Ethiopia Antimicrobial Resistance
Surveillance Plan

The Surveillance of Antimicrobial Resistance Using Public Health Laboratory-Based Sentinel Sites in Ethiopia2016–2020

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ABBREVIATIONS AND ACRONYMS

AAU	Addis Ababa University
AMR	Antimicrobial Resistance
AST	Antibiotic Susceptibility Testing
ATCC	ATCC American Type Culture Collection
CDC	Centers for Disease Control and Prevention
CLSI	Clinical and Laboratory Standard Institute
EMA	Ethiopian Medical Association
EMLA	Ethiopia Medical Laboratory Association
EPHA	Ethiopian Public Health Association
EPHI	Ethiopian Public Health Institute
EQA	External Quality Assurance
FMHACA	Food, Medicine and Health Administration and Control Authority
FMOH	Federal Ministry of Health (Ethiopia)
GHSA	Global Health Security Agenda
GLASS	The Global Antimicrobial Resistance Surveillance System (WHO)
IHR	International Health Regulation
ISO	International Organization for Standardization
IQC	Internal Quality Control
JEE	Joint External Evaluation
LIMS	Laboratory Information Management System
MIC	Minimum Inhibitory Concentration
NACARC	National Advisory Committee on Antimicrobial Resistance Prevention and Containment
NAHDIC	National Animal Health Diagnostic and Investigation Center
NCC	National Coordinating Committee
NRL	National Reference Laboratory
PFSA	Pharmaceuticals Fund and Supply Agency
RRL	Regional Reference Laboratory
SOP	Standard Operating Procedures
STG	Standard Treatment Guideline
VDAFACA	Veterinary Drug and Animal Feed Administration and Control Authority of Ethiopia
WHO	World Health Organization

1. INTRODUCTION

1.1. The Problem of Antimicrobial Resistance

Emergence of antimicrobial resistance is a result of the use, overuse and misuse of antibiotics both in humans and animals. In Ethiopia, there are indications on the misuse of antibiotics by health care providers, unskilled practitioners, and drug consumers. These coupled with rapid spread of resistant bacteria and inadequate surveillance contributed to the problem. Bacterial infections are the major causes of death in Ethiopia. Studies on antibacterial resistance and on bacterial infections have shown that emerging antibacterial resistance threatens the management of bacterial infections; however, the prevention and containment has received far too little attention. The consequences of these states of affairs include increased mortality, morbidity, costs of treatment, and loss of production in animals (Drug Administration and Control Authority of Ethiopia (DACA), 2009).

1.2. The Problem of AMR in Ethiopia

Today's health security threats arise from at least five sources (*Global Health Security Agenda-GHSA*) and one of them is the rise of drug-resistant pathogens. AMR is an increasing threat to global health security that threatens economic, social and political ramifications globally and puts an extra burden on resource-poor countries.

In Ethiopia, there are indications of the misuse of antibiotics by health care providers, unskilled practitioners, and drug consumers. These, coupled with rapid spread of resistant bacteria and inadequate surveillance, contributed to the problem. Bacterial infections are the major causes of death in Ethiopia. Studies on AMR and bacterial infections have shown that emerging AMR threatens the management of bacterial infections; however, the prevention and containment has received thus far too little attention. The consequences of these states of affairs include increased mortality, morbidity, costs of treatment, and loss of production in animals (*Drug Administration and Control Authority-DACA, 2009*).

A five-year baseline Ethiopian survey in 2009 revealed increasing resistance in many pathogens, including *Streptococcus pneumoniae*, *Salmonella* species, and *Staphylococcus aureus*. Coagulase negative staphylococci showed an increase in resistance to Erythromycin from 21.6% in 1996 to 51.9% in 2000; *Streptococcus pneumoniae* showed an increase in resistance to Erythromycin from 0% in 1996 to 18.2% in 2000; and resistance to Chloramphenicol from 0% in 1996 to 17.4% over the same period. *Salmonella* species showed an increase in resistance to Cotrimoxazole from 33.3% in 1997 to 62.5% in 2000. Resistance to Methicillin in *S. aureus* increased from 87.5% in 1996 to 100% in 2000. Some organisms have also shown high level of multidrug resistance (MDR). *Shigelladysentriae*, for example, showed an overall resistance of 31.8% to Chloramphenicol, 43.8% to Cotrimoxazole, 81% to Ampicillin, and 89.5% to Tetracycline over the five-year period (*DACA, 2009*).

Antimicrobial therapy in medical inpatients is widespread. On average every inpatient is prescribed 1.5 antibacterials, with >70% receiving from 1 to 6 different antibacterial treatments. Rational prescribing as measured by the extent of adherence to the Standard Treatment Guideline (STG) 2004 was strikingly low. For example, the drug(s) chosen and the duration of therapy comply with the STG for pneumonia in 19.6%, meningitis in 33.3%, typhoid in 24.7%, urinary tract infection in 22.6%, and relapsing fever 14.8% only (*DACA, 2009*).

A recent study from surgical site infections at St. Paul Specialized Hospital Millennium Medical College and Yekatit 12 Referral Hospital Medical College, Addis Ababa, showed that out of 107 surgical site infected patients, 84.1 % (90) were culture positive and 104 organisms were isolated. *Escherichia coli* is the predominant pathogen accounting 23.1% and MDR *Acinetobacter* species 22.1 %. More than 58 (75 %) of the Gram-negative isolates showed multiple antibiotic resistance (resistance ≥ 5 drugs). Pan-antibiotic resistance was observed in eight (34.8%) of *Acinetobacter* species and three (12.5 %) of *E. coli* (*Waleligh, et al. 2016*).

A cross-sectional study conducted from January to May 2013 at Gondar town and 55 of oral, intranasal, and locally administered herbal medicines revealed that the products contain important bacterial pathogens, including *Shigella dysentery*, *Salmonella spps*, and *Enterobacter spps*. More importantly, 125 isolates were found to be resistant to two or more antibiotics indicating the presence of antibiotic resistant pathogens in the environment such as medicinal herbs that are of public health importance (*Abdela Y, et. al.2016*)

Another cross-sectional study was conducted between January and May 2015 in and around Kombolcha town, Eastern Ethiopia among dairy animals. The study revealed that in 150 dairy cows involved in the study, *S. aureus* was isolated from 11 (73.3%) cows with clinical and 29 (42%) cows with subclinical mastitis. *S. aureus*-associated clinical mastitis was significantly higher than subclinical mastitis (p=0.028) and *S. aureus* was resistant to Penicillin G (100%), Amoxicillin (100%), Cefoxitin (42.7%) and Tetracycline (77.4%). Interestingly, all the isolates were found to be susceptible (100%) to the Gentamycin and 45.3% of the isolates were MDR (*Asmelash T, 2015*)

To determine the *E.coli* resistance pattern in poultry, 65 selected isolates from cloacal swab of broiler chickens in selected farms in Eastern Harrarge zone were subjected to nine antimicrobial agents to determine their resistance. Accordingly, the resistance of *E.coli* was tetracycline (90%), streptomycin (78%), ampicillin (60%), amoxicillin (56%), erythromycin (45%), ciprofloxacin (38%), and chloramphenicol (15%). None of the isolates showed resistance to gentamicin. Sensitivity was observed in case of 80%, 77%, 44%, 32%, 26%, 20%, 20%, 15%, and 10% of the isolates for chloramphenicol, gentamicin, ciprofloxacin, amoxicillin, ampicillin, streptomycin, erythromycin, and tetracycline, respectively. 92.3% of the isolates tested showed MDR for two or more antimicrobials and the highest levels (18.5%) of MDR *E. coli* were observed for three antimicrobials: 7.7% for tetracycline-ampicillin-streptomycin and 10.8% for tetracycline-ampicillin-amoxicillin. This study showed resistance against the antibiotics that are commonly used in poultry (*Tesfaheywet Z, et al. 2013*).

Another report from a retrospective study from Dessie Regional Referral Laboratory (RRL) conducted between September 2002 and September 2011 on urinary tract infection in the East Amhara region indicated that out of 2486 samples collected, 680 (27.35%) were bacterial isolates and the most common isolates were *E. coli*, 410 (60.29%), Pseudomonas species 59 (8.68%), Proteus species 53 (7.79%), *S. aureus* 50 (7.35%) and Klebsiella species 40 (5.88%). The *E.coli* were susceptible to

Nitrofurantoin, 43 (89.6%), Furantoin 124 (87.3%), Nalidixic acid 91 (86.7%), Kanamycin 116 (80%), and Ciprofloxacin 66 (71.7%); and vast majority of the isolates were resistant to Ampicillin, Tetracycline, and Trimethoprim-Sulfamethoxazole. Pseudomonas and Proteus species were resistant to almost all antibiotics listed above (except for Gentamycin) (*Asrat A, et al. 2016*).

In Ethiopia, reports indicate that there are wide practices of misuse of antimicrobials by health care providers, unskilled practitioners, animal husbandry operations, and drug users. These, coupled with the rapid spread of resistant microbes and inadequate surveillance, have exacerbated the problem.

Surveillance and research are essential in guiding management of infectious diseases and updating infection control policies and practices, antimicrobial use, medicines lists, and STGs. Inadequate surveillance and research means that resistance prevalence and trends are not known and that baseline data for evaluating potential interventions are unavailable (*Food, Medicine and Health Administration and Control Authority-FMHACA, 2011*).

Although, different data are available about AMR, they are fragmented and not presented in a systematic manner to address the prevailing problem of the country. In Ethiopia, there is no formal AMR surveillance system in place; hence, a working AMR surveillance system with the active involvement of all regions and partners is urgently needed.

It is known that AMR threatens the effectiveness of successful treatment of infections in humans, animals, and infections acquired from environments that require a range of interventions and multidisciplinary team approaches.

Several published and unpublished research data have been generated from the various health sciences universities in Ethiopia. These indicate that drug resistant bacteria, including MDR, are also isolated from humans, animals, food, water, and other environmental samples that need a multidisciplinary intervention through a One Health approach that emphasizes humans, animals, and environmental microorganisms.

1.3. AMR and One Health

Humans and animals are often susceptible to the same disease-causing microbes, including AMR pathogens. To combat AMR appropriately and effectively, concerted collaborative efforts are necessary across the human health (human medicine), animal health (veterinary medicine), and environment sectors. Therefore, it needs an integrated approach, a One Health approach that considers humans, animals, and the environment, thereby ensuring a robust response to the threat of AMR.

Approximately 60% of all human infectious diseases recognized so far, and about 75% of emerging infectious diseases that have affected people over the past three decades, have originated from animals (*WHO*). In the past 30 years, more than 30 new infectious diseases have emerged (*WHO*). The contact between human and wild animal habitats is increasing, introducing the risk of exposure to new viruses, bacteria, and other disease-causing pathogens.

Ethiopia is an agrarian (agricultural) society with over 80% of the population located in rural areas living in close proximity to domestic and wild animals in a sensitive ecosystem. The public health is inextricably linked to animal health and production. This intense contact can lead to a serious risk to public health, including emerging and re-emerging zoonoses.

Antimicrobials used in both humans and animals are similar and can be over-prescribed for therapeutic and prophylactic purposes, and as feed additives, and can cause resistance.

1.3.1. One Health and AMR threat in Ethiopia

FMOH and the robust Ethiopian scientific community have embraced a One Health approach considering the interaction of human, livestock, and environment/ecology as a binding factor in addressing the health of these populations. The recently-enforced Ethiopian AMR containment strategies (*Strategy for the Prevention and Containment of Antimicrobial Resistance for Ethiopia, FMHACA*) include promotion of optimized use of antimicrobials in human and animal health through effective stewardship practices, and strengthening the knowledge and evidence on antimicrobial use and resistance through One Health surveillance and research.

A recent Global Health Security Agenda (GHSA) and Ethiopian FMOH joint external evaluation (2016), using the WHO's International Health Regulation (IHR) Joint External Evaluation (JEE) tool, declared that in Ethiopia both the animal and public health sectors have AMR testing capacity. Based on the joint assessment the team recommended the following priority actions: strengthen AMR surveillance systems; increase AMR laboratory capacity, improve infection prevention and control activities in the health facility, foster inter-sectoral collaboration, AMR networking and continuous stakeholder communication, and implement an AMR stewardship program within the animal health and public health sectors.

It is the expectation of the Ethiopia AMR Surveillance System that parallel surveillance will be established for the monitoring of animal and environmental AMR, including an AMR network with a shared database and planning of activities to maximize the outcome of surveillance activities. Discussions are currently in progress on the planning and implementation of these parallel surveillance systems. The consideration of the information from these distinct but interrelated surveillance systems will provide a One Health AMR perspective and strengthen the conclusions that can be drawn. In line with this, a national AMR advisory committee and AMR sub-technical working groups have been established, including representatives from human, animal, and environmental sectors, to facilitate and ensure the national strategy to combat AMR is functional. Moreover, the current collaboration with the Ohio State University (OSU) that advances One Health globally would pave the way to the integration of One Health in the Ethiopian health system. The important implication of the One Health approach is that it can have significant impacts on Ethiopia's strategies in control of infectious diseases, including AMR-caused health challenges, and would ultimately lead to promoting optimal health outcomes for people, animals, and the environment.

The goal of this national AMR surveillance plan is following the national AMR strategy and based on public health laboratories to generate evidence on the burden of AMR among priority pathogens isolated in hospitals from inpatients and outpatients during the initial 2017–2020 implementation period.

2. Ethiopian Public Health Laboratory-Based AMR Surveillance Plan

2.1. Objectives

The objectives of the present AMR surveillance plan are to:

1. Asses and support in building the capacity (antimicrobial susceptibility testing, AST, AMR) of identified AMR surveillance sentinel laboratories
2. Establish a nationwide surveillance network
3. Estimate the extent and burden of priority AMR pathogens
4. Analyze and report national data on a regular bases
5. Detect emerging resistance and characterize national spread
6. Generate evidence to inform the implementation of targeted prevention and control programs
7. Eventually transfer the AMR surveillance data to the national One Health system.

2.2. Major Activities

The AMR surveillance plan will attain its goal through undertaking the following major activities:

1. Identify and prioritize sites for AMR surveillance
2. Develop and implement manuals, standard operating procedures and forms
3. Standardize antimicrobial susceptibility testing across the network
4. Conduct training
5. Strengthen the laboratory supply chain system
6. Create national and site level databases for AMR
7. Establish systems for the regular reporting of AST results
8. Develop and implement a national repository system for AMR isolates
9. Prepare and disseminate AMR annual reports.

3. Implementation of the Plan

AMR surveillance will be conducted in public health laboratories that have the capability of performing microbiology laboratory tests. The initial implementation period will be between 2017 and 2020. For the purpose of implementing this plan, existing microbiology laboratories in the country are categorized into three levels:

- Level-1: Laboratory site has microbiologic capability (isolation and identification); AST and EQA participation with enhanced specimen collection and patient clinical data capture.
- Level-2: Laboratory site has microbiologic capability and is regularly performing testing according to established national testing requirements.

- Level-3: Laboratory site has limited microbiologic capability and is not regularly performing AST on patient samples.

Ethiopia's most recent assessment (FMOH) indicated that 35 laboratories can provide microbiology testing services with varying capacities that fall into one of the three categories. In this regard, 16 sites were identified to belong to Level-1; 9 to Level-2; and 10 to Level-3. The ultimate goal is to enroll all labs into the surveillance network by 2020.

Sixteen Level-1 laboratory sites are proposed for initial rollout of this plan (Table 1). There will be rapid expansion to additional facilities based on success in building capacity. Program success will guide scaling-up of the surveillance sites.

Table 1: Level-1 Antimicrobial Resistant Surveillance Sites, Ethiopia.

S.N.	Sites	Region
1	Yekatit 12 Hospital	Addis Ababa
2	TikurAnbessa Specialized Hospital	Addis Ababa
3	St. Paul Hospital	Addis Ababa
4	Zewditu Hospital/Addis Ababa Regional Laboratory	Addis Ababa
5	Ayder Referral University Hospital	Tigray
6	Metu Karl Hospital	Oromia
7	Nekemte Hospital/Nekemt Regional Laboratory	Oromia
8	Adama Referral Hospital/Adama Regional Laboratory	Oromia
9	Jimma Referral University Hospital	Oromia
10	FelegeHiwot Referral Hospital/BD Regional Laboratory	Amhara
11	Dessie Referral Hospital/ Dessie Regional Laboratory	Amhara
12	Gondar Referral University Hospital	Amhara
13	Hawassa Referral University Hospital	SNNP
14	HiwotFana Hospital/Harari Regional Laboratory	Harari
15	Alert Hospital	Addis Ababa
16	EPHI (National Bacteriology Reference Laboratory)	Addis Ababa

SNNP: Southern Nations, Nationalities, and Peoples' Region

3.1. Surveillance Site Preparation

The Ethiopian Public Health Institute (EPHI) used a standardized assessment tool (Appendix 1 & 2) to define the proposed AMR surveillance level for that site. The tool included document and record, data management and reporting, organization, personnel, facility and safety, equipment, purchasing

/inventory, quality management (quality control/quality assurance), and bacteriology (isolation, identification, and AST).

It will be the primary step of the implementation plan to build the AMR testing capacity by filling the gaps identified for each site. The laboratory sites within Level-1 have been further divided into three implementation sub-groups based on the recent AMR capacity assessment results (Table 2).

Table 2. Level-1 AMR Surveillance Implementation Sub-Groups.

Implementation Sub-groups	Sites
I	• EPHI (National Bacteriology Reference Laboratory) • Tikur Anbessa Specialized Hospital • Ayder Referral University Hospital • Dessie Referral Hospital/Dessie Regional Laboratory
II	• Yekatit12 Hospital • Gondar Referral University Hospital • FelegeHiwot Referral Hospital/BD Regional Laboratory • Hawassa Referral University Hospital • Jimma Referral University Hospital • Adama Referral Hospital/Adama Regional Laboratory
III	• Alert Hospital • HiwotFana Hospital/Harari Regional Laboratory • Zewditu Hospital/Addis Ababa Regional Laboratory • Nekemte Hospital • St. Paul Referral Hospital • Metu Karl Hospital

Sub-groups are designated as better, moderate, and relatively less performing. In order to implement the stated plan, the following activities will be implemented for Level-1 laboratory sites.

Table 3. Key Activities and Timeline to be performed for Level-1 Sites, Ethiopia, September 2016.

Serial No,	Key Activities	Responsible Organizations	Timeline	Remarks
1	Conducting laboratory assessment at sites	EPHI	November 2016	Standard tools developed by CDC and ASM shall be used
2	Harmonizing AMR SOPs and other manuals	EPHI, ASM	February 2017	SOPs will be developed when needed
3	AMR supplies will be distributed to sub-group I and II sites	EPHI, CDC. ASM	June 2017	AMR training and surveillance supplies

4	Conducting workshop (AMR sensitization) with all sites	EPHI, ASM	June 2017	All AMR surveillance participating sites shall be invited
5	Conducting AMR training for sub-group- I	EPHI, ASM	June 2017	Hands on AMR laboratory training. This depends on the availability of procured AMR supplies
6	Conducting AMR Data management training for sub-group I	EPHI, WHO	June 2017	"WHO net" Software This applies also for sub-group II and III following their scheduled AMR trainings
7	Post-AMR training follow up	EPHI, ASM	July, 2017for sub-group I	This applies also for sub-group II and III two weeks following their scheduled AMR trainings
8	Strengthening quality management system including EQA follow-up	EPHI, ASM	April 2017	Continuous process as of this period
9	Conduct clinical specimen training for AMR surveillance sites	EPHI, OSU	August 2017	Finalized clinical specimen training curriculum by April 2017
10	AMR workshop for clinicians (harmonizing laboratory and clinics)	EPHI, OSU	August 2017	All Level-1 sites
11	Conducting AMR training for sub-group II	EPHI, ASM	July 2017	Hands on AMR laboratory training. This depends on the availability of AMR supplies
12	AMR supplies will be distributed to sub-group III sites	EPHI, ASM	End of July 2017	
13	Conducting AMR training for sub-group III	EPHI, ASM	September 2017	Hands on AMR laboratory training
14	In-country capacity building for panel production	EPHI, CDC, ASM, ASLM	September 2017	At EPHI

Both Level-2 and Level-3 sites will obtain training, mentorship, supplies and fulfilling workforce to be enrolled in the surveillance system. Finally, overall evaluation of the Ethiopian AMR Surveillance System based on this surveillance plan will be performed during the beginning of 2020.

3.2. Surveillance System Sustainability and Resource Dedication

The Ethiopian FMOH has made a commitment to fund and support the Ethiopia AMR Surveillance System during and after the initial 2017–2020 implementation period. This commitment will be mandated in the (forthcoming) legislation on National Reporting of AMR Organisms. In review of the final AMR Surveillance System evaluation and in light of national priorities, FMOH will determine the extent this commitment will be maintained into the future.

Activities and Timetable	2016		2017				2018				2019				2020
	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Strategic plan preparation															
Plan ratified															
Basic training equipment & supplies to all levels															
Level-1 site															
Conducting workshop (sensitization) on AMR surveillance															
AMR Training Laboratory															
AMR workshop for clinicians (harmonizing laboratory and clinics)															
Surveillance activities															
First round surveillance evaluation															
First-Year AMR Report															
Level-2 site															
Conducting workshop (sensitization) on AMR surveillance															
AMR Training Laboratory															
AMR workshop for clinicians (harmonizing laboratory and clinics)															
Surveillance activities															
Second surveillance evaluation															
Second AMR report															
Level-3 site															
Conducting workshop (sensitization) on AMR surveillance															
AMR Training Laboratory															
AMR workshop for clinicians (harmonizing laboratory and clinics)															
Surveillance activities															
Third surveillance evaluation															
Third-Year AMR Report															
Overall evaluation of the AMR system															

4. Description of the AMR surveillance plan

4.1. Surveillance approach

In this surveillance plan, clinical specimens will be collected from sites. Specimens will be cultured and, for culture positive priority organism(s), AST will be performed. Patient information and laboratory data will be collected using a standardized form. AMR surveillance data will be entered into a computerized database at the site level and also saved as hard copy. Collected data and all isolates will be transported to National Reference Laboratory (NRL) (Figure 1).

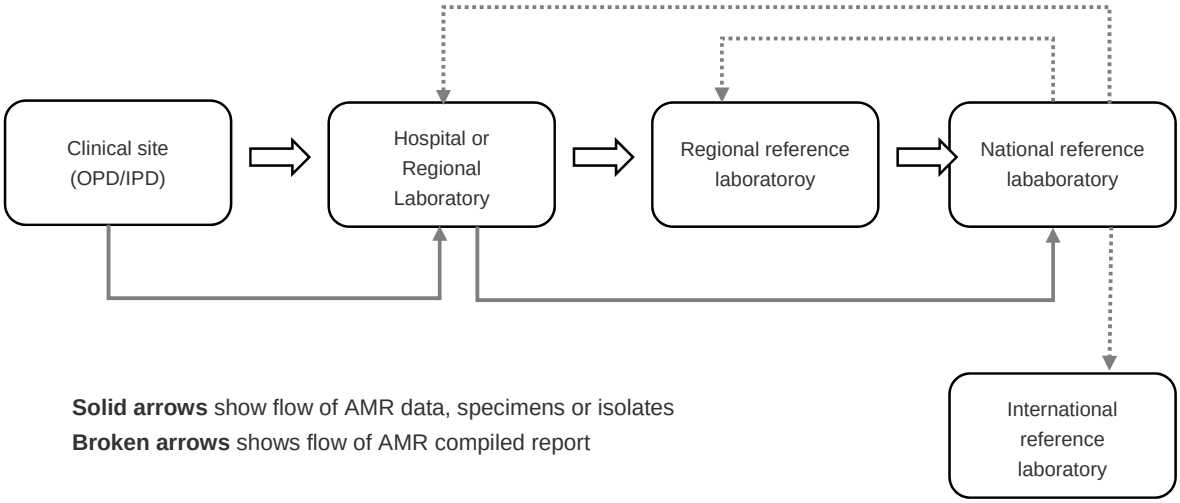

Figure 1. Describing Flow of AMR Isolate, Data and Report, Between Sites, Regional Laboratories and NRL.

All AMR data will be entered into the WHO.net database at sites and NRL, and back-up data will be generated regularly. All AMR priority isolates will be transported to NRL for isolate repository and possible further testing based on isolate transportation the SOP. The isolates which were not identified at the site level will be done at NRL. Ten percent of all isolates collected from sites will be cultured for quality assurance at NRL. Discrepant results will be further investigated by NRL for correction.

4.2. Data Reporting

All AMR data generated at all sites will be entered into the WHO.net database at sites and NRL. AMR back up data will be generated at NRL regularly.

5. Priority Organisms and Antibiotic Sensitivity Testing (AST)

AST will be conducted according to Standard Operating Procedures (SOPs) that have been reviewed and harmonized, as needed, through the NRL. All SOPs will adhere to the most current Clinical and Laboratory Standard Institute (CLSI) guidelines. Priority specimens and organisms for this surveillance plan are shown on Table 5. Priority organisms and antimicrobial combinations for which susceptibility testing will be conducted are shown on Table 6.

If necessary, specimens, pathogens, and pathogen-antimicrobial combinations identified may change during the surveillance period (2017-2019). Prioritized specimen types and pathogens will consider current public health priorities and public health laboratory capacity. Principles for considerations of priority pathogen-antimicrobial combinations selections include:

- Current Ethiopian Standard Treatment Guidelines (STG)
- Antibiotic availability
- Current international guidelines (e.g., CLSI)
- WHO's Global Antimicrobial Resistance Surveillance System (GLASS)

Based on WHO's GLASS, the following priority pathogens are identified to be considered for the Ethiopian AMR surveillance (Table 5).

Table 5. Priority surveillance pathogens by specimen for inclusion in Ethiopia AMR surveillance.

Specimen	Basic Laboratory Case Definition	Priority Surveillance Pathogens
Urine	Significant growth in urine specimen	• *Escherichia coli* • *K. pneumoniae*
Wound	Isolation of pathogen in the presence of pus (Gram smear shows presence of pus with associated organism)	*Staphylococcus aureus*
Other (any specimen)	Significant growth	Carbapenem resistant: • *Acinetobacter spp* • *Pseudomonas aeruginosa* • *Enterobactericeaespp*

Similarly, priority pathogens and corresponding antimicrobials targeted for the plan are selected based on WHO's Global AMR Surveillance System (GLASS) and CLSI M100, 2017 (Table 6). Specimen types and priority pathogen list and corresponding antimicrobial agents may be revised depending on the implementation and progress of the surveillance strategy.

Table 6: List of Priority Pathogens and Corresponding Antimicrobials, September 2016.

Pathogen	Antibacterial Class	Agents that may be used for AST
Escherichia coli	Sulfonamides and Trimethoprim	Co-trimoxazole,
	Fluoroquinolones	Ciprofloxacin or Levofloxacin
	Third-generation Cephalosporins	Ceftriaxone or Ceftazidime
	Fourth-generation Cephalosporins	Cefepime,
	Carbapenems	Imipenem, Meropenem, Ertapenem Doripenem,
	Polymyxins	Colistin
	Penicillins	Ampicillin
Klebsiella pneumoniae	Sulfonamides and trimethoprim	Co-trimoxazole
	Fluoroquinolones	Ciprofloxacin or Levofloxacin
	Third-generation Cephalosporins	Ceftriaxone or Cefotaxime and Ceftazidime
	Fourth-generation Cephalosporins	Cefepime,
	Carbapenems	Imipenem, Meropenem, Ertapenem or Doripenem,
	Polymyxins	Colistin
Acinetobacter baumannii	Tetracyclines	Tigecycline or Minocycline,
	Aminoglycosides	Gentamicin and Amikacin,
	Carbapenems	Imipenem, Meropenem, Ertapenem or Doripenem,
	Polymyxins	Colistin
Staphylococcus aureus	Penicillinase-stable beta-lactams	Cefoxitin
Pseudomonas aeruginosa	Aminoglycosides	Gentamicin, Tobramicin, Amikacin
	Fluoroquinolones	Ciprofloxacin, Levofloxacin
	Penicillin	Piperacillin, Piperacillin/Tazobactam
	Third-generation Cephalosporins	Ceftazidime
	Carbapenems	Imipenem, Meropenem, Doripenem

6. AMR Surveillance Standards

6.1. Laboratory Standards

Minimum AMR surveillance laboratory site capabilities and requirements are outlined in Table 7. Laboratory surveillance sites must meet the basic technical laboratory skill, IQC, EQA, and data management minimum capabilities to participate in the Ethiopia AMR Surveillance System. A standardized assessment tool (Appendices 1 and 2) will be used to assess each proposed site. The assessment will be used to both determine eligibility to participate and to identify any deficient areas to be addressed prior to the AMR surveillance start.

Table 7. Minimum Requirements for Laboratory Participation as a Surveillance Site in the Ethiopia AMR Surveillance System

Capacity	Minimum Requirements
Technical laboratory	• Identify priority organisms and perform AST in accordance with WHO or CLSI standards • Perform AST by using disc diffusion, semi-automated, or manual testing for minimum inhibitory concentration and gradient diffusion
skills	• Utilize a NRL-approved IQC system • Maintain IQC data records for potential review by NRL
IQC	• Participate in a recognized international EQA program • Achieve acceptable performance reviews on periodic EQA dispatches
EQA	• Make commitment to collect and report good-quality data in accordance with reporting timelines • Employ staff trained in collecting, analyzing, and reporting epidemiological, clinical, and laboratory data • Dedicate time for staff member(s) to regularly input, analyze, and report data

6.2. Clinical Specimen Submission Standards

As part of routine clinical care, clinicians at surveillance hospitals will send specimens for culture and AST from patients with suspected infection to the laboratory. The hospital or regional referral laboratory director will ensure that physicians and other healthcare workers are provided with specimen collection SOPs and a laboratory requisition form (Appendix 3), which is to be submitted to the hospital or regional diagnostic laboratory with each specimen. The laboratory requisition form will include patient-level data that should be submitted with specimen.

It is the responsibility of the laboratory/surveillance site to ensure that clinicians have the appropriate containers and materials for priority specimen collection and that an adequate supply of these materials is maintained at all times. Laboratorians who suspect that specimen collection SOPs are not being followed (e.g., high level of specimen contamination with environmental organisms, hemolyzed

samples) should meet directly with the clinical team to review and agree upon measures to improve specimen collection procedures.

Laboratory/surveillance site leadership together with NRL will meet with relevant clinical department leadership and other stakeholders to discuss the initiation of hospital AMR surveillance. The National AMR surveillance system will allow laboratorians to review the format and implications of AST results provided to clinicians, alert clinicians to the availability of hospital AMR data, and foster clinician-laboratory communication for discussion of AMR organisms in individual patients, at the hospital, and the regional level.

6.3. Pathogen Isolations, Identification, and AST

Surveillance laboratories must have the capacity to identify priority organisms and perform AST. Sampling, culturing, and species identification according to good clinical laboratory practice (GCLP) as described in current CLSI manuals. For AST, the disc diffusion methods recommended by CLSI, semi-automated or manual testing for minimum inhibitory concentration (MIC), and gradient diffusion can be used. All AST methods must conform to ISO (International Organization for Standardization) standards, which are compatible with CLSI standards. In addition to susceptible (S), intermediate (I), and resistant (R) classifications, MIC (if available) and inhibition zone diameter will be recorded by participating laboratories. When a new antibiotic is introduced into clinical practice, laboratories should routinely test susceptibility to the drug in order to identify emerging resistance. The NRL will be primarily informed when unusual or unexpected findings in routine samples encounters at surveillance laboratories.

6.4. Clinical Isolates Transportation of Standards

Clinical isolates will be transported to NRL following the standard SOP for isolate transportation. The isolate will be transported from site to NRL bimonthly by using the excising postal system.

6.5. IQC and EQA

Surveillance site laboratories are required to follow current guidelines for microbiology laboratory IQC as published by CLSI. Surveillance site laboratories will review the components of their IQC system with NRL in their initial assessment before implementation. All laboratories supposed to be part of the AMR sentinel site must participate and score more than 80% in EQA program facilitated by EPHI. IQC data records (e.g., testing of batch/lot of media, reagents, discs) should be kept and available for review with the RRL or NRL, as requested.

6.6. Laboratory Supply, Procurement, and Equipment Maintenance

Surveillance site laboratories participating in the Ethiopia AMR Surveillance system are responsible for ensuring appropriate inventory management of all necessary reagents and supplies that are mandatory for isolation, identification, and AST of priority pathogens. Surveillance site laboratories are

required to request their annual need of reagents and supplies to NRL for replenishment before stock out. They are also responsible for adhering to and keeping records of proper equipment maintenance and replacing equipment when needed.

A primary concern with commercial media purchase is the shelf life and consistency of the supply. Therefore, reagents and supply procurements need to be coordinated with NRL and RRL. Additionally, the NRL will coordinate procurement and supply of American Type Culture Collection (ATCC) Strains form approved supplier for respective priority organisms.

If necessary, surveillance laboratories can receive training support for inventory management, supply purchasing, and equipment maintenance from the NRL. The NRL will also maintain a list of quality supplies and suppliers.

6.7. Data Reporting Standards

The validity and efficiency of data collection, transmission, and analysis is a principle concern of any surveillance program. AMR surveillance sites should enter patient clinical and lab results data in a reliable digital data management system. As needed, the NRL will assist laboratories in data management setup and training. Where possible, automated data entry (i.e., from testing equipment to laboratory information systems), data export, and report generation will be used to help ensure the quality and consistency of AMR data and to decrease work burden for laboratory staffs.

Although AST data for all isolates received by a surveillance laboratory could be reported as AMR surveillance (isolate-based surveillance), it is more informative to report AST results specifically linked to patient infections and reported with some clinical data. Under patient-based surveillance, AST results might not be reported if they are from a duplicate specimen or if multiple specimens are submitted for culture during the course a single patient infection. Patient-based surveillance strives to count the AST profiles of each individual infection only once.

The surveillance definition for patient-based reporting is: priority pathogen isolated from a single specimen taken from a clinically ill patient (e.g., *E. coli* in the blood of a septic patient). If that same patient has another *E.coli*-positive blood culture, it would not be counted. However, if the same patient has a blood culture positive for a different organism (e.g., *K. pneumoniae*), or if the original organism is later found in another specimen type (e.g., *E. coli* in urine), both these incidents would be counted as separate infections. To comply with the surveillance definition, de-duplication of non-unique infections will be conducted prior to reporting.

6.8. Clinical and Regional Laboratory Reporting system

All sentinel sites send AMR raw data to the NRL on monthly bases through email. NRL aggregates and analyzes the data and send report to the sites quarterly.' who.net' software will be used for AMR data management. For each priority specimen type (i.e., urine, wound), the following raw will need to be sent to NRL:

- Total number of submission of that specimen type
- Number of culture-negative submissions
- Number of submissions positive for each priority pathogen
    - Pathogen type
    - Patient age
    - Patient sex
    - Duration of stay in hospital at time of specimen collection
- All AST results for each priority pathogen-specimen combination, by:
    - Patient age
    - Patient sex
    - Time in hospital at time of specimen collection.

Hospital laboratory sends data to the NRL in a monthly basis between the first day and third day of the next month (that means for e.g. data from the month of January will be reported February 1-3). Each laboratory must also save all electronic files and hard copies on a local computer or data server as a redundancy. The data should be submitted using a uniform file name format that includes a three-character laboratory code (will be designated for each laboratory), month, year. For example, "BMH012016.xls" would be the name of the January 2016 Monthly AMR data for BMH laboratory.

Once a year, surveillance laboratories will be asked to provide updated estimates of hospital and population data, including:

- Number and demographics of patients seeking care (separately for inpatient and outpatient)
- Size and demographics of population served by hospital

In addition to providing prompt patient laboratory results to individual clinicians on a daily basis, it is recommended that monthly AMR summaries be shared with the relevant clinical department and hospital committees, as applicable, at the hospitals of the surveillance site laboratories. It should be a goal of surveillance laboratories to create individualized hospital reports, such as antibiograms, to assist in the overall understanding of AMR organisms in that hospital and community. Diagnostic stewardship, the use of an individual patient's culture and AST results to determine the most appropriate and effective treatment plan, should be an important goal for participating hospitals.

6.9. National and Global Reporting

AMR data from surveillance sites will be centrally stored and managed at each responsible tiered level. NRL will be responsible for conducting data analysis and generating official AMR summary reports of the country and will send all AMR data to the FMOH. Reports will be published and distributed annually, and when indicated, as special interim reports or focused analyses. Reporting of aggregate national and regional AMR data may be used to efficiently prioritize resources and inform policies directed at control of AMR.

Every 12 months, data gathered from all AMR surveillance sites will be aggregated at NRL and reported to WHO. In accordance with the WHO's GLASS suggested protocol, NRL may submit population, laboratory, and patient data. Reporting of national aggregate AMR data to WHO, or other

international stakeholder, will help ensure that the AMR situation in Ethiopia is captured by the global health community.

7. Roles and Responsibilities of the Surveillance Network

AMR surveillance will engage hospitals and public health microbiology laboratories at different levels throughout the public health system to allow more informed decision-making. Roles and responsibilities at each level are presented throughout this document and summarized below:

7.1. Hospital Clinical Sites

- *Clinical Stakehold*ers: Hospital administrators and health care providers who will be responsible for AMR surveillance activities.
- Assign a clinical focal person, with commitment to the AMR.
- Frequent communication between the clinical focal personnel and laboratory.
- Requesting the necessary laboratory tests based on the symptomatic and clinical diagnosis.
- Filling the required requisition forms completely and accurately.
- Submission of priority specimens per approved specimen collection SOP.
- Annual provision of background hospital and population data to NRL.

7.2. Hospital / Regional Reference Laboratories (RRL)

- Manage priority specimens according to the SOP.
- Identify the pathogen accurately and perform the AST according to the SOP.
- Send all identified priory pathogen isolates to the NRL.
- Report aggregate AST data as described in this document.
- Prompt communication of patient-level AST results to clinical providers.
- Train new staff on necessary SOPs when applicable.
- Ensure overall quality assurance including sustainable supply chain management.
- Compile the antibiogram data and share for the hospital therapeutic committee.
- Send raw data to NRL.

7.3. Regional Reference Laboratories (RRL)

- Regional storage of AMR data.
- Prepare regional report on AMR data Provide trainings and mentorship on AMR to sentinel sites with NRL and other partners.
- Monitoring and evaluation of the AMR sentinel site level implementation.
- Engage in overall quality assurance including sustainable supply chain management.

7.4. National Reference Laboratory NRL/EPHI

- Lead and coordinate the implementation of the AMR surveillance plan of the country.
- Ensure SOPs used by individual laboratories as harmonized for AMR surveillance.
- Set minimum requirements for the execution of AMR surveillance.
- Ensure that reporting of aggregate AST results met AMR surveillance system requirements.
- Maintain the national AMR surveillance database and serve as repository of isolates.
- Perform confirmatory and additional advanced tests for AMR isolates.
- Continually ensure AMR data quality.
- Perform annual surveillance program evaluations.
- Report annual aggregate AMR data to FMOH, WHO, and other stakeholders as needed.
- Provide trainings to sentinel sites with RRL and other stakeholders.
- Ensure the sustainable supply chain system for AMR surveillance.
- Feed data from this AMR surveillance into the national One Health system as per the national guidance.
- Overall quality assurance of the implementation of AMR surveillance.

7.5. International Stakeholders

- In general, support in building the laboratory capacity in Ethiopia in identifying and reporting AMR microorganisms
- Provide technical (trainings, mentorships, workshops, assessments, monitoring visits, etc) and material (reagent, equipment, training materials, ex, books, etc) support in implementation of the Ethiopia AMR surveillance works
- Work in close contact with EPHI, among others in capacity building of laboratories and assuring quality AMR data
- In consultation with FMOH/EPHI, include Ethiopia AMR data in global reporting of AMR burden

7.6. AMR National Advisory Committee

Secretary: EPHI

Member organizations:

FMHACA; Pharmaceuticals Fund and Supply Agency (PFSA); Veterinary Drug and Animal Feed Administration and Control Authority of Ethiopia (VDAFACA); WHO; U.S. Centers for Disease Control and Prevention (CDC); Ethiopian Medical Association (EMA); Ethiopia Medical Laboratory Association (EMLA); Ethiopian Public Health Association (EPHA); National Animal Health Diagnostic and Investigation Center (NAHDIC); Addis Ababa University (AAU) Schools of Pharmacy, Laboratory Technology, and Medicine; and Ethiopian FMOH.

Roles and responsibilities:

A multi-sectorial advisory committee (including Ministry of Health, Ministry of Livestock and Fishery, and others) was convened to revise the national plan to align with the Global Action Plan for AMR

(GAPAMR). GAPAMR is the result of resolution WHA67.25 from the Health Assembly in May 2014, reflecting a global consensus that antimicrobial resistance poses a profound threat to human health.

7.7. GHSA-AMR Sub-Technical Working Group (GHSA-AMR TWG)

Secretary: will be assigned

Member organizations: EPHI directorates and teams: Bacteriology and Zoonosis, Regional Capacity Building; Food Microbiology; FMHACA; CDC-Ethiopia; FMOH directorate for Infection Prevention; VDAFACA; Aklilu Lemma Institute of Pathobiology; and WHO.

Roles and responsibilities: Provide technical assistance and technical leadership on antimicrobial resistance (AMR) surveillance, AMR detection, prevention and control programs and antimicrobial stewardship activities and assist in the development and implementation of a coherent national framework for current and future work related to AMR surveillance. This will ensure that issues are identified within a congruent One Health framework, and that there is accountability for progress and outcomes on AMR.

8. Monitoring and Evaluation (M & E)

Monitoring and evaluation of the Ethiopia AMR Surveillance System will begin at the end of 2017 (6-month surveillance evaluation) (Table 3). M & E of the AMR surveillance system will be conducted by an evaluation team from EPHI/NRL. M & E indicators (performance indicators) will be used to describe performance of the AMR site and determine the overall effectiveness of the program (Appendix 4). Results of surveillance evaluations will be reported to NRL and RR, and disseminated by EPHI to decision-makers to assist in making adjustments to the Ethiopia AMR surveillance system for the next year. This evaluation process will be repeated annually.

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