THE UNITED REPUBLIC OF TANZANIA

POLICY GUIDELINES FOR IMPLEMENTING ANTIMICROBIAL STEWARDSHIP

TANZANIA MAINLAND

JUNE, 2020

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FOREWORD

Rational use of antimicrobial agents is an important strategy for preserving their efficacy in the treatment of infectious diseases. This document has been formulated to guide responsible professionals to manage antimicrobial agents appropriately. This document aims to promote stewardship of antimicrobial use through prevention of the emergence and spread of antimicrobial resistance (AMR) resulting from unnecessary use of antimicrobial agents in human, livestock, fisheries and agriculture sectors.

It is believed that all responsible cadres have responsibility and role to play towards prudent use of antimicrobial agents. As the interests and welfare of the patient remain foremost, antimicrobials should be prescribed and administered in a manner that allows maximum therapeutic or prophylactic value. Use of antimicrobial agents should minimize the potential to cause harm, particularly as a result of emergence of resistant microorganisms. Hence, an effective strategy to limit the effect of multidrug resistance must be multifaceted and must include the education of patients and professionals about appropriate drug, dose and duration, use of effective infection-control practices to prevent transmission from infected to uninfected patients, surveillance of AMR and antimicrobial use, and prohibition of the use of antimicrobial agents in animal feeds.

The development pipeline for new antimicrobials is at an all-time low. We must therefore conserve the antimicrobials we have left by using them optimally. All health, agriculture, veterinary and nutritional professionals should aim to adhere to this guidance and be able to demonstrate this. The Ministry of Health, Community Development, Gender, Elderly and Children, Ministry of Livestock and Fisheries and Ministry Agriculture are confident that this document will be of great value in promoting prudent use of antimicrobial medicines in the country.

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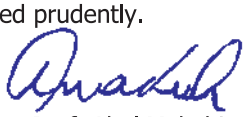
ACKNOWLEDGEMENTS

In 2017, the National Action Plan (NAP) on AMR was developed using the "One Health Approach". Several key issues including the formulation of a national guidance on antimicrobial use were emphasized in the NAP. Hence, I would like to acknowledge the AMR Stewardship Technical Working Group and other stakeholders for taking on-board the recommendations, which have led to the development of these policy guidelines.

I would like also to express my gratitude to the National AMR Multi-Sectoral Coordinating Committee (MCC) for guidance and approval of the document. Additionally, I would like to thank all individuals who contributed directly or indirectly towards the completion of the guidelines. I hope implementers from various sectors will abide to this document and ensure that antimicrobial medicines are used prudently.



Prof. Abel Makubi

CHAIRPERSON- NATIONAL AMR MULTI-SECTORAL COORDINATING COMMITTEE

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ABBREVIATIONS AND ACRONYMS

ADDO	Accredited Drug Dispensing Outlets
AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship
AMU	Antimicrobial Use
AST	Antibiotic Susceptibility Tests
AWaRe	Access Watch and Reserve
CPD	Continuous Professional Development
CVL	Central Veterinary Laboratory
EQA	External Quality Assessment
FAO	Food and Agriculture Organization
GAP	Global Action Plan
GLASS	Global Antimicrobial Resistance Surveillance System
IPC	Infection Prevention and Control
JEE	Joint External Evaluation
MCC	Multi-sectoral Coordinating Committee
MSD	Medical Stores Department
MTC	Medicines and Therapeutic Committee
NAP	National Action Plan
NEMC	National Environmental Management Council
NEMLIT	National Essential Medicines List for Tanzania
NHLQATC	National Health Laboratory Quality Assurance and Training Centre
OIE	World Organization for Animal Health
PPS	Point Prevalence Survey
R&D	Research and Development
RTI	Research and Training Institution

SADCAS	Southern African Development Accreditation Services
SLMTA	Strengthening Laboratory Management Towards Accreditation
SOP	Standard Operating Procedure
STG	Standard Treatment Guidelines
TMDA	Tanzania Medicines and Medical Devices Authority
TPRI	Tropical Pesticides Research Institute
WHO	World Health Organization

GLOSSARY

Animal	Refers to livestock, poultry, farmed wildlife and fisheries
Antimicrobial	Is a medicine/agent used to treat infections caused by bacteria, fungi, protozoa or viruses. It includes antibiotics, antifungals, antiprotozoal, and antivirals
Antimicrobial Resistance	Is the natural or acquired genetic ability of a microorganism to survive the effects of an antimicrobial to which it was previously susceptible
Antimicrobial Stewardship	A coherent set of actions which promote the responsible use of antimicrobials. This definition can be applied to actions at the individual level as well as the national and global level, and across human health, animal health and the environment.
Antimicrobial Stewardship Programme	An organizational or system-wide health-care strategy to promote appropriate use of antimicrobials through the implementation of evidence-based interventions
Medicine outlets	Refers to any licensed Pharmacy, Accredited Drug Dispensing Outlets (ADDO) and Veterinary centers
Prudent or rational use of antimicrobial	Is an act that maximizes therapeutic effect of the antimicrobial agent while minimizing the development of antimicrobial resistance
Surveillance of antimicrobial resistance	Refers to collection, validation, analyses, interpretation and reporting of relevant clinical, microbiological and epidemiological data on antimicrobial resistance in targeted pathogens from different sources including human, animal, plant, food and environment for action
A sentinel site	Is a selected site responsible for collecting data on AMR and reporting these data through the appropriate channel

HOW THE DOCUMENT WAS DEVELOPED

The formulation of the Policy Guidelines on Implementing Antimicrobial Stewardship (AMS) was first developed through desk review by the Pharmaceutical Services Unit (PSU) under the Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC). In December, 2018 the Technical Working Group (TWG) on AMS in collaboration with other stakeholders worked on the draft document. The first draft of the Policy Guidelines on AMS was shared in the 8th Multi-sectoral Coordination Committee (MCC) meeting in April, 2019 for members to approve the document.

The MCC is an advisory committee with responsibility of coordinating all activities of fighting the spread of AMR in the country. Amongst its role is to ensure that all AMS activities are implemented under One Health approach. The MCC meeting recommended that **the guidelines need a wide stakeholder's consultations from all professionals to gain its ownership**. Moreover, the MCC was also recommended the developed documents to include information on one health approach; that it should include information of both human, animal, plant and environmental health to help stakeholders to use a single document while implementing AMS interventions in the country.

In viewing that, in June, 2019 two days' stakeholders workshop to solicit their inputs on the developed Policy Guidelines for Implementing AMS as recommended by the MCC was conducted. The workshop attended by stakeholders from different professional background including those from human, animal, agriculture and environmental health sectors (**see list of contributors in the annex**).

Thereafter, followed by a three days' small group meeting of technical experts from responsible ministries to aggregate and harmonize the collected stakeholders' opinions before making the document final. Then, the improved version of the document was circulated to MCC members for further review. Also, the document was shared to additional AMR stakeholders for improvements and editing. During the MCC quarterly meeting in February 2020, the Policy Guidelines on AMS was approved.

EXECUTIVE SUMMARY

Antimicrobial resistance is well recognized as a global threat to human, animal and environmental health. In 2015, the World Health Organization (WHO) released the Global Action Plan (GAP) to combat AMR followed by other relevant documents from the World Organization for Animal Health (OIE) and Food and Agriculture Organization (FAO) of the United Nations. The Government of the United Republic of Tanzania adopted the Sixty-eighth World Health Assembly Resolution and responded by developing a National Action Plan (NAP) on AMR using the One Health Approach, launched in April, 2017. The Strategic Objective Number Four of the NAP underlines the development of AMS programs in addressing inappropriate use of antimicrobial agents.

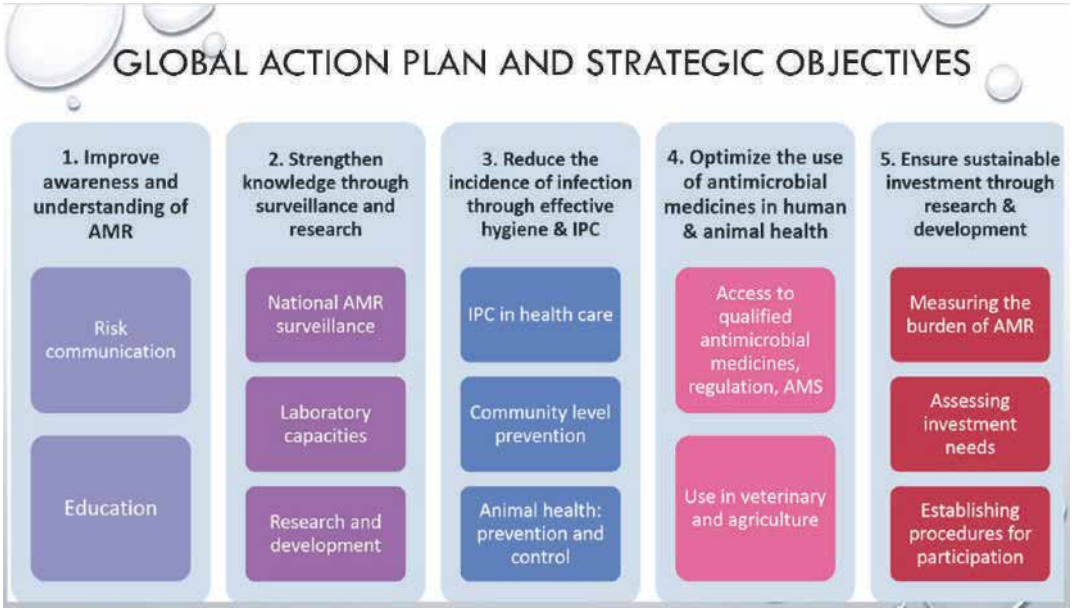
AMS is a systematic multi-sectoral approach for optimizing antimicrobial therapy, through a variety of structures and interventions. The absence of national policy guidelines for prudent use of antimicrobial agents is a major contributing factor in abuse of antimicrobial agents. Hence, this Policy Guideline has been developed to guide AMS programs using the One Health Approach. It includes the components of research and development, antimicrobial regulations and manufacturing; selection of antimicrobials; supply chain management; diagnostics, prescribing, dispensing and responsible use of antimicrobials.

Various interventions for AMS programs have been proposed: developing a national research agenda on AMS and supporting Research and Development (R&D) on antimicrobial use; enforcing regulations on antimicrobial manufacturing, handling, distribution, prescribing, dispensing, use and disposal in all responsible sectors; establishment of AMS programs; adherence to Standard Treatment Guidelines for empirical treatment; strengthening diagnostics by performing Antibiotic Susceptibility Tests (AST); and collecting and analysing data on antimicrobial use.

It is anticipated that hospitals and facilities where antimicrobials are used will establish AMS programs and perform antimicrobial susceptibility tests; that empirical systemic antimicrobial therapy will be prescribed according to Standard Treatment Guidelines and Essential Medicines List (STG/NEMLIT) or related clinical guidelines; that antimicrobial usage data will be collected and interpreted to identify trends and areas for improvement; that research on AMS will be conducted in human, animal and environmental sectors; and regulations on antimicrobial manufacturing, handling, distribution and use in humans, animal, agriculture and animal feeds will be enforced.

CHAPTER ONE
BACKGROUND

Antimicrobial resistance is well recognized as a global threat to human, animal and environmental health. In 2015, the World Health Organization (WHO) released the Global Action Plan (GAP) to combat AMR followed by other relevant documents from the World Organization for Animal Health (OIE) and Food and Agriculture Organization (FAO) of the United Nation. The goal of the GAP was to ensure the successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way and accessible to all who need them. The GAP comprises of five strategic objectives elaborated in figure I below:



Source: Global Action Plan, 2015

The Government of the United Republic of Tanzania adopted the Sixty-eighth World Health Assembly resolution and responded by developing a National Action Plan (NAP) on AMR using the One Health Approach, launched in April, 2017. The Tanzania NAP on AMR is aligned to the Global Action Plan on AMR with similar strategic objectives.

The Strategic Objective Number Four of the NAP underlines the development of AMS programs in addressing inappropriate use of antimicrobial agents. It aims at optimizing antimicrobial selection, dosing, route, and duration of therapy to maximize clinical cure or prevention of infection at hospital and farm levels, while limiting the unintended consequences. Priority areas under this strategic objective are to optimize antimicrobial use, improvement of regulatory framework for preservation of antimicrobial agents and revisiting the policies, regulations, guidelines and directives on the use of antimicrobials in the country.

Other interventions include strengthening regulatory systems in controlling quality, distribution and use of antimicrobial agents including inappropriate or unregulated use of antimicrobial agents in animal and agriculture sectors. These efforts should go hand in hand with Infection Prevention and Control measures in hospital settings and biosecurity measures in farms to curb emergence and spread of AMR.

Specifically, under ***strategic intervention 8.1***; the NAP emphasizes the development and review of policies, laws and guidelines on the use of antimicrobial agents in human, animals and agriculture sectors. In addition, ***activity 8.1.1*** calls for developing policy guidelines for handling, prudent use and preservation of antimicrobial agents in the country.

At Global level, the World Health Organization, the Food and Agriculture organization of the United Nations and the World Organization for Animal Health have developed a Global Framework for Development and Stewardship to Combat AMR caused by inappropriate antimicrobial use. The framework supports the development, control, distribution, and appropriate use of new antimicrobial agents, diagnostic tools, vaccines and other interventions while preserving the existing antimicrobial agents. According to the World Health Assembly's resolution 68.7 the framework should cover the whole spectrum of antimicrobial agents from research and development to use. Hence, these policy guidelines on antimicrobial use are adopting the components addressed in the global framework as elaborated in the figure II below:

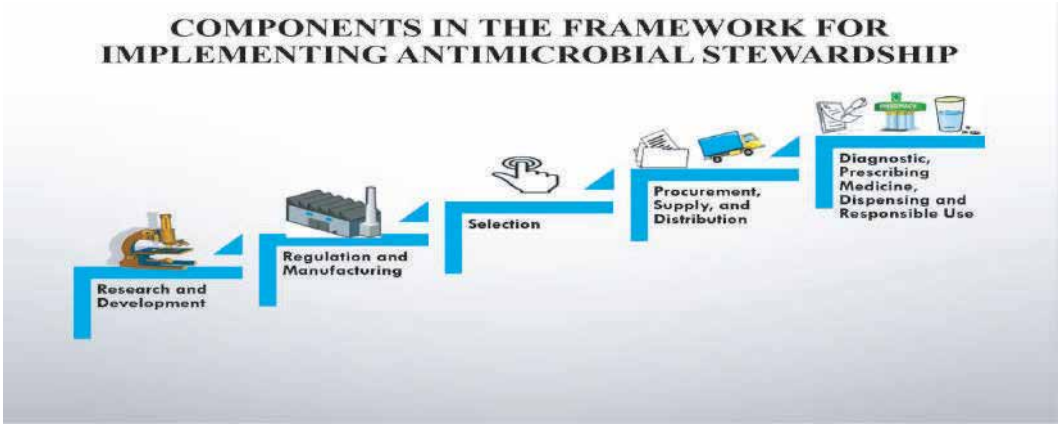


Figure II: Components for implementing antimicrobial stewradship

Source: WHO, FAO, UNEP & OIE 2018

The content of AMS programmes heavily depends on the context and the capacity of national regulatory authorities relevant for human and animal health, plant production and the environment. This could include, for example the following levels:

i. Global level: how new antimicrobials are introduced to the market, labelled, priced and distributed;
ii. National level: legislation, regulation and national treatment guidelines;
iii. Hospital/Farm level: optimizing the use of antimicrobials for patients in hospitals and farms, and at
iv. Community level: fostering access and prudent use in primary health care settings and in animal health through awareness raising and targeted interventions.

Stewardship and access cannot be dealt with in isolation. Any stewardship framework must also ensure that access to antimicrobial agents is not compromised and is expanded where needed. A wider recognition of antimicrobial agents, in particular antibiotics, as a global public good is needed to undertake stewardship at the various levels.

CHAPTER TWO
SITUATIONAL ANALYSIS

This chapter highlights strengths, weaknesses, opportunities and challenges (SWOC) in relation to antimicrobial use in human, animal, food and agriculture.

2.1 Antimicrobial Use in Humans

The development of AMR is a normal evolutionary process for microorganisms but is accelerated by selective pressure exerted by widespread use and handling of antimicrobials. The association between antimicrobial use and resistance has been well documented in some health care facilities, communities and countries (CDDEP 2015)

In 1993, Massele *et al,* studied antibiotics use in Tanzania and found that approximately 39% of studied patients were prescribed with antibiotics. In a baseline study on rational use of medicines by WHO in Tanzania (WHO, 2002), almost 42% of patients were prescribed with antibiotics. In 2014, the Rational Use of Medicines (RUM) survey conducted by Ministry of Health indicated that 67.7% of patients were prescribed with antibiotics. The results above established the overuse of antimicrobials, a plausible reason for increased AMR in the country.

In the RUM assessment, the household survey contacted persons who were ill and had recently recovered from their illness. Results indicated that of the 180 patients who got their medicines and had recovered from their illness, 61% (n=110) did not complete their doses. Additionally, self-medication, sharing of medicines, as well as using medicines without consultations were observed as key findings. This could be a common practice by many patients who do not know the importance of completing their doses, hence posing a threat of development and spread of AMR. These results implied irrational use of medicines including antimicrobials at community level that can lead to AMR development.

In North-eastern Tanzania, Horumpende *et al*., (2017) indicated that, self-medication with antibiotics was practiced by more than a half of Siha district residents; 92% of respondents said they used to go to pharmacy for care when they fall sick. The study further revealed that antibiotic self-medications were mostly used for treatment of cough, fever and diarrhea without prescriptions. In another study by Horumpende *et al*., (2017) in Moshi Municipal

Council, it was found that 92.3% of retail drug outlets dispensed antibiotics without prescription. The antibiotics most commonly dispensed without a prescription were Ampiclox for cough and Azithromycin for painful urination and 71.43% of these prescriptions were dispensed with incomplete doses.

Furthermore, the situational analysis conducted by Global Antimicrobial Resistance Partnership (GARP) group in 2015 emphasized on inappropriate antimicrobial use in Tanzania. For example, 1) "inappropriate prescription of antibiotics by physicians and other healthcare workers may be prevalent, often without establishment of an infection needing antibiotics, 2) consumers often purchase antimicrobials directly from drug outlets, and 3) drug outlets also dispense without prescriptions and sell incomplete doses of antibiotics in an accredited drug-dispensing outlets (ADDOs), especially in the rural areas of the country.

Data from the Medical Store Department (MSD) and the then Tanzanian Food and Drugs Authority (TFDA) in 2017 indicated the most commonly used antimicrobials as listed in table 1 below.

Table 1: Mostly consumed antimicrobials in Tanzania for the year 2016

	Antimicrobial	Class	Percentage (%)
1	Amoxicillin	Broad-spectrum penicillin	19
2	Ciprofloxacin	Quinolone	14
3	Doxycycline	Tetracycline	9
4	Tetracycline	Tetracycline	9
5	Cephalexin	Cephalosporin (1st generation)	8
6	Sulfamethoxazole + trimethoprim	Sulfonamide + trimethoprim	6
7	Erythromycin	Macrolide	4
8	Amoxicillin + clavulanic acid	Broad-spectrum penicillin	3.5
9	Metronidazole	Imidazole derivative	2.7
10	Gentamicin	Aminoglycoside	2.5

In addition, the point prevalence survey (PPS) conducted in selected hospitals in 2018 indicated the following: a) antibiotics were used more in Intensive Care Units (ICUs), surgery and medical wards; b) most of the antibiotics were prescribed without the performance of antibiotic susceptibility testing; and c) there was a lack of AMS programs in hospitals.

2.2 Antimicrobial use in Animals, Food and Agriculture

As global demand for animal protein grows, antimicrobials have increasingly been used in livestock and poultry for more than half a century to treat and prevent disease. They are also used in low doses in animal feed to promote growth and increase yield in animal production.

The GARP situational analysis in 2015, revealed that in various ADDO shops, unauthorized veterinary medicines were being sold, unqualified personnel dispensed drugs, and record keeping and documentation remained inadequate. Furthermore, the report revealed that antimicrobials for animals were commonly bought from informal vendors, and that antimicrobials were prone to degradation due to poor marketing and storage conditions.

Significant amounts of the antimicrobials used by people and animals eventually find their way into the environment, particularly in surface and ground water and in soil. As a result, antibiotic-resistant bacteria may develop and spread in animals and in the environment and may cause human disease, and vice versa. The situation is more serious particularly where clean water and adequate sanitation are not available.

There is some evidence to show the relationship between the use of antimicrobials in animal and in human health. This includes the direct transmission of resistance genes and pathogens from animal to human and from animal-sourced foods to human; outbreaks of food-borne infections; and correlated trends of antimicrobial use in animals and resistance in humans.

High demands for foods of animal, crop and fish origins have resulted in the overuse of antimicrobials and biologicals to control diseases and pests in livestock (poultry), fish and crops. This remains a global health threat because the producer may aggravate antimicrobial use without consideration for human, animal and environmental health.

Hounmanou and Mdegela (2018) have recently revealed that the trend of antimicrobials use in the livestock sector is alarming. Antimicrobials are openly sold on the streets and are distributed over the counters without prescriptions. Further, they showed that, farmers do not adhere to withdrawal periods as recommended by the manufacturers with implications on increased residues in animal products. They also showed that majority of the Tanzanian poultry farmers (up to 90%) treat their chicken by themselves with antibiotics.

CHAPTER THREE
RATIONALE, GOAL AND OBJECTIVES

3.1 Rationale

It is estimated that globally, 50% of antimicrobial use is improper. In spite of existing policies, laws and regulations in the country, the desired objectives of enforcement and effective interventions on rational use of antimicrobials is not yet realized. Additionally, there is inadequate awareness among the community on the need for adherence to antibiotics dosage and all aspects of their rational use. There are also difficulties in evaluating the use and effects of antimicrobial agents due to lack of reliable information, among others.

These have accelerated inappropriate antimicrobial use across all sectors with undesirable health impacts. Several sub-populations in the community, hospitals, farms, and other health care settings and the agricultural sector are at increased risk of facilitating the spread of AMR.

The absence of national policy guidelines that oversee the prudent use of antimicrobial agents is a major contributing factor in abuse of antimicrobial agents. These challenges highlight the need for guidance on proper use of antimicrobials in the country. A coordinated systematic approach to improve the appropriate manufacturing, selection, procurement, distribution and use will prevent the spread of AMR pathogens among Tanzanians.

3.2 Goal

The goal of antimicrobial policy guidelines is to strengthen AMS from manufacturer to the end user in the value chain.

3.3 Objectives

i. To strengthen research and development on antimicrobial resistance and stewardship
ii. To develop and strengthen quality management systems in production and use of antimicrobials
iii. To safeguard appropriate selection of antimicrobial agents for specific disease conditions

iv. To enhance rational procurement, supply and distribution of antimicrobial agents throughout the supply chain

v. To strengthen diagnostic capacity for detection of AMR pathogens and quantification of antimicrobial residues

vi. To promote appropriate prescribing, dispensing and use of antimicrobial agents in human, animal, food and agriculture sectors.

CHAPTER FOUR
STRATEGIES FOR IMPLEMENTING ANTIMICROBIAL STEWARDSHIP PROGRAMS

The aims of an AMS programme in health facilities are:

- to optimize the use of antibiotics;
- to promote behaviour change in antibiotic prescribing and dispensing practices;
- to improve quality of care and patient outcomes;
- to save on unnecessary health-care costs;
- to reduce further emergence, selection of antimicrobials and spread of AMR;
- to prolong the lifespan of existing antibiotics;
- to limit the adverse economic impact of AMR; and
- to build the best-practices capacity of health-care professionals regarding the rational use of antibiotics

AMS is a key component in the prevention and control of AMR. This chapter provides a summary of the achievements, constraints and proposed interventions for AMS programs under the following components:

i. Research and development
ii. Regulation and manufacturing
iii. Selection of antimicrobials
iv. Supply chain management
v. Diagnostics
vi. Prescribing, dispensing and responsible use

4.1 Research and development for antimicrobials

Preamble

Research and development is needed in AMS to promote availability of innovative means of preventing and controlling AMR. Operational researches can also be done e.g. antibiotic utilization studies, point prevalence studies and antibiotic audit data to understand antibiotic prescribing, dispensing and use habits. The main purpose of collecting data on the use of antibiotics is to assess the extent and quality of antibiotic use, identify problematic prescribing practices, and compare appropriate use across health-care facilities and within a health-care facility, department or ward over time. Measuring the quantity and appropriateness of antibiotic prescribing and use will identify where there is room for

improvement in targeting and monitoring AMS interventions. Antibiotic Data Auditing refers to the prospective (real-time) or retrospective collection of antibiotic prescription data on hospitalized patients. The data are analysed and then fed back to the prescribers. This method can begin with weekly or bimonthly quick audits (only a few patients) during ward rounds, with real-time feedback to the prescribers, similar to a repeated and small-scale PPS.

There should be a mechanism to oversee research work and ways to harmonize and advance research agenda on antimicrobials to facilitate Policy Makers, health workers and the community in general to use research findings in decision-making.

Achievements

Existence of a development plan for strengthening R&D in higher learning and research institutions and availability of pharmaceutical training institutions will increase human resource and collaboration in research and development. Availability of local markets and availability of regulatory institutions such as TFDA and National Environmental Management Commission (NEMC) will regulate use of antimicrobials and control establishment of manufacturing companies.

Constraints

A number of research works has been documented, however there is no national research agenda specific for AMR. Also, there is still inadequate coordination and sharing of the available research findings among stakeholders.

- Most of the research carried out are driven by donor's interests and does not cover national or regional specific issues
- Available information is limited since data are limited in coverage
- Research capacity in terms of trained human resource and facilities is limited

Objective

To strengthen Research and Development on antimicrobial resistance and stewardship

Statements: Human, animal, agriculture and environment sectors

i. *The Government in collaboration with stakeholders shall develop a national research agenda on antimicrobial stewardship*

ii. *The Government in collaboration with stakeholders will support R&D for improving appropriate use of antimicrobial agents*

iii. *Research Institutions will be encouraged to undertake basic research and translational studies to support the development of new treatments, diagnostic tools, vaccines and conventional new antimicrobial agents*

iv. *At Regional, district and facility levels, operational research on AMR and AMU will be encouraged and supported to guide appropriate antimicrobials consumption and use*

4.2 Regulation and manufacturing of antimicrobials

Preamble

To curb the potential for misuse of antimicrobials in the human, animal and agriculture sectors, there should be appropriate policy objectives, supported by adequate legislation, regulatory control and enforcement mechanisms. However, at the same time, it is important to ensure that while restricting overuse access to life saving antimicrobials is not compromised.

Achievements

The system to regulate antimicrobials is present in human, animal and agriculture sectors. The Tanzania Food, Drugs and Cosmetics Act, 2003 regulates the importation, manufacture, labeling, marking or identification, storages, promotion, sales, distribution and their rational use of medicines including antimicrobials use in human and animals. The Tanzania Medicines and Medical Devices Authority (TMDA) is equipped with a central Laboratory and mini laboratories prequalified by World Health Organization to monitor quality of pharmaceuticals including antimicrobials.

For the agriculture sector there exists the Plant Protection Act 1997, which is enforced by Tropical Pesticides Research Institute (TPRI), Tanzania, and monitors registration of agricultural pesticides.

Constraints

Domestic manufacturers of antimicrobials to be used in humans, animals and agriculture may contribute to AMR through poor waste disposal with unintentional release of antimicrobials in the environment. There appear to be unsatisfactory compliance with laws and regulations that guide the antimicrobial manufacturing. NEMC should be more proactive in enforcing regulations on disposal of industrial wastes.

In addition, due to limited resources there is inadequate enforcement of post market surveillance for antimicrobial agents used in the country. Currently, the existing laws, namely the Animal Diseases Act 2003, the Veterinary Act 2003, the Grazing-Land and Animal Feed Resources Act 2010 and the TFDC Act 2003, do not have provisions for regulating the use of antimicrobials in animal feeds. This means that the manufacturers of animal feeds in Tanzania are not regulated or restricted from incorporating antimicrobials either as growth promoters in animal feeds or for prophylactic purposes possibly leading to AMR.

With regards to the agricultural sector, the existing Plant Protection Act 1997 does not provide for the accountability of product owners and distributors on the disposal of obsolete antimicrobials used in agriculture. Moreover, the Act does not have any provision for use of organic manure from animal origin which may potentially be contaminated with antimicrobials used in animals.

Another major yet often overlooked constraint is lack of guidance to manage effluents including; farm level effluents, hospital waste, industrial level effluents, abattoir effluents, wash-off, seepages and run-off from crop farming.

Objective

To develop and strengthen quality management systems in production and use of antimicrobials

Statements: Human, animals, food, agriculture and environment sectors

i. *The government will ensure Good Manufacturing Practices of antimicrobials for humans, animals and agricultural practices*
ii. *The Government will enforce compliance to regulations on antimicrobial use in humans, animal, food/feeds and agriculture*
iii. *The Government will enforce compliance to regulations that guides disposal of antimicrobials in the environment*

4.3 Selection of antimicrobials

Preamble

Precise selection of antimicrobial medicines is an important factor in the successful implementation of AMS program. Selection of antimicrobials in national essential medicines list should be based on evidence of safety, efficacy, quality and cost-effectiveness.

Achievements

The NEMLIT guides selection of antimicrobials in the human health sector. The current edition of STG/NEMLIT (fifth edition of December, 2017) has included the recommended WHO AWaRe categorization (Annex I) of antibiotics (A-Aware, Wa-Watch, Re-Reserve). The AWaRe categorization will further be improved in the next editions of STG/NEMLIT according to existing AMR patterns.

The selection of AMU in livestock and agriculture sectors is partially supported by the presence of Acts that register practitioners to manage animal, fish and crop diseases basing on their level of qualifications. These Acts include the Animal Diseases Act 2003, Veterinary Act 2003 and TPRI Act 1979. Concurrently, this aspect is cemented by the existence of public and private Livestock, Fisheries and Agricultural Training Institutions which train manpower at different levels of qualifications.

Constraints

Even though STG/NEMLIT in the human sector has been used for decades, there is still lack of evidence or data at country level that guides inclusion/exclusion of antimicrobials agents in STG/NEMLIT. The selection of antimicrobials to be included in STG/NEMLIT is based on clinical experience and international evidence-based data. However, antimicrobial selection in animal and agriculture sectors is weakened by the absence of treatment protocols.

Objective

To safeguard appropriate selection of antimicrobial agents for specific disease conditions

Statements: Human, animal and agriculture sectors

i. *One of the selection criteria for antimicrobials to be included in the essential antimicrobial list for human and livestock sectors shall be evidence based on AMR surveillance data*
ii. *The Ministries responsible for human, animal and plant health will ensure the empirical treatment guidelines is based on evidence which are in line with WHO/OIE/FAO classification*

4.4 Supply chain management for antimicrobials

Preamble

Addressing stock-out of antimicrobials in the procurement and supply chain system can help in combating AMR. Also, ensuring a strong supply chain of reliable diagnostic tests, reagents,

and consumables is one of the key factors for creating a sustainable, strong diagnostic laboratory system on antimicrobial use. Hence, a robust procurement and supply chain system is essential in implementing AMS in human, animal and agriculture sectors. However, the establishment of the supply chain and procurement in these sectors are inadequate and in different stages of development.

Achievements

The establishment of MSD as an agent for procurement in the public health sector; and the registration of importers and wholesalers regulated by TMDA and TPRI enable the monitoring of antimicrobial consumption in the country. Also, this is significant to the sector as it obligates importers to comply with stipulated regulations guiding the antimicrobial importation, distribution and storage. Though separate, the procurement of antimicrobials in the public sector is in line with the essential medicines list.

Constraints

The Pharmacy Act 2011 Section 34 stipulates that "*A person shall not sell, dispense or supply medicinal products except in premises registered under the Act".* However, there is weak enforcement with regard to supply and distribution of antimicrobial agents to pharmacy premises located in the community, private clinics, hospitals, health centres and dispensaries.

There is no database for monitoring the supply and distribution of antimicrobials from importers or distributors to wholesalers and retail drug outlets. Such situations may lead to distribution of antimicrobials to unlicensed dealers. Another constraint is the inadequate number of qualified personnel throughout the procurement and supply chain. Similar challenges exist in the animal and agriculture sectors.

The distribution of antimicrobials in the country for the use in animals is hampered by among others lack of: distribution guidelines, unstructured system to support the central procurement system (central stores) and standard treatment guidelines. Hence, decision on import of antimicrobials by most importers is based on financial considerations rather than industry/market needs.

Objective

To ensure rational procurement, supply and distribution of antimicrobial agents throughout the supply chain to enhance their prudent use

Statements: Human, animal and agriculture sectors

i. *Regulatory Authorities will ensure that antimicrobial agents are only stocked and supplied by licensed medicines outlets, health/veterinary facilities and agriculture input outlets Regulatory Authorities will ensure availability and maintenance of the database to track supply and distribution of antimicrobial agents from importers, distributors to wholesalers and retail medicine outlets*

ii. *Professional Regulatory Bodies shall ensure minimum requirements of qualified personnel are available throughout the supply chain management*

4.5 Diagnostics

Preamble

Rational use of antimicrobial agents requires proper diagnosis. For proper diseases diagnosis in human and veterinary practices presence of functional and efficient diagnostic facilities is crucial. Being able to make the right diagnosis is usually a criterion to providing effective antimicrobial therapy. Hence, accurate identification of the pathogens and antimicrobial susceptibility testing are fundamentals of optimal AMS. The main function of microbiologists (or laboratory technicians) in an AMS programme is to interpret and communicate microbiology results to prescribers, and to develop and update antibiograms and communicate their value and limitations. Microbiology laboratories play a key role in informing the appropriate use of antibiotics, ensuring first and second-line antibiotics are used whenever possible.

Achievements

The laboratory capacity in Tanzania is supported by the existence of a policy for ensuring quality of laboratory diagnostic capacities. The national laboratory quality standards/guidelines have been established, and some laboratories at National, Zonal and Regional Referral Hospital levels participate in international External Quality Assessment (EQA) schemes. In addition, members of staff at all levels (regional, zonal and reference

laboratories) have been trained in microbiological analysis of samples which include isolate identification and antimicrobial susceptibility testing performance. To date, in the human health sector, there are 32 laboratories in Tanzania with the capacity of performing culture and sensitivity with limitations, the main being limited supply of reagents and consumables. These include: National, Zonal Referral Hospital, Regional Referral Hospitals and public specialized laboratories. Others among the 32 laboratories those of private hospitals such as Aga khan, stand-alone private laboratories such as the Lancet, academic institutions laboratories such as MUHAS and CUHAS and research institutions laboratories such as Ifakara Health Institute. Of the 32 laboratories, 11 including the National Reference Laboratory (NHLQATC) have been accredited by Southern African Development Community Accreditation Services (SADCAS) under ISO 15189:2012 although in 5 of them the microbiology section was not included for accreditation. The NHLQATC has been designated to be the reference laboratory for AMR surveillance in human health while the Central Veterinary Laboratory (CVL) will serve as a reference laboratory for AMR surveillance in animal health. Currently, there is a program involving the regional and faith-based human laboratories on accreditation process through Strengthening Laboratory Management Towards Accreditation (SLMTA) of which 54 Laboratories are enrolled.

Constraints

The Joint External Evaluation (JEE) report of the International Health Regulations (2005) (IHR) core capacities conducted in the Tanzania Mainland in 2016 indicated a lack of capacity for AMR detection and surveillance for infectious diseases caused by AMR pathogens. The FAO's Situation analysis assessment report 2017, clearly indicated the country's capability to manage AMR and their associated threats as being below the global recommended levels. One of the limitations is lack of standardized methods in laboratories practicing AST and data collection for the monitoring of indicators of AMR for human, animal, agriculture and environment.

There is also limited laboratory diagnostic capacity for culture, identification and AST at regional and district levels often due to inadequate supply chain and human resource issues.

Interventions

Objective

To strengthen diagnostic capacity for detection of AMR pathogens and quantification of antimicrobial residues for proper antimicrobial use.

Statements: Human sector

i. *The Ministry responsible for health will ensure hospitals perform culture or serology prior to empirical treatments.*

ii. *The Ministry responsible for health will ensure hospitals establish antibiogram for priority bacteria of public health importance.*

iii. *The hospitals will ensure that AST data are regularly communicated to prescribers and submitted to the National database for country data aggregation, analysis and use*

Statements: Animal and agriculture sectors

i . The Ministry responsible for animal health will ensure veterinary facilities perfom necessary diagnostic test prior to antimicrobial use

ii . The Ministry responsible for animal health will establish antibiogram for priority bcteria of public health

iii. The veterinary facilities will ensure that AST data are regularly communicated to prescribers and submitted to the National database for country data aggregation, analysis, and use.

iv. The ministry responsible for animal and plant health will ensure antimicrobial residues monitoring system is developed and implemented to safeguard public health.

4.6 Prescribing, Dispensing and Responsible Use of Antimicrobial Agents

Preamble

Antimicrobials are among the most commonly prescribed medications in human health and veterinary facilities. The Pharmacy Act Cap 311 and Tanzania Food, Drugs and Cosmetics Cap 219, and the Veterinary Act Cap 319 are in place to safeguard and promote the provision of pharmaceuticals and other health products and services.

The main goal is to achieve adequate therapeutic outcomes for health and improve quality of life of humans and animals as well as provide useful information to the public. Similarly, the Medical, Dental and Allied Health Professionals Act No.11 of 2017 provides guidance on rational prescribing of all medicines including antimicrobial agents.

Proper diagnosis, prescribing and dispensing contribute to rational use of antimicrobials in the treatment of human and animal infections while prolonging the therapeutic active life of the agents. One main outcome of performing AMS interventions in a health-care facility is behaviour change in antibiotic prescribing practices, leading to more responsible use of antibiotics. Implementing AMS programmes is a strategy for changing this behaviour over time. The following are some of the interventions for improving antibiotic prescribing practices.

Types of AMS interventions for improving antibiotic prescribing practices at facility level

Persuasive (education)	• Educational meetings (e.g. basics on antibiotic use, case-based discussions, morbidity and mortality, significant event analysis, lectures on specified topics) • Distribution of and training on educational material (e.g. clinical practice guidelines) • Using local key opinion leaders (champions) to advocate for key messages • Reminders provided verbally, on paper or electronically • AMS e-learning resources made available to all health-care personnel • AMS education as part of continuing medical education
Persuasive (feedback)	• Audit with feedback to prescribers on their prescribing practice • AMS as a component of ward rounds (real-time feedback with educational component) • Patient handover meetings between two shifts with real-time feedback by consultants • Local consensus processes for changes in antibiotic treatment or surgical prophylaxis
Restrictive	• Formulary restrictions • Restricted prescribing of identified antibiotics (expert approval prior to prescription) (see Annex V) • Compulsory order forms for targeted antibiotics • Automatic stop orders (e.g. after a single dose of surgical prophylaxis) • Selective susceptibility reporting from the lab

Structural	• Rapid laboratory testing made available • Therapeutic drug monitoring

Achievements

In an effort to combat AMR in the country the following achievements have been attained:

First, there are clear policies and laws with regard to prescribing, dispensing and use of antimicrobials in the country. The Pharmacy Act Cap 311, Sections 39, 40 & 41 provide for all antimicrobial agents to be prescribed and dispensed by qualified personnel after presentation of a legal prescription countersigned by relevant professional. Also, the Medicines and Therapeutic Committee (MTC) have been established to advocate for responsible use of medicines including antimicrobials in health facilities;

Secondly, the presence of professional Councils, which regulate practices, is an added strength in diagnosis, prescribing and dispensing of antimicrobial agents. Professional Councils such as Medical Council of Tanganyika, Pharmacy Council, Veterinary Council of Tanzania, Nursing and Midwifery Council and Private Health Laboratory Board, promote enforcement of regulations that are geared towards ensuring rational use of antimicrobial agents both in human and animal health;

Thirdly, the presence of animal health facilities registration/guidelines and widespread qualified animal health professionals provide for opportunities of improving the practices of prescribers and dispensers; and fourthly, availability of training institutions is an opportunity that facilitates proper utilization of antimicrobial agents and that provides Continuous Professional Development (CPD) in the field.

Constraints

Weaknesses at service delivery points in the human sector include poor use of STG/NEMLIT for disease management. Additionally, in most private and public health facilities, antimicrobials are being prescribed without reference to laboratory confirmation. For example, Fourth Generation Cephalosporin's and new classes of antimicrobials are preferred for prescription by clinicians compared to lower generations. With regards to private pharmacies, enforcement of regulations to ensure adherence to prescription-only-medicine (POM) is not done. In addition, scheduling of products and restriction of over-the-counter (OTC) sales of antibiotics without a prescription; and in the animal health sector, to restrict or prohibit the use of antimicrobials as growth promoters are not adhered to.

Weak enforcement of regulations directly impacts on prescription and dispensing of antimicrobials and health professional ethics. In addition, lack of STG in veterinary and agriculture practices affects rational use of antimicrobial agents. Furthermore, in the veterinary and agriculture sectors, antimicrobials are sometimes sold in the open markets or stored inappropriately with implications on their potency.

The knowledge gap on antimicrobials (use, resistance and disposal) impact negatively on the antimicrobial use in livestock and agriculture practices which may end up polluting water bodies and environment. Absence of regulations guiding disposal of obsolete agricultural antimicrobials is also another impediment.

Furthermore, absence of regulations and guidelines on the implementation of effective biosecurity measures exacerbate the use of antimicrobial agents at farm level.

Interventions

Objective

To promote appropriate prescribing, dispensing and use of antimicrobial agents in human, animal, food and agriculture.

Statements: Human sector

i. *The Ministry responsible for health in collaboration with other relevant ministries will ensure creation of community awareness and engagements to promote appropriate antimicrobial use and disposal*

ii. *The Ministry responsible for health will ensure that prescribing of antimicrobials is guided by standard treatment guidelines and or specific program treatment protocols*

iii. *Hospital Medicine and Therapeutic Committees will ensure that antimicrobial therapies are periodically reviewed based on microbiology result and the patients' progress*

iv. *Hospital Medicine and Therapeutic Committees will ensure that prescribers are documenting clearly the prescription/patient files for the indication prescribed antimicrobial agents*

v. *Pharmacy Council will ensure that antimicrobial agents are dispensed with appropriate information upon presentation of legal prescription.*

vi. *Ministry responsible for health will ensure that antimicrobial stewardship program is established in district, regional referral, and tertiary hospitals*

vii. *Hospital Medicines and Therapeutic Committee will ensure a system for monitoring the use of antimicrobial is in place*

Statements: Animal and agriculture sectors

i. *Ministry responsible for animal health will ensure that antimicrobial agents are dispensed with appropriate information upon presentantion of legal prescription*

ii. *The Ministry responsible for animal health will ensure that prescribing of antimicrobials is guided by standard treatment guidelines and or specific program treatment protocols.*

iii. *The Ministry responsible for plant health will ensure appropriate use of antimicrobial agents in crop production to avoid development of AMR.*

iv. *The government through responsible institution will ensure that antimicrobial residues monitoring system is developed and implemented to safeguard the public health.*

CHAPTER FIVE
IMPLEMENTATION OF THE POLICY

5.1 Coordination, Roles and Responsibilities

Intersectoral coordination among responsible sectors is imperative for efficient implementation of these Policy Guidelines using the One Health Approach. At national level, the AMR Multi-Sectoral Coordinating Committee (MCC) will oversee the implementation of the guidelines. The AMS TWG will be responsible for advising the MCC on technical issues on antimicrobial use and stewardship while linking with other stakeholders on operationalization of these guidelines using One Health Approach.

Line Ministries will work closely with the AMS TWG to ensure effective implementation of these guidelines at all levels (health facilities, animal health centers and crop farms etc.). For human health, the MTC, will be an important organ in implementing the guidelines at all levels. Independent of the characteristics of the health-care facility, including size, an AMS programme should be adapted to the facility's human, financial, structural and organizational resources, and to the patient mix. For effective implementations of the policy guidelines; laws and/or regulations shall be amended when deemed necessary.

Roles of other key stakeholders are outlined below:

A: LABORATORY PERSONNEL

Microbiologists and other laboratory personnel play a critical role in the implementation of AMS programs. The following are recommended to be implemented:

i. *Receiving, testing and interpreting laboratory results*

ii. *Ensure timely communication of laboratory results on AST with practitioners and other relevant stakeholders.*

B: CLINICIANS (HUMAN AND ANIMAL)

Clinicians have major influences for decision-making with regard to antimicrobial prescribing, appropriate prescriber strategies, and guidance and support. It is the obligation of all prescribers to follow good prescribing and AMS principles. The following are recommended to be implemented:

i. *Prescription of antimicrobials, either for treatment or prophylaxis, should follow standard treatment guidelines or program treatment protocols*
ii. *Clinicians should take an "antimicrobial time-out" after 48-72 hours of a patient's use of antimicrobial to assess the outcome*
iii. *All prescribers shall use authorized prescription forms and should be duly filled and counter signed.*
iv. *Clinicians should stimulate inter-communication among the case management team (Pharmacists, nurses, lab personnel and administrative staff).*
v. *Perform detailed assessment on antimicrobial use including side effects.*

C: PHARMACEUTICAL PROFESSIONALS

Pharmaceutical personnel are important in AMS programs. The following are their responsibilities in AMS programs:

i. *Ensure continuously availability of antimicrobial agents in the supply chain.*
ii. *To adequately keep records on antimicrobial consumptions*
iii. *Strengthen communication between prescribers and other case management team Ensure regular audit of antimicrobial use at all levels*
iv. *The dispenser shall read the prescription and label antimicrobial agents to patients as per dispensing SOP.*
v. *The dispenser shall issue antimicrobial agents only upon presentation of legal prescription*
vi. *If there is any error, the dispenser shall communicate with the prescriber for corrections*
vii. *Educate patients/legal guardians on rational use of antimicrobials including the provision of adequate information on the proper use of antimicrobial agents dispensed for their conditions.*
viii. *Perform detailed assessment on antimicrobial use including side effects.*

D: NURSES AND VETERINARY NURSES /WARD IN CHARGES

An effective AMS Program should include a collaboration of nursing. Communication between nursing and other experts is essential in improving stewardship programs. The following are recommended to be implemented:

i. *Provide antimicrobial agents to patients as per SOP*

ii. *When cultures are ordered, obtain cultures sample and send to microbiology laboratory, monitor culture results and report these to physicians*
iii. *Perform detailed assessment on antimicrobial use including side effects.*
iv. *Keep proper records on antimicrobial use*
v. *Enhance communication with clinicians, laboratory staff, pharmacist, veterinarian/paraprofessionals with regards to antimicrobial use and resistance*
vi. *Educate patients on rational use of antimicrobials.*

E: PROCUREMENT AGENTS

The Medical Stores Department has a major role to ensure availability of quality essential antimicrobial agents in the public sector health facilities. In the animal sector, this activity is privately led, however, the authority can have forms of control to ensure regular availability of antimicrobial agents.

F: ANTIMICROBIAL IMPORTERS, DISTRIBUTORS AND WHOLESALERS

Importers, distributors and wholesalers have a major role to preserve the safety, efficacy and safety of antimicrobials and therefore they have the following obligations:

i. *Comply with legal requirements for importation, handling and distribution of antimicrobials*
ii. *Comply with Good Storage Practices*
iii. *Sales antimicrobial agents to authorized drug outlets only*
iv. *Keep records on importation and sales of antimicrobials*

G: ANTIMICROBIAL RETAILERS

The retail drug outlets shall:

i. *Source antimicrobial agents from approved distributors and wholesalers only*
ii. *Comply with Good Storage and Dispensing Practices*
iii. *Stock antimicrobial agents as per category of the outlets*
iv. *Sales antimicrobials upon presentation of legal prescriptions*
v. *Keep records and retain prescriptions as per regulations*

H: REGULATORY AUTHORITIES

The Tanzania Medicines and Medical Devices Authority has been given a mandate to regulate antimicrobials in both human and animal sector. TPRI is mandated with similar role in

agriculture sector. The TMDA and TPRI have a major role of strengthening post-marketing surveillance and pharmacovigilance for adequate implementation of these guidelines.

I: PROFESSIONAL BODIES AND ASSOCIATIONS

All professional bodies and related associations shall regulate the professionals within their domains to adhere to rational prescribing and use of antimicrobial agents as per stipulated regulations. These include but are not limited to MCT, MAT PC, NMC, TANA, PST, PHLB, Lab association for human health and for animal sector VCT, TVA and TAVEPA.

J: RESEARCH AND TRAINING INSTITUTIONS (RTI)

Research and training institutions have been key in providing empirical information on AMR. The RTI shall carry out focused and relevant research in response to country needs and priorities. The RTI will also support diagnosis of pathogens, surveillance and monitoring of antimicrobials. Teaching on the principles of 1) prudent use of antimicrobials; 2) prescribing; 3) dispensing and 4) disposal of obsolete antimicrobials should be core mandate of the RTIs.

K: Patients/ Community

Patients and farmers are among the main targeted group for effective implementation of these guidelines. The role of patients and farmers should be;

1) *Adherence to treatment instructions.*
2) *Observe withdrawal periods in case of farmers.*
3) *Implement biosecurity measures in farms.*
4) *Avoid self-medication*
5) *Obtain antimicrobial agents from approved sources.*
6) *Proper handling of antimicrobials as per manufacturers or dispenser's instructions.*
7) *Comply with statutory requirements for disposal of antimicrobials and associated containers in order to minimize environmental contamination.*
8) *Community to observe hygiene and sanitation, vaccination programs and nutritional requirements to minimize infections and antimicrobial usage.*

5.2 Establishing Stewardship Programme in Health Facilities

The AMS in health-care facilities shall be established on existing structure. Should not be vertical programmes rather, they should cut across other existing programmes to optimize antibiotic use, thereby improving quality of care and infection management. It is therefore

important that healthcare facility management and an AMS committee and/or AMS team together decide which strategies best fit their local setting, based on a situational analysis and development of an action plan.

Recommended steps in establishing antimicrobial stewardship programs:

STEP 1: UNDERTAKE A FACILITY AMS SITUATIONAL/SWOT (STRENGTHS, WEAKNESSES, OPPORTUNITIES, AND THREATS) ANALYSIS

Before an AMS programme is developed and implemented, a situational or SWOT analysis should be performed. For AMS programmes, this information is important in determining what needs to be done and what can be done. This analysis does not need to be a complex exercise, but rather a pragmatic one that includes the following:

- mapping which core elements are in place in the facility;
- undertaking a baseline antibiotic use analysis;
- identifying main challenges related to antibiotic prescribing and use; and
- identifying available human and financial resources.

The situational analysis should include:

- strengths, weaknesses, opportunities and threats (SWOT) at different levels in the facility;
- possible barriers and enablers for the full participation of the different health-care professionals and departments in the AMS programme.

Example of a SWOT – Health Facility Perspective

	HELPFUL	HARMFUL
INTERNAL/PRESENT FACTORS	**Strengths** *Core elements:* • AMR and AMS are a leadership priority. • IPC programme/committee is active. *Human resources:* • There is enthusiasm for AMS in the facility/wards. • There is clinical knowledge of AMS. *Antimicrobial use and resistance data:* • Prescription audit is conducted in one ward. • Facility aggregate antibiogram is available. *AMS activities:* • A pharmacist is involved in some AMS activities in one ward.	**Weaknesses** *Core elements:* • No medical record or prescription pad is available. *Human resources:* • No dedicated health-care professional is available to lead the AMS team. *Antimicrobial use and resistance data:* • The supply of microbiology reagents is poor. • The supply of antibiotics is poor. *AMS activities:* • Health-care professionals have competing priorities and little time for AMS work.
EXTERNAL/FUTURE FACTORS	**Opportunities** *Core elements:* • Active implementation of the NAP on AMR • Increasing national awareness of AMR and its consequences for health *Human resources:* • Incorporating AMS responsibility into the IPC committee *Antimicrobial use and resistance data:* • Funds for conducting a facility PPS *AMS activities:* • Presenting findings from AMS activities to other wards/ health-care professionals	**Threats** *Core elements:* • Unstable access to essential antibiotics • Increased costs for antibiotics • Prioritization of issues other than AMS in the facility • Low facility budget *Human resources:* • Too many nonfunctional committees in the health-care facility *Antimicrobial use and resistance data:* • Increasing AMR rates, including carbapenem-resistant Enterobacteriaceae (CRE) *AMS activities:* • Opposition from clinical leaders

SWOT

***Source**: WHO 2019*

STEP 2: ESTABLISH A SUSTAINABLE AMS GOVERNANCE STRUCTURE

It is essential to have a governance structure that includes the different functions needed to effectively implement a health-care facility AMS programme. The governance structure may vary in size and complexity depending on the facility. It is essential that the health-care facility leadership/management endorse the health-care facility AMS governance structure to empower the AMS committee, AMS team and/or AMS champions to implement the AMS programme effectively.

An **AMS committee** in the health-care facility should provide leadership and overall coordination of the AMS programme. The AMS committee can be a stand-alone committee or be integrated into an existing structure, such as the infection control, patient safety or drug and therapeutics committee with clear terms of reference. It can be an opportunity to revitalize or empower existing committees. If integrated into an existing committee, AMS must be a standing item on the committee's agenda.

A **multidisciplinary AMS team** (or individual, depending on availability and the size of the health-care facility) of different health-care professionals should be established, who collectively possess the competencies and undertake functions to successfully deliver and implement AMS programmes health-care facilities. Ideally, the AMS team should comprise a prescribing clinician, a pharmacist, a nurse and a (clinical) microbiologist or laboratory technician in facilities with a microbiology laboratory. If available, an infectious disease specialist, a clinical pharmacologist, and/or a nurse with expertise in infections or IPC are also recommended. Additional expertise is essential to complement the skills of the AMS team, such as local champions and health-care professionals who can participate in performing and facilitating stewardship interventions on their wards. Also, if a health-care facility has a quality improvement, patient safety or IPC programme with dedicated staff, securing some of their time to focus on AMS activities is advantageous.

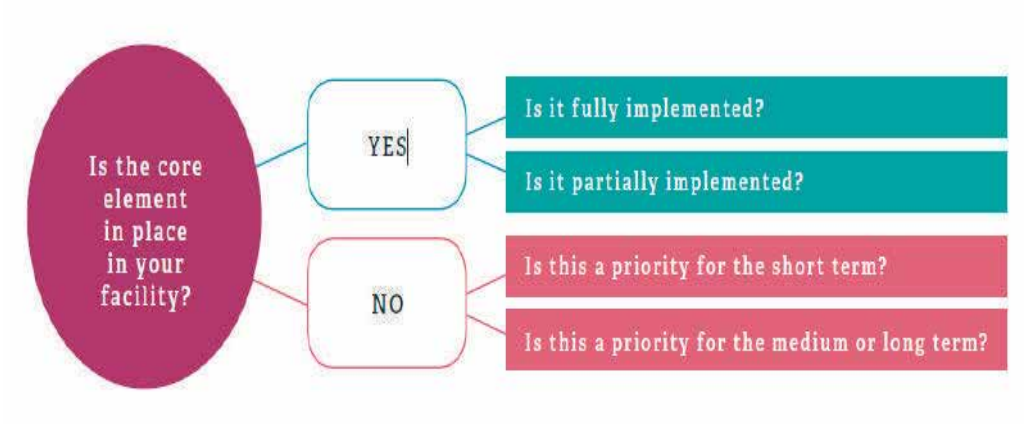
STEP 3: PRIORITIZE THE HEALTH-CARE FACILITY CORE ELEMENTS BASED ON THE SITUATIONAL ANALYSIS

The WHO recommends that health facilities adopt, at a minimum of the AMS Core Elements (Annex II)[3]. This information will help in developing a stepwise implementation plan over the short and medium/long term for the prioritized missing core elements and accelerate implementation of existing ones.

STEP 4: IDENTIFY AMS INTERVENTIONS STARTING WITH THE LOW-HANGING FRUITS

Health facilities need to prioritize interventions based on resources available; start with low hanging fruits.

Prioritizing Interventions



***Source**: WHO,2019*

After identifying and prioritizing the key missing core elements, it is recommended to determine the root. You may use the fishbone template in Annex III.

STEP 5: DEVELOP AMS ACTION PLAN

After conducting a situational analysis and prioritizing interventions, it is important to develop AMS Action Plan to:

- Ensure accountability
- Prioritize activities
- Measure progress

The AMS Action Plan should:

- Specify human and financial resources required
- Determine priority core elements to be implemented in the short term, including accountability, timeline, and indicator

- Identify leadership commitment and oversight, and establish an AMS committee
- Identify areas for improvement, implement AMS interventions (who, what, where, when, and how), monitor and evaluate, and report and feedback results
- Specify human and financial resources required
- Determine priority core elements to be implemented in the short term, including accountability, timeline, and indicator
- Identify leadership commitment and oversight, and establish an AMS committee
- Identify areas for improvement, implement AMS interventions (who, what, where, when, and how), monitor and evaluate, and report and feedback results

STEP 6: IMPLEMENT AMS INTERVENTIONS

AMS interventions should be implemented in a stepwise approach, build on existing structures and reporting, maximize teamwork, and encourage champions and clinical staff – including prescribers – to participate. It is recommended to start small interventions and keep it simple and doable. The continuous quality improvement model, may be used to implement AMS interventions.

Different types of AMS interventions included in facility AMS programmes to improve antibiotic prescribing. The following are the basic ASM Interventions[3]and Annex IV provide more detailed AMS interventions to improve antibiotic prescribing.

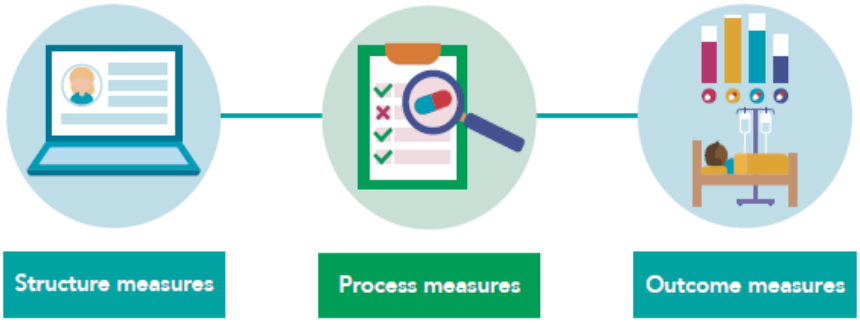
- Educate prescribers and health personnel involved in antibiotic use
- Develop and update a standardized medical record and medical chart to ensure that information on patients' medicines is all in one place
- Review whether patients who receive antibiotic treatment have written indications
- Review antibiotic treatment for patients prescribed three or more broad-spectrum antibiotics
- Review the dose of antibiotics prescribed
- Review surgical antibiotic prophylaxis where it is prescribed for >24 hours and where a single dose is appropriate
- Develop local guidelines for surgical prophylaxis and treatment of common clinical conditions such as community acquired pneumonia, UTIs, skin and soft tissue infection (SSTIs), as well as common health-care-associated infections such as pneumonia, UTIs and catheter-related infections

- Work to ensure leadership and identify expertise in infection management
- Improve the supply and management of medicines, including essential antibiotics, e.g. by establishing a drug and therapeutics committee
- Work to establish basic microbiology laboratory facilities
- Work to establish regular surveillance activities (e.g. AMR, AMC, health-care-associated infections).

STEP 7: MONITOR AND EVALUATE AMS INTERVENTIONS

AMS programmes are encouraged to select the most relevant and feasible indicators.

Structural, process and outcome measures for assessing AMS programmes[79]



Measuring the quantity and appropriateness of antibiotic prescribing and use will identify where there is room for improvement in targeting and monitoring AMS interventions. Annexv indicates step-by-step guide for setting up an AMC surveillance programme at the facility level.

STEP 8: OFFER BASIC AND CONTINUED EDUCATIONAL RESOURCES AND TRAINING ON OPTIMIZED ANTIBIOTIC PRESCRIBING AND USE

Educating Clinicians, Pharmacists, Laboratory personnel, Nurses and other service providers on AMS is essential for successful implementation of ASM programme. AMS competencies are the guiding set of knowledge, skills and attitudes that result in durable, trainable and measurable behaviours facilitating better prescribing and use of antibiotics. The capacity building shall include:

- Educational meetings (e.g., ATB use, case-based discussions)
- Distribution of and training on educational material (e.g., clinical practice guidelines)

- Using opinion leaders (champions) to advocate key messages
- AMS education as part of continuing medical education

CHAPTER SIX: MONITORING AND EVALUATION OF THE IMPLEMENTATION OF THE POLICY GUIDELINES ON ANTIMICROBIAL USE

Monitoring the appropriateness of antimicrobial use is a key element of an effective AMS program. A continuous monitoring and evaluation of antimicrobial usage will be done at all sectors and at all levels. Surveillance of both antimicrobials use and resistance shall be conducted on regular basis.

Surveillance data on antimicrobial consumption and use will be collected at MSD, TMDA, health facilities, veterinary facilities and agriculture antimicrobial outlets. The Government shall establish a National Antimicrobial Surveillance program. The program shall report and track antimicrobial use in both public and private sector by:

i. Collecting data at MSD, TMDA, importers and manufacturers
ii. Collecting data from health facilities and community pharmacies, veterinary health facilities and agriculture antimicrobial outlets
iii. Collecting data from Veterinary Investigation centers (VICs), Tanzania Veterinary Laboratory Agency (TVLA) and NHLQATC
iv. Collecting data from farm level

Annual audit of the antimicrobials usage shall be done by MTC in each health facility and designated veterinary facilities and share the report with the line Ministries. At national level the reports on surveillance of AMR and AMU will be compiled and shared with all stakeholders in the human, animal and agriculture sectors for interventions. Furthermore, it is desirable that supervision on rational antimicrobial use will be conducted in all sectors at all levels. There will be a baseline assessment on the usage of antimicrobials in the country and a two yearly evaluation will be conducted.

It is anticipated that all line Ministries, development partners and institution responsible for this thematic area will support the implementation of these guidelines by providing needed resources.

ANTIMICROBIAL STEWARDSHIP PERFORMANCE INDICATORS

1. 80% of hospitals established antimicrobial stewardship programs by 2022
2. Empirical systemic antimicrobial therapy prescribed according to Standard Treatment Guidelines (STG/NEMLIT) or related clinical guidelines by 2022
3. 80% of hospitals perform antibiotic susceptibility tests by 2022
4. Antimicrobial usage data collected and interpreted to identify areas for improvement by 2022
5. Number of researches on antimicrobial stewardship conducted in human, animal, agriculture and environmental sectors in Tanzania increased by 2022
6. Number of regulations/guidelines on antimicrobial manufacturing, handling, distribution and use in humans, animal, animal feeds and agriculture developed by 2022
7. Presence of database to track supply and distribution of antimicrobial agents from importers or distributors to wholesalers and retail medicine outlets by 2022
8. List of qualified personnel and area of competence provided by professional Regulatory Bodies by 2022
9. Number of CPD activities conducted by Professional Association and Councils on antimicrobial use, resistance and stewardship increased

ANNEX I: THE WORLD HEALTH ORGANIZATION AWaRe MODEL

ACCESS GROUP

This group includes antibiotics and antibiotic classes that have activity against a wide range of commonly encountered susceptible pathogens while showing lower resistance potential than antibiotics in Watch and Reserve groups. Access antibiotics should be widely available, affordable and quality-assured to improve access and promote appropriate use.

Selected Access group antibiotics (shown here) are included on the WHO EML as essential first-choice or second-choice empirical treatment options for specific infectious syndromes.

- Amikacin
- Amoxicillin
- Amoxicillin + clavulanic acid
- Ampicillin
- Benzathine benzylpenicillin
- Benzylpenicillin
- Cefalexin
- Cefazolin
- Chloramphenicol
- Clindamycin
- Cloxacillin
- Doxycycline
- Gentamicin
- Metronidazole
- Nitrofurantoin
- Phenoxymethylpenicillin
- Procaine benzylpenicillin
- Spectinomycin
- Sulfamethoxazole + trimethoprim

WATCH GROUP

This group includes antibiotics and antibiotic classes that have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials (CIA) for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance. Watch group antibiotics should be prioritized as key targets of national and local stewardship programmes and monitoring.

Selected Watch group antibiotics (shown here) are included on the WHO EML as essential first-choice or second-choice empirical treatment options for a limited number of specific infectious syndromes.

- Azithromycin
- Cefixime
- Cefotaxime
- Ceftazidime
- Ceftriaxone
- Cefuroxime
- Ciprofloxacin
- Clarithromycin
- Meropenem
- Piperacillin + tazobactam
- Vancomycin

RESERVE GROUP

This group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi drug-resistant organisms, and treated as "last-resort" options. Their use should be tailored to highly specific patients and settings, when all alternatives have failed or are not suitable. They could be protected and prioritized as key targets of national and international stewardship programmes, involving monitoring and utilization reporting, to preserve their effectiveness.

Selected Reserve group antibiotics (shown here) are included on the WHO EML when they have a favourable risk-benefit profile and proven activity against "Critical Priority" or "High Priority" pathogens identified by the WHO Priority Pathogens List, notably carbapenem-resistant Enterobacteriaceae.

- Ceftazidime + avibactam
- Colistin
- Fosfomycin (intravenous)
- Linezolid
- Meropenem + vaborbactam
- Plazomicin
- Polymyxin B

ANNEX II: HEALTH FACILITIES CORE ELEMENTS FOR ANTIMICROBIAL STEWARDSHIP PROGRAMS

	CORE INDICATOR	Yes	No
LEADERSHIP COMMITMENT	**1.AMS identified as a priority for health-care facility management** The facility management has formally identified AMS as a priority objective for the facility and included it in its key performance indicators. Financial and human resources have been allocated for AMS activities		
	2. Health-care facility AMS action plan endorsed that prioritizes activities and measures progress and accountability A health-care facility AMS action plan is endorsed that prioritizes activities and measures progress and accountability for ensuring appropriate antibiotic use, based on existing national or international guidelines and/or an existing national strategy. The AMS action plan is updated regularly as required.		
	3. Dedicated financial support for the health-care facility AMS action plan There is dedicated, sustainable and budgeted financial support for AMS activities in the action plan (e.g. support for salary, training and information technology (IT) support).		
ACCOUNTABILITY	**4. Multidisciplinary AMS leadership committee in place with clear terms of reference*** This AMS committee can be either stand-alone or embedded in another existing committee structure (e.g. drug and therapeutics committee, pharmacy committee, infection control committee, patient safety committee). If embedded in another committee, AMS must be a standing item on the committee's agenda. The AMS committee is explicitly in charge of setting and coordinating the AMS programme/strategy according to its terms of reference.		
	5. Dedicated AMS leader/champion identified for the health-care facility A health-care professional has been identified as a leader/champion for AMS activities at the facility and is responsible for leading the AMS team in implementing the AMS programme.		
	6. Multidisciplinary AMS team with terms of reference* An AMS team of multidisciplinary health-care professionals who will implement the day-to-day AMS activities in the health-care facility. In resource-limited settings or small facilities it is often difficult to have an AMS team, and an AMS champion can be identified instead. The composition of the AMS team is flexible and should be based on existing recommendations and adapted to the local context: • option 1: >2 health-care professionals constituting a multidisciplinary team (e.g. tertiary hospitals);		

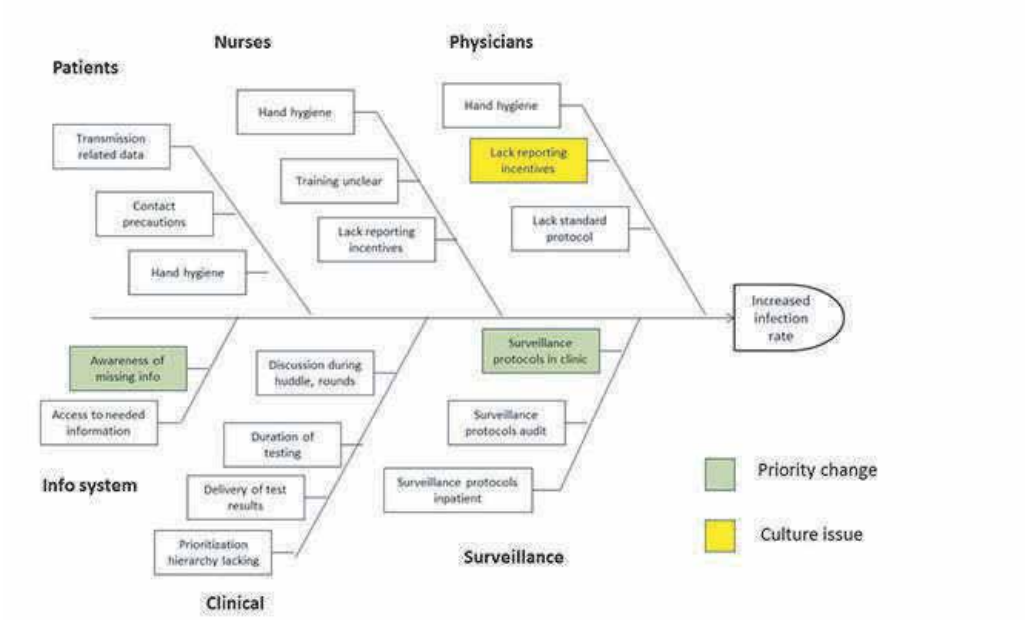
	• option 2: a prescriber and a nurse or pharmacist (e.g. secondary or small hospitals); or • option 3: an AMS champion, e.g. a physician, nurse or pharmacist leading the stewardship programme, with access to expert advice.		
	7. Other health professionals identified and involved in AMS activities Other health-care professionals apart from the AMS team (e.g. from the ICU, internal medicine and surgery, health informatics, or pharmacy or nursing personnel) participate in AMS activities based on the priorities of the health-care facility AMS action plan.		
	8. Clearly defined collaboration between the AMS and IPC programmes A document clearly specifies the process of collaboration between the AMS team/committee and the IPC programme and/or committee. In many low-resource settings the IPC and AMS committees may be merged into one.		
	9a. Regular (descriptive) activity reports on the implementation of the AMS programme Regular activity reports are produced and disseminated to health-care facility personnel and regional/ national AMS TWGs. These reports include data on antibiotic use/consumption and describe the interventions implemented by the AMS team.		
	9b. Regular activity reports (status and outcomes) on the implementation of the AMS programme Regular activity reports are produced and disseminated to health-care facility personnel and regional/ national AMS TWGs with timelines for measurable short- and long-term targets/goals, based on analysis of local antibiotic use and evaluation of the impact of stewardship interventions.		
AMS ACTIONS	**10. Up-to-date standard treatment guidelines** The health-care facility has available, up-to-date recommendations for infection management based on international/national evidence-based guidelines and local/national susceptibility patterns (where possible), to assist with antibiotic selection for common clinical conditions (indication, agent, dose, route, interval, duration). A process is in place for regular review and updating of the guidelines based on new evidence or other external input.		
	11. Regular AMS team review/audit of specified antibiotic therapy or clinical conditions at the healthcare facility Depending on available resources, this can be conducted by prioritizing wards or specific patient conditions.		

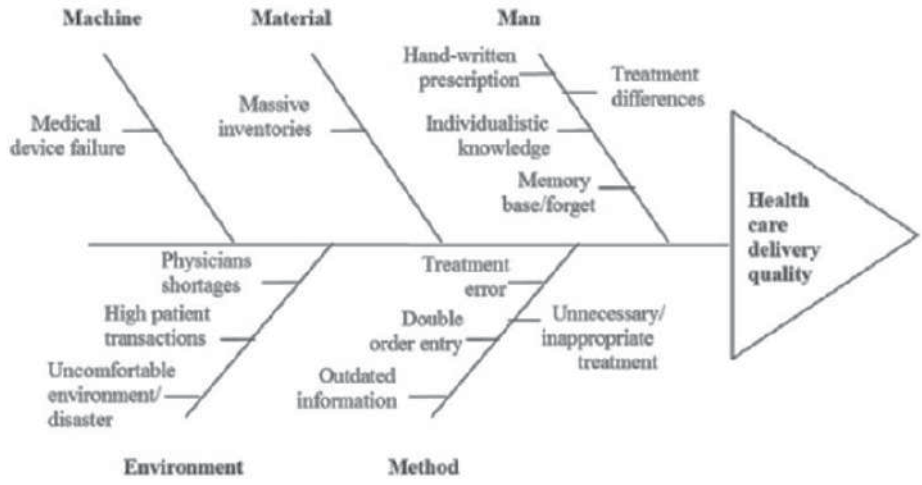
	12. Advice/feedback from AMS team members is easily accessible/available to all prescribers This can be achieved through various methods, including facility ward rounds, bedside consultations and dedicated telephone lines.		
	13. The AMS team conducts regular ward rounds and other AMS interventions in select health-care facility departments The AMS team conducts regular ward rounds (in one or more wards) and other AMS interventions in select facility departments (one or more) identified in the health-care facility AMS action plan.		
	14a. Health-care facility formulary with a list of approved antibiotics The health-care facility has a formulary with a list of approved antibiotics that may be based on national recommendations or the WHO EML.		
	14b. Health-care facility formulary with a list of restricted antibiotics The health-care facility has a formulary with a list of antibiotics approved for use in the facility and specifies a list of restricted antibiotics that require approval by the designated AMS team member (or infectious disease physician if available, physician or AMS champion) when used and/or are only permitted for specific conditions, e.g. the WATCH and RESERVE groups of antibiotics.		
	15. Laboratory and imaging services accessible to support AMS interventions The health-care facility has access to (on-site or off-site) laboratory and imaging services, and to timely, quality-assured results to support diagnosis of the most common infections.		
	16. Health-care facility access to IT services to support AMS activities The specific requirements need to be defined at local/regional/national level. This could include, for example, measurement of antibiotic use.		
	17a. Standardized facility prescription chart and medical records The health-care facility ensures the availability and use of standardized prescription charts, medical records and transfer notes.		
	17b. Health-care facility policy for documenting prescribed medicines The health-care facility has a written policy that requires prescribers to clearly document the indication and antibiotics prescribed (agent, dose, route, interval, duration and review dates) in the prescription chart, medical record and transfer notes to other health-care institutions.		

Education & training	**18. Basic training in optimal antibiotic use for health-care professionals** The health-care facility offers basic induction training (e.g. sensitization on AMR and use of standard treatment guidelines) to staff on how to optimize antibiotic prescribing, dispensing and administration.		
	19. Continued training in optimal antibiotic use for health-care professionals The health-care facility offers continued educational resources (e.g. regular training on infection management) to train staff on how to optimize antibiotic prescribing, dispensing and administration.		
	20. Initial and regular training of the AMS team in infection management The health-care facility offers initial and regular training of the AMS team in infection management (diagnosis, prevention and treatment) and AMS. This training is usually not offered at the facility level, but is likely to be available at the regional, national or international level. The facility should, however, ensure that members of the AMS team are adequately trained, according to local/national requirements.		
Monitoring & Surveillance	**21. Monitoring appropriateness of antibiotic use at the unit and/or facility-wide level through audits or PPSsi** The AMS team undertakes audits or PPSs, at the unit and/or health-care facility level, to assess the appropriateness of infection management and antibiotic prescription (e.g. indication, agent, dose and duration of antibiotic therapy in specific infectious conditions such as pneumonia or surgical prophylaxis) according to policy/guidance.		
	22. Monitoring quantity and types of antibiotic use (purchased/prescribed/dispensed) at the unit and/or facility-wide level In collaboration with the facility pharmacy, the AMS team monitors the quantity and types of antibiotic use (purchased/prescribed/dispensed) at the unit and/or health-care-facility level.		
	23. Monitoring of antibiotic susceptibility and resistance rates for a range of key indicator bacteria The AMS team monitors antibiotic susceptibility and resistance rates for a range of key indicator bacteria at the health-care facility-wide level, in alignment with national and/or international surveillance systems (e.g. GLASS).		
	24. Monitoring compliance of AMS interventions by the AMS committee The AMS committee monitors compliance with one or more of the specific interventions put in place by the AMS team (e.g. indication captured in the medical record for all patients on antibiotics).		

Reporting & Feedback	**25. Regular evaluation and sharing of health-care facility data on antibiotic use with prescribers** Health-care-facility reports on the quantity of antibiotics purchased/prescribed/dispensed are reviewed and analysed, and key findings are shared with prescribers along with specific action points.		
	26. Regular evaluation and sharing of health-care facility resistance rates with prescribers The facility reports on antibiotic susceptibility rates are reviewed, and analyses and key findings are shared with prescribers along with specific action points.		
	27. Evaluation of appropriateness of data on antibiotic use is shared with prescribers Findings from audits/reviews of the quality/appropriateness of antibiotic use are communicated directly to prescribers along with specific action points.		
	28. Health-care facility antibiogram for key antibiotics informed by data on antibiotic use and resistance The health-care facility aggregate antibiogram is developed and regularly updated based on a review and analysis of facility antibiotic use and antibiotic-resistant bacteria. The antibiogram may help to inform updates of clinical guidelines.		

ANNEX III: TEMPLATE FOR ROOT CAUSE ANALYSIS





ANNEX IV: COMPREHENSIVE LIST OF INTERVENTIONS FOR ANTIMICROBIAL STEWARDSHIP PROGRAMME

INTERVENTION	HOW TO DO IT	ADVANTAGES	DISADVANTAGES
EDUCATION Formal or informal teaching and training to engage prescribers and other HCWs in improving antibiotic prescribing, dispensing and administration practices	Basic and continuous education of clinical staff, clinical case discussions, classes and regular sharing of information, reminders and AMS e-learning resources.	Can be performed by well-informed HCWs in informal settings (i.e. ward rounds). Necessary for better adoption of most AMS interventions. Results in improved prescribing behaviours when combined with other AMS interventions (bundle).	Few AMS team members a barrier for formal training of HCWs.
TREATMENT GUIDELINES Facility treatment recommendations for common infection syndromes based on national or facility clinical guidelines, and on local susceptibility data, if available.	STG and NEMLIT	Empirical antibiotic prescribing guidelines and standard treatment guidelines lead to improved, standardized care for common infectious diseases, help prescribers select initial therapy, improve antibiotic use, and decrease cost and length of stay.	Requires broad dissemination through multiple formats and channels to ensure uptake.
SURGICAL PROPHYLAXIS GUIDELINES Facility recommendations for common surgical procedures.	Adapt surgical prophylaxis guidelines to local needs, providing antibiotic choice, dose and duration. Disseminate well: poster in the operating theatre, leaflet, apps,	Ensure timely administration and stop of appropriate antibiotic(s). Significantly reduce surgical site infections. Easier to implement than other guidelines due to few controversies around the recommendations.	Require coordination and collaboration of many disciplines in the facility.

	electronic platform. Automatic stop orders might be incorporated (see below).	Need to be disseminated to surgeons and/or anaesthetists, and supervised by pharmacists. Low-hanging fruit: once the process is optimized, only periodic monitoring and feedback are required.	
AUDIT WITH FEEDBACK Refers to the assessment of prescribed antibiotic treatment, with feedback on antibiotic treatment considered as inappropriate. Prospective (preferred) or retrospective assessment of antibiotic therapy in in-patients, performed by trained HCWs or AMS team members.	See above for audits and AMC surveillance	Essential to prescribers' education; provides specific feedback on what antibiotics they prescribe and how they prescribe them. Identifies antibiotic prescribing challenges in the unit, and shows the impact of AMS interventions on antibiotic prescribing and use (e.g. de-escalation, duration). Data may include information on indication for treatment, prescribed antibiotic(s), dosage, interval, administration route, timing of administration of first dose and duration if collected after stop of treatment. Can be performed from very basic (only indication and antibiotics prescribed per patient) to more advanced.	Time-consuming. Can be perceived as intrusive; if so, ensure data is only used confidentially for improvement in the unit.

WARDS ROUNDS Real-time assessment of antibiotics to be prescribed, or which are already prescribed, with instant feedback to prescriber.	Assess appropriateness of prescribed antibiotics for all inpatients or a group of patients (ICU, surgery, etc.), and provide real-time feedback. AMS members do ward rounds preferably with clinical staff, providing oral or written feedback. Issues to consider are redundant therapy, antibiotics prescribed (compliance with guidelines or microbiology test results), dose optimization, IV-to-oral switch and duration	Provide real-time feedback on inpatient antibiotic treatment and training of prescribers. Can be performed by clinical experts who are not AMS team members (e.g. on handover meetings between shifts).	Ward rounds are often performed by AMS teams. Frequency of ward rounds depends on human resources and burden of antibiotic use.
ANTIBIOTIC SELF-REVISION BY PRESCRIBERS Scheduled reassessment of need for and choice of antibiotics.	Involves prescribers performing a post-prescription review of antibiotics, combined with audit and feedback. A checklist may improve compliance. Consider indication for treatment, redundant therapy, antibiotics prescribed (compliance with guidelines or microbiology test results), dose	Directly involves prescribers in charge of patients in reviewing prescribed antibiotic treatment. Facilitates prescriber education and maintains prescriber autonomy. Less resource-intensive than audit and feedback.	Opposition from prescribers and lack of facility policy for implementing it. May not happen if prescribers are not prompted or comfortable with making changes. May not lead to improved appropriateness if prescribers lack expertise in infection management.

	optimization, IV-to-oral switch, duration		
FEEDBACK INTERVENTIONS			
REDUNDANT THERAPY Review of antibiotic therapy, revealing unnecessary or undesirable therapy.	A quick review of a patients' antibiotic therapy may reveal undesirable antibiotic combinations: duplication of treatment, overlapping bacterial spectra (e.g. metronidazole and clindamycin) or interactions with other medicines.	A relatively easy target for AMS interventions. Cost savings on antibiotics, and potentially reduces AMR. Reduces adverse events (e.g. nephrotoxicity, gastrointestinal side effects).	Need for trained staff who can review antibiotic therapy and provide expert advice.
REVIEW OF PRESCRIBED ANTIBIOTICS 1. DE-ESCALATION by prescribers. 2. DE-ESCALATION changes. according to guidelines. 3. DE-ESCALATION according to microbiology test results +/– 48 hours	1. Self-revision by prescriber irrespective of time and availability of microbiology test results. 2. Self-revision by prescribers or review on ward rounds on whether empirical treatment is according to guidelines (diagnosis, drug, dose, interval, administration route, duration) and patient characteristics	Can reduce costs for broad-spectrum antibiotics, and potentially reduces AMR and further facility and patient costs.	1–2. May not occur if prescribers are not prompted or are not comfortable making changes 3. Requires that microbiology sampling be done correctly, as well as quality-assured microbiology testing, timely release of results

after prescription.	3. When microbiological results become available, antibiotic treatment should be streamlined accordingly: choose the most active antibiotic(s) with least toxicity, narrowest spectrum and lowest cost. De-escalation is safe for sepsis and septic shock, and is associated with decreased mortality.		and good communication with trained prescribers.
DOSE OPTIMIZATION Review of antibiotic doses based on infection, patient characteristics, antibiotic(s) and guidelines.	Optimize dose based on age, weight, organ dysfunction (kidney) and tissue penetration. Consider therapeutic drug monitoring, if available, especially for nephrotoxic antibiotics (aminoglycosides). Evaluate the need for loading dose and/or prolonged/continuous infusions. Integrate into pharmacists' review during ward rounds or other audit processes.	Improves patient outcomes, and reduces suboptimal drug concentrations and adverse events (mainly nephrotoxicity).	Requires patient-specific data to perform the assessment, e.g. weight, renal function, indication and recommendations for dosing in special patient populations (e.g. obesity, renal dysfunction), which are not always available. May also require microbiology laboratory results (minimum inhibitory concentration) for correct dose.

IV-TO-ORAL SWITCH Promotes the use of oral antibiotics instead of IV when clinically indicated.	Consider based on: • clinical condition and availability of adequate oral antibiotic; • oral intake and gastrointestinal absorption (not impaired); • adequacy of oral intake in terms of diagnosis (e.g. not in the case of endocarditis or meningitis).	Reduces unnecessary days of IV lines and common complications. Reduces length of stay, as patients can complete antibiotic treatment at home.	May meet opposition from prescriber (and patient).
DURATION Review (real-time or retrospective) of stop dates for antibiotic treatment in patients.	Can be performed: • by prescribers during self-revision; • the entire AMS team during ward rounds; • pharmacists collecting prescriptions in every unit; • retrospectively.	Addresses a common area for improvement with regard to antibiotic prescribing. Improves patient outcomes, and prevents selection of MDR bacteria and adverse events (i.e. Clostridium difficile infection and nephrotoxicity).	May need to be individualized in e.g. immune-compromised patients or patients with central nervous system or bone infection.
RESTRICTIVE INTERVENTIONS (LIMITATIONS TO PRESCRIBING TARGETED ANTIBIOTICS)			
RESTRICTION Restricted dispensing of targeted antibiotics on the hospital's formulary, according to approved criteria (e.g. use the AWaRe categories). Use of restricted	Restrictions on antibiotics are by diagnosis or unit. Selection of restricted antibiotics is done by facility authorities, the AMS team and heads of units based on spectrum, cost or toxicities.	Controlling targeted antibiotics defined by the AMS team or hospital formulary. Shown to be highly effective, especially in the early stages of an AMS programme, in an outbreak situation or as part of a response to an increase in	May delay initiation of treatment. Opposition from prescribers due to lack of autonomy. Risk of misusing other antibiotics that do not require authorization. Labour-intensive and time-consuming because it requires enforcement to

antibiotics may be limited to certain indications, prescribers, services, patient populations or a combination of these.	Antibiotics are restricted before use; ensures expert approval before initiation. Practical approach that allows attending physician to use the drug pending approval by physician or AMS team after +/– 48 hours.	or current high use of certain antibiotics in the facility. Has been shown to reduce medicine costs for hospitals over time.	be effective.
Selective susceptibility reporting.	Report susceptible first-line narrow spectrum antibiotics to regular wards.	May reduce use of broad-spectrum antibiotics.	Opposition from prescribers, lack of guidelines, poor system support, insufficient resources.
AUTOMATIC STOP ORDERS Stop dates automatically applied to an antibiotic order when the duration is not specified to ensure that antibiotics are continued no longer than necessary.	Automatic stop orders are mostly used for a single dose of surgical antibiotic prophylaxis, or prescribing some antibiotics. Useful in small facilities and with limited pharmacy staff. Use only in a context with good control mechanisms to avoid unsafe treatment interruptions.27 Nurses can play a role in alerting the attending physician.	A simple measure, considering the high burden of antibiotics unnecessarily used for surgical prophylaxis	IT is needed, which is often missing. Unintended treatment interruptions if not properly supervised by the AMS team.
RAPID LABORATORY TESTING Stop dates	Rapid diagnostic tests allow for more accurate diagnosis and targeted	Provides quicker diagnostic results than traditional	Tests are often expensive and/or require advanced, expensive equipment that

automatically applied to an antibiotic order when the duration is not specified to ensure that antibiotics are continued no longer than necessary	antibiotic treatment.	microbiology testing	is not available in many facilities.
THERAPEUTIC DRUG MONITORING To be performed for concentration dependent antibiotics when used >3 days. This can be done especially at tertiary levels if they have the services eg MNH.	There should be a standardized procedure for collecting blood samples. The concentration of the antibiotic is measured in blood to allow for optimal adjustment of daily dose.	Fewer adverse events related to specific antibiotic treatments.	Therapeutic drug monitoring is not available in many health-care facilities.

ANNEX V: STEP-BY-STEP GUIDE FOR SETTING UP AN AMC SURVEILLANCE PROGRAMME AT THE FACILITY LEVEL

Step 1: Structures and governance

• Appoint a person/team to manage and coordinate the local surveillance system at the facility level (part of an already existing structure such as the AMS or IPC committee).

• Assign tasks and responsibilities with clear terms of reference.

Step 2: Objectives and methodology

• Define the objectives and outputs of the facility surveillance programme.

• Determine the surveillance framework with respect to hospital structure, antimicrobial classes and frequency of

data collection.

• Identify the sources of consumption data and the type of hospital activity indicator.

Step 3: Data collection and validation

• Collect consumption and hospital activity data.

• Validate and clean the data.

Step 4: Data analysis and reporting

• Identify the target groups for the results.

• Analyses and report data, taking into account the identified target groups.

• If applicable, report the data to the national surveillance system.

Step 5: Use of the data and follow-up

• Support the AMS and hospital medicines management in analysing the data.

• Improve the system to meet the requirements of the target groups.

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