Draft global action plan on antimicrobial resistance

Draft for consultation with Member States October 2014

In May 2014 the Sixty-seventh World Health Assembly adopted resolution WHA67.25 on antimicrobial resistance, requesting the Director-General to develop a draft global action plan to combat antimicrobial resistance, including antibiotic resistance, and to submit the draft to the Sixty-eighth Health Assembly in May 2015, through the Executive Board at its 136th session.

Antibiotic resistance is the ability of bacteria to overcome the effect of antibiotic medicines. Bacteria adapt to grow in the presence of antibiotics, so the rate and prevalence of resistance are linked to the frequency of use of antibiotics. Many antibiotics belong to the same class of medicine so resistance to one can mean resistance to the whole class, and resistance that develops in one context can spread rapidly to affect treatment of a wide range of infections and diseases. Some of these features are also true for medicines used to treat viral, parasitic and fungal diseases, leading to the broader concept of antimicrobial resistance (AMR).

Within the wider scope of AMR, the draft action plan refers, where appropriate, to existing action plans for viral, parasitic diseases including HIV/AIDS, malaria and tuberculosis (TB). Antibiotic resistance is covered in more detail. Most of the actions proposed in this plan are equally applicable to antifungal resistance.

AMR affects all areas of health, involves many sectors, and impacts on all of society. Drug resistance can circulate between humans, animals, food, water and the environment, and transmission is influenced by trade, travel and migration (both human and animal). International multisectoral collaboration and cooperation are essential requirements in the action plan since action is needed in all countries and sectors simultaneously. Sustainable coalitions are needed at all levels within countries to bring different sectors and stakeholders together.

Action now is imperative. AMR (and particularly antibiotic resistance) is spreading, and there are few prospects for new antibiotics in the short term. However, there is now a much higher level of awareness of, and political support for, action to address AMR. Support is multisectoral to an extent

1 WHO (2012) WHO global strategy for the surveillance and monitoring of HIV drug resistance


WHO (2013). Emergency response to artemisinin resistance in the Greater Mekong Subregion

not seen before, with recognition of the economic impact and with collaboration between the human health, animal health and agriculture sectors (including the tripartite collaboration between WHO, FAO and OIE). The action plan addresses concerns not well considered previously, including economic assessment and a business case for investment, and commitments by Member States, WHO and others to report progress against measurable goals and targets.

1 PREPARATION OF THE DRAFT ACTION PLAN

In response to the request of the Health Assembly in Resolution WHA67.25, the recommendations of WHO’s Strategic Technical Advisory Group (STAG) on Antimicrobial Resistance were taken into account in the development of the draft global action plan and a multisectoral approach was followed in the drafting process.2

The STAG heard the views of over 30 representatives of civil society, nongovernmental organizations, public health and regulatory agencies, industry associations and professional organizations at its meeting of 14–16 April 2014.3 FAO and OIE were consulted regularly throughout the development of the draft global action plan, including through meetings of the tripartite collaboration and by their participation in other consultations for development of the action plan.

In July and August 2014 a web-based consultation was organized. A letter was sent to Member States on 18 July 2014 describing the process and inviting comments. To encourage as broad a response as possible, other relevant stakeholders were contacted and information about the web consultation was widely disseminated through networks on AMR. By 1 September 2014, 130 comments and contributions had been received, including 54 from Member States, 40 from nongovernmental organizations and 16 from private-sector entities.4

Member States, key stakeholders and the Secretariat convened a number of high-level technical, political and interagency discussions to contribute to the action plan. These included a meeting on human and animal health and agriculture co-hosted by the Netherlands in collaboration with FAO and OIE (The Hague, 25–26 June 2014); a meeting on the Global Health Security Agenda including AMR, hosted by Indonesia (Jakarta, 20–21 August 2014). A further meeting to address research gaps and needs, hosted by Brazil (Brasilia, 28–29 October 2014); responsible use of antibiotics is to be hosted by Brazil, France, Indonesia, Norway, Senegal, South Africa and Thailand (Oslo, 13–14 November 2014); and a meeting to promote development of global surveillance capacity, systems and standards will be hosted by Sweden (Stockholm, 2–3 December 2014).

The outcomes of the Brasilia, Oslo and Stockholm consultations, as well as of a further web-based consultation and a meeting of Member States in the early months of 2015, will be taken into account in revisions to the draft action plan before submission to the Health Assembly. Guidance will continue to be sought from the STAG.

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4 Details of the consultation and responses will be published at http://www.who.int/drugresistance/en/
5 Information on the programme, participants and outcome from this meeting are available at http://www.conferenceamr2014.nl/scope-of-the-conference/666/, accessed 7 August 2014.
The draft global action plan takes into account a number of existing national and regional action plans, WHO guidance and action plans for specific diseases and health topics, including AMR, and a range of available data, research evidence and analysis.6

2 BACKGROUND
Hard-won gains in global health are under threat because the organisms that cause many common human diseases have become resistant to the drugs designed to destroy them. Resistance exists across very different types of conditions – from TB, pneumonia, HIV and malaria to respiratory and urinary tract infections, blood-stream infections and food poisoning. Diseases previously regarded as relatively easy to manage are much harder to treat as doctors must use “last-resort” drugs that are more costly, take longer to work and are often unavailable or unaffordable in low- and middle-income countries.

Resistance is a natural process of adaptation when microbes are exposed to antimicrobial drugs, such as antivirals and antibiotics. Resistance develops far more quickly through the misuse and overuse of these medicines, yet antibiotic use by humans7 increased by 36% between 2000 and 2010. High-income countries consume most antibiotics per person but consumption is rising rapidly in emerging economies. Antibiotics are needed to treat sick animals but are also used to prevent disease in healthy animals and, in many countries, to promote growth through mass administration to herds. The total gross weight of antibiotics used in animals is growing significantly and is expected to grow further as animal production increases by a projected 70% by 2050 to meet rising demands of a growing world population. Antimicrobials are also commonly used in plant agriculture and commercial fish and seafood farming.

Resistance spreads in ways that cannot be predicted, such as through exchange of genetic material between different bacteria. For instance, antibiotic resistance in bacteria that cause food poisoning can transfer to bacteria that cause pneumonia. Resistant microbes can circulate between animals and humans, and patterns of resistant bacteria in food animals can be found in meat and milk destined for sale to consumers. Resistance can spread rapidly. NDM-1-producing bacteria, which are highly resistant to treatment, were first discovered in 2008, but by mid-2011 patients with NDM-1 bacteria had been identified on all continents except Central and South America.

For patients and families, the consequences of AMR can be most profound for children. The commonest childhood diseases in developing countries – malaria, pneumonia, other respiratory infections and dysentery – can no longer be cured by many older antibiotics or medicines. In lower-income countries, effective antibiotics – if accessible – are critical for saving the lives of children with conditions such as acute diarrhoea, bacterial blood infections and severe acute malnutrition. In higher-income countries, some routine surgical operations and cancer chemotherapy will become unavailable or be very high-risk without effective antibiotics to prevent or treat associated infections. Surveys in a wide range of countries show that many patients believe antibiotics will cure viral infections that lead to coughs, colds and fever. Patients may also fail to complete a course of antimicrobial treatment or may self-medicate without an accurate diagnosis.

Health-care workers have a vital role in preserving the power of antimicrobials. Inappropriate prescribing and dispensing of antimicrobials in health-care facilities lead to misuse and overuse of medicines, often because medical staff lack up-to-date information, cannot access diagnostic facilities to identify the type of infection, yield to patient pressure to prescribe antibiotics, or benefit financially from supplying the drugs. Inadequate hygiene and infection prevention in hospitals help

6 Details of national and regional action plans, WHO guidance and action plans for specific diseases and health topics, including AMR, and other information taken into account will be documented in supplementary material that will be published at http://www.who.int/drugresistance/en/

7 Across the 71 countries for which there was data.
to spread infections. Hospital patients with drug-resistant methicillin-resistant *Staphylococcus aureus* (MRSA) have an estimated 61% higher risk of dying than those with the non-resistant form of the bacteria, and a risk of death almost three times higher than similar patients without this infection. Health-care associated infections are a growing challenge in developing countries.

For **farmers, animal husbandry and the food industry**, drug resistance means the loss of effective antimicrobials to treat sick animals, thus damaging food production and family livelihoods. An additional risk is the exposure of livestock workers to resistant bacteria in animals; farmers working with cattle, pigs and poultry with MRSA have a much higher risk of testing positive for the bacteria. Exposure through food is the most important of many ways for resistant bacteria to be transmitted from animals to humans, and there is evidence that human consumption of food carrying antibiotic-resistant bacteria has led, directly or indirectly, to acquisition of antibiotic-resistant infections. Other routes for human exposure include crops treated with antimicrobials or contaminated by manure or slurry, and farmyard run-offs into groundwater.

Many of the required actions on resistance depend on **political will** to adopt controversial policies, including controlling the use of antimicrobial drugs in human health and animal and food production. In a majority of countries, antibiotics can be purchased in markets, shops, pharmacies or over the Internet with no prescription or involvement of a health professional or veterinarian, leading to overuse and inappropriate self-medication. Substandard/spurious/false-labelled/falsified/counterfeit medical products are widespread, often lacking active ingredients or with too low a dose, putting human and animal health at risk and encouraging emergence of resistant microbes. Strong laws are needed to ensure that medicines are safe, effective and of good quality, and should be enforced by regulators with resources to control the manufacture, importation, distribution, marketing authorization and sale of medicines.

Among **economic policy-makers, development agencies, research funding organizations and other potential investors**, there is little awareness of the potential overall social, economic and financial impact of drug resistance. The World Economic Forum has identified AMR as a global risk beyond the capacity of any organization or nation to manage or mitigate alone. The effects of resistance on a developed country’s economy include higher health-care costs and decreases in labour supply, productivity, household incomes, national income and tax revenues. In the European Union alone, a subset of drug-resistant bacteria is responsible annually for some 25 000 deaths, equivalent to an economic loss of at least EUR 1.5 billion. Similar analyses are needed for low- and middle-income countries. Resistance to common veterinary antimicrobials causes increased mortality in animals with consequent production losses and extra costs. AMR is a drain on the global economy and it is urgent to build a business case for long-term sustainable investment to tackle the problem.

For the **pharmaceutical sector**, medicines and drugs that are no longer effective lose their value. Industry leaders will be important partners in combating AMR, both by supporting the responsible use of drugs to prolong their effectiveness and in research and development (R&D) 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. Current low levels of investment in R&D on antibiotics could suggest that the traditional investment model is failing patients in this area. New business models are needed to incentivize innovation and promote cooperation between policy-makers, researchers and the pharmaceutical industry to ensure that new technologies are available globally to prevent, diagnose and treat resistant infections.

### 3 ACTION PLAN GOALS

The overall public-health goal of the action plan is to ensure, for as long as possible, continuity of treatment and prevention of infectious diseases with effective and safe medicines that are of appropriate quality, used in a responsible way, and accessible to all who need them.
To monitor the effectiveness of the action plan, the following measures of outcome and impact are proposed:

- A reduction in the prevalence of AMR, based on data collected through integrated AMR surveillance programmes and specific infectious disease control programmes in all countries.
- A reduction in the mortality attributable to AMR (subject to availability of data, and for defined diseases).
- A reduction (to zero) in the number of serious infectious diseases that cannot be prevented or treated (achieved through conservation of the effectiveness of current antimicrobials or the development of new medicines and vaccines).
- A reduction in the prevalence of selected infectious diseases, and in particular preventable infections (achieved through effective prevention and control measures).
- An increase in the number of organisms for which specific rapid diagnostic tests are available, including for use in low- and middle-income countries.
- The number of new medicines entering phase II clinical studies, and for which mechanisms are in place to ensure preservation, and access in low- and middle-income countries.
- A reduction in global human consumption of antibiotics, recognizing the need for improved access in some settings, with specific reporting on the use of the critical classes of antibiotics and other antimicrobial medicines.
- A reduction in the consumption of antibiotics used in food production (terrestrial and aquatic livestock, and other agricultural practices) and reduction in the use in animals of antibiotics critically important for human health.
- Progressive reduction (to zero) in the use of medical and veterinary antimicrobials for applications other than human and animal health.

Actions are described in this plan to enable the achievement and measurement of these targets.

### 3.1 Proposed actions by Member States

To have in place the means to measure and report the data required to monitor impact of the global action plan.

### 3.2 Actions by the Secretariat

To consult with Member States and other stakeholders (including FAO and OIE through the tripartite collaboration) to define and agree on the measurable indicators and time-bound outcome targets of the effectiveness of the global action plan.

### 4 ACTION PLAN: PRINCIPLES AND STRATEGIC OBJECTIVES

The action plan is based on six guiding principles:

1) **Whole-of-society engagement.** Antimicrobial resistance will affect everyone, regardless of where they live, their health or economic circumstances, lifestyles or behaviours. It will have an impact on sectors beyond human health, such as agriculture, food security and economic development. Everyone – all sectors and disciplines – should therefore be engaged in the implementation of this action plan on a personal, societal or professional basis.

2) **Actions based on best available knowledge and evidence.** The actions and investment needed to address AMR must be supported wherever possible by clear and compelling evidence of, risk analysis, or rationale for their benefit and cost-effectiveness.

3) **Prevention first.** Every infection prevented (without use of antimicrobial medicines) is one that needs no treatment. Many interventions for the prevention of infection are cost-effective and can be implemented in all resource settings and sectors.
4) **Access not excess.** The overall goal is to preserve the ability to treat serious infections. Actions to address AMR need to take into account the need to maintain equitable access to, and appropriate use of, existing and new antimicrobial medicines.

5) **Sustainability.** Actions are more likely to be sustainable where they are integral to health systems or practices in other sectors, and where there is evidence of continuing health and economic benefit. Action will be more sustainable if all parties accept accountability for implementation and report regularly against agreed targets.

6) **Incremental targets for implementation.** All countries and other stakeholders need to be able to demonstrate progress towards implementation of the global action plan, and achievement of action plan objectives and goals, whatever their current status. A step-wise approach to targets and performance indicators for implementation of the plan, based on a series of “building-blocks”, will allow for different priorities and capacities of Member States and other stakeholders.

This action plan is structured around five strategic objectives:

1) **Objective 1: Improve awareness and understanding of AMR through effective communication, education and training.**

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

3) **Objective 3: Reduce the incidence of infection through effective hygiene and infection prevention measures.**

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

5) **Objective 5: Develop the business case for sustainable investment that takes account of the needs of all countries, as well as the need for investment in new medicines, diagnostic tools, vaccines and other interventions.**

## 5 ACTIONS TO ACHIEVE THE STRATEGIC OBJECTIVES

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

Reducing the impact of AMR requires changes in behaviour across all sectors of society from individuals through to professionals in health and other sectors, organizations and governments worldwide. Despite many global, regional and national campaigns and programmes there is still a need for better awareness, understanding and knowledge.

Key concepts that need to be understood and accepted include:

- Antimicrobial drugs, including antibiotics, are among the most important achievements of modern medicine, providing the means to treat common infections that might otherwise be deadly.
- AMR can affect everyone everywhere regardless of their health and economic circumstances.
- Everyone can and should contribute to reducing the threat of AMR.
- Antimicrobial resistance has high social, health, financial and economic impacts and there is a compelling need for investment to reduce these impacts.
- Development of AMR is driven by use in human and animal/animal agriculture settings. Individuals, health-care facilities, organizations and industries need to take responsibility for proper use of these life-saving medicines.
5.1.1 Proposed actions by Member States
Increase national awareness of AMR 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.

Ensure that AMR is a core component of professional education, training, certification and development for the health and veterinary sectors and agricultural practice.

Include antimicrobial use and resistance in school curricula 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.

Ensure that AMR 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.

5.1.2 Actions by the Secretariat
Develop and implement global communication programmes and campaigns, including an annual World Antibiotic Awareness campaign in November each year, building on existing regional and national campaigns. Provide core communication materials and tools (including for social media and to assess public awareness and understanding) that can be adapted and implemented by Member States and others.

Develop, with FAO and OIE through the tripartite collaboration, core communication, education and training materials that can be adapted and implemented regionally and nationally, including on the need for responsible use of antibiotics, the importance of infection prevention in human and animal health and agricultural practice, and measures to control spread through food and the environment. Support Member States with the integration of education on AMR into professional training, education and registration.

Publish regular reports on the implementation of the global action plan, and on progress towards meeting impact targets, in order to maintain commitment to reducing AMR.

Maintain AMR 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.

5.1.3 Proposed actions by international and national partners
Professional organizations and societies should ensure that AMR is a core component of education, training, examination, professional registration or certification, and professional development.

OIE should continue to support its Member States with the implementation of veterinary professional standards and training, including application of the PVS Pathway. 8

FAO should support awareness-raising on AMR and promote good animal production and hygiene practices among animal production and health workers, animal producers, food animal value chain operators and other stakeholders.

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Intergovernmental organizations, including FAO, OIE and the World Bank, should maintain awareness and understanding of AMR and, in collaboration with WHO, should mirror the actions of the Secretariat within their constituencies.

Other stakeholders – including civil society organizations, trade and industry bodies, employee organizations, foundations with an interest in science education, and the media – have a role to play in promoting public awareness and understanding of infection prevention and use of antimicrobial medicines across all sectors.

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

Sound scientific knowledge, underpinned by basic research, is vital to finding and implementing long-term solutions to AMR. In turn, the planning, monitoring and evaluation of interventions depend on accurate information about the extent of the problem and its impact. Governments, agencies, professional organizations, NGOs, industry and academia have important roles in developing such knowledge and translating it into practice.

It is important to better understand the causes, prevalence and impact of AMR. In particular:

- Epidemiological data on AMR is needed to guide treatment of patients and to inform actions at local, national and regional levels. The same information over time is essential for monitoring the effectiveness of interventions.
- Understanding the impact of AMR on health systems and the economy will lead to appropriate investment decisions.
- Robust evidence on the mechanisms of resistance development, spread and other risk factors is vital if new tools are to be developed and new policies and regulations implemented to combat AMR.
- An understanding is needed of the circulation of resistance within and between humans, animals, food, water and the environment, and of the impact that resistance in one has on the others. Particular research is needed to quantify the scale and impact of antibiotic use on resistance in animal and zoonotic pathogens and the impacts of AMR on agriculture, food animal production and food security. Conversely, research is needed on the impacts of agricultural practices on AMR development and spread.
- Newly emerged resistance or mechanisms for resistance must be rapidly identified and characterized.

WHO’s global report on AMR surveillance\(^9\) revealed many gaps in information on pathogens of major public health importance and we need a better picture of the level of drug resistance in the population as a whole. There are significant gaps in surveillance, and standards are lacking for methods, data-sharing and coordination. Fragmented efforts to collect information on the occurrence of AMR have been made in several areas, but there is no global consensus on standards for data collection and reporting on antibacterial resistance (ABR) in human health and harmonization is lacking across medical, veterinary and agricultural sectors.

The knowledge gaps apply not only to a lack of understanding of the distribution of AMR in the population, but also to needs in many other areas, including:

- Studies in social science and behaviour, to support Objective 1 (above)
- Research, including clinical trials, to assess treatments for common bacterial infections in low-resource settings

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- Pre-competitive research and translational studies to support development of new treatments, vaccines, diagnostics and other interventions
- Research to assess the benefits and harms of non-therapeutic uses of antimicrobials in agriculture and aquaculture, including use for growth promotion and crop protection, and to identify alternative means to achieve these benefits
- Economic research, including the development of economic models to assess the cost of AMR and the cost and benefits of taking action as set out in this plan.

Member States of the European Union (EU), through the Joint Programming Initiative on AMR (JPI AMR), have recently launched an AMR Strategic Research Agenda. This initiative, which includes some countries outside the EU, could provide an initial framework for further development of a global strategic research agenda.

5.2.1 Proposed actions by Member States

All WHO Member States should begin to develop the capacity to collect, analyse and report data on the prevalence of AMR. This capacity should include:

- Ability to collect and analyse data to inform national policies and decision-making.
- Ability to collect, analyse and report data on a core set of organisms/antimicrobial medicines, including from both health-care facilities and the community.
- Access to at least one reference laboratory capable of susceptibility-testing to meet the core data requirements, using standardized tests and operating to agreed quality standards.
- Ability to meet the surveillance needs of specific disease strategies and action plans (such as for artemisinin-resistant malaria, multidrug-resistant TB and other infections of regional or national importance)\(^1\).
- Meeting the recommendations of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) for antimicrobial susceptibility-testing of foodborne pathogens\(^2\), the standards published in the OIE terrestrial and aquatic animal codes,\(^3\) the FAO/WHO Codex Alimentarius Code of Practice to minimize and contain antimicrobial resistance\(^4\) and the Codex Alimentarius guidelines for risk analysis of foodborne AMR.\(^5\)
- Sharing of information so that national, regional and global trends can be detected and monitored.
- The capacity to detect and report newly emerged resistance of potential public health concern, as required under International Health Regulations (2005).

Member States should consider implementing the agreed global public health research agenda on AMR, including research to promote responsible use of antimicrobial medicines, defining improved practices for preventing infection in human and animal health and agricultural practice, developing practical and feasible approaches to extend the lifespan of antimicrobial medicines, and encouraging development of novel diagnostics and antimicrobial medicines.

5.2.2 Actions by the Secretariat

Develop and implement a global programme for surveillance of AMR in human health, including surveillance and reporting standards, case definitions, quality assessment schemes, and a network of WHO Collaborating Centres to support AMR surveillance and quality assessment in each WHO region.

\(^1\) See footnote on page 1
\(^2\) Integrated surveillance on antimicrobial resistance: guidance from a WHO advisory group available at http://apps.who.int/iris/bitstream/10665/91778/1/9789241506311_eng.pdf
\(^4\) See http://www.codexalimentarius.org/committees-task-forces/?provide=committeeDetail&idList=6.

Work with FAO and OIE, under the tripartite collaboration, to support integrated surveillance and reporting of AMR across human and animal health and agriculture, and develop measures of AMR in the food chain for use as indicators of risk to human health.

Consult with Member States and other multisectoral stakeholders to develop a global public health research agenda to address major gaps in knowledge on AMR, including methods to assess the health and economic burdens of AMR, cost-effectiveness of actions, mechanisms of resistance development and spread, and research to underpin development of new interventions, diagnostic tools and vaccines. Monitor and report on implementation of the research agenda, including through the use of the global health research and development observatory.

Work with partners to establish a sustainable repository for information on AMR 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.

5.2.3 Proposed actions by international and national partners

FAO, with WHO, will 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 AMR.

The international research community and FAO should support studies to improve understanding of the impact of AMR on agriculture, animal production and food security, as well as the impacts of agricultural practices on AMR development and spread.

OIE should regularly update the terrestrial and aquatic animal codes (particularly with reference to AMR), revise the guideline on laboratory methodologies for bacterial antimicrobial susceptibility-testing, and support the establishment of veterinary laboratory services through the PVS Pathway.

Global health donors, international development bodies, and aid and technical agencies should support developing countries to build capacity to collect and report data on prevalence of AMR.

Research funding organizations and foundations should support implementation of the agreed global public health research agenda on AMR.

5.3 Objective 3: Reduce the incidence of infection through effective hygiene and infection prevention measures

A high proportion of the most serious and difficult-to-treat antibiotic-resistant infections occur in health-care facilities. This is due not only to admission of patients with serious infections who do not respond to treatment but also to intensive use of antibiotics (both appropriate and inappropriate) to treat sick patients and inadequate measures to prevent and control infection, resulting in the spread of drug-resistant infections both within and outside the facility. Better hygiene and infection prevention measures are essential to limit the development and spread of antimicrobial-resistant infections, and particularly multidrug-resistant bacteria.

Over 30 bacterial, viral and parasitic pathogens are transmitted sexually, and every day nearly a million people acquire a sexually transmitted infection, including diseases such as HIV/AIDS and gonorrhoea for which antimicrobial drug resistance is critical. Effective policies and plans to prevent...
and control sexual transmission of infections, as well as other behavioural modes of transmission such as drug injection, will be important for reducing infection and consequential need for treatment.

Waterborne and foodborne diseases, and especially diarrhoeal diseases, are important causes of morbidity and mortality worldwide. Waterborne and foodborne pathogens that cause disease include campylobacter, *Escherichia coli*, salmonella, shigella species and cholera, as well as viral and parasitic pathogens. Diarrhoeal diseases alone account for some 2 million deaths globally every year. Sanitation, food and water safety must be a core component of infectious disease prevention.

Of the vector-borne infectious diseases, malaria has the greatest public health impact globally and is the most affected by AMR. Vector control is key to malaria control and elimination.

Immunization to prevent infectious diseases is one of the most successful and cost-effective public health interventions. Use of vaccines can contribute to action on AMR in three ways:

1. Use of existing vaccines to prevent infectious diseases such as pneumonia or TB that would otherwise require antimicrobial medicines.
2. Use of existing vaccines to reduce the prevalence of infections (such as influenza or rotaviral diarrhoea) that are often inappropriately treated with antibiotics.
3. Development of new or improved vaccines to prevent diseases (such as malaria, gonorrhoea and other diseases caused by multidrug-resistant bacteria) that are becoming difficult to treat or are untreatable due to AMR.

Much antibiotic use in agriculture and aquaculture is linked to intensive animal production systems. 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 the feed and water. Alternative management and biosecurity practices, including use of vaccines, will reduce infection and thereby the dependence on antibiotics and the risk that antibiotic-resistant organisms will develop and spread through the food chain.

### 5.3.1 Proposed actions by Member States

Member States may consider the following actions:

Promote food and water safety at national level and among professionals and the public, with capacity-building and communication campaigns at different levels and in specific sectors involved in control of foodborne and waterborne infections.

Take urgent action to strengthen hygiene and infection prevention and control in health-care facilities, to prevent sexually transmitted infections and to prevent pneumonia and diarrhoea.

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.

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Ensure that national surveillance for AMR includes the collection and reporting of data on antimicrobial susceptibility in health-care-associated infections.

Implement national immunization programmes and consider their expansion, taking into account the prospects for reduced treatment options due to AMR and the additional benefits of reduced use of antimicrobials, including antibiotics.

Implement the standards published in the OIE terrestrial and aquatic animal codes and FAO/WHO Code of Practice to Minimize and Contain Antimicrobial Resistance.

Promote vaccination as a method of reducing infections in food animals.

5.3.2 Actions by the Secretariat
Facilitate the design and implementation of policies and tools to strengthen hygiene and infection prevention and control practices, particularly to combat AMR, and promote the engagement of civil society and patient groups in improving practices in hygiene and infection prevention and control.

Develop evidence-based guidance and strategies to promote health and healthy lifestyles, including for the prevention of HIV, sexually transmitted infections and substance use.

Ensure that policy recommendations for new and existing vaccines take into account the prospects for reduced treatment options due to AMR, and the additional benefits of reduced use of antimicrobials, including antibiotics.

Work with partners and other organizations to facilitate the development and clinical evaluation of specific priority vaccines to address the threat of difficult-to-treat or untreatable infections.

Work with FAO and OIE, within the tripartite collaboration, to develop recommendations for the use of vaccines to prevent foodborne infections in animals, including recommendations for new vaccines, as a means to prevent infectious diseases in humans and animals and reduce antimicrobial use.

5.3.3 Proposed actions by international and national partners
Professional societies and accreditation bodies should support training and education on infection-prevention measures as an obligatory requirement in professional development, accreditation and registration.

OIE should update its codes and manuals to take account of new developments in vaccines.

FAO should continue to engage and support producers and other value chain stakeholders to adopt good animal husbandry, management, health and biosecurity practices aimed at reducing the use of antibiotics and the risk of AMR development and spread.

5.4 Objective 4: Optimize the use of antimicrobial medicines in human and animal health
Evidence that AMR is driven by the volume of use is compelling. Antibiotic use for human health alone increased by 36% globally from 2000 to 2010. This may indicate that antibiotics are overprescribed and that people have easy access to them through over-the-counter sales and, more recently, via the Internet. Non-prescription use of antibiotics, even for human health, is widespread and has reached high levels in many countries.

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19 See http://www.codexalimentarius.org/committees-task-forces/?provide=committeeDetail&dList=6
Growth in the livestock sector has consistently exceeded that of the crop sector. Total demand for animal products in developing countries is expected to more than double by 2030. Satisfying increasing and changing demands for animal food products, while at the same time sustaining the natural resource base (land, water, air and biodiversity), is a major challenge to agriculture today, particularly in developing countries. Despite measures taken by some Member States, antibiotic use in human and animals and agriculture is still increasing, and the projected increase in demand for animal food products may have a consequent impact on antibiotic use.

Seasonal fluctuations in consumption indicate that antibiotics are improperly used to treat seasonal viral infections. Some classes of antibiotics are overused and misused. Use of antimicrobial medicines should be guided by adequate guidelines or protocols for prescription, dispensing, administration and the use of diagnostic tools.

Data on antibiotic use are regularly collected and analysed in a number of high- and middle-income countries in order to inform development of national plans, implementation of interventions and monitoring of their impact. However, data are lacking on antibiotic use at the point of care, yet such data would give decision-makers and health professionals a better understanding of patterns of prescribing and use, helping them to plan and implement relevant interventions and monitor their impact. There is also a lack of data from lower-income countries and a lack of harmonization of data collection across sectors.

Recognition of antimicrobial medicines as a public good could promote R&D investment, regulation, distribution and use in the public interest. In some cases, industry spending on promotion of products is greater than investment by governments in promoting rational use or providing independent information.

Decisions to prescribe antibiotics are infrequently based on definitive diagnosis. There is a compelling need for effective, rapid, low-cost diagnostic tools that can be used to guide optimal use of antibiotics in human and animal health, and that can be easily integrated into clinical, pharmacy and veterinary practice. Evidence-based prescribing and dispensing should be the standard of care.

Regulation is inadequate or lacking in many areas, including over-the-counter and Internet sales and veterinary and agricultural use. Where regulations exist, they may not be enforced or enforceable. Development of AMR is accelerated by poor patient compliance (e.g. failure to complete the prescribed course), the prevalence of substandard medicines in human and veterinary products, and agricultural use.

Indiscriminate use of any antibiotic can render it (or even the whole of that class of antibiotic) ineffective. New antimicrobials need to be selectively used to delay emergence of resistance. This requires concerted actions at policy and practice levels.

5.4.1 Proposed actions by Member States
All Member States are urged to develop and implement comprehensive action plans to address AMR that incorporate the following:

- 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.
- Ensuring that access to antimicrobials is by prescription only or by an equivalent form of authorization by accredited health or veterinary professionals.
- Ensuring that marketing authorization is given only to antimicrobials that are of good quality, safe and efficacious according to the recommendations of the Working Group of Member
States on Substandard/Spurious/Falsely-Labelled/Falsified/Counterfeit Medical Products and the VICH Guidelines, and that there is appropriate oversight of the supply chain.

- Development and use of Essential Medicines Lists, reimbursement lists and standard treatment guidelines to guide purchasing and prescribing of antimicrobials, and that promotional practices by industry are regulated and controlled.
- Provision for stewardship programmes that monitor and promote optimization of antimicrobial use at national and local levels in accordance with international standards to ensure the correct choice of medicine at the right dose on the basis of evidence.
- Identification and elimination of economic incentives in all sectors that encourage inappropriate antimicrobial use, and introduction of incentives to optimize use.
- 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.
- Policies to address antimicrobial use in terrestrial and aquatic animals and agriculture, including implementation of 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 antimicrobials in animal health, including metaphylaxis.

5.4.2 Actions by the Secretariat

Develop a framework for monitoring and reporting on antimicrobial consumption in human health, including standards for data collection and reporting on use in different settings, building on the work of OECD.

With FAO and OIE, under the tripartite collaboration, collect, consolidate and publish information on the global consumption of antimicrobials.

Strengthen, under the tripartite collaboration with FAO and OIE, the concept of critically important antibiotics and ensure that this concept includes use of new antibiotics so that a common position on restriction of antimicrobials for human use can be established.

Implement the recommendations of the Working Group of Member States on Substandard/Spurious/Falsely-Labelled/Falsified/Counterfeit Medical Products to ensure oversight of the supply chain and to prevent substandard, spurious, falsely-labelled, falsified, or counterfeit medicines reaching patients.

Develop technical guidelines and norms to support access to, and evidence-based selection and responsible use of, antimicrobial medicines, including follow-up to treatment failure.

Provide leadership to strengthen medicines regulatory systems at national and regional levels, so that appropriate practices for optimizing use of antimicrobials are supported by appropriate and enforceable regulation, and that promotional practices can be adequately regulated.

Consult with Member States and pharmaceutical industry associations on innovative regulatory mechanisms for new antimicrobial medicines, including considering them as a class of medicine that will require a different set of regulatory controls, to address the need for preservation of

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21 See http://www.vichsec.org/guidelines/biologicals/bio-quality/impurities.html

effectiveness and for global access. Consider new approaches to product labelling that focus on public health needs rather than marketing claims.

Develop standards (under the tripartite collaboration with FAO and OIE), based on best available evidence of harms, for the presence of antimicrobials and antimicrobial residues in the environment, water supply and food (including aquatic and terrestrial animal feed).

5.4.3 Proposed actions by international and national partners
OIE should regularly update the terrestrial and aquatic animal codes, particularly with reference to AMR.

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 antimicrobials in agricultural practice.

OIE, supported by FAO and WHO within the tripartite collaboration, should build and maintain a sustainable global database on the use of antimicrobials in animals.

The pharmaceutical industry should invest in the development of effective and low-cost tools for infectious disease diagnosis and antimicrobial susceptibility-testing for use in human and animal health at points of care and dispensing (pharmacies).

Donors, philanthropic organizations and NGOs should ensure that their efforts to increase access to antimicrobial medicines are accompanied by measures to protect the continued efficacy of such medicines.

Professional bodies and associations, including industry associations, health insurance providers and other payers should develop a code of conduct for appropriate training, education, marketing, purchasing, reimbursement and use of antimicrobials. This 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.

5.5 Objective 5: Develop the business case for sustainable investment that takes account of the needs of all countries, as well as the need for investment in new medicines, diagnostic tools, vaccines and other interventions
Cost can be a substantial barrier to implementation of the action plan. Capacity development, including training, will be essential, especially in low-resource settings. Investment in new and accessible interventions, including medicines, vaccines and diagnostics, needs to be taken into account.

Economic impact assessments need to be done on the health and economic burden of AMR, and should include the cost of doing nothing versus the cost and benefit of action. There is a need to quantify national and global investment needs, to develop the business case for investment, and to establish mechanisms for securing and managing the investment funds. The lack of such data has been identified as one of the barriers to implementation of the Global Strategy for Containment of Antimicrobial Resistance. However, the case for action is already compelling, and must not be delayed because of gaps in scientific evidence or knowledge.

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There are few studies on the economic cost of AMR, and most of these have focused on developed countries. The current and future cost of AMR (the cost of doing nothing) must be better assessed as a key component of the case for investment. However, it is already clear that this cost is high:

- **AMR increases the costs of health care.** When available, treatment with second-line or later drugs is more expensive, and sometimes dramatically so. Longer duration of illness and treatment, often in hospitals, increases health-care costs further. On average, the cost of treating one case of multidrug-resistant TB is equivalent to the cost of treating 100 antibiotic-susceptible TB cases.

- **AMR reduces incomes and takes a toll on families.** Illness and premature death lead to economic losses as workers cannot work and farmers and herders lose their livestock and livelihoods. As a growing proportion of the human population suffers from protracted illness, achieving goals to expand health-care coverage for the poor becomes harder. In many poor countries AMR will further increase the proportion of people without access to care.

- **Emerging evidence of economic impacts.** In January 2013, the World Economic Forum estimated the cost of AMR, based on limited data, as 0.4–1.6% of GDP. The European Union has estimated that infections due to selected multidrug-resistant bacteria result in extra health-care costs and productivity losses of at least EUR 1.5 billion each year. On this basis, the business case for investment in action to combat AMR is compelling.

There is an urgent need for investment in the development of new medicines, vaccines and diagnostic tools. Fears that resistance will develop rapidly and that returns on investment will be limited due to restrictions in use make antibiotics a less attractive investment than medicines for chronic diseases. Today most pharmaceutical companies have stopped research in this area. WHO’s Consultative Expert Working Group on Research and Development: Financing and Coordination\(^\text{24}\) termed this situation as “a serious market failure” and low level of investment in R&D on antibiotics as “a particular cause for concern”. New market models are therefore needed which will result in renewed investment in R&D, while also ensuring that use of new products is governed by public-health needs within the framework of stewardship programmes to conserve the products’ effectiveness and that there is equitable and affordable global access to them.

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

Many fora have been convened in recent years to discuss these issues and to identify sustainable and effective approaches to incentivising R&D while preserving new drugs resulting from this research and ensuring equitable access in developing countries\(^\text{25}\).

### 5.5.1 Proposed actions by Member States

Member States should consider assessing investment needs for implementation of their national action plans on AMR, and to develop plans to secure and utilize the required financing.

Member States should participate in international collaborative research to support the development of new medicines, diagnostic tools and vaccines through:


\(^{25}\) Several existing initiatives were reviewed at a Technical Consultation on Innovative Models for New Antibiotics’ Development and Preservation organized by WHO on 13 May 2013 in Geneva (http://www.who.int/phi/implementation/consultation_imnadp/en/).
• Increasing national funding for basic scientific research on infectious diseases, and promoting partnerships between research institutions in developed and in developing countries.
• Collaborate in the investigation of natural sources of biodiversity and biorepositories as sources for the development of new antibiotics.
• Strengthening existing and creating new public-private partnerships for encouraging research and development of new antimicrobials and diagnostics.
• Piloting innovative ideas for financing such R&D and for the adoption of new market models to encourage investment and ensure access to new antimicrobial products.

5.5.2 Actions by the Secretariat
Work with the United Nations Secretary-General and United Nations bodies to identify the best mechanism(s) to realize the investment needed to implement the global action plan on AMR, particularly with regard to the needs of developing countries.

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 AMR, and to collate and summarize these needs.

Work with the World Bank and with FAO and OIE, within the tripartite collaboration, to assess the economic impact of AMR and of implementation of the action plan in animal health and agriculture.

Explore with Member States, intergovernmental organizations, industry associations and other stakeholders, options for the establishment of a new partnership(s) to:
• Coordinate the work of many unlinked initiatives aiming to renew investment in antibiotics R&D (including that of the Consultative Expert Working Group on Research and Development26).
• Identify priorities for new treatments, vaccines and diagnostics on the basis of emergence and prevalence of serious or life-threatening infections caused by resistant pathogens.
• Act as the vehicle(s) for securing and managing the investment in new medicines, vaccines, diagnostics and other interventions and for facilitating access to such products while ensuring their proper and optimal use.
• Establish open collaborative models of R&D in a manner that will both ensure access and also provide incentives for investment.

5.5.3 Proposed actions by international and national partners
Partners in the finance and economic sectors should develop the business case for national and global investment in combatting AMR, including an assessment of the cost of implementing this action plan and the consequential cost of no action. This could be led by the World Bank.

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 AMR) in different production settings.

6 IMPLEMENTATION, MONITORING AND EVALUATION

Despite proposals and initiatives to combat AMR over many years, there is little indication that the situation is improving. Monitoring and reporting of progress in implementing action at national, regional and global levels, together with monitoring of the impact of these actions will be the most effective means of driving change in the future. Countries, international organizations, partners and other stakeholders must be accountable for their actions to combat AMR. At national level, the focus will be on developing and implementing action plans to combat AMR. For each country the priorities for implementation of individual actions will depend on the local context and resources, but all countries should regularly report progress towards full implementation.

The Secretariat has been working with Member States to collate information on the status of national action plans on AMR, and related information on regulation and use of antimicrobial medicines. A report of these data will be published before the Sixty-eighth Health Assembly and will provide a baseline against which future progress and national and global levels can be monitored and reported.

6.1 Proposed actions by Member States

All Member States are urged to develop and implement a comprehensive action plan towards addressing AMR, using a stepwise approach that describes priorities for action and national targets for implementation for each of the core building blocks set out below:

- Mechanisms for sustainable coalitions and governance arrangements at all levels to bring together different sectors and stakeholders.
- Hygiene promotion and infection prevention and control programmes.
- Awareness, education and training programmes and campaigns.
- Evidence-based guidance for clinical use (including use of diagnostics for both human and animal health).
- Stewardship programmes to control misuse and overuse in health-care facilities and community health practice.
- A functioning surveillance system, integrated across sectors with access to at least one reference laboratory, quality-assured and with the ability to detect resistance and provide data to support primary indicators.
- A system for monitoring and reporting on antibiotic use in all sectors.
- Regulation to ensure effective licensing and quality control of medicines for both medical and veterinary use.
- Procedures, including legislation, to ensure that access to antimicrobials is by prescription only, or an equivalent form of authorization by accredited health or veterinary professionals.
- Monitoring, evaluation and assessment of plan implementation and impact, including mechanisms and resources to monitor compliance across all parts of the plan.
- Policies to address use in terrestrial and aquatic animals and agriculture, including implementation of the standards published in the terrestrial and aquatic animal health codes and recommendations of the OIE list of antimicrobials of veterinary importance.
- Application of OIE’s PVS Pathway to ensure good governance of animal health systems and professional veterinary services.
- Capacity to detect and report newly emerged resistance of potential public health concern, as required by the International Health Regulations (2005), including provision for reporting notifiable diseases to national authorities.
- National immunization policy that incorporates the need to reduce the incidence of infections that may require antimicrobial treatment, and the introduction of vaccines for diseases that may be difficult to treat.
• Inclusion of AMR in national risk registers (or equivalent).
• Assessment of the financial investment needs for implementation of the national action plan, including good governance, appropriate legislation and laboratory capacity, and plans to secure and manage resources.

Member States should support the Secretariat by providing information on progress in implementing national action plans on AMR, measured against national priorities and targets, for inclusion in the Secretariat biennial reports (see 6.2 below). Where possible, such information should be based on audit information or other validated data.

6.2 Actions by the Secretariat
Support countries to develop and implement national plans.

Incorporate the Secretariat’s actions in the global action plan into the Programme Budget and General Programme of Work, and provide a biennial report of progress to the Executive Board.

Monitor development and implementation of action plans by Member States and other partners. Publish biennial progress reports, including an assessment of countries and organizations that have plans in place, and their progress in implementation.27

WHO, FAO and OIE will report on progress in implementing actions undertaken within the tripartite collaboration.

6.3 Proposed actions by international and national partners
All partners and other stakeholders, including FAO, OIE, the World Bank, industry associations and foundations should put in place their action plans to address AMR, and should report progress in implementing the plans as an integral part of their reporting cycle.

27 Potential measures of implementation of action at national, regional and global levels are listed at Annex 1
7 ANNEX 1: POTENTIAL MEASURES OF ACTION PLAN IMPLEMENTATION

- Number of countries with published national action plans on AMR
- Number of countries with cost assessment and finance plan for action on AMR
- Number of countries reporting data to OIE database on use of antimicrobials in animals
- Number of countries reporting data on use of antimicrobials in humans
- Number of countries reporting the minimum data sets as part of global AMR surveillance
- Number of countries with access to accredited reference laboratory for AMR
- Number of countries with antibiotic stewardship programmes
- Number of countries with national immunization policies
- Number of countries reporting economic and health economic costs of AMR
- % regions or Member States participating in world antibiotic awareness annual campaign
- % Member States, federations and organizations signed up to global codes of conduct
- Number of countries implementing prescription only access or equivalent for human health
- Number of countries implementing prescription only access or equivalent for veterinary and agricultural use
- Number of countries eliminated use for growth promotion in livestock
- Number of countries with education and training on antimicrobial use built into professional registration requirements
- % antibiotic prescriptions based on diagnostic test results
- % prescriptions conforming to guidelines or protocols
- Number of countries complying with OIE terrestrial and aquatic animal codes
- Number of countries complying with relevant standards in Codex Alimentarius
- Number of countries participating in OIE PVS Pathway
- Number of OIE national focal points trained on AMR
- % increase in global financing for basic scientific research on infectious diseases
- % increase in global investment in research and development for new antimicrobial medicines, diagnostics and vaccines