reduce the need for antimicrobial therapy and prevent the spread of AMR. According to WHO estimates, over 400 000 people die each year from such diseases, with more than one third of the deaths occurring among children under 5 years of age. Diarrhoeal diseases are the most common infections resulting from consumption of contaminated food.

The large volumes of antimicrobials given to food-producing animals in some countries can have important public health consequences, because antimicrobial-resistant bacteria in the animal gut can potentially be transmitted to humans through the food chain or the environment. Some bacteria isolated from foods of plant origin are also resistant to critically important antimicrobials. When these bacteria become resistant, the resulting disease becomes more difficult to treat. Soil, water, manure used as fertilizer and human handling are probable sources of contamination in food production.

***Current responses*:** These challenges can be addressed largely by ensuring good hygiene and biosecurity and by finding and adopting effective, practical alternatives for preventing and treating microbial infections in plants and animals. Adequate resources for research on food safety and foodborne AMR in LMICs and the development of regulatory frameworks, stewardship and enforcement in those countries are also needed.

[16] http://www.oie.int/index.php?id=169&L=0&htmfile=titre_1.4.htm
[17] OIE, 2017. Terrestrial Animal Health Code Vol. I. General provisions, section 5: Trade measures, import/export procedures and veterinary certification, and Vol. II. Recommendations applicable to OIE Listed diseases and other diseases of importance to international trade.
[18] OIE, 2017. Annual report on antimicrobial agents intended for use in animals. Better understanding of the global situation. http://www.oie.int/fileadmin/Home/fr/Our_scientific_expertise/docs/pdf/AMR/Annual_Report_AMR_2.pdf.
[19] OIE, 2016. TheOIE strategy on AMR and the prudent use of antimicrobials. http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/PortailAMR/EN_OIE-AMRstrategy.pdf.

Two decades of work and publications by FAO, OIE and WHO on AMR as a food safety issue[20,21,22] and issuance of pertinent standards by the Codex Alimentarius Commission[23] have raised global awareness of the need to reduce the risk of AMR in the food chain. Tools, guidance documents and guidelines are available to prioritize risk management while preserving the effectiveness of antimicrobials with medical importance in humans.[24,25,26] To complement these, OIE has made a list of antimicrobial agents of veterinary importance, and recently updated recommendations on their use.[27]

Guidance is also available for designing surveillance programmes to monitor AMR and antimicrobial use in the food chain with an integrated One Health approach, and to generate data on use as a basis for stewardship.[28,29,30,31,32,33,34,35,36]

Successful implementation of Codex and relevant FAO, OIE and WHO guidelines and standards will require multisectoral, multistakeholder collaboration at global, regional and country levels, and international solidarity to promote and further disseminate good food production practices (such as hygiene, husbandry and vaccination). The three organizations ("the Tripartite") will work further to support a scientific basis for updating the Codex code of practice to minimize and contain AMR in the food chain. They will also prepare a plan for countries on implementing recommendations, including those of the Codex Alimentarius, for containing the development and spread of AMR in food production systems.

Moreover, FAO promotes Integrated Pest Management (IPM) as a pillar of sustainable intensification of crop production and pesticide risk reduction. IPM is an ecosystem approach to crop production and protection that combines different management strategies and practices for growing healthy crops and minimizing the use of pesticides. The FAO IPM programme currently comprises three regional programmes, in Asia, the Near East and West Africa.

[20] http://www.who.int/foodsafety/publications/antimicrobial-resistance/en/
[21] http://www.fao.org/antimicrobial-resistance/resources/publications-archive/en
[22] http://www.oie.int/en/for-the-media/amr/
[23] http://www.fao.org/fao-who-codexalimentarius/thematic-areas/antimicrobial-resistance/en/
[24] http://www.fao.org/3/a-i4296t.pdf
[25] http://www.who.int/foodsafety/publications/antimicrobials-fifth/en/
[26] http://www.who.int/foodsafety/publications/cia_guidelines/en/
[27] http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/AMR/A_OIE_List_antimicrobials_May2018.pdf
[28] http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/Eng_OIE_List_antimicrobials_May2015.pdf
[29] http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/PortailAMR/EN_OIE-AMRstrategy.pdf
[30] http://www.who.int/foodsafety/publications/agisar_guidance2017/en/
[31] http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_antibio_harmonisation.htm
[32] http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_antibio_monitoring.htm
[33] http://www.oie.int/index.php?id=171&L=0&htmfile=chapitre_antibio_quantities_usage_patterns.htm
[34] http://www.oie.int/index.php?id=171&L=0&htmfile=chapitre_antibio_development_harmonisation.htm
[35] http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-804-05%252FWD%252Fam05_06e.pdf
[36] http://www.fao.org/3/a-i5996e.pdf

6. Environmental contamination

The challenge: AMR has been addressed mainly from the perspectives of human and animal health. The environment must also be considered in determining how antimicrobials, antibiotic resistance genes (ARGs), mobile genetic elements (MGEs) and resistant microbes spread from humans, animals, plants and waste (industrial or from households) (see Fig. 1 below).[37]

More data are essential to determine whether the spread of antimicrobials into the environment significantly increases the risk of AMR infections.[38] There is evidence that the environment can act as a reservoir of antimicrobial residues and resistance genes and can therefore be a "hidden incubator" for the selection, proliferation and dissemination of antimicrobial-resistant pathogens.[39] There is, however, little information on the potential impact of antimicrobial residues and antimicrobial resistance genes in the environment on human and animal health, and on the functioning of ecosystems. Other challenges include the lack of routine, standardized monitoring to determine the trends in AMR from environmental sources, and difficulty in defining the intersecting environment and therefore in designating leadership and responsibility. There are high risks of duplication and of neglect of important areas.

Current responses: During the third session of the United Nations Environment Assembly, UNEP was instructed to prepare a report on the impact of environmental AMR on human and animal health and on the environment. UNEP and WHO have signed a memorandum of understanding (MoU) to strengthen their cooperation, including on AMR-related issues. Likewise, a MoU between UNEP and FAO paves the way for the two organizations to work together on the linkages between conservation, production, the sustainable use of natural resources, climate change and achieving the Sustainable Development Goals.

Multiple complementary actions are under way. FAO, WHO, the Centres for Disease Control and Prevention (USA), the Government of the United Kingdom and the Wellcome Trust have held a number of expert meetings on the links between WASH, environmental health and AMR. Meeting reports will add understanding and guidance. The Joint Programming Initiative on Antimicrobial Resistance (JPI AMR) promotes research and shared knowledge about the causes and consequences of AMR in the environment include. Formed in 2011 by 15 European countries with the support of the European Commission, the JPI AMR now comprises 27 countries globally, and calls for research proposals on environmental AMR.[40] The European Environment Agency is preparing an expert workshop to determine the current understanding of, and the level of risk represented by, transmission of AMR through urban wastewater treatment. Specialized academic centres such as the Centre for Antibiotic Resistance Research at the University of Gothenburg[41] are also increasingly studying the environment, and the Global Sewage Surveillance Project includes over 150 participating countries.[42] The European Statistical Office (EUROSTAT) organizes regular and harmonized surveys across all EU Member States to gather information on land cover and land use.

[37] Christou A, Agüera A, Bayona JM, Cytryn E, Fotopoulos V, Lambropoulou D et al. The potential implications of reclaimed wastewater reuse for irrigation on the agricultural environment: the knowns and unknowns of the fate of antibiotics and antibiotic resistant bacteria and resistance genes. A review. Water Res. 2017; 123:448–67.
[38] Lundborg JS, Tamhankar AJ. Antibiotic residues in the environment of South East Asia. BMJ 2017; 358:j2440.
[39] Bengtsson-Palme J, Kristiansson E, Larsson DGJ. Environmental factors influencing the development and spread of antibiotic resistance. FEMS Microbiol Rev. 2018;42:68–80.
[40] https://www.jpiamr.eu/environmental-dimensions-of-amr-in-focus/
[41] https://care.gu.se/
[42] http://www.compare-europe.eu/library/global-sewage-surveillance-project/

This survey, known as LUCAS (Land Use/Cover Area frame statistical Survey), includes sampling of topsoil, coordinated by European Commission's Joint Research Centre. In 2018, the survey will include, for the first time, the most extensive EU assessment of soil biodiversity targeting bacteria, fungi and eukaryotes. Antimicrobial gene resistance distribution will be also assessed in agricultural soils across the European Union.

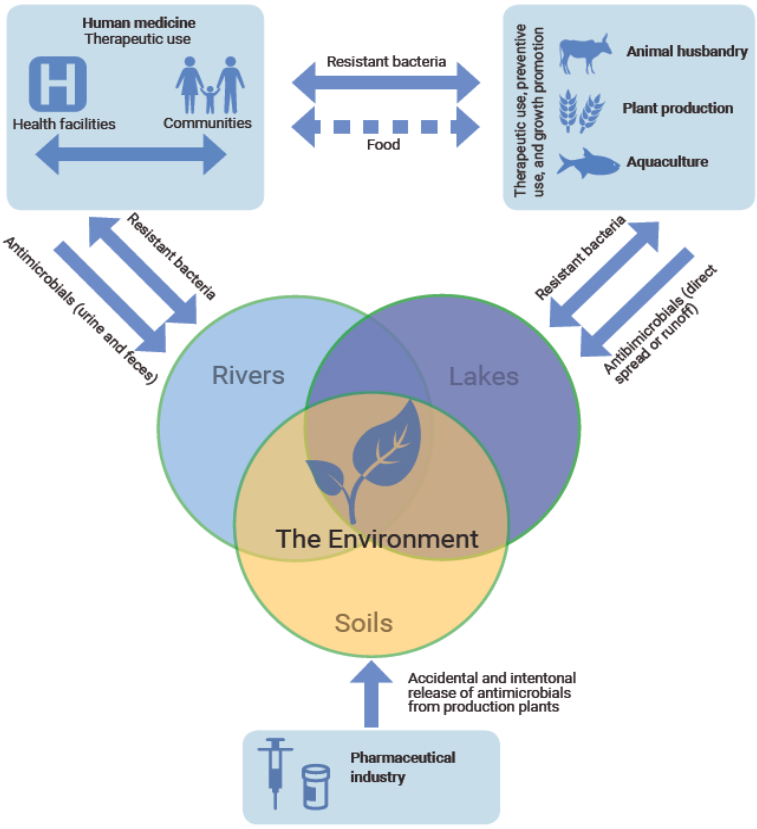

Figure 1. Pathways for the release of antimicrobial residues into the environment

Adapted from Anderson DI, Hughes D. Microbiological effects of sublethal levels of antibiotics. Nat Rev Microbiol 2014;12(7):465–78.

The Tripartite has a number of standards and guidelines relevant to reducing the release of antimicrobials into the environment. OIE has prepared standards for responsible and prudent use for terrestrial[43] and aquatic[44] animals and is collecting global data on the use of antimicrobials in animals[45] for future capacity building, decreased use and awareness-raising. The Task Force on AMR of the Codex Alimentarius Commission has requested FAO and WHO, in collaboration with OIE, to provide scientific advice on AMR in the food production environment. FAO is collecting data, reviewing the literature and designing a tool to follow the movement and fate of residues in soil and water.

[43] http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_antibio_use.htm
[44] http://www.oie.int/index.php?id=171&L=0&htmfile=chapitre_antibio_resp_prudent_use.htm
[45] http://www.oie.int/fileadmin/Home/fr/Our_scientific_expertise/docs/pdf/AMR/Annual_Report_AMR_2.pdf

Work to address the release of antimicrobial residues from the pharmaceutical industry is also under way. The European Commission recently closed a consultation on a strategic approach to pharmaceuticals in the environment.[46] The OECD recently started to develop policy guidance on contaminants of emerging concern in fresh water, including antimicrobial residues. The AMR Industry Alliance is setting target values for the pharmaceutical industry based on an assessment of risk for the development of resistance in the environment.

7. Optimizing human use

The challenge: Challenges associated with inappropriate use of antimicrobials in humans concern surveillance, legislation and regulation (including the capacity of LMICs to enforce regulation), structural weaknesses in health services, behaviour change, accessibility and affordability.

Surveillance of antimicrobial use and of AMR is crucial for identifying problems and undertaking corrective action, such as stewardship interventions and policy changes. Data on antimicrobial consumption in LMICs are sparse, patchy and usually aggregated at national level with little or no information on the place of use (for example, public or private sector; hospital or community level facilities).

In response to the increase in AMR, some countries have taken measures to establish or strengthen their laws and regulatory systems to ensure the safety, efficacy and quality of antimicrobials. Enforcement of such regulations is challenged, however, by weak regulatory capacity, lack of or poor collaboration between national medicine regulatory authorities and law enforcement bodies, increased circulation of substandard and falsified medical products and low awareness within government institutions and the general population. Sales of antibiotics in the private sector are particularly difficult to regulate in some countries.

Limited access to health services and frequent shortages of antimicrobials affects all settings in the public sector and –may lead patients to seek care from drug vendors and pharmacies. This often results in unnecessary or suboptimal use of antibiotics. It also results in the development of strong informal markets that allow the entry of substandard and falsified medicines. Furthermore in LMICs, laboratory services may be limited to higher-level hospitals, making it difficult to apply up-to-date treatment guidelines based on local resistance patterns. Finally, older antibiotics for which there are few global producers may be difficult to obtain. Lack of first-choice antibiotics results in the prescription and dispensing of broader-spectrum antibiotics. These difficulties are complemented by insufficient expertise globally, in particular the numbers of physicians and pharmacists trained in infectious diseases.

While overuse of antimicrobials is the main concern with regard to AMR, access to and the affordability of medicines, including antimicrobials, remain a challenge in LMICs. Paradoxically, underuse of antimicrobials (for example the relatively widespread practice of purchasing and consuming a single tablet) can also cause the development and spread of AMR. This is confounded by another common practice of sharing medicines with family members and friends without expert advice.

[46] https://ec.europa.eu/info/law/better-regulation/initiatives/ares-2017-2210630_en

Studies of antimicrobial prescribing and use among health professionals and the public indicate gaps in knowledge, attitudes and practices. While the drivers of poor prescribing practices and inappropriate use are well documented, little is known about the effectiveness of interventions to change them.

Funding to address these challenges and to take actions remains limited. Ministries of health and national regulatory agencies in low-resource settings are frequently understaffed. At local levels, resources are often insufficient to dedicate staff for antimicrobial stewardship and drug and therapeutics committees.

Current response: The Global Action Plan on AMR and the Global Framework for Development and Stewardship to Combat AMR under development by WHO, OIE and FAO provide important guidance for global and national strategies. Both documents focus on the appropriate use of antibiotics in humans, animals and plants. The Global Action Plan aims to increase awareness and address misunderstanding of AMR through effective communication, education and training. The annual World Antibiotic Awareness Week (WAAW) provides the public, policy makers and professionals with information on AMR and suggests actions they can take to address it. Other tools such as the WHO Essential Medicines List and Priority Pathogens List support the rational use of antimicrobials in countries.

Antimicrobial stewardship is an important part of AMR national action plans. Guidance and tools for stewardship programmes adapted to low-resource settings are being prepared by WHO, non-state actors and academic institutions. WHO has categorized antibiotics to guide prescribing and regulation and is preparing tools to assist countries in updating their national lists of essential medicines and therapeutic guidelines. The Organization is also working to improve the accessibility and use of diagnostics and laboratory services to reduce diagnostic uncertainty and inform treatment choices.

In response to the lack of data and standardized data collection, particularly in LMICs, WHO has launched global surveillance programmes on antimicrobial consumption and on AMR, with the aim of supporting countries to set up national surveillance systems. WHO is also preparing tools for complementary surveys on the use of antibiotics in hospitals and the community. In parallel, countries are being supported to strengthen the supply chain and ensure the quality of products on the market.

Open questions for stakeholders

- What kind of support (other than financial) is needed to translate the existing guidance into implementable actions?
- How can policy makers be assisted to further develop and implement infection prevention and control in human and animal health and plants and be convinced to invest now to mitigate the escalating and future costs and obtain benefits far beyond preventing AMR?
- What incentives or initiatives are needed for behaviour change towards responsible use in the health sector (hospitals, community health centres) and in the food and animal production sectors (animal and plant health professionals, food producers and manufacturers, consumers).
- What is needed to generate evidence-based data that link the misuse of antimicrobials and the development and spread of AMR via the environment? How can we use the available data to develop effective policy solutions influence policy makers?
- What approaches are needed to ensure the industry and investors manufacture and market antimicrobials responsibly, and not stimulate overuse or contribute to environmental pollution?
- Changing practices needs the support of the industry - how can we balance the availability of a public good such as effective antimicrobials, with a private industry perspective?
- What are the mechanisms to enhance the availability and utility of global resources for the end user (communities and individuals) to optimize or reduce the need for the use of antimicrobials and mitigate the unintentional exposure to the environment?