



Food and Agriculture Organization  
of the United Nations



World Health  
Organization



# Global Framework for Development & Stewardship to Combat Antimicrobial Resistance

## Draft Roadmap

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## ABBREVIATIONS

<b>AMR</b>	Antimicrobial resistance
<b>AMU</b>	Antimicrobial use
<b>CARB-X</b>	Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator
<b>CEPI</b>	Coalition for Epidemic Preparedness Innovations
<b>CEWG</b>	Consultative Expert Working Group
<b>DNDi</b>	Drugs for Neglected Diseases <i>initiative</i>
<b>EC</b>	European Commission
<b>EML</b>	Essential Medicines List
<b>FAO</b>	Food and Agriculture Organization of the United Nations
<b>FIND</b>	Foundation for Innovative New Diagnostics
<b>GAP-AMR</b>	Global Action Plan on Antimicrobial Resistance
<b>GARDP</b>	Global Antibiotic Research and Development Partnership
<b>GHIT</b>	Global Health Innovative Technology Fund
<b>IACG</b>	Interagency Collaboration Group
<b>IAVI</b>	International AIDS Vaccine Initiative
<b>IMI</b>	Innovative Medicines Initiative
<b>IPM</b>	International Partnership of Microbicides
<b>MMV</b>	Medicines for Malaria Venture
<b>MVI</b>	Malaria Vaccine Initiative
<b>NAPs</b>	National action plans
<b>NGO</b>	Non-governmental Organization
<b>OIE</b>	World Organisation for Animal Health
<b>PDP</b>	Product Development Partnership
<b>R&amp;D</b>	Research and development
<b>STAC</b>	Scientific and Technical Advisory Committee
<b>TB</b>	Tuberculosis
<b>TDR</b>	Special Programme for Research and Training in Tropical Diseases

**This document provides additional background information to WHA document A70/12 Global Action Plan on Antimicrobial Resistance.<sup>1</sup> It describes the current state of play and the way forward with respect to the establishment of a global framework for development and stewardship to combat antimicrobial resistance. The document was developed in close collaboration with the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO). It builds upon the options for the development of such a framework presented to the Sixty-ninth World Health Assembly.<sup>2</sup>**

## **CONTEXT**

In September 2016, the United Nations General Assembly in its “Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance” called upon the World Health Organization, together with the Food and Agriculture Organization of the United Nations and the World Organisation for Animal Health, to finalize a global development and stewardship framework.<sup>3</sup> As mandated in WHA68.7, the framework will support the development, control, distribution and appropriate use of new antimicrobial medicines, diagnostic tools, vaccines and other interventions, while preserving existing antimicrobial medicines, and promoting affordable access to existing and new antimicrobial medicines and diagnostic tools, taking into account the needs of all countries and in line with the Global Action Plan on Antimicrobial Resistance (GAP-AMR).<sup>4,5</sup> The WHO Director-General submitted options for establishing such a global development and stewardship framework to the Sixty-ninth World Health Assembly.<sup>2</sup>

## **OBJECTIVES**

On the basis of resolution WHA68.7 and as described in A69/24.Add. 1, the objectives of a global development and stewardship framework can be described as follows:

- Stewardship: preserve antimicrobial medicines by taking measures to promote control, appropriate distribution as well as appropriate use;
- Research & Development: develop new antimicrobial medicines, diagnostic tools, vaccines and other interventions for detecting, preventing and controlling antimicrobial resistance;
- Access: promote affordable access to existing and new antimicrobial medicines, vaccines and diagnostic tools.

## **WHAT DO WE UNDERSTAND BY ‘FRAMEWORK’?**

At the outset, one of the key questions is how to reach a common understanding of the character and function of a framework. In drafting resolution WHA68.7, the World Health Assembly deliberately chose the term ‘framework’ to provide flexibility with respect to the selection of the most appropriate instrument(s). The term ‘framework,’ in general, refers to a basic conceptual structure. The framework will provide an overarching structure for various tools and instruments aimed at addressing three key objectives: 1) stewardship, 2) fostering research and development (R&D), and 3) access. In doing so, the framework will build on existing standards, guidelines and tools that are currently being implemented by FAO, OIE, and WHO.<sup>6-17</sup> Indeed, while WHO is the lead agency for human health and related

issues, animal health and welfare related standards fall within the competence of OIE. The joint FAO/WHO Codex Alimentarius Commission develops food standards with the dual objective of protecting consumer health and ensuring fair trade practices. While these instruments need to be taken into account and can be used to further the objectives of the framework, elements of the framework that have repercussions for human, animal, and plant health sectors could be endorsed by the constituencies of the three organizations.

Where gaps remain, new tools need to be developed, for example, to address the need for economic incentives for the development of new treatments and to enhance stewardship along the lifecycle of antimicrobial treatments. This roadmap proposes a modular approach through which the framework can be developed and built over time.

The framework is envisaged to form an “umbrella” uniting different instruments. Ultimately, there may be a need for an overarching instrument that defines overall objectives, principles, governance, and possible accountability and financing mechanisms. The fact that the framework will unite different instruments also means that different elements of the framework could take different legal forms.<sup>2</sup>

Independent activities within the three organizations contribute to and complement the work of the tripartite collaboration on AMR. For example, in 2016, the FAO governing body adopted the FAO Action Plan on Antimicrobial Resistance.<sup>18</sup> The Plan focuses on four areas or work: improve awareness and advocacy on AMR and related threats; develop capacity for surveillance and monitoring of AMR and antimicrobial use (AMU) in food and agriculture; strengthen governance related to AMU in food and agriculture, and; promote good practices in food and agricultural systems and the prudent use of adding antimicrobials to the five objectives of the Global Action Plan. Also, during the 84<sup>th</sup> OIE General Session in May 2016, the World Assembly of Delegates adopted Resolution No. 36 requesting the development of an OIE Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials that was published in November 2016.<sup>32</sup>

## **HOW DOES THE FRAMEWORK RELATE TO THE GLOBAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE?**

A key question is how the framework relates to the Global Action Plan on AMR. As stated in WHA68.7, the global framework aims at developing new antimicrobial products, conserving them and ensuring affordable access. The framework, therefore, addresses objectives 4 and 5 (optimize the use of antimicrobial medicines in human and animal sectors, develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions) of the Global Action Plan. Notably, the scope of the framework as defined in WHA68.7 will not address improving awareness and understanding of antimicrobial resistance through effective communication, education and training (objective 1), strengthening the knowledge and evidence base through surveillance and research (objective 2) or reducing the incidence of infection through effective sanitation, hygiene and infection prevention measures (objective 3). Activities to address objectives 1-3 are already at various stages of implementation under the Global Action Plan.

Within this context, it is important to highlight that the framework is not intended to replace the Global Action Plan. Rather, it will provide focus for work under objectives 4 and 5 with full understanding that some overlap exists between the five objectives of the plan; for example, appropriate use of antibiotics relies heavily upon the availability of data on resistance and on information data on the use of antimicrobial agents. The fact that the framework should focus on some elements of the GAP is not a prioritization of these elements, but is meant to further develop objectives 4 and 5 of the Global Action Plan.

The framework is meant to be a global framework. It will support but not interfere with or replace the national action plans (NAPs) that will remain the primary tool of implementation at country level of the Global Action Plan.

## **SCOPE**

Resolution WHA68.7 is very broad, encompassing new antimicrobial medicines, diagnostic tools, vaccines and other interventions. The term ‘antimicrobial medicines,’ which subsumes antibiotics and other medicines, includes antiviral, antifungal, antibacterial and anti-parasitic agents. In principle, it also includes therapies for viral infections such as influenza or HIV. All such medicines are susceptible to the emergence of resistance.

Fortunately, special programmes and initiatives have been established over the past few years to address some, but not all, of the most concerning conditions and diseases, such as HIV/AIDS, tuberculosis (TB), malaria and other neglected tropical diseases. These programmes/initiatives aim to foster the development of new treatments, improve access to existing treatments and, in part, address disease-relevant issues surrounding resistance.<sup>19,20</sup>

As illustrated in Table 1, the level of market failure varies significantly. Neglected tropical diseases are a typical example where the costs of the R&D cannot be offset by future product sales. Fostering R&D for neglected diseases is, therefore, addressed within the follow-up process of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG). Other disease groups (hepatitis C and B, for example) harness market forces and attract investments by industry. In some cases, global public health market mechanisms create a commercial market that drives investments in R&D.

Likewise, the speed with which antimicrobial resistance emerges and spreads varies considerably from one pathogen to another. Given that a specific function of the framework is to harmonize stewardship policies in the human health, animal, plant and food sectors across the three organizations, the framework will mainly focus on health technologies that can be used for human health and either animal or plant protection.

Another difference to highlight is that the chances of success for developing effective treatments or vaccines, the speed of their development, the investment needed and the impact of use of new products differ between diseases.

In A69/24 Add.1, the WHO Secretariat suggested to follow a stepwise approach starting with antibiotics, including for the treatment of TB. The reason is that antibiotics are used in humans and animals and plant protection; therefore, there seems to be consensus on the

growing threat of resistance to antibiotics and on the need for further research and development investment.

Table 1: Characterizing antimicrobial pathogens by sector involvement, level of market failure and R&D entities/initiatives

<b>Disease/Disease group</b>	<b>Targeted towards human health, animal health, and/or food production</b>	<b>Level of market failure<sup>c</sup></b>	<b>Dedicated global and regional R&amp;D entities/initiatives</b>
<b>Bacterial infections<sup>a</sup></b>	All three sectors	High	WHO/DND <i>i</i> GARDP, CARB-X, IMI
<b>Fungal infections</b>	All three sectors	High	--
<b>HIV</b>	Humans	Low, but very high for paediatric applications	IAVI, IPM
<b>Influenza</b>	Humans and animals	Low	--
<b>Malaria</b>	Humans	High	MMV, MVI
<b>Neglected tropical diseases</b>	Mostly humans; for some, possible use in animals to decrease transmission to humans	Very high	TDR, DND <i>i</i> , Sabin Institute, FIND, GHIT
<b>Emerging diseases with pandemic potential<sup>b</sup></b>	Mostly humans; for some, possible use in animals to decrease transmission to humans	Very high	WHO R&D Blueprint CEPI, FIND
<b>Tuberculosis</b>	Humans and animals <sup>d</sup>	High	Global Alliance for TB Drug Development, TB Vaccine Initiative
<b>Viral hepatitis</b>	Humans	None	--

<sup>a</sup> Bacterial infections that are not classified as neglected tropical diseases. TB is listed separately.

<sup>b</sup> R&D Blueprint: Revised list of priority diseases. Arenaviral hemorrhagic fevers (including Lassa Fever); Crimean Congo Haemorrhagic Fever; Filoviral diseases (including Ebola and Marburg); Middle East Respiratory Syndrome Coronavirus; other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome; Nipah and related henipaviral diseases; Rift Valley Fever; Severe Fever with Thrombocytopenia Syndrome; Zika; Disease X.<sup>21</sup>

<sup>c</sup> Very high: no commercial market/no financing mechanisms; High: limited commercial markets; Low: significant commercial markets/financial incentives (adapted from the Special Programme for Research and Training in Tropical Diseases<sup>22</sup>).

<sup>d</sup> Streptomycin is used to treat fruit trees in certain countries.

## **DEVELOPMENT OF NEW ANTIMICROBIAL MEDICINES, DIAGNOSTIC TOOLS AND VACCINES**

In line with the stepwise approach outlined in this document, the framework will consider R&D incentives to foster development of tools to tackle bacterial infections in humans and animals as a first step, with the possibility of expanding subsequently to other areas where there is inadequate investment. WHO, together with DNDi, has already set up a new product development partnership, the Global Antibiotic Research and Development Partnership (GARDP), which will develop new antibiotic treatments while endeavouring to ensure sustainable access as described in Box 1.

In February 2017, the WHO Secretariat published a list of priority pathogens for research and development. The list focuses on 12 bacteria or families of bacteria that, in addition to TB, pose great threats to human health. The objective of the list is to highlight research and development priorities in the area of antibiotic resistance.<sup>23</sup>

As a next step, the WHO Secretariat is analysing the pipeline for antibacterial treatments, extending the scope to include novel products such as monoclonal antibodies and bacteriophages. This analysis is focusing on both the quantity and the potential added value of products in the pipeline. The outcome of this assessment will feed into WHO's Global Observatory on Health Research and Development and will inform the WHO Expert Committee on Health Research and Development which will be established by end 2017.

The WHO Secretariat is also undertaking an evidence-based prioritization exercise for potential human vaccines to reduce the impact of AMR which will help determine future priority R&D investments. The report of this study is likely to be available by end 2017.

Priorities for R&D focused on the animal sector will include, for example, work to support the development of quality and affordable animal vaccines to decrease the use of antibiotics in food-producing animals. A report highlighting priority animal diseases for which the development of a vaccine would have potential to reduce the use of antimicrobials in pigs, poultry, swine and fish has already been published by OIE.<sup>24</sup> This work will be extended to other animal species. Another area that urgently requires more research is finding alternatives to antibiotics and other antimicrobials as growth promoters for animal husbandry.

More investment is also needed to develop rapid and affordable point-of-care/point-of-use diagnostics to guide treatment decisions in both the human and animal sector. WHO will be developing in the next 18 months a list of essential in vitro diagnostic tests for human use. One demonstration project (established as a follow up of the report of the WHO Consultative Expert Working Group (CEWG) on health research and development) focuses on the development of a "Multiplexed Point-of-Care Test for Acute Febrile Illness" that attempts to deliver a low-cost, multiplex point-of-care diagnostic test for the differential diagnosis of fever/sepsis, thus enhancing treatment options and reducing inappropriate use of antibiotic drugs.<sup>25</sup>

**Box 1: The WHO/DNDi Global Antibiotic Research and Development Partnership**

The Global Antibiotic Research and Development Partnership (GARDP) is a not-for-profit research and development organization that addresses global public health needs by developing new antibiotic treatments while endeavouring to ensure sustainable access. GARDP is part of the implementation of the Global Action Plan on Antimicrobial Resistance that calls for new public-private partnerships for encouraging research and development of new antimicrobial agents and diagnostics. GARDP is a joint initiative of WHO and Drugs for Neglected Diseases *initiative* (DNDi) who is hosting it during the start-up phase. GARDP has received seed funding and pledges from the governments of Germany, Netherlands, South Africa, and Switzerland, the United Kingdom of Great Britain and Northern Ireland as well as from the medical humanitarian organization Médecins Sans Frontières which exceed €5 million for 2016-2018. It currently has a staff of 10 people with additional support staff from DNDi contributing directly to GARDP programmes.<sup>26</sup>

A number of studies have been published in the recent past<sup>27-29</sup> suggesting different funding mechanisms for R&D and ways to implement the concept of delinkage. To fill the R&D pipeline beyond GARDP, several national and regional initiatives have been set up including the CARB-X initiative launched by the Biomedical Advanced Research and Development Authority (BARDA) in the United States of America; the European Commission's (EC) Innovative Medicines Initiative (IMI); the EC Joint Programming Initiative on Antimicrobial Resistance; and prize funds for diagnostics, such as the UK Longitude Prize on diagnostics for AMR. How to incentivize the development of antibiotics is also on the agenda of the G20, including the possibility to create some kind of global funding or coordination mechanism for research and development for AMR.<sup>31</sup> This framework would address the lack of R&D investment and build upon existing studies, reports and initiatives in this area considering both push (for example, research grants) and pull (for example, market entry rewards or prize funds) mechanisms taking into account the principle of delinkage.

**A FRAMEWORK FOR STEWARDSHIP AND ACCESS**

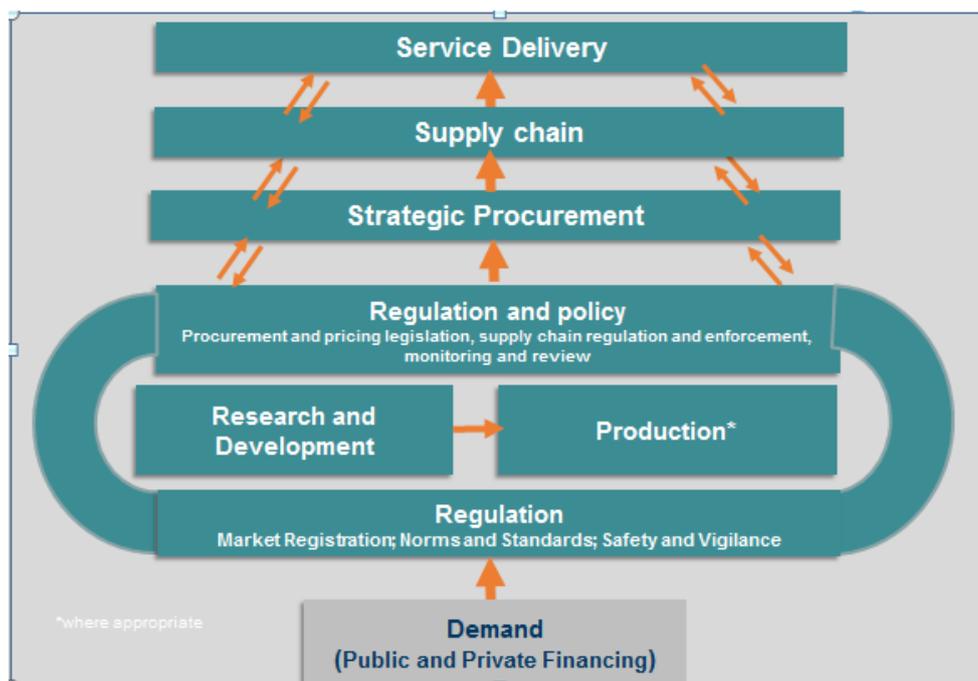
The term 'stewardship' describes the careful and responsible management of something entrusted to one's care. For antimicrobials, this means appropriate use to improve patient outcomes while minimizing the development and spread of resistance. Regarding animal health, such management is mostly addressed through the concept of responsible and prudent use and emphasizes prevention (for example, hygiene at farm and marketing levels, routine vaccination schedules for flocks, herds, or aquaculture farms). Any stewardship framework must also ensure that access to needed treatment is not compromised. Stewardship and access cannot be dealt with in isolation.

According to WHA68.7, the framework should cover the development, control, distribution and appropriate use of different tools to tackle AMR. The framework will thus encompass the whole lifecycle of a product from product development, marketing authorization and regulatory requirements to end-users; for example, labelling requirements, the manufacturing process and its impact on the environment, the selection of the right antimicrobials, how they are marketed and promoted, distributed, prescribed, used and discarded as waste (see figure 1). Regarding human use, the question on how they are paid

for or reimbursed as well as how antimicrobials are dispensed in inpatient and/or outpatient settings and finally used by patients and users also needs to be addressed. This includes developing new reimbursement or pay-for-service models that further appropriate use and conservation of new antibiotics and provide incentives for companies to develop new treatments. Disposal of unused or expired medicines also needs to be explored. Stewardship also entails that professional groups (for example, physicians, veterinarians, dentists, and pharmacists) are well-qualified and proficient in prescribing the right medicine at the most appropriate dose for optimal duration and correct indication.

The lifecycle approach entails the definition of clear roles and obligations for the various stakeholders involved within the cycle: manufacturers, including generics and food-animal producers, regulatory authorities, prescribers, dispensers, wholesale and retail distributors, physicians and veterinarians, farmers and citizens.

Overall, more work is needed to assess the feasibility and impact of measures to foster appropriate use and to identify the most cost-effective measures, including on behavioural change amongst physicians, veterinarians, and farmers.



**Figure 1: Stewardship covers the whole lifecycle from research to human use**

In parallel, the global framework will address responsible and prudent use of antimicrobials in the animal and crop agriculture sectors without depriving veterinarians and farmers the needed access to antimicrobial medicines of ensured quality. The OIE standards on responsible and prudent use of antimicrobial agents published in the Terrestrial and Aquatic Animal Health Codes cover each step from production to use.<sup>10,11</sup> The challenge of how to deal with antibiotic use without veterinary oversight, as routine preventive measures, or for growth promotion will require particularly close collaboration with FAO and OIE. As noted above, other relevant standards and instruments will need to be considered to avoid duplication of work. Importantly, the following must be taken into consideration as a

prerequisite to a reduction in the use of antimicrobials in animal and crop agriculture: improved biosecurity at sites of primary production, good husbandry and farming practices, veterinary oversight, adequate and safe animal feed, increased animal welfare, improved hygiene along the production and marketing chain, awareness, capacity development among farmers, agronomists, and feed producers. Further work will be required to the extent that these aspects fall within the scope of the framework.

From human health, animal health and plant protection perspectives, any global agreement on stewardship (and access) would need to establish principles and rules on how they should be used, taking into account existing work. There is a strong need for good regulatory practices ensuring appropriate regulatory oversight along the entire lifecycle, including disposal practices. These are areas that will have to be further developed as part of the framework.

For human health purposes, A69/24 Add.1 included a suggestion to develop a global priority list of antibiotics that would be subject to a global stewardship framework.<sup>2</sup> This work is currently underway (see next section).

### **REVIEW OF THE WHO ESSENTIAL MEDICINES LIST(S)**

WHO is undertaking a comprehensive review of the antibiotics' chapters in the WHO Model List of Essential Medicines (EML). The objective of the revision is to summarize the evidence supporting antibiotic use for the most common and relevant infections, define a subset of antibiotics that should always be available in any health post, and define the antibiotics that should be primarily used for targeted uses or be conserved. The 21<sup>st</sup> Expert Committee on the Selection and Use of Essential Medicines, held from 27 to 31 March 2017, considered the review of 21 syndromes.

The review also included a separate review of antibiotic dosing for children, a review of antibiotics for specific sexually transmitted infections, as well as an evaluation of antibiotic awareness campaigns that could contribute to more appropriate use of antibiotics.<sup>30</sup> The Committee's report is expected to be published by mid-2017.

### **USE OF ANTIMICROBIAL AGENTS IN THE ANIMAL AND AGRICULTURE SECTORS**

OIE, FAO and WHO have been working over the past years to foster appropriate use of antibiotics in the animal and the agriculture sector. In 2003 and 2004, two expert workshops on Non-Human Antimicrobial Usage and Antimicrobial Resistance, jointly convened by FAO, OIE and WHO, recommended that:

- WHO should develop a list of antimicrobial agents critically important for humans with a view to enabling specific resistance-prevention actions for these antimicrobials within the context of non-human use;
- OIE should identify antimicrobials that are critically important in veterinary medicine to complement the identification of such antimicrobials used in human medicine.

OIE adopted, based on scientific criteria, a list of antimicrobial agents of veterinary importance that takes into account the animal health needs of the major food-producing animal species and addresses the needs to treat animal diseases with a global perspective.<sup>12</sup>

Among the OIE list, some classes of antibiotics are considered to be critically important both for human and animal health. This is the case for fluoroquinolones and for the third and fourth generation of cephalosporins. Therefore, these treatments should:

- not be used as preventive treatment applied by feed or water in the absence of clinical signs in the animal(s) to be treated;
- not be used as a first line treatment unless justified and when used as a second line treatment; this should ideally be based on the results of bacteriological tests.

Extra-label/off label use should be limited and reserved for instances where no alternatives are available. Such use should be in agreement with the national legislation in force.

In November 2016, OIE published its Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials.<sup>32</sup> Aligned with the Global Action Plan, the strategy recognizes the importance of a “One health” approach involving human and animal health, as well as agricultural and environmental needs.

WHO regularly reviews the WHO List of Critically Important Antibiotics. The objective of this list is to preserve the effectiveness of antimicrobials and to help formulate and prioritize risk assessment and risk management strategies for containing resistance coming from the food chain. The list ranks antimicrobial agents as:

- Critically important
- Highly important
- Important

The Fifth Revision was published in April 2017.<sup>7</sup> This list was also taken into account in the revision of the EML. The intent and purpose of the EML includes different factors than the List of Critically Important Antibiotics, namely efficacy and access while the purpose of the List of Critically Important Antibiotics is to assess the impact of resistance as well as the risk of transmission through the food chain. Hence, while there is considerable overlap between the two lists, there will be some differences due to the varying purposes.

Taking into account the WHO List of Critically Important Antimicrobials for Human Medicine, WHO is developing guidelines to preserve the effectiveness of critically important antimicrobials for human medicine that will provide guidance on how to use antimicrobials in food-producing animals. These guidelines are being developed following WHO guideline development rules and are likely to be published in 2017. FAO and OIE were invited to sit on the Steering Group as special members and also to attend the Guideline Development Group meetings. The outcome guidelines will inform the forthcoming revision by Codex member countries of the Codex (FAO/WHO) Code of Practice to Minimise and Contain Antimicrobial Resistance, pending confirmation of the 40<sup>th</sup> Session of the Codex Alimentarius Commission (July 2017). WHO and FAO will consider providing additional scientific advice to Codex in this area, upon request. To reflect the need of relevant stakeholders and taking a multisectoral approach, FAO, OIE, and WHO are considering convening a tripartite expert consultation to develop recommendations relative to the OIE and WHO Lists of Critically Important Antimicrobials after the next revision of the OIE list.

After their completion, the WHO guidelines, among others, could inform the development of future Codex Alimentarius guidance on AMR with inputs from FAO and WHO in collaboration with OIE.

Regarding food safety, standards have been developed by the FAO/WHO Codex Alimentarius Commission on minimizing and containing antimicrobial resistance, risk analysis of foodborne antimicrobial resistance, good animal feeding and the maximum residue limits of veterinary drugs in food. They provide methodologies to appropriately reduce the risk of the emergence of resistance or spread of resistant bacteria through food that result from the use of antimicrobial agents in food-producing animals and crops.

The framework will build on these existing workstreams in the three organizations. Stewardship policies will be developed taking into account the WHO Essential Medicines List, the WHO List of Critically Important Antimicrobials for Human Medicine and the OIE List of Antimicrobials of Veterinary Importance and other regional or national lists supporting the preservation of the efficacy of antimicrobial agents. However, more work needs to be done, in particular, to implement standards, guidelines and establish good regulatory practices on the production, marketing and use of antibiotics in the animal and agriculture sectors.

### **PROMOTING AFFORDABLE ACCESS**

While some antibiotics should be used in a more restrictive way, affordable access to quality essential medicines, vaccines, as well as diagnostics also needs to be increased in both the human and animal sectors. As pointed out, stewardship and access are closely linked and should not be dealt with separately. Access considerations need to be built into any future global stewardship and access framework.

In that context, the quality of antimicrobials that are sold is an important consideration both in the human and animal sectors. Antibiotics are the most frequently reported category of falsified and substandard medicines in human medicine.<sup>34</sup>

There are numerous barriers to access and many are rooted in deficiencies of national health systems. While it is beyond the scope of the framework to address general shortcomings of national health systems, any stewardship measures need to be designed in a way that does not impede access and amplify the negative impact of the current system of controlled drugs on access for human health. Antimicrobial medicines also need to be affordable for those who need them which can be challenging with respect to new patented products. Voluntary licenses and the use of WTO TRIPS flexibilities are possible means to overcome such barriers.<sup>2</sup> The principle of delinkage can help to ensure affordability. GARDP, by applying this principle, will ensure that any products that will be developed will be available at affordable prices. On the other hand, very few quality manufacturers remain on the market that produce certain cheap injectable antibiotics which may be due to too-low profit margins in that market. Initiatives such as the WHO Fair Pricing Forum to be held in May 2017 will address ways to improve access to medicines and ways to achieve universal health coverage.<sup>35</sup>

## **PROPOSED WAY FORWARD**

The development of a global framework is work in progress by FAO, OIE and WHO. All three organizations will proceed further with building elements of the overall framework and, in parallel, develop the overall concept and content. As outlined in this document, a number of elements are already in place or will be established throughout 2017. Work is expected to continue into 2018 on these and other elements.

### **1) Setting up a team in the WHO Secretariat**

A dedicated group is being set up within the WHO Department of Essential Medicines and Health Products to work toward the development of the global framework. The group will work closely with the AMR Secretariat, and other relevant internal and external entities.

### **2) Working with FAO and OIE**

Working closely together with FAO and OIE is an essential prerequisite for success. To ensure close collaboration, the framework will be a standing agenda item in the discussions of the tripartite group. Specific face-to-face tripartite meetings will be arranged when necessary. The three organizations will regularly inform their governing bodies and the Interagency Coordination Group (IACG) of ongoing work and progress.

### **3) Creating a sub-group of the AMR Scientific and Technical Advisory Committee**

The WHO Secretariat will convene a dedicated subgroup of the current STAC for AMR that will include some experts of the main STAC and additional experts, including from the animal and agriculture sectors. FAO and OIE will be invited to participate in this group to ensure a tripartite approach.

### **4) Consultations with stakeholders**

Involvement of stakeholders will be key for the development of the framework. In collaboration with FAO and OIE, consultations with relevant stakeholders will be held, including with the animal and agricultural sector, professional associations, civil society and industry. The WHO Secretariat will develop a workplan in collaboration with FAO and OIE to appropriately prepare and schedule these consultations subject to guidance received from the World Health Assembly and the IACG.

### **5) Consultation of and reporting to Member States**

The WHO Secretariat will ensure appropriate consultation of Member States throughout the process subject to further guidance from the World Health Assembly.

WHA68.7 requests the Director-General to submit biennial reports on progress achieved in implementing resolution WHA68.7 These need to be submitted to the Seventieth (2017), Seventy-second (2019) and Seventy-fourth (2021) World Health Assemblies. The Director-General will report on progress in the development of the framework according to additional guidance received by the World Health Assembly.

The United Nations high-level meeting on antimicrobial resistance that took place during the Seventy-first UN General Assembly requested the UN Secretary-General to submit a report for Member State consideration by the Seventy-third session (September 2018 –

September 2019) of the General Assembly on the implementation of the declaration which includes the mandate to WHO to finalize the global framework together with FAO and OIE.

The tripartite collaboration will also regularly inform the IACG on progress achieved and challenges encountered drawing on its expertise and guidance where necessary.

### **TIMELINES**

The development of the framework will follow a stepwise approach. Thus, over the next years, FAO, OIE, and WHO will develop different elements of the tripartite framework. Some parts may require a formal endorsement by the governing bodies of the responsible organization(s). A more detailed timeline will be prepared based on the recommendations of the Seventieth World Health Assembly and the first meeting of the IACG.

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