AFRICA CDC FRAMEWORK FOR ANTIMICROBIAL RESISTANCE, 2018-2023

1. Executive Summary

Antimicrobial resistant (AMR) organisms are increasing globally, threatening to render existing treatments ineffective against many infectious diseases. In Africa, AMR has already been documented to be a problem for HIV and the pathogens that cause malaria, tuberculosis, typhoid, cholera, meningitis, gonorrhea, and dysentery. Recognizing the urgent need for action, the World Health Assembly adopted the Global Action Plan on Antimicrobial Resistance in May 2015. In accordance with the Global Action Plan and to meet needs specific to Africa, Africa CDC will establish the Anti-Microbial Resistance Surveillance Network (AMRSNET). AMRSNET is a network of public health institutions and leaders from human and animal health sectors who will collaborate to measure, prevent, and mitigate harms from AMR organisms.

Within the next 5 years, AMRSNET's four goals are:

1. Improve surveillance of AMR organisms among humans and animals

2. Delay emergence of AMR

3. Limit transmission of AMR

4. Mitigate harm among patients infected with AMR organisms

To achieve these goals, AMRSNET will conduct three essential cross-cutting activities:

1. Advocate for policies and laws to enable long-term prevention and control of AMR

2. Civil society engagement

3. Develop human resources

2. The Threat of Antimicrobial Resistant Infections

Antimicrobial agents, of which antibiotics are a subset, have saved hundreds of millions of lives from infectious diseases. Antimicrobial resistant (AMR) organisms are increasing globally, threatening to render existing treatments ineffective against many infectious diseases. Drug resistant strains of bacteria, fungi, parasites, and viruses prolong illness, increase case-fatality, facilitate transmission, and increase treatment costs. ,

Many factors contribute to the emergence, persistence, and transmission of AMR. Although AMR strains arise naturally due to genetic changes in microorganisms, their emergence is accelerated by inappropriate use of antimicrobial agents in humans, animals, and the environment, including self-treatment of illness by lay persons, non-indicated administration by healthcare providers, and addition of antibiotics to feed to "promote growth" and prevent illness among animals reared for food consumption. AMR emergence may be further amplified by substandard and/or counterfeit antibiotics, which impair treatment of existing infections and may help select for AMR strains. Transmission of AMR is accelerated by inadequate infection prevention and control in healthcare facilities, by contamination of the food supply with AMR bacteria, by impaired access to potable water, and by limitations in public health prevention programmes, including immunisation, sanitation, and sexual health. Globally, drug resistance causes an estimated 700,000 deaths each year, and, if current trends continue, AMR could result in over 10 million deaths per year and over 100 trillion USD in lost output globally by 2050.

Recognising the urgent need for action, the World Health Assembly adopted the Global Action Plan on Antimicrobial Resistance in May 2015. The Global Action Plan sets the following objectives: "(1) to improve awareness and understanding of AMR; (2) to strengthen knowledge through surveillance and research; (3) to reduce the incidence of infection; (4) to optimise the use of antimicrobial agents; and (5) to ensure sustainable investment in countering antimicrobial resistance." To address the Global Action Plan's objectives of improving awareness and strengthening knowledge, the World Health Organisation (WHO) established the Global Antimicrobial Resistance Surveillance System (GLASS). Available information from GLASS and other programmes indicate increasing drug resistance across the African region, particularly among HIV and the pathogens that cause malaria, tuberculosis, typhoid, cholera, meningitis, gonorrhea, and dysentery. There is also increasing recognition that delayed diagnosis and treatment of these infections leads to sepsis, an underappreciated cause of mortality across Africa. ,

3. Africa CDC's Response to AMR

In accordance with the Global Action Plan and to meet needs specific to Africa, Africa CDC will establish the Anti-Microbial Resistance Surveillance Network (AMRSNET). AMRSNET is a network of public health institutions and leaders from human and animal health sectors who will collaborate to measure, prevent, and mitigate harm from AMR organisms. Core members of AMRSNET will be derived from African National Public Health Institutes (NPHI). Activities will be implemented by Africa CDC's Regional Collaborating Centres (RCCs) in collaboration with NPHIs, NGOs, and existing AMR focal points and Collaborating Centres at WHO

(specifically GLASS) , the Food and Agriculture Organisation of the United Nations (FAO), and the World Organisation for Animal Health (OIE), the Inter-African Bureau for Animal Resources (AU-IBAR), and the African Union Pan-African Veterinary Vaccine Centre (AU-PANVAC). AMRSNET will work across the range of infectious pathogens (bacteria, viruses, parasites, fungi) and across human and animal health. Where necessary, AMRSNET will prioritise based on burden of disease, prevalence, and trends in AMR, and feasibility of interventions.

Within the next 5 years, AMRSNET's four goals are:

1. Improve surveillance of AMR organisms among humans and animals

2. Delay emergence of AMR

3. Limit transmission of AMR

4. Mitigate harm among patients infected with AMR organisms

To achieve these goals, AMRSNET will conduct three essential cross-cutting activities:

1. Advocate for policies and laws to enable long-term prevention and control of AMR

2. Develop human resources

4. Collaboration and Integration with Existing Initiatives

Many organisations have mobilised resources to address AMR. WHO, for example, serves as the lead implementer for the Global Action Plan, and its regional and country offices are working directly with national governments to develop and implement national action plans on AMR . Many research networks and academic centres are conducting studies to assess the burden of AMR and how to reduce transmission. Non-governmental organisations, such as ReACT and the Global Antimicrobial Resistance Partnership, have gathered data, synthesised evidence, issued reports, recommended policy change, educated the public, mobilised partners, and advocated with stakeholders at all levels of government, industry, and global health.

AMRSNET seeks to serve as the primary coordinator for AMR surveillance and control on the African continent, complementing existing activities by WHO, Ministries of Health, AU agencies (IBAR, PANVAC), and non-governmental organisations working on AMR. Following the OneHealth model, AMRSNET will incorporate Ministries of Agriculture, veterinary health organisations, and networks working on animal and environmental health. Africa CDC's RCCs will convene these diverse partners to facilitate data and specimen sharing and dissemination of new findings. Because it derives its institutional authority from the African Union, Africa CDC will be uniquely positioned to promote continent-wide policy and advocate across all sectors of government and society, based on the work of WHO, FAO, OIE, non-governmental organisations, and other AMRSNET partners.

5. Improve Surveillance of AMR Organisms among Humans and Animals

Understanding the full extent of AMR and its impact in Africa is challenged by a lack of continent-wide AMR surveillance data, especially for pathogens that require complex testing methods. Although gains have been made in collecting data on AMR as it relates to TB and malaria, several challenges remain, including inadequate: demand by clinicians for diagnostic testing; laboratory infrastructure; resources to continuously collect, transport and test specimens for AMR surveillance; use of standardised protocols, quality assurance; and collaboration between human and animal health sectors.

For this section, we differentiate between public health laboratories and clinical diagnostic laboratories. We consider public health laboratories to be facilities supported by a government agency to provide confirmatory and specialised testing services in a specific administrative area. Such laboratories may test primary specimens (e.g., blood, urine, sputum) or other biological materials, such as bacterial isolates or purified nucleic acid. We consider clinical diagnostic laboratories to be government or non-government facilities that diagnose infection in a person who presents to a clinic or hospital. Such laboratories usually only test primary specimens from patients, though they may also perform susceptibility testing using isolates or nucleic acid. In some settings, laboratories may serve dually as public health and clinical diagnostic laboratories. For this section, we use the term quality assurance to refer to systematic and routine use of standard operating procedures, documentation, quality control, and proficiency testing.

5.1. Increase the Number of Tests Performed on Humans and Animals for AMR Organisms

The first step to continuously monitor the burden of AMR is to increase the number of ill persons (or animals) tested for an infectious etiology and, if an etiology is identified, tested for AMR. This approach, known as diagnostic stewardship, involves making high-quality diagnostic tests readily available, appropriately using these tests, and applying test results to make patient care safer and more effective. WHO has published guidelines on diagnostic stewardship for facilities that participate in GLASS. Extensive work is also being conducted by national governments, international organisations, and NGOs to increase clinical diagnostic testing in Africa. Most of these efforts, however, are focused on single diseases, such as HIV, TB, or malaria, for which dedicated funding exists. Susceptibility testing for bacteria and other pathogens requires personnel and infrastructure that, while not particularly expensive, is rarely supported by governments. For some diseases, unique opportunities exist to integrate data. Some hospitals may already collect antimicrobial resistance data for bacteria in a laboratory information management system. Newer devices designed primarily for diagnosis of TB and HIV can continuously transmit data on usage and test results via mobile phone networks. Since AMR is a potential problem for all infectious organisms and is clearly established as a problem for some of these organisms.

Africa CDC will help convene the broadest possible set of partners in each region to:

1) Map available human and animal testing sites, including facilities that offer point-of-care diagnosis of infectious diseases (e.g., microscopy, HIV testing) and any bacteriology services (e.g., culture, antimicrobial susceptibility testing).

2) Identify legal, technological, policy, administrative, logistical, and financial barriers to expansion of clinical testing.

3) Advocate for policies and mobilise resources to expand testing in areas with limited capacity and to alleviate other barriers.

Africa CDC will also need to advocate for diagnostic stewardship among animals that are reared for food and are known hosts and/or vectors of high priority human pathogens. Africa CDC's RCCs will need to engage directly with private sector agriculture businesses and, where necessary, make a strong business case for expanded testing.

5.2. Increase the Proportion of Clinical Diagnostic Laboratories with Quality Assurance Programs

Only a small proportion of clinical laboratories in Africa are certified as compliant with international standards for quality assurance. Since AMR testing for bacteria and other pathogens occurs primarily at clinical diagnostic laboratories, rather than public health laboratories, Africa CDC will need to advocate strongly for policies and practices that promote high quality testing in these facilities.

After identifying the location and capacity of facilities, Africa CDC will:

1) Promulgate guidelines for assessing clinical laboratories' adherence to quality standards, such as those by GLASS .

2) Collaborate with Member States to apply these guidelines and periodically issue reports that track adherence.

3) Promote and promulgate proficiency testing programmes for diagnostic laboratories focused on susceptibility testing of high-priority pathogens.

4) Identify barriers to quality assured laboratory testing and, where necessary, work with external partners to remove those barriers.

5) Consider African Union statutes to mandate standards in Member States for diagnostic testing of human specimens

5.3. Increase the Proportion of Public Health Laboratories with Quality Assurance Programs and International accreditation

As referral and specialized testing centres, public health laboratories will play an essential role in generating high-quality data about AMR. Part of that role involves isolation and susceptibility testing, and part of that role involves verifying procedures and results from clinical diagnostic laboratories. To perform these roles,

public health laboratories must participate in external quality assurance programmes and strive to achieve international accreditation, particularly if their data is used for GLASS or AMRSNET.

Africa CDC will work with the African Society of Laboratory Medicine and other partners to:

1) Define an Africa CDC approach to assessing African public health laboratories' adherence to quality standards, using established international approaches, such as ISO or American College of Pathology, for reference.

2) Consider the designation of AMR supra-national reference laboratories to provide specialty testing, training, and capacity building in national laboratories.

3) Collaborate with Member States to assess adherence of public health laboratories to standards.

5.4. Increase the Number of National Public Health Laboratories Conducting Surveillance for AMR Using Standardized Protocols

Producing valid data about the burden of AMR requires clinical diagnostic and public health laboratories all adhering to standardised protocols. Critical challenges to doing this include lack of agreement about: pathogens to be monitored for AMR, methods for identifying pathogens (e.g., culture vs. molecular), antimicrobial agents to test for susceptibility, methods for susceptibility testing, and interpretation of susceptibility test results. WHO GLASS has promulgated approaches to these challenges, but wider adoption is needed. Reference laboratories are required at multiple levels (including supra-national level) to confirm identification and susceptibility testing, perform genotyping, and provide surge capacity.

Africa CDC will work with a diverse group of partners in each region to:

1) Develop consensus regarding a specific set of pathogens and, for each pathogen, antimicrobial agents that should be continuously monitored, recognizing that some important pathogens may not be included.

2) Collaborate with WHO, laboratory standards organisations (CLSI, EUCAST), and other partners to harmonise susceptibility testing and interpretation for these pathogens and antimicrobial agents.

3) Adopt or adapt standardised training materials and conduct training through RCCs.

4) Collaborate with non-governmental organisations, including private industry, to supply testing kits or essential testing materials to high priority sites.

5.5 Increase the Number of Member States that Continuously Collect, Analyse, Report, And Disseminate Data about AMR for High Priority Pathogens in their Respective Countries

The final – and most critical - step in AMR surveillance is disseminating data to policy makers to increase awareness and help translate awareness into action. Even if protocols are effectively harmonised, substantial barriers exist, including policies and attitudes that prevent data sharing, agreement on data interpretation, conclusions, and authorship, and resources to analyse data and prepare reports.

Given that it will take substantial time until coverage of testing is high enough to yield representative results, Africa CDC will work with partners to synthesise existing data from surveillance, hospital microbiology laboratories, research studies, and other sources to provide periodic estimates of AMR prevalence. Africa CDC may also consider working with partners to harmonise protocols for special surveys to provide point-prevalence estimates

Africa CDC will work with partners in each Region to:

1) Develop and maintain agreements for sharing of specimens, isolates, other materials, and data across countries and between regions.

2) Convene partners periodically in each region and annually at continental level to review protocols for data sharing, interpretation, and authorship.

3) Mobilise resources for sufficient staffing, infrastructure, administrative and policy support, and funding for surveillance and data dissemination.

4) Establish a comprehensive, continuously updated, and publically available database of AMR on the African continent.

5) Assist Member States with interpreting AMR surveillance data and revising treatment guidelines or other policies appropriately

6. Delay Emergence of AMR

6.1. Increase the Proportion of Physicians Adhering to Prudent Antibiotic Use Guidelines

Extensive studies have been conducted in the United States, Europe, and other industrialised settings on approaches to promoting prudent antibiotic prescribing – an approach known as antimicrobial stewardship. Few studies have demonstrated a substantial, sustained response when antimicrobial stewardship only focuses on awareness. Even though physicians seem to understand the potentially negative consequences of prescribing antibiotics when they are not indicated or of prescribing antibiotics with an overly broad spectrum of coverage, this awareness does not consistently change their behavior. Greater success has been achieved when stewardship programmes include structural changes and behavioral modification techniques, e.g., posting guidelines and antibiotic prescribing pledges inside examination rooms, providing alternatives to antibiotic prescribing for physicians to give to patients, limiting access to 'second-line' or 'reserve' antibiotics, and providing feedback to clinicians about non-judicious antibiotic prescribing patterns by them in comparison to their peers. , , Economic incentives vary by country but can be particularly problematic when healthcare facilities rely on antibiotic sales to fund operations, when physicians sell antibiotics themselves, and when physicians receive additional reimbursement for selling antibiotics.   There are limited studies about the effectiveness or essential components of antimicrobial stewardship programmes in Africa and other resource-limited settings.

In many settings, persons obtain antibiotics directly from pharmacies with no evaluation by or prescription from a physician. More work needs to be done to understand whether persons who staff pharmacies (whether they are trained pharmacists or not) are more responsive to training and behavioral modification than physicians and whether regulatory approaches are essential.

It is important to note that prudent antibiotic use is also likely to improve outcomes of ill persons. The vast majority of treatment is empiric, i.e., symptoms and examination but no laboratory confirmation. When based on best available evidence, guidelines for prudent antibiotic use can potentially improve individual outcomes and delay emergence of resistance.

Africa CDC will:

1) Convene experts to review existing AMR surveillance data from Africa and disseminate Africa-specific antimicrobial treatment and stewardship guidelines for facilities and clinicians.

2) Convene experts to review evidence for promoting prudent antibiotic prescribing and disseminate guidance to countries periodically about best practices.

3) Support demonstration projects in multiple countries throughout Africa to evaluate the impact of policies and programmes focused on prudent antibiotic prescribing, including hospital-based antimicrobial stewardship programmes.

4) Collaborate with partners working on access to care for serious infectious conditions
such as TB, HIV, malaria, pneumonia, and sepsis—to assure that all Africa CDC guidance on antimicrobial use considers problems of access and excess.

5) Develop an "African Union Formulary" that classifies antimicrobial agents into first-line agents and second-line or reserve agents that should require higher-level approval or justification for use. The formulary could also delineate drugs for use by authorised non-physician prescribers.

6) Promote adoption of national-level policies, potentially through an African Union statute, for formularies and stricter control of second-line (reserve) antimicrobial agents.

6.2. Increase the Proportion of Veterinarians and Food Producers Adhering to Prudent Antibiotic Use Guidelines

Inappropriate antibiotic use among animals, particularly those reared for human consumption, is a major driver of AMR. Promoting prudent antibiotic use is particularly challenging, because food producers have a strong economic incentive to use antibiotics for disease prevention and growth promotion and little economic incentive to use therapeutic antimicrobials prudently. Veterinary antibiotics can be purchased on the open market and added to feed, with the negative public health consequences effectively invisible to the food producer. Furthermore, little data exist about the individual prescribing practices of veterinarians in industrialised settings and in Africa. It is reasonably assumed that most animal consumption of antibiotics occurs during food production, not through prescriptions to treat illness. Use of antimicrobial agents in plants

may also be contributing to the emergence of human fungal infections (such as aspergillosis) resistant to azoles. The African Union has made a high-level commitment to food safety, engaging partners from multiple sectors, including industry. Africa CDC can leverage this commitment by making policy makers more aware of the link between food production, AMR emergence, and foodborne illness.

To begin addressing this complex problem, Africa CDC will:

1) Convene a broad set of stakeholders from government, agriculture industry, veterinary health, and consumers to review current practices and barriers to prudent antibiotic use.

2) Collaborate with relevant AU agencies working on food safety to develop antibiotic use guidelines for specific agriculture industries, such as poultry, and advocate among large-scale producers and governments for their adoption.

3) Develop and encourage adoption of model regulations for sales of antibiotics to the animal and agriculture sectors.

4) Encourage and consider policies that promote procurement of poultry and other meats only from producers who adhere to prudent antibiotic use guidelines.

6.3. Reduce Availability and Sales of Sub-Standard and Counterfeit Antibiotics

Sub-standard and counterfeit antibiotics are widely available in Africa and have a substantial negative impact on health. Sub-standard antibiotics can promote AMR by containing levels of an agent sufficient to exert selective pressure for resistant organisms but insufficient level to kill those organisms. Both sub-standard and counterfeit antibiotics can delay correct treatment of an infection, prolonging illness and worsening case-fatality, promoting spread of pathogens, including resistant ones, and, for patients who eventually receive a higher level of care, necessitating use of second-line (reserve) medications. Most countries lack sufficient resources to evaluate and approve drugs and to withdraw substandard drugs from the market. Countries also need to implement policies that ensure that drugs that are procured or donated meet standards for quality, that this quality is not unduly compromised during storage, and that drugs are used for appropriate purposes

Africa CDC will:

1) Conduct a formal review of regulatory standards and regulatory capacity across the continent and consider African Union legislation to promote a common scheme for prohibiting sale of non-standard antibiotics.

2) Promote education of pharmacists in identifying fake drugs and using innovative tests to measure drug quality.

3) Collaborate with governmental and non-governmental partners (including community groups) to increase awareness by clinicians, pharmacists, and patients of sub-standard and counterfeit antibiotics.

4) Consider advocacy by African Union with international partners and multi-lateral organisations to impose penalties on entities that manufacture and distribute sub-standard or counterfeit agents in Africa.

7. Limit Transmission of AMR

7.1. Increase the Proportion of Healthcare Facilities Implementing Infection Control and Prevention Programs

Transmission of AMR occurs frequently in healthcare facilities. Such transmission can have severe consequences, because resistant organisms in healthcare facilities are often resistant to a broader spectrum of agents compared with resistant organisms found in the community and because the hospitalised population is more susceptible to severe illness. Transmission can occur via all modes, including direct contact, droplet, airborne, and injection. The basic components of all programmes include: strong political commitment and dedicated resources for infection control; strict adherence to protocols for hand hygiene and for identification, isolation, and management of potentially infectious patients; adequate supplies and equipment for patient care; systems for infectious waste management, building design, and maintenance to reduce transmission; and continuous monitoring of process, outcome, and impact indicators. The West Africa Ebola response demonstrated that effective hospital-based infection prevention and control programmes require intensive support to initiate and maintain. While Africa CDC aspires to support comprehensive infection prevention and control programmes, a more limited objective may be necessary in the near term, such as strengthening immediate containment of and response to recognised outbreaks of multidrug-resistant organisms.

Africa CDC will work to:

1) Advocate for Member States to establish national infection prevention and control programmes that address staffing, supplies, monitoring, and building design, and advocate for African Union statutes that mandate Member States to implement these programmes.

2) Work with governments and healthcare delivery partners at all levels to develop and measure a minimum set of indicators to assess adequacy of infection control programmes in healthcare facilities.

3) Promote education and training of healthcare workers and related staff in infection prevention and control, particularly hand hygiene, standard precautions, and isolation techniques.

4) Collaborate with government and non-government donors and with private industry to assure a stable supply chain for personal protective equipment, hand hygiene stations, water, safety-engineered injection devices, autoclaves, and other essential infection control items.

5) Develop and assess regional and country-specific implementation strategies for procurement, training, and education of environmental services, including cleaning and sound waste management.

6) Develop partnerships with global, regional, and national organisations already advocating for stricter infection control related to TB, influenza and respiratory viruses, Ebola, and blood borne infections.

7.2. Increase the Availability and Sales of Animal Products Raised with Prudent Antibiotic Use

In the community setting, food products contaminated with AMR organisms or antibiotic residue can increase the burden of AMR infections in humans. Once consumed, AMR organisms may not cause human illness, but may exchange genetic components with other organisms that do cause human illness. Humans can develop illness themselves due to these organisms with newly-acquired resistance or transmit pathogens to others. As noted above, the challenge with reducing AMR organisms in food products is that antimicrobials are commonly used in the rearing of animals for food consumption.

To reduce this threat, Africa CDC will work to:

1) Convene a diverse group of stakeholders to summarise the evidence base and periodically issue reports about this issue.

2) Advocate among African policy makers to increase awareness about this threat to human health.

3) Encourage and consider policies regarding procurement by government agencies of poultry and other meats only from producers who adhere to prudent antibiotic use guidelines.

8. Mitigate Harm among Patients Infected

8.1. Increase the Number of Healthcare Facilities with Quality Diagnostic Tests for Infection and AMR

Efforts described above to increase diagnostic testing at clinical and public health laboratories will directly benefit patients by providing information to guide initiation, discontinuation, or other changes to antibiotic therapy. WHO GLASS has promulgated procedures for performing susceptibility testing, and healthcare facilities need to use such standardised procedures to ensure the validity of results for patient care and for surveillance. In addition to conventional approaches to susceptibility testing, healthcare facilities are increasingly adopting point-of-care diagnostic tests for infectious diseases, specifically HIV, TB, and malaria. Platforms for some of these systems, such as Xpert, are not limited to a single pathogen and could be adopted for diagnosis of other infectious agents. Advantages include speed and accuracy of diagnosis to tailor use (or non-use) of antimicrobial agents. Barriers to adopting multi-platform systems include resources to procure and maintain equipment and reagents, awareness by healthcare leadership, acceptability of providers, and technical training of staff.

To address this challenge, Africa CDC will:

1) Work with regional and national agencies to develop a continent-wide approach to improve the standardisation, sensitivity, and reliability of antimicrobial susceptibility tests.

2) Collaborate with non-governmental organisations and industry partners to evaluate specific tests and, where appropriate, include in antimicrobial resistance guidelines.

3) Identify gaps in regulatory programmes for diagnostic tests at the national level and promote training in regulatory science for health agencies throughout Africa.

8.2. Reduce the Availability and Use of Substandard Diagnostic Tests and Supplies

Substandard diagnostic tests and laboratory supplies remain common across Africa and can lead to AMR when tests lead to unnecessary antibiotic treatment. Limiting their availability will be extremely challenging, given the large number of healthcare delivery sites that may be using such products.

Africa CDC will:

1) Work with partners to inventory the types of tests performed for AMR across the continent as part of the work described above to increase the number of sites testing humans for AMR.

2) Apply the regulatory framework for diagnostic tests described above at the continental, regional, and national level to begin limiting sales of further substandard tests and supplies and, if possible, recall tests and supplies already on the market.

8.3. Increase the Proportion of Physicians and Healthcare Facilities Adhering to Guidelines for Treatment Of Susceptible and AMR Infections in Humans

As noted above, Africa CDC will promote stewardship programmes to increase the proportion of physicians adhering to prudent antibiotic use guidelines. By adhering to guidelines, physicians will both help delay emergence of AMR and improve outcomes among patients already infected with AMR organisms. Depending on the context in each country, Africa CDC could consider expanding such programmes to include other persons who dispense antimicrobial agents, such as pharmacists, chemists, and non-physician clinicians. In addition to the steps noted above to increase guidelines adherence,

In addition to the steps noted above to increase guidelines adherence, Africa CDC will:

1) As noted above, convene experts to review existing AMR surveillance data from Africa and disseminate guidance regarding prudent antibiotic treatment for patients.

2) Collaborate with academic institutions, industry, and non-governmental organisations to evaluate patient outcomes for those treated according to guidelines to continuously improve treatment approaches

8.4. Maintain Access to Essential Antibiotics

A major ethical dilemma for Africa CDC's strategy will be to balance antibiotic access versus excess. Although antibiotic usage is excessive at a population level, many vulnerable groups lack access to effective antimicrobial treatment, leading to high rates of illness and death from pneumonia, influenza, malaria, TB, HIV infection, typhoid fever, parasitic diseases, and other highly treatable infections. Sepsis, for example, remains a major causal pathway for death from many of these infectious diseases, and early empiric antibiotic treatment can have a major impact on reducing case-fatality. If prescribing authority was limited to physicians – rather than allowing non-physician prescribing or direct purchase from pharmacies – excess and access could be limited

simultaneously for vulnerable groups.

Cognisant of these challenges, Africa CDC will:

1) Include at least one patient representative on all committees convened to develop policies or guidelines.

2) Assure adequate consultation from community and advocacy groups in the development and implementation of programmes and studies.

3 Convene stakeholder consultations across Africa to identify critical barriers to access, then advocate for policies and mobilise resources to enhance access

9. Implementation

9.1. Advocating Policies and Laws to Enable Long-Term Prevention and Control of AMR

Laws and policies play a critical role in framing, enabling, and protecting public health. Africa CDC will leverage its stature and authority as a specialised agency of the African Union to advocate for laws and policies to monitor, prevent, and mitigate AMR. Africa CDC will develop a policy unit focused on approaches that can be taken at the African Union, through Regional Economic Communities, in countries, and, in some situations, at the sub-national level, particularly large urban settings. Africa CDC will specifically work with partners to review existing laws across the continent, identify gaps, and propose laws through the African Union and its partners that could serve as a model for other countries or at other levels. These laws would ideally strengthen and harmonise policies that countries are including in their own AMR national action plans.

Africa CDC will focus its efforts on:

1) Increasing adoption and enforcement of regulations related to surveillance of AMR at national and regional level.

2) Increasing adoption and enforcement of regulations that limit inappropriate antibiotic use in humans.

3) Increasing adoption and enforcement of regulations that limit inappropriate antibiotic use in animals.

4) Increasing adoption and enforcement of regulations that mandate infection prevention and control in healthcare facilities.

5) Implementing a continent-wide regulatory framework for high quality diagnostics for AMR.

6) Increasing adoption of agreements to share data and specimens across NPHIs and other stakeholders.

9.2. Civil Society Engagement

Large-scale public health efforts can only succeed with the robust involvement of civil society. With HIV, community based organisations and individual activists played an essential role in mobilising resources, accelerating access, combating stigma, and enacting laws and policies that have averted infections and saved millions of lives. To date, engagement of civil society has been challenging, because the science can be

complex to explain, the threat often characterised as distant, patients' stories of illness and death often not told because of under-diagnosis, interventions not readily distilled into high-impact slogans, and public health agencies investing too little in civil society engagement. Enacting laws and policies for AMR control depends critically on robust engagement of civil society; the demand of its citizens, far more than science alone, will convince governments to take concerted action.

In addition to incorporating civil society voices into technical discussions, Africa CDC will seek to engage civil society, specifically for:

1) Ensuring that excess is curtailed, while access is not.

2) Promoting public awareness of the harms of antimicrobial overuse and antimicrobial resistance.

3) Promoting consumer demand for food free from antimicrobial residue and antimicrobial-resistant pathogens.

4) Promoting patient demand for healthcare free from nosocomial infections

9.3. Developing Human Resources for AMR Surveillance and Control

The activities in Africa CDC's AMR plan must be supported by sufficient human resources. Each country will need leadership and staff that have the adequate education and skills to implement AMR control programmes in both human and animal health sectors. The most pronounced human resources gaps are likely in laboratory services—from bench microbiologists to managers—and in healthcare infection prevention and control. The first strategy to address this involves mobilising resources to support hiring, training, and retaining staff. Many countries in Africa already receive substantial external donor assistance for health-related conditions, particularly HIV. By highlighting the urgency and severity of the AMR threat, Africa CDC can advocate for both donors and government ministries to review their existing budgets and allocate more funding to laboratory services and infection prevention and control personnel. A second strategy involves training existing staff, using the RCCs as a platform for region-specific education of cadres. Africa CDC's RCCs will work to increase human workforce capacity by establishing Centres of Excellence. An early priority of these Centres of Excellence will be developing a series of short training courses; courses will be focused on assuring that policy makers, public health officials, clinicians, microbiologists, veterinarians and other relevant stakeholders share a common body of knowledge and approach to addressing AMR in their populations. A final strategy will involve Africa CDC engaging health systems leaders, economists, and policy experts in estimating the gap between current and optimal human resources, providing country and sub-national estimates of the cost for filling that gap, building the business case for meeting that gap, and continuously monitoring progress in closing the gap.

Africa CDC will focus its human resource efforts on:

1) Implementing a structured advocacy campaign targeted at policy makers, donors, and private partners from the healthcare delivery and agricultural sectors to highlight the need for sufficient human resources for AMR surveillance and control.

2) Collaborate with other partners on training personnel from the public and private sector in laboratory methods and healthcare infection prevention and control through RCCs.

3) Commission analysis of human resources needs and costs and develop systems to continuously monitor government, donor, and other resources dedicated to AMR-related activities

9.4. Early Priorities

Recognising that successfully implementing this plan may take decades, Africa CDC will first convene stakeholders and members of AMRSNET to define a framework for governance, operations, and evaluation.

Among the components of the AMR plan, the highest priorities in the first two years will include

1. Surveillance

   a. Map available human diagnostic testing sites, including facilities that offer point-of-care testing for infections and those that perform antimicrobial susceptibility testing.

   b. Identify legal, policy, administrative, logistical, and financial barriers for expanded clinical testing.

   c. Define an Africa CDC approach to assessing African public health laboratories' adherence to quality standards, using established international approaches, such as ISO or American College of Pathology, for reference.

   d. Develop consensus regarding a specific set of pathogens and, for each pathogen, antimicrobial agents that should be continuously monitored, recognising that some important pathogens may not be included.

   e. Collaborate with WHO and enroll sites in WHO GLASS to harmonise susceptibility testing and interpretation for these pathogens and antimicrobial agents.

   f. Develop standardised training materials and conduct training through RCCs

   g. Develop and maintain agreements for sharing of specimens, isolates, other materials, and data across countries and between regions.

2. Delay emergence

   a. Convene experts to review existing AMR surveillance data from Africa and disseminate guidance regarding prudent antibiotic treatment for patients.

   b. Convene experts to review evidence for promoting prudent antibiotic prescribing and disseminate guidance periodically about best practices.

   c. Convene a broad set of stakeholders from government, agriculture industry, veterinary health, and consumers to review current practices and barriers to prudent antibiotic use.

3. Limit transmission

   a. Advocate for African Union policies and statutes regarding national policies for infection prevention and control protocols, staffing, supplies, monitoring, and building design.

b. Work with governments and healthcare delivery partners at all levels to develop and measure a minimum set of indicators to assess adequacy of infection prevention and control programmes in healthcare facilities

4. Mitigate harm

   a. Work with partners to inventory the types of tests (equipment, supplies, protocols) performed for AMR across the continent as part of the work described above to increase the number of sites testing humans for AMR..

5. Civil society engagement

   a. Work with activists and community organisations to increase awareness about AMR and define specific actions that these groups can take.

6. Developing human resources

   a. Begin a structured advocacy campaign targeted at policy makers, donors, and private sector partners from the healthcare delivery and agricultural sectors to highlight the need for sufficient human resources for AMR surveillance and control.

10. Monitoring and Evaluation

This plan will only succeed if Africa CDC collaborates effectively with WHO, OIE, FAO, Ministries of Health, and the many other organisations dedicated to improving public health. Monitoring the plan's success will be challenging, because many of the objectives described above do not have sufficient data to establish an accurate baseline nor is there sufficient evidence to indicate how much of an increase in a specific target will have a meaningful impact on preventing or mitigating harm from AMR.

Africa CDC will work with its partners to develop a dedicated monitoring team that will:

1. Compile best available evidence from African countries to estimate baselines for each activity in the plan.

2. Identify five year targets for each activity that are likely to have a meaningful impact on public health using expert opinion and established methods of achieving consensus among experts.

3. Produce annual reports of progress toward completing activities and achieving targets.

In addition to the targets specific to each component of the plan, Africa CDC will also convene experts to identify high-level targets, including:

1. Reduced mortality rate in populations specifically vulnerable to AMR infections, including infants

2. Reduced percentage of resistant organisms for selected high priority pathogens

11. Acknowledgements

Africa CDC thanks the many persons and institutions that provided critical input into the conception, research, writing, and production of this document.

12. Acronyms

Africa CDC	Africa Centres for Disease Control and Prevention
AMR	Antimicrobial resistance
AMRSNET	Anti-Microbial Resistance Surveillance Network
AU	African Union
CLSI	Clinical Laboratory Standards Institute
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organization of the United Nations
GLASS	Global Antimicrobial Resistance Surveillance System
HIV	Human immunodeficiency virus
IBAR	African Union's Inter-African Bureau for Animal Resources
MDR	Multidrug resistant
NPHI	National public health institutes
OIE	World Animal Health Organization
PANVAC	African Union's Pan-African Vaccine Centre
RCC	Regional Collaborating Centre
TB	Tuberculosis
USD	United States dollars
WHO	World Health Organization

13. References

World Bank. Drug-resistant infections: a threat to our economic future. Washington DC; 2016. Available at: http://pubdocs.worldbank.org/en/689381474641399486/1701381-AMR-Lab-Report-Web.pdf

Ndihokubwayo, JB, et al. Antimicrobial resistance in the African Region: Issues, challenges and actions proposed. Key Determinants for Health in the African Region. 2013;16.

WHO. Drug resistant tuberculosis is now at record levels. Geneva; 2010. Available at: http://www.who.int/mediacentre/news/releases/2010/drug_resistant_tb_20100318/en/

Levy SB, Marshall B. Antibacterial resistance worldwide: causes, challenges and responses. Nat Med. 2004;10:S122-9.

Newton PN, Green MD, Fernández FM, Day NP, White NJ. Counterfeit anti-infective drugs. Lancet Infect Dis. 2006;6:602-13.

Okeke IN, Lamikanra A, Edelman R. Socioeconomic and behavioral factors leading to acquired bacterial resistance to antibiotics in developing countries. Emerg Infect Dis. 1999 Jan-Feb;5(1):18-27.

Review on Antimicrobial Resistance. Available online from: https://amr-review.org/home.html

World Health Organization. (2015). Global Action Plan on Antimicrobial Resistance. Available online from: http://apps.who.int/iris/bitstream/10665/193736/1/9789241509763_eng.pdf

http://www.who.int/drugresistance/surveillance/glass-enrolment/en/

Essack SY, Desta AT, Abotsi RE, Agoba EE. Antimicrobial resistance in the WHO African region: current status and roadmap for action. J Pub Health 2016;39:8-13

Le Doare K, Bielicki J, Heath PT, Sharland M. Systematic review of antibiotic resistance rates among gram-negative bacteria in children with sepsis in resource-limited countries. J Pediatric Infect Dis Soc. 2015;4:11-20.

Musicha P, Cornick JE, Bar-Zeev N, et. al. Trends in antimicrobial resistance in bloodstream infection isolates at a large urban hospital in Malawi (1998-2016): a surveillance study. Lancet Infect Dis. 2017;S1473-3099(17)30394-8.

http://www.who.int/drugresistance/ surveillance/glass-enrolment/en/

WHO. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Available at: http://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf

WHO/OIE/FAO. Antimicrobial resistance: a manual for developing national action plans. 2016. Available at: http://apps.who.int/iris/bitstream/10665/204470/1/9789241549530_eng.pdf

Ndihokubwayo, JB, et al. Antimicrobial resistance in the African Region: Issues, Challenges and Actions Proposed. Key Determinants for Health in the African Region. 2013;16.

East Africa Public Health Laboratory Networking Project. Report by Center for Disease Dynamics, Economics, and Policy. 2016; Washington DC. Available at: https://www.cddep.org/sites/default/files/wb_report_32.pdf

Morgan DJ, Malani P, Diekema DJ. Diagnostic Stewardship—Leveraging the Laboratory to Improve Antimicrobial Use. JAMA. 2017;318:607–608.

WHO. Diagnostic stewardship: a guide to implementation in antimicrobial resistance surveillance sites. Available at: http://apps.who.int/iris/bitstream/10665/251553/1/WHO-DGO-AMR-2016.3-eng.pdf

Nkengasong JN, Birx D. Quality matters in strengthening global laboratory medicine. Afr J Lab Med. 2014;3:239.

Available at: http://www.who.int/antimicrobial-resistance/AMR-Surveillance-QA-CCs-network-meeting/en/

Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. Therapeutic Advances in Drug Safety. 2014;5(6):229-241.

Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD003539. DOI: 10.1002/14651858.CD003539.pub2.

Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, Gould IM, Ramsay CR, Michie S. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub4.

Hulscher, Marlies EJL, et al. Antibiotic prescribing in hospitals: a social and behavioural scientific approach. Lancet Infect Dis 2010;10:167-175.

WHO. The World Medicines Situation 2011. Geneva: The World Health Organization; 2011.

Morel CM, Edwards SE, Harbarth S. Preserving the 'commons': Addressing the sustainable use of antibiotics through an economic lens. Clin Microbiol Infect. 2017;pii:S1198-743X(17)30427-5.

Cox JA, Vlieghe E, Mendelson M, Wertheim H, Ndegwa L, Villegas MV, Gould I, Levy Hara G. Antibiotic stewardship in low-and middle-income countries: 'same, but different'? Clin Microbiol Infect. 2017 Jul 13. pii: S1198-743X(17)30365-8.

Morgan DJ, Okeke IN, Laxminarayan R et al. Non-prescription antimicrobial use worldwide: a systematic review. Lancet Infect Dis 2011; 11: 692–701.

Landers TF, Cohen B, Wittum TE, Larson EL. A Review of Antibiotic Use in Food Animals: Perspective, Policy, and Potential. Public Health Reports 2012;127:4-22.

Azevedo MM, Faria-Ramos I, Cruz LC, Pina-Vaz C, Rodrigues AG. Genesis of azole antifungal resistance from agriculture to clinical settings. J Agric Food Chem. 2015;63:7463-8.

Newton PN, Green MD, Fernández FM, Day NP, White NJ. Counterfeit anti-infective drugs. Lancet Infect Dis. 2006;6:602-13.

Weinstein, R.A. Controlling antimicrobial resistance in hospitals: infection control and use of antibiotics. Emerg. Infect. Dis. 2001;7:188–192.

WHO. Guidelines on core components of infection prevention and control. 2016. Available at: http://www.who.int/gpsc/ipc-components/en/

Courvalin P. Predictable and unpredictable evolution of antibiotic resistance. J Intern Med. 2008;264:4–16.