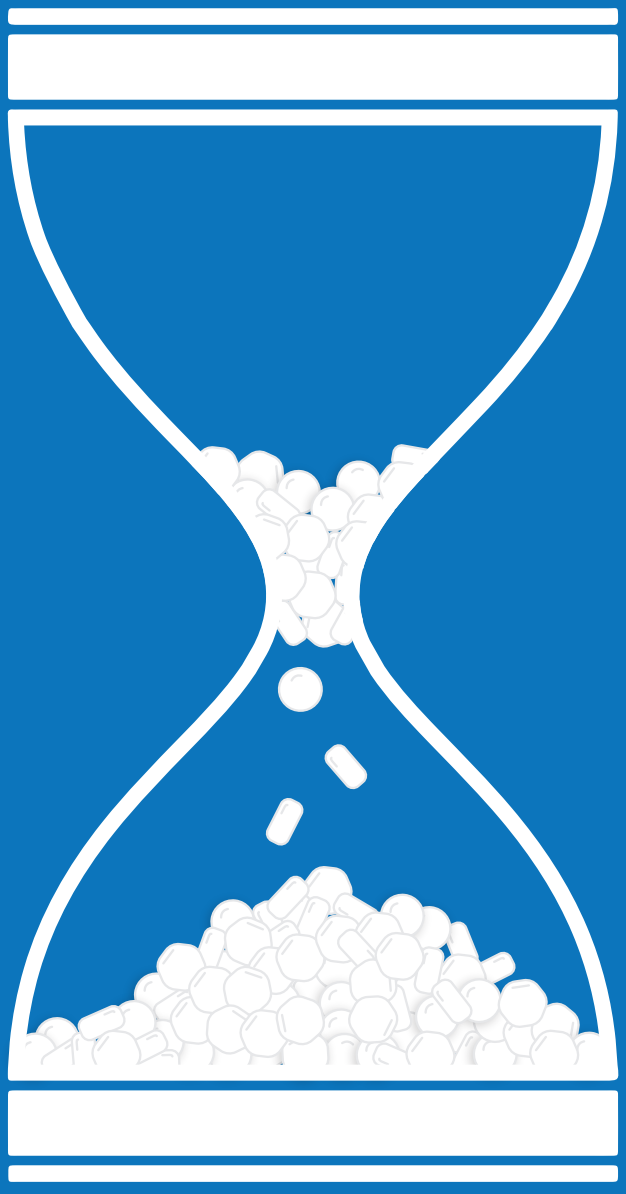

NO TIME TO WAIT:
SECURING THE FUTURE FROM DRUG-RESISTANT INFECTIONS

REPORT TO THE SECRETARY-GENERAL OF THE UNITED NATIONS

APRIL 2019

IACG | Interagency Coordination Group on Antimicrobial Resistance

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KEY MESSAGES IN THIS REPORT

Antimicrobial resistance is a global crisis that threatens a century of progress in health and achievement of the Sustainable Development Goals.

- Antimicrobial (including antibiotic, antiviral, antifungal and antiprotozoal) agents are critical tools for fighting diseases in humans, terrestrial and aquatic animals and plants, but they are becoming ineffective.
- Alarming levels of resistance have been reported in countries of all income levels, with the result that common diseases are becoming untreatable, and lifesaving medical procedures riskier to perform.
- Antimicrobial resistance poses a formidable challenge to achieving Universal Health Coverage and threatens progress against many of the Sustainable Development Goals, including in health, food security, clean water and sanitation, responsible consumption and production, and poverty and inequality.
- Misuse and overuse of existing antimicrobials in humans, animals and plants are accelerating the development and spread of antimicrobial resistance.
- Inadequate access to clean water, sanitation and hygiene in health care facilities, farms, schools, households and community settings; poor infection and disease prevention; lack of equitable access to affordable and quality-assured antimicrobials, vaccines and diagnostics; and weak health, food and feed production, food safety and waste management systems are increasing the burden of infectious disease in animals and humans and contributing to the emergence and spread of drug-resistant pathogens.

There is no time to wait. Unless the world acts urgently, antimicrobial resistance will have disastrous impact within a generation.

- Drug-resistant diseases already cause at least 700,000 deaths globally a year, including 230,000 deaths from multidrug-resistant tuberculosis, a figure that could increase to 10 million deaths globally per year by 2050 under the most alarming scenario if no action is taken. Around 2.4 million people could die in high-income countries between 2015 and 2050 without a sustained effort to contain antimicrobial resistance.
- The economic damage of uncontrolled antimicrobial resistance could be comparable to the shocks experienced during the 2008-2009 global financial crisis as a result of dramatically increased health care expenditures; impact on food and feed production, trade and livelihoods; and increased poverty and inequality.
- In higher-income countries, a package of simple interventions to address antimicrobial resistance could pay for itself due to costs averted. In lower-income countries, additional but still relatively modest investments are urgently needed.
- If investments and action are further delayed, the world will have to pay far more in the future to cope with the disastrous impact of uncontrolled antimicrobial resistance.

Because the drivers of antimicrobial resistance lie in humans, animals, plants, food and the environment, a sustained One Health response is essential to engage and unite all stakeholders around a shared vision and goals.

- National Antimicrobial Resistance Action Plans are at the heart of a multisectoral One Health response, but financing and capacity constraints in many countries need to be urgently addressed to accelerate implementation.
- Strengthening infection prevention and control in health care facilities and farms using available tools and ensuring access to clean water, sanitation and hygiene in health facilities, farms, schools, household and community settings are central to minimizing disease transmission and the emergence and transmission of antimicrobial resistance in humans, animals, plants, food and the environment.
- Strengthening surveillance, regulatory frameworks, professional education and oversight of antimicrobial prescription and use, and increasing awareness among all stakeholders are also significant challenges that need to be urgently addressed to ensure the responsible use of antimicrobials and to minimize resistance in humans, animals, plants, food and the environment.
- Immediately stopping the use of the antimicrobials on the WHO List of Highest Priority Critically Important Antimicrobial Agents for Human Medicine as growth promoters is an essential first step towards completely phasing out the use of antimicrobials for growth promotion.
- Additional effort, investments and incentives are needed to spur innovation in antimicrobial medicines, diagnostics, vaccines, waste management tools, safe and effective alternatives to antimicrobials and alternative practices, as well as operational and implementation research, in human, animal and plant health.
- Many people around the world still do not have access to antimicrobials. Ensuring equitable and affordable access to quality antimicrobial agents and their responsible and sustainable use is an essential component of the global response to antimicrobial resistance.
- Stronger political leadership, advocacy, coordination and accountability are needed at all levels to enable a sustained One Health response to antimicrobial resistance. All stakeholder groups – including governments, civil society and the private sector – need to be engaged and to collaborate in an unprecedented effort across the human, animal, plant, food and feed production and environmental sectors, based on a shared vision and goals.
- The challenges of antimicrobial resistance are complex and multifaceted, but they are not insurmountable. Implementation of the recommendations in this report will help to save millions of lives, maintain economic and other development gains, and secure the future from drug-resistant diseases.

SUMMARY OF IACG RECOMMENDATIONS

A. ACCELERATE PROGRESS IN COUNTRIES

A1: The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials as well as alternatives, vaccines and diagnostics, and their responsible and prudent use by competent, licensed professionals across human, animal and plant health.

A2: The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs.

A3: The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO) and Codex Alimentarius, starting with an immediate end to the use of antibiotics categorised as the Highest Priority Critically Important Antimicrobial Agents on the WHO List of Critically Important Antimicrobials for Human Medicine.

B. INNOVATE TO SECURE THE FUTURE

B1: The IACG calls on public, private and philanthropic donors and other funders to increase investment and innovation in quality-assured, new antimicrobials (particularly antibiotics), novel compounds, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials for human, terrestrial and aquatic animal and plant health, as well as implementation and operational research.

B2: The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new, quality-assured antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

B3: The IACG calls on public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts for new antimicrobials, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials; and to strengthen implementation and operational research and research coordination and collaboration in a One Health context.

C. COLLABORATE FOR MORE EFFECTIVE ACTION

C1: The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels.

C2: The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels.

D. INVEST FOR A SUSTAINABLE RESPONSE

D1: The IACG calls on governments; global, regional, national, bilateral and multilateral financing and development institutions and banks; and private investors to systematically apply standards to assess risks and impacts related to antimicrobial resistance (an antimicrobial resistance and One Health "lens") when making investments.

D2: The IACG emphasizes the need for increased investments in the response to antimicrobial resistance, including from domestic financing in all countries; urges existing and future financing mechanisms in human, animal and plant health, food and feed production and the environment to give greater priority to antimicrobial resistance in their resource allocations; calls on public, private and philanthropic donors to contribute additional funding, including to support implementation of National Antimicrobial Resistance Action Plans.

E. STRENGTHEN ACCOUNTABILITY AND GLOBAL GOVERNANCE

E1: The IACG requests the Tripartite agencies (FAO, OIE and WHO) together with UN Environment, other UN agencies and the World Bank, in the context of UN reform, to further strengthen joint One Health action, based on target-setting, country priorities and needs, by enhancing their organizational capacity and providing adequate and sustainable core funding for antimicrobial resistance-related activities.

E2: The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Joint Secretariat managed by the Tripartite agencies (FAO, OIE and WHO).

E3: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UN Environment and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.

E4: The IACG recognizes the ongoing process led by Member States to develop the Global Development and Stewardship Framework to Combat Antimicrobial Resistance and urges the Tripartite agencies (FAO, OIE and WHO) and UN Environment to expedite its development in line with the scope described in the 2015 World Health Assembly resolution on antimicrobial resistance (WHA68.7). As Member States finalize this process, they should also consider the need for new international instruments.

1. CONTEXT FOR THIS REPORT

The 2016 *Political Declaration of the High-level Meeting of the United Nations General Assembly on Antimicrobial Resistance (1)* represented a landmark in the world's commitment to tackling antimicrobial resistance, calling for greater urgency and action in response to its many challenges. In the political declaration, Member States requested the Secretary-General, in consultation with the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and the World Health Organization (WHO) to convene an ad hoc interagency coordination group (IACG) co-chaired by the Executive Office of the Secretary-General and the Director-General of WHO to provide practical guidance for approaches needed to ensure sustained, effective global action to address antimicrobial resistance. It also requested the Secretary-General to submit a report for consideration by Member States by the seventy-third session of the General Assembly in 2019 on the implementation of the political declaration and on further developments and recommendations emanating from the IACG, including on options to improve coordination, considering the 2015 Global Action Plan on Antimicrobial Resistance *(2)*.

This report presents the IACG's response to the request from Member States in the 2016 political declaration and makes recommendations for urgent action for consideration by the Secretary-General, Member States and other stakeholders in the global response to antimicrobial resistance.

2. PROCESS OF DEVELOPING THE IACG RECOMMENDATIONS

The IACG was convened in March 2017. Its membership consisted of representatives of United Nations and multilateral agencies and individuals with expertise across human, animal and plant health, as well as the food, animal feed, trade, development and environment sectors. The IACG's mandate was to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance. Its terms of reference included promoting, planning and facilitating collaborative action to align activities so that gaps are closed and resources are optimally utilized; exploring the feasibility of developing global goals and targets related to antimicrobial resistance; and reporting back to the Secretary-General by the seventy-third UN General Assembly in 2019. The IACG was supported by a Secretariat hosted by WHO with staff seconded from FAO, OIE and WHO.

Between March 2017 and December 2018, the IACG met formally either in-person or by teleconference eight times, and held many other conference calls, including meetings of thematic sub-groups. To guide its activities, the IACG developed a workplan *(3)* and an IACG Framework for Action on Antimicrobial Resistance *(4)* that describes key content areas and relevant levers to address them, building on the 2016 political declaration, the Global Action Plan on Antimicrobial Resistance and the Sustainable Development Goals (SDGs). Country visits by IACG members to Argentina, Thailand and Vietnam in 2018 provided valuable insights into successes and challenges in national and local responses to antimicrobial resistance.

In the course of its deliberations, the IACG analysed critical issues in the response to antimicrobial resistance to inform its report and recommendations. In 2018, it developed discussion papers for public consultation in six thematic areas: 1) Public awareness, behaviour change, and communication; 2) National Action Plans on Antimicrobial Resistance; 3) Optimizing use of antimicrobials; 4) Innovation, research and development, and access; 5) Surveillance and monitoring; and 6) Global governance and alignment with the SDGs *(5,6,7,8,9,10)*. Targeted outreach and consultations were conducted with key stakeholders during this analytic phase, particularly with regard to governance, access, research and development issues. A web-based public consultation process on the six discussion papers was held between June and August 2018 and received 153 submissions from a wide range of stakeholders.

The IACG conducted a wide range of stakeholder engagement activities, including discussions with FAO, OIE, WHO and UN Member States based in Rome, Paris, Geneva and New York respectively; discussions with civil society and the private sector; and inputs from more than 350 participants attending the Call to Action on Antimicrobial

Resistance event in Accra, Ghana, in November 2018. A mapping exercise and critical appraisal of recommendations made in previous global reports on antimicrobial resistance were conducted by the IACG Secretariat to provide guidance to the IACG and help ensure that its recommendations addressed key bottlenecks in the response, rather than duplicating those in previous reports. In January and February 2019, additional public discussions on the draft IACG recommendations were held with more than 400 people representing 68 Member States, 39 civil society organizations, 49 private sector groups and 11 international organizations. Concurrently, a web-based forum on the draft recommendations drew more than 80 additional written submissions from Member States, civil society organizations, the private sector and individuals.

Further information on the IACG process and relevant materials, including the written submissions received, are available on the IACG website.

3. BACKGROUND TO THE IACG RECOMMENDATIONS

3.1. Antimicrobial resistance is a global crisis that risks reversing a century of progress in health

Antimicrobial agents are critical tools to fight diseases in humans, animals, plants and crops. But growing levels of resistance to these agents is placing a century of progress in human health at risk. Common infections are becoming much more difficult to treat, and lifesaving medical procedures and treatments riskier to perform. At the same time, there is a lack of scientific innovation resulting in part from market failure, with too few new antimicrobials, vaccines, diagnostics tools and alternatives to antimicrobials for use in humans, animals and plants in the research and development pipeline.

Alarming levels of antimicrobial resistance have been reported in countries of all income levels. In some member countries of the Organization for Economic Cooperation and Development (OECD), about 35 per cent of common human infections are already resistant to currently available medicines, and in some low- and middle-income countries (LMICs), resistance rates are as high as 80 to 90 per cent for some antibiotic-bacterium combinations *(11)*. More than a third of countries providing data to WHO in 2017 reported widespread resistance to common pathogens *(12)*. Resistance to second- and third-line antibiotics – the last lines of defence against some common diseases – are projected to almost double between 2005 and 2030 *(11)*. Concurrently, millions of lives are lost every year due to lack of access to existing antimicrobial agents: inadequate access to antibiotics alone kills nearly 6 million people annually, including a million children who die of preventable sepsis and pneumonia *(13,14,15)*.

Although antimicrobial resistance can develop naturally, misuse and overuse of antimicrobial agents in humans, terrestrial and aquatic animals, plants and crops are greatly accelerating its development and spread. In human health, poor medical prescribing practices and patient adherence to therapies, weak regulation and oversight including over-the-counter sales, and the proliferation of substandard and falsified antimicrobials are all contributing to the problem.

The use of antimicrobials to promote growth and routinely prevent disease in healthy animals and crops without appropriate indication and in the absence of good agricultural practices to prevent infectious diseases on farms are further contributing to the development and spread of antimicrobial resistance *(16)*. Drivers of the use of antimicrobials in animal health – especially in many LMICs – include the large and growing burden of animal diseases, the increasing scale of animal production, and underinvestment in veterinary services and animal health. These underlying issues require attention as part of efforts to reduce the unnecessary use of antimicrobials in animals.

3.2 There is no time to wait. Unless the world acts urgently, antimicrobial resistance will have disastrous impact within a generation

Although antimicrobial resistance is not mentioned in the SDGs, it is recognized in the Global Action Plan for Healthy Lives and Well-being for All *(17)* as a barrier to achievement of SDG 3 on human health and directly jeopardizes progress against other SDGs related to food security, clean water and sanitation, and responsible consumption and production. Due to cascading impacts on economic development and inequality, antimicrobial resistance also indirectly threatens progress against the SDGs that aim to reduce poverty and inequality.

The true magnitude of antimicrobial resistance in humans is not fully known, but estimates suggest that resistant infections already cause at least 700,000 deaths every year, including 230,000 deaths from multidrug-resistant tuberculosis *(18,19)*. A worst-case scenario developed by the World Bank has suggested that this figure could rise to 10 million deaths every year by 2050, if no action is taken *(20)*. In countries where resistance can be measured accurately, the OECD predicts that around 2.4 million people could die in Europe, North America and Australia between 2015 and 2050 without a sustained effort to contain antimicrobial resistance *(11)*.

The economic impact of uncontrolled antimicrobial resistance would also be catastrophic. As drug-resistant pathogens spread, health care expenditures would increase dramatically, and sustainable food and feed production – including global trade in food, feed and livestock – will increasingly be at risk. As a result, the World Bank estimates that by 2030 up to 24 million people could be forced into extreme poverty, mainly in low-income countries, and annual economic damage as a result of antimicrobial resistance could be comparable to the shocks experienced during the 2008-2009 global financial crisis – but with no end in sight *(20)*.

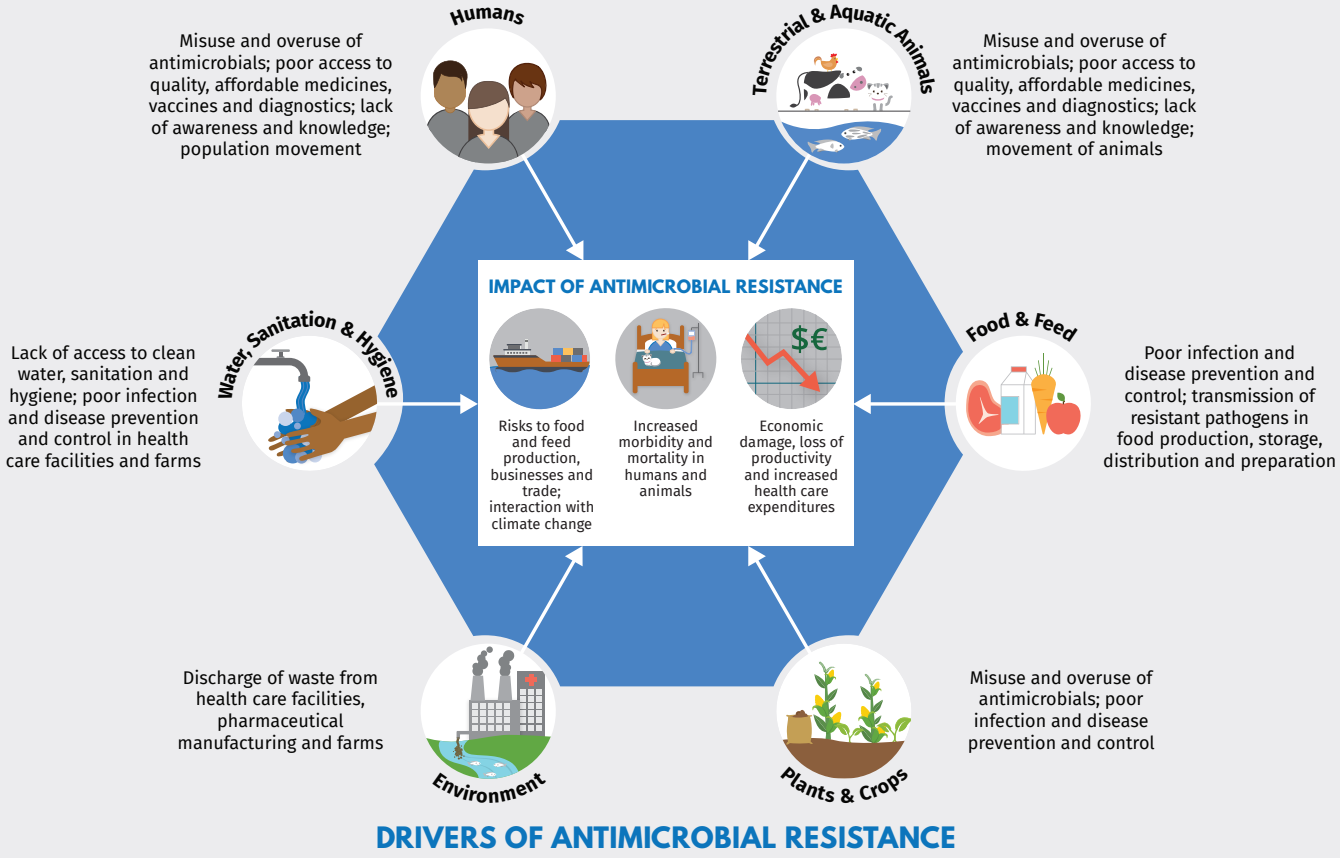
Although evidence remains limited, concerns are also growing about the impact of antimicrobial resistance on the environment and natural ecosystems due to overuse and discharge of antimicrobials and resistant micro-organisms in manure and waste from health care facilities and pharmaceutical manufacturing, commercial livestock and plant production, and fish and seafood farming, a problem that may be fuelled by changes in the world's climate *(21,22)*.

3.3. A sustained One Health response to antimicrobial resistance is essential to engage and unite all stakeholders around a shared vision and goals

Because the drivers and impact of antimicrobial resistance lie in humans, terrestrial and aquatic animals, plants, food, feed and the environment, and are interconnected, a One Health approach is essential to addressing it on multiple fronts (Fig.1).

Fig 1. A One Health response to address the drivers and impact of antimicrobial resistance

"One Health" refers to designing and implementing programmes, policies, legislation and research in a way that enables multiple sectors and stakeholders engaged in human, terrestrial and aquatic animal and plant health, food and feed production and the environment to communicate and work together to achieve better public health outcomes.



3.3.1. Accelerated implementation of One Health national action plans must be at the heart of the global response to antimicrobial resistance

Since the launch of the Global Action Plan on Antimicrobial Resistance in 2015, at least 100 countries have developed National Antimicrobial Resistance Action Plans, and there is a wealth of normative guidance from the Tripartite agencies (FAO, OIE and WHO) and the Codex Alimentarius to support their implementation (*23*). But efforts to implement national action plans are currently too slow and must be accelerated.

Although antimicrobial resistance affects all countries at all levels of development, not all countries are equally equipped to respond effectively, and national plans need to be tailored to local needs, context and capacities. Many LMICs facing a higher burden of disease and risk of antimicrobial resistance still need to improve basic water, sanitation and hygiene in health care facilities, farms, schools, households and community settings; strengthen infection prevention and control in health facilities, farms and food and feed production; and improve waste management and environmental protection. At the same time, they face significant barriers to implementation of National Antimicrobial Resistance Action Plans, including inadequate political awareness and commitment, and lack of informed people to champion a One Health approach. Many countries also lack a compelling narrative to engage policy-makers and the general public in a way that links antimicrobial resistance to core national health and economic interests. At the same time, mechanisms and capacity for One Health collaboration across Ministries and sectors are frequently inadequate or under-resourced.

Many national action plans focus mainly on the health of humans and livestock, paying insufficient attention to plants, food and feed production, of antimicrobials; mainstreaming antimicrobial resistance into existing programming across the SDGs; and mobilizing additional human and financial resources. Depending on country context, additional investments and capacity building are needed to develop and implement critical components such as antimicrobial stewardship programs; professional education, training, certification and development; behaviour change, awareness and communications activities; and strengthening supply chain management and legal and regulatory frameworks across the One Health spectrum.

Strengthening monitoring and surveillance is particularly important to track the use of antimicrobials and the spread of resistance in humans, animals, plants and food; build the evidence base for action; support multisectoral collaboration; and monitor progress. Implementing surveillance systems requires significant, long-term investments in personnel, training, laboratory, data collection and other infrastructure. All countries, as well as their donors and development partners, have a vital interest in building these critical capacities at the country level, ensuring that data is used to guide responses, and supporting global-level surveillance through initiatives such as WHO GLASS and AGISAR and surveillance work undertaken by OIE and FAO.

3.3.2. More innovation is needed to tackle antimicrobial resistance across the One Health spectrum

The research and development pipeline for health technologies to address priority pathogens has long been inadequate (*24,25,26*). A sustained effort is needed to spur increased innovation in medicines, diagnostics, vaccines and safe and effective alternatives to antimicrobials across human, terrestrial and aquatic animal and plant health, as well as waste and environmental management.