

## **Antimicrobial resistance**

### **Draft global action plan on antimicrobial resistance**

#### **Report by the Secretariat**

#### **INTRODUCTION**

1. When microbes become resistant to medicines, the options for treating the diseases they cause are reduced. This resistance to antimicrobial medicines is happening in all parts of the world for a broad range of pathogens, with an increasing prevalence that threatens human and animal health. The direct consequences of infection with resistant microorganisms can be severe, including longer illnesses, increased mortality, prolonged stays in hospital, loss of protection for patients undergoing operations and other medical procedures, and increased costs. Antimicrobial resistance affects all areas of health, involves many sectors and has an impact on the whole of society.

2. The indirect impact of antimicrobial resistance, however, extends beyond increased health risks and encompasses economic losses due to reduced productivity caused by sickness (of both human beings and animals) and higher costs of treatment. Antimicrobial resistance is a drain on the global economy; to counter it needs long-term investment, for instance in financial and technical support for developing countries, development of new medicines, diagnostic tools, vaccines and other interventions, and to strengthen health systems to ensure more effective use of and access to antimicrobial agents.

3. The development of this draft global action plan on antimicrobial resistance, requested by the Health Assembly in resolution WHA67.25 in May 2014, reflects a global consensus that antimicrobial resistance poses a profound threat to human health. It reflects the input received to date from broad multisectoral and Member States' consultations.

4. The goal of the draft global action plan is to ensure, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them. It is expected that countries will develop their own national action plans on antimicrobial resistance in line with the global plan.

5. To achieve this goal, the draft global action plan sets out five strategic objectives: (1) to improve awareness and understanding of antimicrobial resistance; (2) to strengthen knowledge through surveillance and research; (3) to reduce the incidence of infection; (4) to optimize the use of antimicrobial agents; and (5) to ensure sustainable investment in countering antimicrobial resistance. These objectives can be attained through the implementation of clearly identified actions for which Member States, WHO and international partners across multiple sectors should be held accountable.

The actions to optimize use of antimicrobial medicines and to renew investment in research and development of new products must be accompanied by actions to ensure affordable and equitable access by those who need them.

6. With this approach, the main goal of ensuring treatment and prevention of infectious diseases with effective and safe medicines is achievable.

## SCOPE

7. **Antibiotic resistance** develops when bacteria adapt and grow in the presence of antibiotics. The development of resistance is linked to how often antibiotics are used. Because many antibiotics belong to the same class of medicines, resistance to one specific antibiotic agent can lead to resistance to a whole related class. Resistance that develops in one organism or location can also spread rapidly and unpredictably, through for instance exchange of genetic material between different bacteria, and can affect antibiotic treatment of a wide range of infections and diseases. Drug-resistant bacteria can circulate in populations of human beings and animals, through food, water and the environment, and transmission is influenced by trade, travel and both human and animal migration. Resistant bacteria can be found in food animals and food products destined for consumption by humans.

8. Some of these features also apply to medicines that are used to treat viral, parasitic and fungal diseases; hence the broader term **antimicrobial resistance**.

9. The draft global action plan covers antibiotic resistance in most detail but also refers, where appropriate, to existing action plans for viral, parasitic and bacterial diseases, including HIV/AIDS, malaria and tuberculosis.<sup>1</sup> Many of the actions proposed in this plan are equally applicable to antifungal resistance.

10. Antimicrobial resistance (and particularly antibiotic resistance) is spreading, and there are few prospects for the development of new classes of antibiotics in the short term. However, there is today considerable awareness of the need for, and political support for, action to combat antimicrobial resistance. Support is multisectoral, and there is increasing collaboration between the human health, animal health and agriculture sectors (including a tripartite collaboration agreed between FAO, OIE

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<sup>1</sup> World Health Organization global strategy for the surveillance and monitoring of HIV drug resistance. Geneva: World Health Organization; 2012 ([http://www.who.int/hiv/pub/drugresistance/drug\\_resistance\\_strategy/en/](http://www.who.int/hiv/pub/drugresistance/drug_resistance_strategy/en/), accessed 28 October 2014). Guidelines for surveillance of drug resistance in tuberculosis, fourth edition. Geneva: World Health Organization; 2009 ([http://whqlibdoc.who.int/publications/2009/9789241598675\\_eng.pdf](http://whqlibdoc.who.int/publications/2009/9789241598675_eng.pdf), accessed 28 October 2014). Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization; 2014 ([http://apps.who.int/iris/bitstream/10665/130918/1/9789241548809\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/130918/1/9789241548809_eng.pdf), accessed 28 October 2014). Global plan for artemisinin resistance containment. Geneva: World Health Organization; 2011 (<http://www.who.int/malaria/publications/atoz/9789241500838/en/>, accessed 28 October 2014). Emergency response to artemisinin resistance in the Greater Mekong subregion. Geneva: World Health Organization; 2013 (<http://www.who.int/malaria/publications/atoz/9789241505321/en/>, accessed 28 October 2014). Resolution WHA62.15. Prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis. In: Sixty-second World Health Assembly, Geneva, 18–22 May 2009. Resolutions and decisions, annexes. Geneva: World Health Organization; 2009 (document WHA62/2009/REC/1):25–29; [http://apps.who.int/gb/ebwha/pdf\\_files/WHA62-REC1/WHA62\\_REC1-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA62-REC1/WHA62_REC1-en.pdf), accessed 28 October 2014).

and WHO)<sup>1</sup>. The need for urgent action is consistent with the precautionary principle, and national and international multisectoral action and collaboration should not be impeded by gaps in knowledge.

11. This draft global action plan provides the framework for national action plans to combat antimicrobial resistance. It sets out the key actions that the various actors involved should take, using an incremental approach over the next 5–10 years to combat antimicrobial resistance. These actions are structured around the five strategic objectives set out in paragraphs 30–48.

## THE CHALLENGE

12. Improvements in global health over recent decades are under threat because the organisms that cause many common human diseases and medical conditions – including tuberculosis, HIV/AIDS, malaria, sexually transmitted diseases, urinary tract infections, pneumonia, blood-stream infections and food poisoning – have become resistant. Doctors must increasingly use “last-resort” medicines that are more costly, take longer to work, and are often unavailable or unaffordable in low- and middle-income countries. Some cases of tuberculosis and gonorrhoea are now resistant even to antibiotics of last resort.

13. Resistance develops more rapidly through the misuse and overuse of antimicrobial medicines. Antibiotic use for human health is reported to have increased by 36% between 2000 and 2010. Surveys in a wide range of countries show that many patients believe that antibiotics will cure viral infections that cause coughs, colds and fever. Antibiotics are needed to treat sick animals but are also widely used in healthy animals to prevent disease and, in many countries, to promote growth through mass administration to herds. Antimicrobial agents are commonly used in plant agriculture and commercial fish and seafood farming.

14. Antimicrobial resistance can affect all **patients and families**. Some of the commonest childhood diseases in developing countries – malaria, pneumonia, other respiratory infections, and dysentery – can no longer be cured with many older antibiotics or medicines. In lower-income countries, effective and accessible antibiotics are crucial for saving the lives of children with those diseases as well as other conditions such as bacterial blood infections and severe acute malnutrition. In higher-income countries, some routine surgical operations and cancer chemotherapy will become less safe without effective antibiotics to protect against infections.

15. **Health-care workers** have a vital role in preserving the power of antimicrobial medicines. Inappropriate prescribing and dispensing can lead to their misuse and overuse if medical staff lack up-to-date information, cannot identify the type of infection, yield to patient pressure to prescribe antibiotics or benefit financially from supplying the medicines. Inadequate hygiene and infection prevention and control in hospitals help to spread infections. Hospital patients infected with methicillin-resistant *Staphylococcus aureus* have an estimated 61% higher risk of dying than those infected by a non-resistant form of the bacteria.

16. For **farmers, animal husbandry and the food industry**, the loss of effective antimicrobial agents to treat sick animals damages food production and family livelihoods. An additional risk for

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<sup>1</sup> The FAO-OIE-WHO Collaboration: sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces – a tripartite concept note, 2010, available at [http://www.who.int/influenza/resources/documents/tripartite\\_concept\\_note\\_hanoi\\_042011\\_en.pdf](http://www.who.int/influenza/resources/documents/tripartite_concept_note_hanoi_042011_en.pdf) (accessed 20 November 2014).

livestock workers is exposure to animals carrying resistant bacteria. For example, farmers working with cattle, pigs and poultry that are infected with methicillin-resistant *Staphylococcus aureus* have a much higher risk of also being infected with these bacteria. Food is the most important of many vehicles for transmission of resistant bacteria from animals to human beings and human consumption of food carrying antibiotic-resistant bacteria has led to acquisition of antibiotic-resistant infections. Other risks for infection with resistant organisms include exposure to crops treated with antimicrobial agents or contaminated by manure or slurry, and farmyard run-offs into groundwater.

17. Reducing antimicrobial resistance will require the **political will** to adopt new policies, including controlling the use of antimicrobial medicines in human health and animal and food production. In most countries, antibiotics can be purchased in markets, shops, pharmacies or over the Internet without prescription or involvement of a health professional or veterinarian. Substandard/spurious/falsely-labelled/falsified/counterfeit medical products are widespread, and often contain low concentrations of active ingredients, encouraging emergence of resistant microbes. Laws to ensure that medicines are safe, effective, of good quality and accessible to those who need them need to be enacted and enforced.

18. The World Economic Forum has identified antimicrobial resistance as a global risk beyond the capacity of any organization or nation to manage or mitigate alone,<sup>1</sup> but in general there is little awareness of the potential social, economic and financial impacts of drug resistance. In developed economies, these include higher health care costs and decreases in labour supply, productivity, household incomes, and national income and tax revenues. In the European Union alone, a subset of drug-resistant bacteria is responsible annually for some 25 000 deaths, with extra health care costs and lost productivity due to antimicrobial resistance amounting to at least €1500 million. Similar analyses are needed for low- and middle-income countries. Resistance to common veterinary antimicrobial medicines also causes food production losses, poor animal welfare and extra costs. Antimicrobial resistance is sapping the global economy and the full economic case needs to be made for long-term sustainable investment to tackle the problem, including the ensuring of access to financial and technical support for developing countries.

19. For the **pharmaceutical sector**, medicines that are no longer effective lose their value. Industry leaders are important partners in combating antimicrobial resistance, both by supporting the responsible use of medicines in order to prolong their effectiveness and through research and development of innovative medicines and other tools to combat resistance. No major new class of antibiotics has been discovered since 1987 and too few antibacterial agents are in development to meet the challenge of multidrug resistance. New concepts are needed for providing incentives for innovation and promoting cooperation between policy-makers, academia and the pharmaceutical industry to ensure that new technologies are available globally to prevent, diagnose and treat resistant infections.

## THE WAY FORWARD

20. Despite proposals and initiatives over many years to combat antimicrobial resistance, progress has been slow, in part because of, on the one hand, inadequate monitoring and reporting at national, regional and global levels, and, on the other, inadequate accountability of all stakeholders.

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<sup>1</sup> Howell L Ed. Global risks 2013: eighth edition. Geneva; World Economic Forum, 2013.

21. At the national level, operational action plans to combat antimicrobial resistance are needed to support strategic frameworks. All Member States are urged to have in place, within two years of the endorsement of the draft action plan by the Health Assembly, action plans on antimicrobial resistance that are aligned with the global action plan.<sup>1</sup> Partners and other stakeholders, including FAO, OIE, the World Bank, industry associations and foundations, should also put in place and implement action plans to counter antimicrobial resistance, and report progress as part of their reporting cycles. All action plans should reflect the following principles:

(1) **Whole-of-society engagement.** Antimicrobial resistance will affect everybody, regardless of where they live, their health, economic circumstances, lifestyle or behaviour. It will affect sectors beyond human health, such as animal health, agriculture, food security and economic development. Therefore, everybody – in all sectors and disciplines – should be engaged in the implementation of the action plan.

(2) **Prevention first.** Every infection prevented is one that needs no treatment. Prevention of infection can be cost-effective and implemented in all settings and sectors, even where resources are limited. Good sanitation, hygiene and other infection prevention measures that can slow the development and restrict the spread of difficult-to-treat antibiotic-resistant infections are a “best buy”.

(3) **Access not excess.** The aim is to preserve the ability to treat serious infections; to do that requires both equitable access to, and appropriate use of, existing and new antimicrobial medicines.

(4) **Sustainability.** Actions are more likely to be sustained when they are a routine part of systems and practices, and when there is continuing health and economic benefit.

(5) **Incremental targets for implementation.** Member States are at very different stages in terms of developing and implementing national plans to combat antimicrobial resistance. To enable all countries to make the most progress towards implementing the global action plan on antimicrobial resistance, flexibility will be built into the monitoring and reporting arrangements in order to allow each country to determine the priority actions that it needs to take in order to attain each of the five strategic objectives and to implement the actions in a stepwise manner that meets both local needs and global priorities.

## CONSULTATIVE PROCESS

22. In May 2014, the Sixty-seventh World Health Assembly adopted resolution WHA67.25 on antimicrobial resistance, in which it requested the Director-General, among other actions, to develop a draft global action plan to combat antimicrobial resistance, including antibiotic resistance, and to submit the draft to the Sixty-eighth World Health Assembly, through the Executive Board.

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<sup>1</sup> The Secretariat has worked with Member States to collate information on the status of national action plans on antimicrobial resistance and on regulations and policies for use of antimicrobial medicines. A report based on these data will be published before the Sixty-eighth World Health Assembly and will provide a baseline against which future progress at national and global levels can be monitored and reported.

23. To initiate the preparation of a draft global action plan, the Secretariat used the recommendations of the Strategic and Technical Advisory Group on antimicrobial resistance,<sup>1</sup> existing national and regional action plans, WHO's guidance and action plans on related subjects, as well as other available evidence and analysis.<sup>2</sup> The Secretariat regularly consulted FAO and OIE, for example through meetings as part of the tripartite collaboration and through their participation in other consultations.

24. At its second meeting (Geneva, 14–16 April 2014),<sup>3</sup> the Strategic and Technical Advisory Group considered input from more than 30 additional participants, including representatives of intergovernmental organizations, civil society, public health and regulatory agencies, industry associations, professional organizations and patient groups. At a subsequent meeting (Geneva, 17 October 2014), the Advisory Group reviewed the text of the draft global action plan.

25. During July and August 2014 the Secretariat held a web-based consultation for Member States and other relevant stakeholders, attracting 130 comments and contributions, including 54 from Member States, 40 from nongovernmental organizations and 16 from private-sector entities.

26. Between June and November 2014, Member States, stakeholders and the Secretariat convened additional high-level technical, political and interagency discussions to contribute to the action plan.<sup>4</sup> These included the Ministerial Conference on Antibiotic Resistance: joining forces for future health (The Hague, 25 and 26 June 2014); a meeting on the Global Health Security Agenda, including antimicrobial resistance (Jakarta, 20 and 21 August 2014); an informal Member States consultation to provide direct input on the draft plan (Geneva, 16 October 2014); and a meeting on the responsible use of antibiotics (Oslo, 13 and 14 November 2014).

27. Further scheduled meetings include one on global surveillance capacity, systems and standards (Stockholm, 2 and 3 December 2014). The results of these and any other consultations hosted by with Member States and other stakeholders will be taken into account, guided by advice from the Strategic and Technical Advisory Group on antimicrobial resistance, before submission of the final version of the draft global action plan to the Health Assembly.

## STRATEGIC OBJECTIVES

28. The overall goal of the action plan is to ensure, for as long as possible, continuity of the ability to **treat and prevent infectious diseases with effective and safe medicines** that are quality-assured, used in a responsible way, and accessible to all who need them.

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<sup>1</sup> Details of the Strategic and Technical Advisory Group on antimicrobial resistance and its recommendations are available at: <http://www.who.int/drugresistance/stag/en/> (accessed 18 November 2014).

<sup>2</sup> Details of national and regional action plans, WHO guidance and action plans for specific diseases and health topics including antimicrobial resistance, standards and guidelines established by intergovernmental organizations such as FAO and OIE, and other information taken into account will be documented in supplementary material that will be published on the relevant pages of the WHO website (<http://www.who.int/drugresistance/en/>).

<sup>3</sup> The report of the meeting is available at: [http://apps.who.int/iris/bitstream/10665/128675/1/WHO\\_HSE\\_PED\\_AIP\\_2014.4\\_eng.pdf?ua=1&ua=1](http://apps.who.int/iris/bitstream/10665/128675/1/WHO_HSE_PED_AIP_2014.4_eng.pdf?ua=1&ua=1) (accessed 18 November 2014).

<sup>4</sup> Information on these consultations is available at: <http://www.who.int/drugresistance/en/>.

29. To achieve this overall goal, five strategic objectives have been identified. These are set out in paragraphs 30–48 with the corresponding actions for Member States, the Secretariat (including actions for FAO, OIE and WHO within the tripartite collaboration), and international organizations and other partners, in the table following paragraph 52. It is expected that countries will develop their own national action plans on antimicrobial resistance in line with the global plan.

### **Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training**

30. Steps need to be taken immediately in order to raise awareness of antimicrobial resistance and promote behavioural change, through public communication programmes that target different audiences in human health, animal health and agricultural practice as well as consumers. Inclusion of the use of antimicrobial agents and resistance in school curricula will promote better understanding and awareness from an early age.

31. Making antimicrobial resistance a core component of professional education, training, certification and development in the health and veterinary sectors and agricultural practice will help to ensure proper understanding and awareness among professionals.

### **Objective 2: Strengthen the knowledge and evidence base through surveillance and research**

32. Actions and investments to tackle antimicrobial resistance should be supported by clear rationales of their benefit and cost–effectiveness. National governments, intergovernmental organizations, agencies, professional organizations, nongovernmental organizations, industry and academia have important roles in generating such knowledge and translating it into practice.

33. Particularly important gaps in knowledge that need to be filled include the following:

- the incidence, prevalence, range across pathogens and geographical patterns related to antimicrobial resistance are all information that is needed to guide the treatment of patients; to inform local, national and regional actions; and to monitor the effectiveness of interventions
- understanding of how resistance develops and spreads, including how resistance circulates within and between humans and animals and through food, water and the environment, is important for the development of new tools, policies and regulations to counter antimicrobial resistance
- the ability rapidly to characterize newly emerged resistance in microorganisms and elucidate the underlying mechanisms; this knowledge is necessary to ensure that surveillance and diagnostic tools and methods remain current
- understanding of the social science and behaviour needed to support the achievement of Objective 1
- research into, including clinical trials of, treatments for common bacterial infections, especially in low-resource settings
- basic research and translational studies to support the development of new treatments, diagnostics, vaccines and other interventions

- research to identify alternatives to non-therapeutic uses of antimicrobial agents in agriculture and aquaculture, including their use for growth promotion and crop protection
- economic research, including the development of models to assess the cost of antimicrobial resistance and the costs and benefits of this action plan.

34. WHO's global report on surveillance of antimicrobial resistance<sup>1</sup> also revealed many gaps in information on antimicrobial resistance in pathogens of major public health importance. International standards on harmonization of national antimicrobial resistance surveillance and monitoring programmes were adopted by OIE's members in 2012, but there are no internationally agreed standards for collection of data and reporting on antibacterial resistance in human health, and no harmonizing standards across medical, veterinary and agricultural sectors. There is also no global forum for the rapid sharing of information on antimicrobial resistance.

35. In 2013, some Member States of the European Union launched a strategic research agenda on antimicrobial resistance through a joint programming initiative.<sup>2</sup> This initiative, which also includes some countries outside the European Union, could provide an initial framework for further development of a global strategic research agenda.

### **Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures**

36. Many of the most serious and difficult-to-treat antibiotic-resistant infections occur in health care facilities, not only because that is where patients with serious infections are admitted but also because of the intensive use therein of antibiotics and inadequate measures to prevent and control infection.

37. Better hygiene and infection prevention measures are essential to limit the development and spread of antimicrobial-resistant infections and multidrug-resistant bacteria. Effective prevention of infections transmitted through sex or drug injection as well as better sanitation, hand washing, and food and water safety must also be core components of infectious disease prevention. Malaria has the greatest public health impact of all vector-borne infectious diseases and is the most affected by antimicrobial resistance;<sup>3</sup> vector control holds the key to malaria prevention, control and elimination.

38. Immunization can reduce antimicrobial resistance in three ways:

- existing vaccines can prevent infectious diseases whose treatment would require antimicrobial medicines
- existing vaccines can reduce the prevalence of viral infections, which are often inappropriately treated with antibiotics
- development and use of new or improved vaccines can prevent diseases that are becoming difficult to treat or are untreatable owing to antimicrobial resistance.

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<sup>1</sup> Antimicrobial resistance: global report on surveillance 2014. Geneva: World Health Organization; 2014.

<sup>2</sup> Strategic Research Agenda: Joint Programming Initiative on Antimicrobial Resistance. The Hague, JPIAMR, 2013.

<sup>3</sup> World malaria report 2013. Geneva: World Health Organization; 2013.



39. Much antibiotic use is linked to intensive animal production. Antibiotics are sometimes used to prevent infections or to prevent the spread of diseases within a herd when infection occurs, and are often administered through feed and water. Alternative husbandry practices, including the use of vaccines, can reduce infection rates and dependence on antibiotics as well as the risk that antibiotic-resistant organisms will develop and spread through the food chain.

#### **Objective 4: Optimize the use of antimicrobial medicines in human and animal health**

40. Evidence that antimicrobial resistance is driven by the volume of use of antimicrobial agents is compelling. High antibiotic use may reflect over-prescription, easy access through over-the-counter sales and, more recently, via the Internet, which are widespread in many countries. Despite measures taken by some Member States, antibiotic use in humans, animals and agriculture is still increasing. The projected increase in demand for animal food products may lead to yet further increases in antibiotic use.

41. Data on antibiotic use are collected and analysed in many high- and middle-income countries and OIE is developing a database on antibiotic use in animals. However, data are lacking on antibiotic use in human beings at the point of care and from lower-income countries.

42. More widespread recognition of antimicrobial medicines as a public good is needed in order to strengthen regulation of their distribution, quality and use, and encourage investment in research and development. In some cases, industry's spending on promoting products is greater than governmental investment in promoting rational use of antimicrobial medicines or providing objective information.

43. Decisions to prescribe antibiotics are rarely based on definitive diagnoses effective, rapid, low-cost diagnostic tools are needed for guiding optimal use of antibiotics in human and animal medicine, and such tools should be easily integrated into clinical, pharmacy and veterinary practices. Evidence-based prescribing and dispensing should be the standard of care.

44. Regulation of the use of antimicrobial agents is inadequate or poorly enforced in many areas, such as over-the-counter and Internet sales. Related weaknesses that contribute to development of antimicrobial resistance include poor patient compliance, the prevalence of substandard medicines for both human and veterinary use, and inappropriate or unregulated use of antimicrobial agents in agriculture.

#### **Objective 5: 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**

45. The economic case must reflect the need for capacity development, including training in low-resource settings, and the need for new and accessible interventions, including medicines, diagnostics and vaccines.

46. Economic impact assessments are needed on the health and broader socioeconomic burden of antimicrobial resistance, and should compare the cost of doing nothing against the cost and benefit of action. Lack of such data hindered implementation of the 2001 Global Strategy for Containment of

Antimicrobial Resistance.<sup>1</sup> The few studies on the economic cost of antimicrobial resistance are limited chiefly to developed countries.

47. Investment in the development of new medicines, as well as in diagnostic tools and vaccines, is needed urgently. Lack of such investment reflects, in part, fears that resistance will develop rapidly and that returns on investment will be limited because of restrictions in use. Thus research and development of new antibiotics is seen as a less attractive business investment than that of medicines for chronic diseases. Currently most major pharmaceutical companies have stopped research in this area, a situation described by WHO's Consultative Expert Working Group on Research and Development: Financing and Coordination<sup>2</sup> as "a serious market failure" and "a particular cause for concern". New processes are needed both to facilitate renewed investment in research and development of new antibiotics, and to ensure that use of new products is governed by a public health framework of stewardship that conserves the effectiveness and longevity of such products while securing affordability and access to those in need. The cost of investment in research and development may need to be de-linked from the volume of sales. Many forums have been created in recent years to discuss these issues.<sup>3</sup>

48. Antibiotics must also be supplemented by affordable, point-of-care diagnostics to inform health practitioners and veterinarians of the susceptibility of the pathogens to available antibiotics. The applicability and affordability of these techniques in low- and middle-income countries must be considered.

## **FRAMEWORK FOR ACTION ON ANTIMICROBIAL RESISTANCE**

49. The framework presented below tabulates the actions that Member States, the Secretariat and international and national partners need to take in order to attain the goal and meet the objectives of the global plan.

50. Member States are urged to develop their own national action plans on antimicrobial resistance within the next two years of the endorsement of the draft action plan by the Health Assembly that are in line with the global action plan.

51. The Secretariat will facilitate this work by:

- supporting countries to develop, implement and monitor national plans
- leading and coordinating support to countries for assessment and implementation of investment needs

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<sup>1</sup> Implementation workshop on the WHO global strategy for containment of antimicrobial resistance. Geneva: World Health Organization; 2003.

<sup>2</sup> Research and development to meet health needs in developing countries: strengthening global financing and coordination. Report of the consultative expert working group on research and development: financing and coordination. Geneva: World Health Organization; 2012.

<sup>3</sup> Several existing initiatives were reviewed at WHO's Technical Consultation on Innovative Models for New Antibiotics' Development and Preservation (Geneva, 13 May 2014) ([http://www.who.int/phi/implementation/consultation\\_imnadv/en/](http://www.who.int/phi/implementation/consultation_imnadv/en/), accessed 20 November 2014).

- monitoring development and implementation of action plans by Member States and other partners
- publishing biennial progress reports, including an assessment of countries and organizations that have plans in place, their progress in implementation, and the effectiveness of action at regional and global levels. Progress made by FAO, OIE and WHO in implementing actions undertaken within the organizations' tripartite collaboration will also be included in these reports.

52. The Secretariat will also work with the Strategic and Technical Advisory Group on antimicrobial resistance, Members States, FAO and OIE within the tripartite collaboration, and other relevant partners to develop a framework for monitoring and evaluation, including the identification of measurable indicators of implementation and effectiveness of the plan. Examples of such indicators of effectiveness (impact) that could be applied are shown for each of the strategic objectives are shown in the tabulated framework.

<b>Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training</b>		
<b>Potential measures of effectiveness:</b> extent of reduction in global human consumption of antibiotics (with allowance for the need for improved access in some settings), and reduction in the volume of antibiotic use in food production		
<b>Member State action</b>	<b>Secretariat action</b>	<b>International and national partners' action</b>
<p>Increase national awareness of antimicrobial resistance through public communication programmes that target the different audiences in human health, animal health and agricultural practice, including participation in an annual world antibiotic awareness campaign.</p> <p>Ensure that antimicrobial resistance is a core component of professional education, training, certification and development for the health and veterinary sectors and agricultural practice.</p> <p>Include antimicrobial use and resistance in school curricula in order to promote better understanding and awareness, and ensure that public media are provided with accurate and relevant information so that public information and reporting reinforce key messages.</p>	<p>Develop and implement global communication programmes and campaigns, including an annual world antibiotic awareness campaign, building on existing regional and national campaigns and in partnership with other organizations (e.g. UNESCO and UNICEF). Provide core communication materials and tools (including those for social media and for assessing public awareness and understanding) that can be adapted and implemented by Member States and others.</p> <p>Develop, with FAO and OIE through the tripartite collaboration, core communication, education and training materials that can be adapted and implemented regionally and nationally, on subjects that include the need for responsible use of antibiotics, the</p>	<p>Professional organizations and societies should ensure that antimicrobial resistance is a core component of education, training, examination, professional registration or certification, and professional development.</p> <p>OIE should continue to support its members in implementing OIE standards including veterinary professional standards and training, applying its Performance of Veterinary Services Pathway<sup>1</sup> and updating of legislation.</p> <p>FAO should support awareness-raising on antimicrobial resistance and promote good animal production and hygiene practices among animal production and health workers, animal producers, and other stakeholders in the food and agriculture sectors.</p>

<sup>1</sup> See: <http://www.oie.int/support-to-oie-members/pvs-evaluations/> (accessed 20 November 2014).

<p>Ensure that antimicrobial resistance is recognized as a priority need for action across all government ministries through inclusion in national risk registers or other effective mechanisms for cross-government commitment.</p>	<p>importance of infection prevention in human and animal health and agricultural practice, and measures to control spread of resistant organisms through food and the environment. Provide support to Member States with the integration of education on antimicrobial resistance into professional training, education and registration.</p> <p>Publish regular reports on progress in implementing the global action plan and progress towards meeting impact targets, in order to maintain commitment to reducing antimicrobial resistance.</p> <p>Maintain antimicrobial resistance as a priority for discussion with Member States through the regional committees, the Executive Board and Health Assembly, and with other intergovernmental organizations, including the United Nations.</p>	<p>Intergovernmental organizations, including FAO, OIE and the World Bank, should raise awareness and understanding of antimicrobial resistance and, in collaboration with WHO, should mirror the actions of the Secretariat within their constituencies.</p> <p>Other stakeholders – including civil society organizations, trade and industry bodies, employee organizations, foundations with an interest in science education, and the media – should help to promote public awareness and understanding of infection prevention and use of antimicrobial medicines across all sectors.</p>
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**Objective 2: Strengthen the knowledge and evidence base through surveillance and research**

**Potential measure of effectiveness:** extent of reduction in the prevalence of antimicrobial resistance, based on data collected through integrated programmes for surveillance of antimicrobial resistance in all countries

Member State action	Secretariat action	International and national partners' action
<p>Develop a national surveillance system for antimicrobial resistance that:</p> <ul style="list-style-type: none"> <li>includes a national reference centre with the ability systematically to collect and analyse data – including those on a core set of organisms and antimicrobial medicines from both health care facilities and the community – in order to inform national policies and decision-making;</li> <li>includes at least one reference laboratory capable of susceptibility testing to fulfil the core data requirements, using standardized tests and operating to agreed quality standards;</li> <li>meets the recommendations of the WHO Advisory Group on</li> </ul>	<p>Develop and implement a global programme for surveillance of antimicrobial resistance in human health, including surveillance and reporting standards, case definitions, external quality assessment schemes, and a network of WHO Collaborating Centres to support surveillance of antimicrobial resistance and external quality assessment in each WHO region.</p> <p>Report regularly on global and regional trends in the prevalence of antimicrobial resistance in human health and establish a web-based portal for sharing information and data.</p> <p>Work with FAO and OIE, within the tripartite collaboration, to support integrated surveillance and</p>	<p>FAO, with WHO, should review and update regularly the Codex Alimentarius Code of Practice to minimize and contain antimicrobial resistance and the Codex Alimentarius guidelines for risk analysis of foodborne antimicrobial resistance.</p> <p>The international research community and FAO should support studies to improve understanding of the impact of antimicrobial resistance on agriculture, animal production and food security, as well as the impacts of agricultural practices on development and spread of antimicrobial resistance.</p> <p>OIE should regularly update the terrestrial and aquatic animal codes (particularly with reference</p>

<p>Integrated Surveillance of Antimicrobial Resistance for antimicrobial susceptibility testing of foodborne pathogens,<sup>1</sup> the standards published in the OIE terrestrial and aquatic animal codes,<sup>2</sup> the FAO/WHO Codex Alimentarius Code of Practice to Minimize and Contain Antimicrobial Resistance<sup>3</sup> and the Codex Alimentarius Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance;<sup>4</sup></p> <ul style="list-style-type: none"> <li>• shares information so that national, regional and global trends can be detected and monitored;</li> <li>• has the capacity to detect and report newly emerged resistance that may constitute a public health emergency of international concern, as required under the International Health Regulations (2005).</li> </ul> <p>Consider implementing an agreed global public health research agenda on antimicrobial resistance, including: research to promote responsible use of antimicrobial medicines; defining improved practices for preventing infection in human and animal health and agricultural practice; and encouraging development of novel diagnostics and antimicrobial medicines.</p>	<p>reporting of antimicrobial resistance in human and animal health and agriculture, and develop measures of antimicrobial resistance in the food chain for use as indicators of risk to human health.</p> <p>Consult Member States and other multisectoral stakeholders about the development of a global public health research agenda for filling major gaps in knowledge on antimicrobial resistance, including methods to assess the health and economic burdens of antimicrobial resistance, cost-effectiveness of actions, mechanisms of development and spread of resistance, and research to underpin development of new interventions, diagnostic tools and vaccines. Monitor and report on implementation of the research agenda, for instance through the use of WHO's Global Health Research and Development Observatory.</p> <p>Work with partners to establish a sustainable repository for information on antimicrobial resistance and on the use and efficacy of antimicrobial medicines that is integrated with the global health research and development observatory and with a programme for independent evidence assessment and evaluation.</p>	<p>to antimicrobial resistance), revise the guideline on laboratory methods for bacterial antimicrobial susceptibility testing, and support the establishment of veterinary laboratory services through its Performance of Veterinary Services Pathway.</p> <p>Global health donors, international development bodies, and aid and technical agencies should support developing countries to build capacity to collect and analyse data on the prevalence of antimicrobial resistance and share or report such data.</p> <p>Research funding organizations and foundations should support implementation of the agreed global public health research agenda on antimicrobial resistance.</p>
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<sup>1</sup> Integrated surveillance on antimicrobial resistance: guidance from a WHO advisory group. Geneva: World Health Organization; 2013.

<sup>2</sup> See: <http://www.oie.int/en/our-scientific-expertise/veterinary-products/antimicrobials> (accessed 20 November 2014).

<sup>3</sup> See: <http://www.codexalimentarius.org/committees-task-forces//?provide=committeeDetail&idList=6> (accessed 20 November 2014).

<sup>4</sup> See document CAC/GL 77-2011 at: <http://www.codexalimentarius.org/standards/list-of-standards/en/> (accessed 20 November 2014).

<b>Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures</b>		
<b>Potential measures of effectiveness:</b> extent of reduction in the prevalence of preventable infections, and in particular the incidence of drug-resistant infections in health care settings		
<b>Member State action</b>	<b>Secretariat action</b>	<b>International and national partners' action</b>
<p>Member States may consider the following actions:</p> <ul style="list-style-type: none"> <li>• take urgent action to implement and strengthen hygiene and infection prevention and control in health care facilities;</li> <li>• include training and education in hygiene and infection prevention and control as core (mandatory) content in training and education for health care and veterinary professionals and in their continuing professional development and accreditation or registration.</li> </ul> <p>Ensure that national surveillance of antimicrobial resistance includes the collection and reporting of data on antimicrobial susceptibility of pathogens causing health care-associated infections.</p> <p>Implement the standards published in the OIE Terrestrial and Aquatic Animal Health Codes<sup>1</sup> and FAO/WHO Codex Alimentarius Code of Practice to Minimize and Contain Antimicrobial Resistance.<sup>2</sup></p> <p>Promote vaccination as a method of reducing infections in food animals.</p>	<p>Facilitate the design and implementation of policies and tools to strengthen hygiene and infection prevention and control practices, particularly to counter antimicrobial resistance, and promote the engagement of civil society and patient groups in improving practices in hygiene and infection prevention and control.</p> <p>Ensure that policy recommendations for new and existing vaccines take into account the prospects for restricted treatment options because of antimicrobial resistance, and the additional benefits of reduced use of antimicrobial agents, including antibiotics.</p> <p>Work with partners and other organizations to facilitate the development and clinical evaluation of specific priority vaccines for the prevention of difficult-to-treat or untreatable infections.</p> <p>Work with FAO and OIE, within the tripartite collaboration, to develop recommendations for the use of vaccines in food-producing animals, including recommendations for new vaccines, as a means to prevent foodborne diseases in humans and animals and reduce antimicrobial use.</p>	<p>Professional societies and accreditation bodies should support training and education on infection-prevention measures as a mandatory requirement in professional development, accreditation and registration.</p> <p>OIE should update its codes and manuals to take account of new developments in vaccines.</p> <p>FAO should continue to engage and support producers and stakeholders in the food and agriculture sectors in adopting good practices in animal husbandry, health and biosecurity aimed at reducing the use of antibiotics and the risk of development and spread of antimicrobial resistance.</p>

<sup>1</sup> See: <http://www.oie.int/en/our-scientific-expertise/veterinary-products/antimicrobials> (accessed 20 November 2014).

<sup>2</sup> See: <http://www.codexalimentarius.org/committees-task-forces//?provide=committeeDetail&idList=6> (accessed 29 October 2014).

<b>Objective 4: Optimize the use of antimicrobial medicines in human and animal health</b>		
<b>Potential measure of effectiveness:</b> extent of reduction in global human consumption of antibiotics (with allowance for the need for improved access in some settings), the consumption of antibiotics used in food production (terrestrial and aquatic livestock, and other agricultural practices), and the use of medical and veterinary antimicrobial agents for applications other than human and animal health		
<b>Member State action</b>	<b>Secretariat action</b>	<b>International and national partners' action</b>
<p>Develop and implement comprehensive action plans on antimicrobial resistance that incorporate the following elements:</p> <ul style="list-style-type: none"> <li>• collection and reporting of data on use of antimicrobial agents in human and animal health and agriculture so that trends can be monitored and the impact of action plans assessed;</li> <li>• ensuring that prescription, distribution and dispensing of antimicrobials is carried out by accredited health or veterinary professionals;</li> <li>• ensuring that marketing authorization is given only to antimicrobial agents that are quality assured, safe and efficacious;</li> <li>• development and use of WHO Model Lists of Essential Medicines, reimbursement lists and standard treatment guidelines to guide purchasing and prescribing of antimicrobial medicines, and regulation and control of promotional practices by industry;</li> <li>• laboratory capacity to identify pathogens and their antimicrobial susceptibility in order to guide optimal use of antimicrobial medicines in clinical practice;</li> <li>• provision of stewardship programmes that monitor and promote optimization of</li> </ul>	<p>Develop a framework for monitoring and reporting on antimicrobial consumption in human health, including standards for collection and reporting of data on use in different settings, building on the work of OECD.<sup>1</sup></p> <p>With FAO and OIE, within the tripartite collaboration, collect, consolidate and publish information on the global consumption of antimicrobial medicines.</p> <p>Strengthen and align, within the tripartite collaboration with FAO and OIE, the concepts of critically important antibiotics for human and animal health, and ensure that these concepts include use of new antibiotics so that a common position on restriction of antimicrobial medicines for human use can be established.</p> <p>Provide support to Member States in the development and enforcement of relevant regulations that will prevent substandard/spurious/false-labelled/falsified/ counterfeit antimicrobial medical products reaching patients.</p> <p>Develop technical guidelines and standards to support access to, and evidence-based selection and responsible use of, antimicrobial medicines, including follow-up to treatment failure.</p> <p>Provide leadership to strengthen medicines regulatory systems at</p>	<p>OIE should regularly update its Terrestrial and Aquatic Animal Health Codes, particularly with reference to antimicrobial resistance.</p> <p>FAO, in collaboration with WHO, should regularly review and update the Codex Alimentarius Code of Practice to Minimize and Contain Antimicrobial Resistance to take into account not only residues in food but also the need for standards to minimize and control use of antimicrobial agents in agricultural practice.</p> <p>OIE, supported by FAO and WHO within the tripartite collaboration, should build and maintain a global database on the use of antimicrobial medicines in animals.</p> <p>The pharmaceutical industry should invest in the development of effective and low-cost tools for diagnosis of infectious diseases and antimicrobial susceptibility testing for use in human and animal health at points of care and dispensing (pharmacies).</p> <p>Donors, philanthropic and other nongovernmental organizations and civil society should ensure that their efforts to increase access to antimicrobial medicines are accompanied by measures to protect the continued efficacy of such medicines.</p> <p>Professional bodies and associations, including industry</p>

<sup>1</sup> Prescribing in primary care. In: Health at a glance 2013: OECD Indicators. Paris: Organisation for Economic Co-operation and Development; 2013.

<p>antimicrobial use at national and local levels in accordance with international standards in order to ensure the correct choice of medicine at the right dose on the basis of evidence;</p> <ul style="list-style-type: none"> <li>• identification and elimination of economic incentives in all sectors that encourage inappropriate use of antimicrobial agents, and introduction of incentives to optimize use;</li> <li>• effective and enforceable regulation and governance to ensure appropriate licensing, distribution, use and quality assurance of antimicrobial medicines in human and animal health, including a regulatory framework for preservation of new antibiotics;</li> <li>• policies on use of antimicrobial agents in terrestrial and aquatic animals and agriculture, including implementation of Codex Alimentarius and OIE guidelines as well as WHO/OIE guidance on the use of critically important antibiotics, phasing out of use of antibiotics for animal growth promotion and crop protection, and reduction in nontherapeutic use of antimicrobial medicines in animal health.</li> </ul>	<p>national and regional levels, so that appropriate practices for optimizing use of antimicrobial medicines are supported by appropriate and enforceable regulation, and that promotional practices can be adequately regulated.</p> <p>Consult with Member States and pharmaceutical industry associations on innovative regulatory mechanisms for new antimicrobial medicines, for example considering them as a class of medicine that will require a different set of regulatory controls, and on new approaches to product labelling that focus on public health needs rather than marketing claims, in order to address the need for preservation of effectiveness and for global access.</p> <p>Develop standards (within the tripartite collaboration with FAO and OIE), based on best available evidence of harm, for the presence of antimicrobial agents and their residues in the environment, especially in water, wastewater and food (including aquatic and terrestrial animal feed).</p>	<p>associations, health insurance providers and other payers, should develop a code of conduct for appropriate training in, education about, and marketing, purchasing, reimbursement and use of antimicrobial agents. This code should include commitment to comply with national and international regulations and standards, and to eliminate dependence on the pharmaceutical industry for information and education on medicines and, in some cases, income.</p>
<p><b>Objective 5: 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</b></p> <p><b>Potential measures of effectiveness:</b> extent of increase in sustainable investment in capacity to counter antimicrobial resistance for all countries, including investment in development of new medicines, diagnostics and other interventions</p>		
Member State action	Secretariat action	International and national partners' action
<p>Member States should consider assessing investment needs for implementation of their national action plans on antimicrobial resistance, and should develop plans to secure and apply the required financing.</p>	<p>Work with the United Nations Secretary-General and bodies in the United Nations system to identify the best mechanism(s) to realize the investment needed to implement the global action plan on antimicrobial resistance, particularly with regard to the needs of developing countries.</p>	<p>Partners in the finance and economic sectors should define the economic case for national and global investment in combating antimicrobial resistance, including an assessment of the cost of implementing this action plan and the consequential cost of no action; this work could be led by</p>



<p>Member States are encouraged to participate in international collaborative research to support the development of new medicines, diagnostic tools and vaccines through:</p> <ul style="list-style-type: none"> <li>• prioritization and support of basic scientific research on infectious diseases, and promoting partnerships between research institutions in developed and developing countries;</li> <li>• collaborating in the investigation of natural sources of biodiversity and biorepositories as sources for the development of new antibiotics;</li> <li>• strengthening existing and creating new public–private partnerships for encouraging research and development of new antimicrobial agents and diagnostics;</li> <li>• piloting innovative ideas for financing research and development and for the adoption of new market models to encourage investment and ensure access to new antimicrobial products.</li> </ul>	<p>Work with the World Bank and with other development banks to develop and implement a template or models to estimate the investment needed to implement national action plans on antimicrobial resistance, and to collate and summarize these needs.</p> <p>Work with the World Bank and with FAO and OIE, within the tripartite collaboration, to assess the economic impact of antimicrobial resistance and of implementation of the action plan in animal health and agriculture.</p> <p>Explore with Member States, intergovernmental organizations, industry associations and other stakeholders, options for the establishment of a new partnership or partnerships:</p> <ul style="list-style-type: none"> <li>• to coordinate the work of many unlinked initiatives aiming to renew investment in research and development of antibiotics (including follow-up initiatives from the Consultative Expert Working Group on Research and Development)<sup>1</sup>;</li> <li>• to identify priorities for new treatments, diagnostics and vaccines on the basis of emergence and prevalence of serious or life-threatening infections caused by resistant pathogens;</li> <li>• to act as the vehicle(s) for securing and managing investment in new medicines, diagnostics, vaccines and other interventions;</li> <li>• to facilitate affordable and equitable access to existing and new medicines<sup>2</sup> and other</li> </ul>	<p>the World Bank.</p> <p>FAO, OIE and other partners should support appropriate analyses to establish the case for investment and to inform the selection of interventions to improve animal husbandry, management, health, hygiene and biosecurity practices aimed at reducing antimicrobial use (and antimicrobial resistance) in different production settings.</p>
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<sup>1</sup> Research and development to meet health needs in developing countries: strengthening global financing and coordination. Report of the consultative expert working group on research and development: financing and coordination. Geneva: World Health Organization; 2012.

<sup>2</sup> Many of the actions that can support affordable and equitable access to medicines are set out in the Global strategy and plan of action on public health, innovation and intellectual property. Geneva: World Health Organization; 2011.

	products while ensuring their proper and optimal use; <ul style="list-style-type: none"><li>• to establish open collaborative models of research and development in a manner that will both ensure access and provide incentives for investment.</li></ul>	
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**ACTION BY THE EXECUTIVE BOARD**

53. The Board is invited to note this report and to provide further guidance on the draft global action plan with a view to its submission to the Sixty-eighth World Health Assembly for consideration.

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