



# Global Antimicrobial Resistance Surveillance System

Manual for Early Implementation

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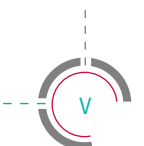
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## Abbreviations

AMR	antimicrobial resistance
AST	antimicrobial susceptibility testing
CAESAR	Central Asian and Eastern European Surveillance of Antimicrobial Resistance
CLSI	Clinical and Laboratory Standards Institute
EARS-Net	European Antimicrobial Resistance Surveillance Network
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GLASS	Global Antimicrobial Resistance Surveillance System
NCC	national coordinating centre
NRL	national reference laboratory
ReLAVRA	Latin American Antimicrobial Resistance Surveillance Network





# 1. Introduction

## 1.1 Background

Antimicrobial resistance (AMR) is the development of resistance in microorganisms—bacteria, viruses, fungi and parasites—to an antimicrobial medicine to which it was previously sensitive. AMR in a wide range of infectious agents is a growing public health threat of huge concern to countries and to many sectors. Especially alarming is the rapid global spread of multi-resistant bacteria that cause common infections and that resist treatment with existing antimicrobial medicines.

In May 2015, the Sixty-eighth World Health Assembly adopted the Global Action Plan on Antimicrobial Resistance,<sup>1</sup> which reflects the global consensus that AMR poses a profound threat to human health. One of the five strategic objectives of the Global Action Plan is to strengthen the evidence base through enhanced global surveillance and research. AMR surveillance is the cornerstone for assessing the burden of AMR and for providing the necessary information for action in support of local, national and global strategies.

Global surveillance programmes that monitor resistance in specific bacterial pathogens, such as *Mycobacterium tuberculosis*<sup>2</sup> and *Neisseria gonorrhoeae*<sup>3</sup>, have been in place for many years. In addition, a number of regional surveillance programmes have been monitoring resistance in selected geographical areas, such as the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR), the European Antimicrobial Resistance Surveillance Network (EARS-Net) and the Latin American Antimicrobial Resistance Surveillance Network (ReLAVRA).

Despite the success of these programmes in gathering data over many years, significant gaps remain in surveillance of many other bacterial pathogens that cause common infections in humans. These gaps, together with a lack of common standards for methods, data-sharing and coordination at local, national, regional and global levels, are hampering efforts to produce meaningful data at a global level to enable comprehensive monitoring and analysis of the occurrence and trends of resistance worldwide<sup>4</sup>.

International standards on AMR surveillance and monitoring programmes exist for some aspects of animal health,<sup>5</sup> however standards across the medical, veterinary, agricultural and environmental sectors are not harmonized, except for foodborne and zoonotic bacteria.<sup>6</sup> Furthermore, the proposed WHO standards for collecting data and reporting on AMR in human health<sup>7</sup> are yet to be widely implemented. No global forum currently exists for rapid sharing of standardized information on AMR.

In a meeting hosted by the Swedish Ministry of Health and Social Affairs and the Public Health Agency of Sweden,<sup>8</sup> 30 WHO Member States, from all WHO regions, reaffirmed the need for a global programme for surveillance of AMR of relevance to human health, to form the basis for local, national and regional action and to monitor the effectiveness of interventions. Participants in the consultation also agreed on the surveillance approach proposed by WHO and presented in this manual.

<sup>1</sup> Global Action Plan on Antimicrobial Resistance, 2015 ([http://apps.who.int/gb/ebwha/pdf\\_files/WHA68/A68\\_20-en.pdf?ua=1](http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_20-en.pdf?ua=1)).

<sup>2</sup> Global tuberculosis report 2014. Geneva: World Health Organization; 2014 ([http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/)).

<sup>3</sup> The Gonococcal Antimicrobial Surveillance Programme (GASP). Geneva: World Health Organization ([http://www.who.int/reproductivehealth/topics/rtis/gonococcal\\_resistance/en/](http://www.who.int/reproductivehealth/topics/rtis/gonococcal_resistance/en/)).

<sup>4</sup> Antimicrobial resistance: global report on surveillance 2014. Geneva: World Health Organization; 2014 (<http://www.who.int/drugresistance/documents/surveillance-report/en/>).

<sup>5</sup> Terrestrial animal health code. Paris: World Organisation for Animal Health (<http://www.oie.int/international-standard-setting/terrestrial-code/access-online/>).

<sup>6</sup> Integrated surveillance of antimicrobial resistance. Guidance from a WHO Advisory Group. Geneva: World Health Organization; 2013 ([http://www.who.int/foodsafety/publications/agisar\\_guidance/en/](http://www.who.int/foodsafety/publications/agisar_guidance/en/)).

<sup>7</sup> Surveillance standards for antimicrobial resistance. Geneva: World Health Organization; 2001 ([http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_5/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_5/en/)).

<sup>8</sup> Surveillance of antimicrobial resistance for local and global action. Stockholm, 2–3 December 2014. Stockholm: Folkhälsomyndigheten; 2014 (<http://www.folkhalsomyndigheten.se/amr-stockholm-2014/about-the-conference/>).



## 1.2 Global Antimicrobial Resistance Surveillance System (GLASS)

The Global Antimicrobial Resistance Surveillance System (GLASS) is being developed to support the Global Action Plan on Antimicrobial Resistance and should be coordinated within the national action plans of countries. The goal of GLASS is to enable standardized, comparable and validated data on AMR to be collected, analysed and shared with countries, in order to inform decision-making, drive local, national and regional action and provide the evidence base for action and advocacy.

GLASS combines patient, laboratory and epidemiological surveillance data to enhance understanding of the extent and impact of AMR on populations. In view of the challenges of collecting all these data, countries should consider gradual implementation of the surveillance standards proposed in this manual on the basis of their priorities and resources.

This manual focuses on early implementation of GLASS, comprising surveillance of resistance in common human bacterial pathogens. The intended readership of this publication is national public health professionals and national health authorities responsible for surveillance of antibacterial resistance in humans.

This manual describes the GLASS standards and a road map for evolution of the system between 2015 and 2019. Further development of GLASS will be based on the lessons learnt during this period.

## 1.3 Objectives of GLASS

GLASS will collect, analyse and report harmonized data on infected patients, aggregated at national level, following the standard definitions described in this manual. The objectives of GLASS are to:

- foster national surveillance systems and harmonized global standards;
- estimate the extent and burden of AMR globally by selected indicators;
- analyse and report global data on AMR on a regular basis;
- detect emerging resistance and its international spread;
- inform implementation of targeted prevention and control programmes; and
- assess the impact of interventions.

Use of the surveillance standards proposed in GLASS could also improve patient safety by promoting diagnostic stewardship (section 3.2.3) for responsible use of antimicrobial agents and ensuring quality-assured, standardized identification of bacteria and antimicrobial susceptibility testing (AST) in patient management. As nationally aggregated data may not provide the specific information required for decisions on treatment at local level, local data should be used as a basis for treatment guidelines whenever possible.

## 1.4 Road map

Early implementation of GLASS will cover the period 2015–2019. During this period, GLASS will provide the standards and tools for routine surveillance based on microbiological and clinical information on priority bacterial infections in humans, start country enrolment and produce global reports on GLASS implementation and AMR rates.

GLASS will initially concentrate on the antibiotic-resistant bacteria that are the greatest threats globally, particularly those that are resistant to several drugs thereby limiting therapeutic options. The priorities of different countries and regions vary; thus the proposed components of GLASS, the specimens to be collected, the pathogens to be surveyed and the types of resistance are not definite but will be updated as necessary.

Cases will be detected from the results of AST of specimens sent to laboratories and core clinical information.

Another surveillance approach to be explored and progressively included in GLASS is case-based surveillance of clinical syndromes (Annex 1). This type of surveillance is more complex but can provide more accurate and less biased information than routine surveillance, and should be pursued at sites with the necessary capacity.

The GLASS data-sharing platform will allow progressive incorporation of information from other surveillance systems related to AMR in humans, such as for foodborne AMR<sup>9</sup>, monitoring of antimicrobial use and surveillance of infections associated with health care (see Table 1).

To support early implementation, GLASS will provide guidance to Member States in compiling harmonized, standardized AMR surveillance data, and in sharing these data to form a global picture. The initiative will also support use of methods for compiling relevant data nationally and locally (at surveillance sites), where systems are not already in place or where the proposed infections and pathogens of global priority are not already covered by surveillance. Patient and population data will be collected from national surveillance sites to monitor resistance among bacteria that are causes of common infections and shared in order to avoid duplication of work. For global containment of AMR, common markers of resistance to different antimicrobial drugs have been defined, which are described in this document.

Subject to the availability of resources, GLASS will promote studies to provide information that is not readily available from routine surveillance, such as supplementary information on the AMR burden (e.g. morbidity, mortality, cost), the effects of interventions and potential drivers of AMR.

Member States can enrol in GLASS in a stepwise manner; participating countries will be requested to provide information on the national surveillance system and on AMR rates. Progress in setting up or strengthening national surveillance and reporting of data to GLASS will be monitored and reported. Member States are not obliged to provide data on all the defined priority pathogens but are encouraged to monitor as many as possible and to build the necessary capacity. GLASS should build upon existing surveillance systems to inform national and global efforts. While coverage of specimens and microorganisms may be limited during early implementation, the results should nevertheless be of good quality and representative of the population monitored.

This manual:

- provides guidance to those responsible for AMR surveillance nationally on participation in global antibacterial resistance surveillance in humans, including the collection, compilation and sharing of data;
- proposes steps for the development of national surveillance systems and adherence to GLASS; and
- provides indicators for measuring implementation of a national surveillance programme.

The results of early implementation will be evaluated, and the lessons learnt will inform revision of the manual and extension of the global network to additional countries.

<sup>9</sup> Integrated surveillance of antimicrobial resistance. Guidance from a WHO Advisory Group. Geneva: World Health Organization; 2013 ([http://www.who.int/foodsafety/publications/agisar\\_guidance/en/](http://www.who.int/foodsafety/publications/agisar_guidance/en/)).

**Table 1.** Five-year road map for implementation of GLASS

Year	Targets
2015	<p>Prepare manual, set up IT hub and plan support for implementation of GLASS.</p> <p>Establish a platform for international collaboration with WHO collaborating centres, national and regional networks and other laboratories and institutions to allow WHO to support countries in implementing GLASS.</p> <p>Initiate country enrolment.</p>
2016	<p>Start collection of baseline data on human antibacterial-resistant infections from WHO Member States.</p> <p>Report on progress in implementation.</p> <p>Target the participation of 15% of Member States.</p>
2017	<p>Consolidate baseline data collection on human antibacterial-resistant infections from WHO Member States.</p> <p>Increase the capacity of the platform to build relations with other AMR surveillance systems (e.g. in animal health, agriculture and use and consumption of antibiotics).</p> <p>Extend Member States participation to 20%.</p>
2018	<p>Report on the global and regional AMR data in human health.</p> <p>Explore the feasibility of case-finding by surveillance of clinical syndromes at selected surveillance sites.</p> <p>Extend Member States participation to 30%.</p>
2019	<p>Review lessons learnt from early implementation to inform further development of GLASS.</p> <p>Extend Member States participation to 40%.</p>

## 2. Surveillance methods

### 2.1 Routine surveillance and case-finding based on routine clinical samples of priority specimen types

Cases will be found among routine clinical samples by AST of defined specimen types from patients selected for sampling at surveillance sites according to local practice. Basic demographic and epidemiological information will be collected on each patient and on the population covered to identify their characteristics. AST results will thus be combined with the patient data that accompany every request for AST (Annex 2) and related to population data from the surveillance site.

The priority specimens and pathogens for AMR surveillance of routine clinical samples are listed in Table 2.

Table 2. Priority specimens and pathogens for surveillance of AMR

Specimen	Laboratory case definition	Surveillance type and sampling setting	Priority pathogens for surveillance
Blood	Isolation of pathogen from blood <sup>a</sup>	Selected sites or national coverage Continuous Patients in hospital and in the community	<i>E. coli</i> <i>K. pneumoniae</i> <i>A. baumannii</i> <i>S. aureus</i> <i>S. pneumoniae</i> <i>Salmonella</i> spp.
Urine	Significant growth in urine specimen <sup>b</sup>	Selected sites or national coverage Continuous Patients in hospital and in the community	<i>E. coli</i> <i>K. pneumoniae</i>
Faeces	Isolation of <i>Salmonella</i> spp. <sup>c</sup> or <i>Shigella</i> spp. from stools	Selected sites or national coverage Continuous Patients in hospital and in the community	<i>Salmonella</i> spp. <i>Shigella</i> spp.
Urethral and cervical swabs	Isolation of <i>N. gonorrhoeae</i>	Selected sites or national coverage Continuous Patients in hospital and in the community	<i>N. gonorrhoeae</i>

<sup>a</sup> Any pathogen isolated from a blood culture may be significant for surveillance locally and nationally; only the prioritized pathogens for global surveillance are listed here.

<sup>b</sup> Pure culture according to local laboratory practice. Catheter samples should be excluded if possible.

<sup>c</sup> Diarrhoeal surveillance is for non-typhoid salmonella species; for local clinical purposes, typhoid and paratyphoid should be included.

The surveillance targets for GLASS are:

- all patients sampled for prioritized specimens (both positive and negative samples)
- all patients sampled for prioritized specimens with growth of priority species (only positive samples).

### 2.1.1 Population

GLASS will collect information on the population of individuals from whom data are obtained. In order to estimate the extent of AMR in a population accurately, the population size in the catchment area of surveillance sites should be known for accurate estimation of surveillance coverage and the AMR burden in the population. It may be difficult to obtain this information and particularly to use a consistent method globally. Although this information will not be requested at this stage of GLASS implementation, countries that already routinely collect this information are encouraged to continue. For the purposes of early implementation of GLASS, countries will be requested to submit the following information:

- the total national population;
- the numbers of patients seeking care over 12 months at surveillance sites in outpatient clinics (e.g. number of consultations) and in inpatient facilities; and
- the numbers of patients with positive and negative cultures per specimen type and with susceptible and non-susceptible pathogens for each priority pathogen–antibiotic combination per specimen type, stratified according to core patient data:
  - age: the age groups reported in the Global Health Observatory;
  - gender;
  - hospital or other type of in-patient care facility: patient admitted for > 2 calendar days when the specimen was taken or admitted to the health care facility for < 2 calendar days but transferred from another health care facility where he or she was admitted for ≥ 2 calendar days; and
  - community: patients cared for at outpatient clinics or patients in hospital for ≤ 2 calendar days when the specimen was taken.

Specimens collected from hospital patients will be used as a proxy for hospital-acquired infections, and those collected from patients in the community will be considered a proxy for community infections.

All data must be aggregated at national level before submission to GLASS. It is recommended that the surveillance coordination centre maintain individual data for detection of errors and quality control. The WHONET software has been adapted to facilitate data entry at surveillance sites, reporting to national surveillance centres and aggregation of data at national level for automatic generation of the reporting forms.

Examples of the metrics to be generated are given in Annex 1.

### 2.1.2 Removal of duplicate results

When several cultures are collected during patient management, duplicate findings for the same patient should be excluded (de-duplication). For each surveillance period (e.g. 12 months), only one result should be reported for each patient per surveyed specimen type and surveyed pathogen. For example if two blood cultures from the same patient yield growth of *E. coli*, only the first should be included in the report; if growth of *E. coli* detected in one culture and of *K. pneumoniae* in the other, both results should be reported. If there is growth of *E. coli* in one blood culture and in one urinary culture from the same patient, both specimen types should be reported. If possible, repeated negative results for the same specimen type in the

same patient should also be de-duplicated.

### 2.1.3 Period for national surveillance

Surveillance should be continuous and aggregated at national level every 12 months and as per the national surveillance schedule.

### 2.1.4 Reporting to WHO

The national coordination centre (NCC) should report aggregated data to WHO annually. Outbreaks of resistant pathogens, new resistance or unexpected findings should be reported to the relevant national authorities as soon as they are confirmed by a reference laboratory, and WHO should be informed.

WHO will update data on a web-based platform regularly and will issue a global report every second year.

## 2.2 Priority pathogen–antibacterial combinations on which GLASS will gather data

AMR can be detected only by microbiological methods; therefore, samples must be taken from patients for species identification and AST. At this stage of GLASS, AST results will be used as a marker of AMR. Other properties of microorganisms that might be characterized for different aspects of antibacterial resistance (e.g. resistance mechanisms, genetic markers) could be addressed later in the development of GLASS.

During early implementation of GLASS, AST results will be classified according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI)<sup>9</sup> or the European Committee on Antimicrobial Susceptibility Testing (EUCAST).<sup>10</sup> The results for the priority pathogens and antibiotics listed in Table 3 will be classified as susceptible (S), intermediate (I), resistant (R), or not tested or not applicable.

<sup>9</sup> Performance standards for antimicrobial susceptibility testing: twenty-fifth informational supplement. Wayne, Pennsylvania: Clinical and Laboratory Standards Institute; 2015 (M100-S25).

<sup>10</sup> EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance. European Committee on Antimicrobial Susceptibility Testing; 2015 (<http://www.eucast.org>). At time of publication of this manual, EUCAST is available free of charge. National committees for disc diffusion testing in Europe, and an increasing number of countries outside of Europe, now endorse the EUCAST guidelines.

**Table 3.** Pathogen–antimicrobial combinations on which GLASS will gather data

Pathogen	Antibacterial class	Antibacterial agents that may be used for AST <sup>a,b</sup>
<i>Escherichia coli</i>	Sulfonamides and trimethoprim Fluoroquinolones Third-generation cephalosporins Fourth-generation cephalosporins Carbapenems <sup>c</sup> Polymyxins Penicillins	Co-trimoxazole Ciprofloxacin or levofloxacin Ceftriaxone or cefotaxime and ceftazidime Cefepime Imipenem, meropenem, ertapenem or doripenem Colistin Ampicillin
<i>Klebsiella pneumoniae</i>	Sulfonamides and trimethoprim Fluoroquinolones Third-generation cephalosporins Fourth-generation cephalosporins Carbapenems <sup>c</sup> Polymyxins	Co-trimoxazole Ciprofloxacin or levofloxacin Ceftriaxone or cefotaxime and ceftazidime Cefepime Imipenem, meropenem, ertapenem or doripenem Colistin
<i>Acinetobacter baumannii</i>	Tetracyclines Aminoglycosides Carbapenems <sup>c</sup> Polymyxins	Tigecycline or minocycline Gentamicin and amikacin Imipenem, meropenem or doripenem Colistin
<i>Staphylococcus aureus</i>	Penicillinase-stable beta-lactams	Cefoxitin <sup>d</sup>
<i>Streptococcus pneumoniae</i>	Penicillins Sulfonamides and trimethoprim Third-generation cephalosporins	Oxacillin <sup>e</sup> Penicillin G Co-trimoxazole Ceftriaxone or cefotaxime
<i>Salmonella</i> spp.	Fluoroquinolones Third-generation cephalosporins Carbapenems <sup>c</sup>	Ciprofloxacin or levofloxacin Ceftriaxone or cefotaxime and ceftazidime Imipenem, meropenem, ertapenem or doripenem
<i>Shigella</i> spp.	Fluoroquinolones Third-generation cephalosporins Macrolides	Ciprofloxacin or levofloxacin Ceftriaxone or cefotaxime and ceftazidime Azithromycin
<i>Neisseria gonorrhoeae</i>	Third-generation cephalosporins Macrolides Aminocyclitols Fluoroquinolones Aminoglycosides	Cefixime Ceftriaxone Azithromycin Spectinomycin Ciprofloxacin Gentamicin

<sup>a</sup> The listed substances are priorities for surveillance of resistance in each pathogen, although they may not be first-line options for treatment. One or more of the drugs listed may be tested.

<sup>b</sup> One or more of the drugs listed may be tested in countries. S, I, R and nominator and denominator data for each shall be reported separately.

<sup>c</sup> Imipenem or meropenem is preferred to represent the group when available.

<sup>d</sup> Cefoxitin is a surrogate for testing susceptibility to oxacillin (methicillin, nafcillin); the AST report to clinicians should state susceptibility or resistance to oxacillin.

<sup>e</sup> Oxacillin is a surrogate for testing reduced susceptibility or resistance to penicillin; the AST report to clinicians should state reduced susceptibility or resistance to penicillin.

The antimicrobial substances against which resistance or non-susceptibility will be monitored were selected because either they are commonly recommended first-line treatment or surrogate substances for resistance in drugs commonly used to treat patients, or the pathogen–antimicrobial combination is of particular concern because of limited treatment options. As GLASS evolves, the list may be modified and other pathogens and antimicrobial substances included.

### 2.3 Priority specimen types to be assessed

Data on bacterial resistance in human infections to be entered into GLASS will be obtained from the following specimens:

- blood
- urine
- faeces
- urethral and cervical swabs.

The rationale for choosing these specimen types is that they represent infections in the bloodstream, urinary tract, gastrointestinal tract and gonorrhoea. These infections are common, and an alarming increase has been seen in resistance to drugs of last resort. Although patients with uncomplicated urinary tract infection are not routinely sampled, these samples are most likely to give an indication of emerging resistance in Gram-negative bacteria. Furthermore, blood and urinary tract pathogens can often be identified by accurate, uncomplicated laboratory methods.

Although respiratory tract infections are also common, collection of respiratory tract samples is not included in early implementation because of the difficulty in correlating the pathogens found with infection. They may be included in later stages of implementation. Other important sites of infection and pathogens are not covered in this initial phase. The purpose of drawing up a limited list is to simplify global data gathering and reporting for early implementation. **Countries should cover the sites of infection, pathogens and AST that they consider to be priorities in their surveillance systems.**

Early implementation will indicate the global relevance and feasibility of extending the infection sites and pathogens in the next phases. Its aim is to collect information on defined priority pathogen–specimen combinations; however, **countries can join GLASS even if they can provide information on only some of the combinations** and increment coverage progressively, according to their needs and resources.



## 3. Participation in GLASS

### 3.1 Enrolment

WHO will invite Member States to participate in GLASS by an open call on the WHO website (<http://www.who.int/drugresistance/surveillance/en/>). Member States that commit themselves to collecting and sharing the data required by GLASS will participate in early implementation and will be given capacity-building IT tools (see 3.4). As countries have different surveillance systems at different stages of development, flexibility will be built into the system, so that each country can implement or strengthen the core components of a national AMR surveillance system and generate high-quality data to meet both local needs and GLASS requirements. Therefore, enrolled countries may start reporting to GLASS only on the implementation status of the surveillance system prior to sending actual AMR data. Countries that are already producing the data required by GLASS can submit these data upon enrolment.

### 3.2 Requirements for participation

#### 3.2.1 National coordinating centre

A national coordinating centre (NCC) should be set up to oversee the national AMR surveillance system, including the collection and aggregation of data from surveillance sites, to ensure that the system is functional. Its mandate should include defining national AMR surveillance objectives within the national AMR strategy, preparing and coordinating dissemination of national protocols, coordinating data collection, analysis and reporting, and sharing nationally aggregated data with WHO (GLASS). The NCC should continuously monitor and evaluate the national surveillance system. The NCC function is usually undertaken by a public health institute; other institutes may be considered more suitable, but they must have access to both laboratory and epidemiological expertise and have a defined structure for surveillance coordination and data management. The NCC should define a strategy for gradual implementation of the surveillance standards proposed by GLASS and identify a focal point for communication with WHO.

Ideally, the NCC should have links to AMR surveillance in animals, so that ultimately it can coordinate AMR surveillance in both human and animals, with a national focal point for AMR surveillance.

#### 3.2.2 National reference laboratory

At least one public health or academic laboratory with expertise in methods for characterizing antimicrobial-resistant pathogens should be nominated as the national reference laboratory (NRL) for AMR surveillance. It will be required to provide participating institutions guidance and technical support in AST and quality management (including participation in external quality assurance schemes) and to confirm unusual or new resistance patterns before they are reported to the relevant national authority. The NRL(s) should liaise with the NCC in standardizing and verifying microbiological results. If capacity for fulfilling NRL tasks is not yet available within a country, collaboration can be temporarily established with an appropriate institute in another country.

#### 3.2.3 AMR surveillance sites

The NCC should organize enrolment of surveillance sites. The number of sites will depend on the country, and no single algorithm applies for determining the appropriate number. Participating countries are expected to establish at least one surveillance site and then extend the number progressively, aiming for a balanced geographical, demographic and socio-economic distribution. Inpatient and outpatient health care facilities are usually appropriate surveillance sites; the inclusion of specialty outpatient clinics may be

considered for some priorities, such as sexually transmitted infection clinics for AMR surveillance in patients with gonorrhoea.

The surveillance site(s) should have access to appropriate epidemiological and laboratory support so as to provide basic demographic, clinical, epidemiological and microbiological information from tested clinical specimens.

### **Epidemiology capacity**

Capacity to collect and report good-quality data and a commitment to undertake and sustain surveillance are two of the most important criteria for selecting a surveillance site. Surveillance sites must have responsible personnel who are trained in collecting, analysing and reporting epidemiological, clinical and laboratory data. This includes the capacity to understand and analyse basic demographic information from the population covered by the surveillance site, to organize and analyse data manually or by means of an IT tool and to produce timely reports on a regular basis.

### **Laboratory capacity**

On-site laboratory capacity for testing specimens facilitates surveillance but is not essential if the site can store and transport samples rapidly to a central testing facility. Surveillance sites must be linked to at least one laboratory with the capacity to identify the pathogens and perform susceptibility tests. Sampling, culture and species identification must be performed according to good laboratory practice, as described in WHO manuals<sup>11</sup> and textbooks, as recommended by the NRL. For AST, the disc diffusion methods recommended by CLSI<sup>12</sup> or EUCAST<sup>13</sup>, semi-automated or manual testing for minimum inhibitory concentration and gradient diffusion can be used. All the methods should be internationally recognized. WHO will collect only susceptibility data categorized as “susceptible”, “intermediate” and “resistant”, but it recommends that the minimum inhibitory concentrations and inhibition zone diametres also be collected at national level whenever possible, to allow quality control of the data, comparing old and new results, tracking microbiological subpopulations in outbreak investigations, etc.

When a new drug is introduced into clinical practice, laboratories should routinely test susceptibility to the drug in order to identify emerging resistance. Staff should be trained to recognize and raise alerts on any unusual or unexpected findings in routine samples.

Laboratories at participating surveillance sites should use a quality management system recognized by the NRL to ensure the accuracy, reliability and timeliness of reported results. All aspects of laboratory testing required to isolate and identify an infectious agent and to detect resistance must be controlled for quality according to appropriate WHO manuals<sup>14</sup> and CLSI or EUCAST guidelines. All laboratories that provide data to an AMR surveillance system must participate in a proficiency testing scheme recognized by the NRL that covers antimicrobial susceptibility testing.

<sup>11</sup> Manual for the laboratory identification and antimicrobial susceptibility testing of bacterial pathogens of public health importance in the developing world. Geneva: World Health Organization; 2003 ([http://www.who.int/drugresistance/publications/WHO\\_CDS\\_CSR\\_RMD\\_2003\\_6/en/](http://www.who.int/drugresistance/publications/WHO_CDS_CSR_RMD_2003_6/en/)) and Basic laboratory procedures in clinical bacteriology. Geneva: World Health Organization; 2003 (<http://whqlibdoc.who.int/publications/2003/9241545453.pdf>).

<sup>12</sup> Performance standards for antimicrobial susceptibility testing: twenty-fifth informational supplement. Wayne, Pennsylvania: Clinical and Laboratory Standards Institute; 2015 (M100-S25).

<sup>13</sup> EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance. European Committee on Antimicrobial Susceptibility Testing; 2015 (<http://www.eucast.org>). At time of publication of this manual, EUCAST is available free of charge. National committees for disc diffusion testing in Europe, and an increasing number of countries outside of Europe, now endorse the EUCAST guidelines.

<sup>14</sup> Laboratory diagnosis of sexually transmitted infections, including human immunodeficiency virus. Geneva: World Health Organization; 2013 (<http://www.who.int/reproductivehealth/publications/rtis/9789241505840/en/>).

### Diagnostic stewardship programme

The quality of surveillance based on routine data can be improved by diagnostic stewardship, which is an integral part of both clinical management and standardized surveillance. “Diagnostic stewardship” is coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate, timely diagnostic testing, collection and identification of specimens and accurate, timely reporting of results to guide patient treatment.

Clinicians must be given timely, systematic guidance and training in conducting relevant diagnostic activities in order to minimize sampling bias due to variations in how patient samples are sent for microbiological analysis. Clinicians should complete a standard form containing patient data, that should accompany every sample sent for AST (see Annex 2). Microbiology laboratories should support clinicians in diagnosing infectious disease syndromes and in choosing the best therapeutic option; they should also provide assistance in detecting new types of AMR and outbreaks of infection. Optimal patient care depends on effective communication between personnel at points of care and microbiology laboratories.

Diagnostic stewardship, as well as encouraging the active participation of clinicians as a means to improving patient outcomes, will also promote participation in the global surveillance system.

### 3.3 Proposed steps in setting up a national AMR surveillance system

The proposed steps in setting up national AMR surveillance are as follows:

1. Establish a national surveillance coordinating body with a focal point and a data management structure.
2. Define the surveillance objectives to:
  - assist the planning and monitoring of the national strategies to control AMR
  - inform global efforts to control AMR.
3. Define a strategy for gradual implementation of the national surveillance system and participation in GLASS.
4. Establish at least one national reference laboratory that participates in an external quality assurance scheme.
5. Identify AMR surveillance sites, that have access to epidemiological support and a microbiology laboratory, and promote diagnostic stewardship.
6. Develop or adapt national protocols for:
  - data collection (see annexes 2 and 3)
  - laboratory protocols
  - diagnostic stewardship
  - data flow.
7. Disseminate protocols and tools, and train staff in their use.
8. Start collecting data on progress or status of implementation (Annex 4) and on AMR (see section 2 and annexes 2 and 3).
9. Report information on the AMR situation to inform the national strategy, and report aggregated data to GLASS to inform global strategies.
10. Ensure that monitoring and evaluation include pilot-testing of any new surveillance approach, a review of steps, and adjustment of processes as necessary.

### 3.4 Collection, management, analysis and reporting of data

#### 3.4.1 Collection and management of data at local surveillance sites

Clinicians at the participating health care facilities will send a sample for culture and AST from patients with suspected infection to the laboratory serving the surveillance site. AST is usually performed locally; however, in countries with limited capacity, samples for AST may be sent to a reference laboratory. The minimum core patient data that should accompany any request for AST are: age, gender, specimen type, date of sampling and whether from a hospital or the community (see section 2.3 and Annex 2 for a sample form).

Participating surveillance sites should enter data into data management software. Sites that do not yet have suitable software for efficient data management and reporting can use the free WHONET<sup>15</sup> software, which can be used on stand-alone computers or linked to through existing information systems. The software is currently used in hospital, public health, veterinary and food laboratories in over 110 countries and is available in over 20 languages. The BacLink software of WHONET can be used in most laboratory information management systems to export local data files to WHONET, so that they can be shared with the national AMR data manager. WHONET includes a feature for exporting resistance statistics into the format required for producing local and national reports and for uploading to the GLASS web interface. Small surveillance sites with few events and without WHONET or another data management system can use paper forms for submission to the national AMR data manager.

Some countries already have systems for sending reports from health care facilities to the national level. Each national surveillance system should decide whether to report anonymized individual test results (“line data”) or aggregated data, depending on capacity. Duplicates should be removed (de-duplication) and the data checked for quality before submission to the NCC, or the NCC should remove duplicates. If de-duplication is done locally, the NCC could conduct new checks for duplicates and data quality.

#### 3.4.2 Collection and management of data at national level

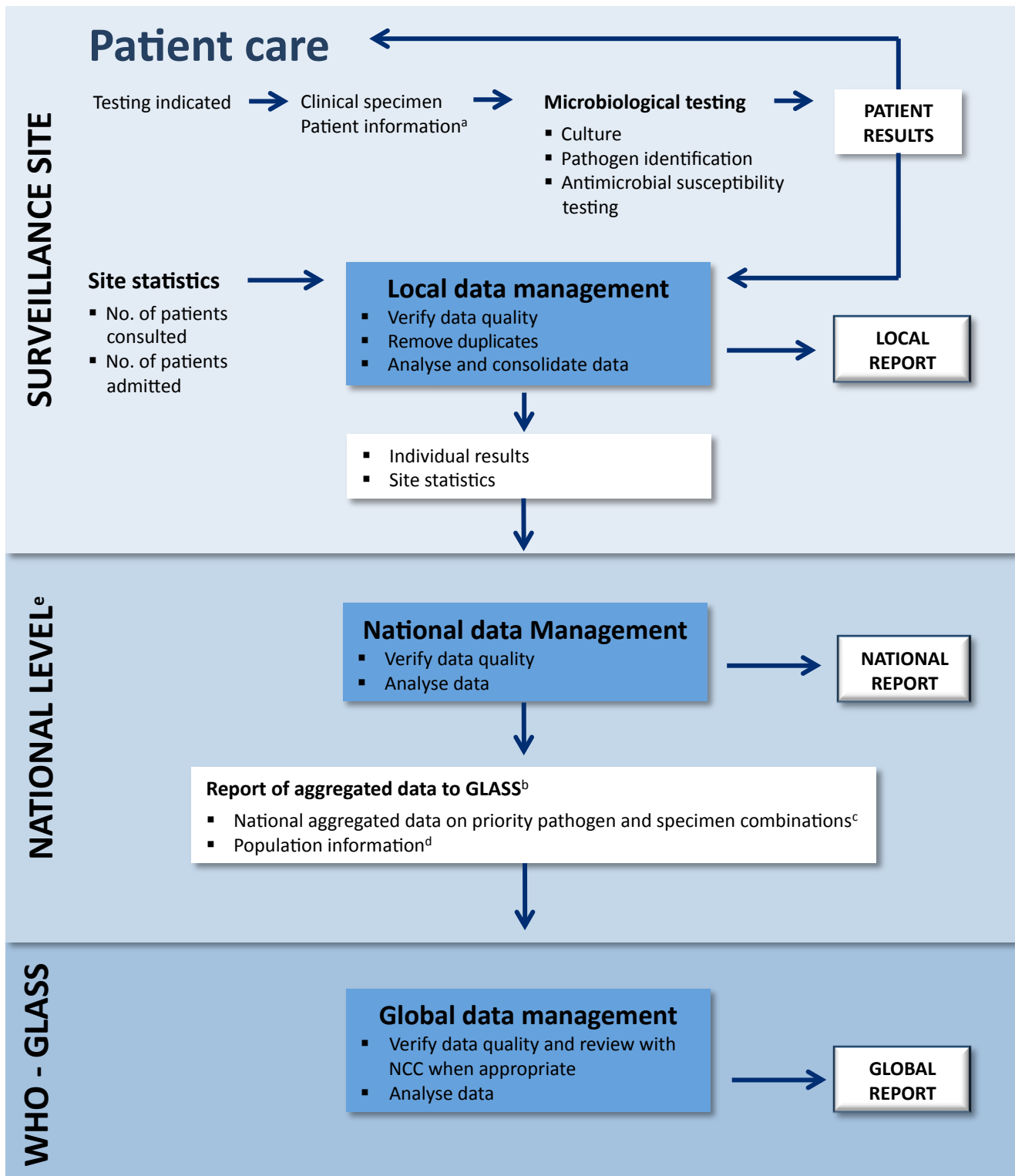
Data received from surveillance sites must be aggregated as described in Annex 3 and submitted electronically to WHO. One of the aims of GLASS is to promote national surveillance systems with harmonized global standards. In addition to the data set required by GLASS, a more comprehensive approach is recommended at national level, including other species and specimen types as per national policy. The benefits of such an approach for countries include:

- characterization of the frequency of resistance, organisms and, when available, antimicrobial agents used in different facilities and regions;
- prospective and retrospective information on emerging public health threats;
- information on the geographical spread of priority pathogens and phenotypes in the country and identification of community and health care-associated outbreaks;
- evaluation and optimization of national standard treatment guidelines;
- assessment of the performance of participating facilities and mentoring them for optimal analysis and presentation of results; and
- prospective collection of new data, including first appearance and spread, which must be reported to GLASS, particularly if any of the priority pathogens shows resistance to all antimicrobial agents.

A schematic view of the AMR information flow is shown in Figure 1.

<sup>15</sup> WHONET software and educational tutorials. (<http://www.who.int/drugresistance/whonetsoftware/en/>).

Figure 1. Schematic view of information flow



- Core patient information: age, date of birth, gender, specimen type, date of specimen collection, hospital or community origin, use of antimicrobial agents (see Annex 2).
- Structure for reporting aggregated data at country level given in Annex 3.
- Priority pathogen-specimen combinations are listed in Tables 2 and 3.
- Population information as described in 2.1.1.
- National level includes the national surveillance coordinating centre and the national reference laboratories.

### 3.4.3 Data to be reported to WHO

WHO should be informed of progress in implementing the core components of national AMR surveillance systems, rates of AMR from the aggregated data required by GLASS and reports of unusual types of AMR.

The proposed indicators of implementation of GLASS are listed in Annex 4. A framework covering both the indicators selected for global reporting and those in the national AMR surveillance plan will be used to monitor and evaluate national AMR surveillance.

The rates of AMR should be submitted with a web-based IT tool, which will be made available to the NCC when a country enrolls. The tool will provide an interface that allows multi-site data entry and centralized data storage, retrieval, analysis and sharing. In due course, it will be extended to form a global AMR repository, which may also include data on use of antimicrobial agents and other types of surveillance, including data from the veterinary and agricultural sectors.

Unusual types of AMR should be confirmed by the NRL and reported to the relevant national authority before being communicated to GLASS.

### 3.4.4 Data quality management, analysis and reporting

A global report on AMR surveillance, including progress in establishing surveillance capacity, quality and reporting at national and regional levels, will be produced every two years. Data showing the progress of countries and trends in resistance will be published and made available on the website.

## 3.5 WHO support for GLASS activities and capacity-building

Countries participating in GLASS will have access to a web-based platform for data sharing, management and reporting; and a support package that includes implementation tools, surveillance software (WHO-NET), capacity-building activities and assistance in monitoring and evaluation for low-income countries.

WHO is establishing a platform for international collaboration among WHO collaborating centres, national and regional networks and other institutions to assist WHO in providing technical support for implementation of GLASS. WHO will also promote exchange and peer support between countries.

Implementation of the global AMR surveillance system will be reported to WHO Member States at the World Health Assembly. WHO will coordinate implementation and ensure respect for Member States' laws on surveillance, data collection, storage and reporting, and patient confidentiality.

## 4. References

### ***Surveillance of antimicrobial resistance***

Antimicrobial resistance: global report on surveillance. Geneva: World Health Organization; 2014 (<http://www.who.int/drugresistance/documents/surveillancereport/en/>).

European Antimicrobial Resistance Surveillance Network. Stockholm: European Centre for Disease Prevention and Control (<http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/Pages/index.aspx>).

Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos. Buenos Aires: Antimicrobianos (<http://antimicrobianos.com.ar/category/resistencia/relavra/>).

Integrated surveillance of antimicrobial resistance. Guidance from a WHO Advisory Group. Geneva: World Health Organization; 2013 ([http://www.who.int/foodsafety/publications/agisar\\_guidance/en/](http://www.who.int/foodsafety/publications/agisar_guidance/en/)).

Guidelines for national surveillance of antimicrobial resistance and quality assurance of antimicrobial susceptibility testing. Manila: WHO Regional Office for the Western Pacific; 2002.

Guidelines for antimicrobial resistance surveillance. Alexandria: WHO Regional Office for the Eastern Mediterranean; 1996.

Guide for establishing laboratory-based surveillance for antimicrobial resistance. Brazzaville: WHO Regional Office for Africa; 2013 (<http://www.afro.who.int/media-centre/afro-feature/item/6768-towards-enhanced-surveillance-of-antimicrobial-resistance-in-the-who-african-region.html?lang=en>).

Technical guidelines for integrated disease surveillance and response in the African Region. 2nd ed. Brazzaville: WHO Regional Office for Africa; 2010 (<http://www.afro.who.int/en/clusters-a-programmes/dpc/integrated-disease-surveillance/features/2775-technical-guidelines-for-integrated-disease-surveillance-and-response-in-the-african-region.html>).

Community-based surveillance of antimicrobial use and resistance in resource-constrained settings: report on five pilot projects. Geneva: World Health Organization; 2009 (<http://apps.who.int/iris/handle/10665/70036>).

Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR). Copenhagen: WHO Regional Office for Europe (<http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/antimicrobial-resistance/central-asian-and-eastern-european-surveillance-of-antimicrobial-resistance-caesar>).

Surveillance of antimicrobial resistance for local and global action, Stockholm, 2–3 December 2014. Meeting report. Stockholm: Public Health Agency of Sweden; 2014 (<http://www.folkhalsomyndigheten.se/documents/projektwebbar/sar/summary/AMR-meeting-summary.pdf>).

WHONET. Geneva: World Health Organization (<http://www.who.int/drugresistance/whonetsoftware/en/>).

### ***Surveillance standards***

WHO recommended surveillance standards, 2nd ed. Geneva: World Health Organization; 1999 (WHO/CDS/CSR/ISR/99.2) (<http://www.who.int/csr/resources/publications/surveillance/whocdscsr992.pdf>).

Surveillance standards for antimicrobial resistance. Geneva: World Health Organization; 2001 (WHO CDS/CSR/DRS/2001/5) ([http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_5/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_5/en/)).



Terrestrial animal health code. 24th ed. Paris: World Organisation for Animal Health; 2015 (<http://www.oie.int/international-standard-setting/terrestrial-code/access-online/>).

### **Microbiological laboratory standards**

Manual for the laboratory identification and antimicrobial susceptibility testing of bacterial pathogens of public health importance in the developing world. Geneva: World Health Organization; 2003 ([http://www.who.int/drugresistance/publications/WHO\\_CDS\\_CSR\\_RMD\\_2003\\_6/en/](http://www.who.int/drugresistance/publications/WHO_CDS_CSR_RMD_2003_6/en/)).

European Committee on Antimicrobial Susceptibility Testing – EUCAST (<http://www.eucast.org/>).

Performance standards for antimicrobial susceptibility testing: twenty-fifth informational supplement. Wayne, Pennsylvania: Clinical and Laboratory Standards Institute; 2015 (M100-S25).

Strategies and laboratory methods for strengthening surveillance of sexually transmitted infections. Geneva: World Health Organization and UNAIDS; 2012:69–92 (<http://apps.who.int/iris/handle/10665/75729>).

Unemo M, Ballard R, Ison C, Lewis D, Ndowa F, Peeling R, eds. Laboratory diagnosis of sexually transmitted infections, including human immunodeficiency virus. Geneva: World Health Organization; 2013 (<http://www.who.int/reproductivehealth/publications/rtis/9789241505840/en/>).

### **Further information**

Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015 ([http://www.who.int/drugresistance/global\\_action\\_plan/en/](http://www.who.int/drugresistance/global_action_plan/en/)).

Jaipur declaration on antimicrobial resistance. New Delhi: WHO Regional Office for South-East Asia; 2011 ([http://www.searo.who.int/entity/world\\_health\\_day/media/2011/whd-11\\_amr\\_jaipur\\_declaration\\_.pdf](http://www.searo.who.int/entity/world_health_day/media/2011/whd-11_amr_jaipur_declaration_.pdf)).

Global action plan to control the spread and impact of antimicrobial resistance in *Neisseria gonorrhoeae*. Geneva: World Health Organization; 2012 (<http://www.who.int/reproductivehealth/publications/rtis/9789241503501/en/>).

Worldwide country situation analysis: response to antimicrobial resistance. Geneva: World Health Organization; 2015 (<http://www.who.int/drugresistance/documents/situationanalysis/en/>).



## Annex 1. Surveillance approaches

The surveillance method used depends on the objectives and the available resources. At a minimum, surveillance in GLASS should include data on AMR combined with patient and microbiological information.

### A. Case-finding based on priority specimens sent routinely to laboratories for clinical purposes

Early implementation of GLASS will be based on this type of surveillance. A benefit of the surveillance approach proposed in GLASS is that epidemiological and clinical data will be combined with microbiological data. This will allow stratification of populations to ascertain e.g. the most frequent type of resistant infection, the age structure of infections, whether most occur in the community or in hospital and the geographical distribution.

This method has also drawbacks. Although infections due to bacteria resistant to antimicrobial agents do not usually present differently from those due to the same but susceptible bacteria, in settings where samples are not routinely sent for microbiological investigation, those examined are more likely to be taken from severely ill patients who have failed first- and perhaps second-line treatment. This type of surveillance is therefore more likely to find resistant strains.

Despite the caveats, data from surveillance based on routinely collected clinical samples can be used for several purposes if core data are collected on patients and the population from which they derive and if duplicated results for the same patient are removed (see 2.1.1):

- A combination of epidemiological and laboratory data allows stratification of populations for ascertaining the type of infection, whether most AMR infections are occurring, e.g. in young or elderly people, in the community or in hospital, and the geographical distribution of infections caused by resistant organisms.
- The extent of AMR infections can be assessed from epidemiological indicators such as incidence and prevalence. Epidemiological and laboratory data must represent a defined population in order to be pertinent. For infections of hospital origin, the most common denominator is the number of hospital admissions or patient-days in hospital. The population denominator for assessing infections occurring in the community may be difficult to determine, as it requires counting the number of infections in a population in a specified catchment area. However, it is crucial for understanding variations in sampling frequency and impact of resistant infections.
- Routine data from antibiograms can be analysed for new trends by comparing them with data from the previous year, to determine any significant change in important resistant bacteria, such as carbapenem-resistant *Enterobacteriaceae*. Information on any increase is critical for designing local measures to prevent transmission of resistant bacteria; a decrease may reflect an impact of interventions.

As one of the objectives of early implementation is to build common understanding by testing the feasibility of collecting and sharing harmonized data, the limitations of surveillance based on routinely collected clinical samples is not considered to be a major problem at this stage.

## B. Case-based surveillance of clinical syndromes

Surveillance based on patients in a defined population who present for medical care with signs and symptoms that meet the case definitions provides more precise data about the burden of AMR in the population.

Case-finding based on clinical syndromes reflects the incidence of a resistant infection in the population under surveillance. The total number of laboratory-confirmed infections in patients seeking medical care should be calculated, regardless of the causative organism, and the calculated rates and proportions of infections caused by susceptible and non-susceptible bacteria.

Case-based surveillance of clinical syndromes is laborious and may require resources that are not available at the surveillance site. Cases may be underreported due, for example, to lack of information and training in health care facilities or lack of time for clinicians. Surveillance sites that can conduct case-based surveillance of clinical syndromes but not continuously could undertake periodic surveys.

## C. Laboratory-based surveillance

Laboratory-based data without linkage to patient information is frequently used to monitor AMR, but this approach does not provide information on the extent of the problem in the population and is not promoted in GLASS.

## D. Examples of measures that can be generated

Various measures of the occurrence of AMR in defined populations can be generated, depending on the information available on the events (numerator) and the group of individuals (population).

### a. Metrics that can be generated by case-finding based on priority specimens sent routinely to laboratories for clinical purposes

#### ***Frequency of patients sampled per specimen type per population covered***

Numerator:	Number of patients sampled per specimen type
Denominator:	Population covered
Example:	Number of urinary cultures per 100 000 inhabitants

#### ***Frequency of patients with growth of non-susceptible bacteria per specimen type, species and antibiotic***

Numerator:	Number of sampled patients with growth of non-susceptible bacteria of the species and antibiotic under surveillance per specimen type
Denominator:	Total number of sampled patients per specimen type
Example:	Number of sampled patients with <i>E. coli</i> resistant to fluoroquinolones out of all patients sampled for blood culture

**Proportion of sampled patients with positive culture of any (susceptible, intermediate or resistant) pathogenic bacteria per specimen type**

Numerator:	Number of patients sampled with positive culture per specimen type
Denominator:	Number of patients sampled per specimen type.
Example:	Number of patients sampled with positive blood cultures out of all patients sampled for blood culture

**Proportion of samples with growth of non-susceptible bacteria of the species and antibiotic under surveillance per specimen type**

Numerator:	Number of samples with growth of non-susceptible bacteria of the species and antibiotic under surveillance
Denominator:	Total number of samples with growth of bacteria of the species under surveillance and tested for susceptibility for the antibiotic in question.
Example:	Proportion of <i>E. coli</i> non-susceptible to fluoroquinolones out of all tested.

**b. Metrics that can be generated by case-based surveillance of clinical syndromes**

**Incidence of monitored infections (regardless of pathogen) in the population**

Numerator:	Total number of infection episodes that fulfil case definitions verified by bacterial culture
Denominator:	Population covered by participating sites
Example:	Number of bloodstream infections per 100 000 inhabitants or further specified per age group, gender etc.

**Incidence of infection in the population per syndrome per organism under surveillance**

Numerator:	Total number of infections caused by the species under surveillance
Denominator:	Population covered by participating sites
Example:	Number of bloodstream infections caused by <i>E. coli</i> per 100 000 population

**Incidence of non-susceptible infections per syndrome per organism under surveillance**

Numerator:	Number of infections caused by non-susceptible bacteria of the species and antibiotic type under surveillance
Denominator:	Population served by participating sites
Example:	Number of bloodstream infections caused by <i>E. coli</i> resistant to fluoroquinolones per 100 000 population

**Proportion of infections caused by non-susceptible pathogens per syndrome, pathogen and antibiotic**

Numerator:	Number of infections caused by non-susceptible bacteria of the species and antibiotic type under surveillance
Denominator:	Total number of infections caused by the species and tested for the antibiotic under surveillance
Example:	Proportion of <i>E. coli</i> resistant to fluoroquinolones of all <i>E. coli</i> that cause bloodstream infections and have been tested for fluoroquinolones

## Annex 2. Information to be collected routinely at points of care on all clinical samples sent for bacteriological culture and testing for susceptibility to antimicrobial agents

The form in this Annex is a generic example of a form that should accompany samples to a microbiology laboratory. Each surveillance site should adapt this form to local needs, ensuring patient privacy. To comply with the GLASS standards, the data fields in the form must be included in the requests that clinicians send with samples for microbiological testing.

In addition, the request form could also include other fields as per the national surveillance system policy, such as the ward or department, hospital number and name, the diagnosis, patient history, other reasons for the request, antimicrobial therapy given, the question to be answered by testing and the name and contact details of the person who requested the test; most fields being essential information recorded as part of clinical diagnosis.

Patient identification		
a. Unique identification number _____	Gender:	
b. Name: (family name, given name(s)) _____	Male <input type="checkbox"/>	
_____	Female <input type="checkbox"/>	
Date of birth: (yyyy/mm/dd) _____		
Years _____	Months (if < 1 year) _____	
Specimen information:		
<input type="checkbox"/> Blood <input type="checkbox"/> Urine <input type="checkbox"/> Faeces <input type="checkbox"/> Urethral secretion <input type="checkbox"/> Cervical secretion		
<input type="checkbox"/> Other		
Date of specimen collection: (yyyy/mm/dd) _____	Had the patient been hospitalized for more than 2 calendar days at the time for sampling? <input type="checkbox"/> Yes <input type="checkbox"/> No	

The same information could be collected in digital format. Collection forms and tools will be provided or made available (WHONET application, specification of digital export files from other systems) to collect data at surveillance sites.

## Annex 3. Structure for reporting aggregated data by a national surveillance coordinating centre

The tables below illustrate the structure of aggregated data and the level of aggregation of data to be collected from participating countries. **The tables are not to be used as collection forms**; other tools (WHONET application, specification of digital export files from other systems) will be provided for that purpose.

To save space, not all the priority pathogens and antibiotic combinations are included in the examples, and only few age groups are shown.

The listed drugs are priorities for surveillance of antibacterial resistance; they may not be options for first-line treatment.

Table A.3.1. Participation in GLASS baseline surveillance

### Contact information

Country: .....

Total population: .....

Contact person: ..... Alternative contact person: .....

Telephone: ..... Telephone: .....

E-mail: ..... E-mail: .....

Address: ..... Address: .....

Priority specimen*	Pathogens*
<input type="checkbox"/> Bloodstream infections (Table A.3.2)	<input type="checkbox"/> <i>E. coli</i> <input type="checkbox"/> <i>K. pneumoniae</i> <input type="checkbox"/> <i>A. baumannii</i> <input type="checkbox"/> <i>S. aureus</i> <input type="checkbox"/> <i>S. pneumoniae</i> <input type="checkbox"/> <i>Salmonella</i> spp.
<input type="checkbox"/> Urinary tract infections (Table A.3.3)	<input type="checkbox"/> <i>E. coli</i> <input type="checkbox"/> <i>K. pneumoniae</i>
<input type="checkbox"/> Acute diarrhoea (Table A.3.4)	<input type="checkbox"/> <i>Salmonella</i> spp. <input type="checkbox"/> <i>Shigella</i> spp.
<input type="checkbox"/> Gonorrhoea, urethra, cervix (Table A.3.5)	<input type="checkbox"/> <i>N. gonorrhoeae</i>

\* Tick the items included in national surveillance and reported to GLASS

**Table A.3.2.** Surveillance of bloodstream infections

(Tables are not to be used as collection forms)

**Period**

yyyy/mm/dd to yyyy/mm/dd

**Number of surveillance sites**

Hospital(s): ..... Outpatient department(s): .....

**Data stratified by age and gender**

Age group (years)																					
0		1–4		5–14		15–24		25–34		35–44		45–54		55–64		65–80		≥ 81		Total	
F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M

Total number of patients from whom a blood culture was taken:

Hospital origin:\*

Community origin:\*\*

Total number of patients with positive blood culture, any species:

\* Hospital origin: hospitalized for > 2 calendar days when the specimen was taken:

- patient admitted to a health care facility for > 2 calendar days; or
- patient admitted to a health care facility for < 2 calendar days but transferred from another health care facility where admitted for ≥ 2 calendar days

\*\* Community origin:

- patient being cared for at an outpatient clinics when the specimen was taken; or
- patient hospitalized for ≤ 2 calendar days when the specimen was taken.



**Table A.3.2** (continued)

**Numbers of patients with susceptible, intermediate and resistant results for each priority pathogen and antibiotic**

This example covers only reporting of aggregated data for *E. coli* in two of the ten age groups. The listed drugs are priorities for surveillance of antibacterial resistance, although they may not be options for first-line treatment.

Antibiotic susceptibility testing (AST) guideline used:  CLSI  EUCAST Other: \_\_\_\_\_

Species	Antibiotics	Age group (years)														
		< 1						1-4								
		Female			Male			Female			Male					
		Hospital origin	Community origin	Hospital origin	Community origin	Hospital origin	Community origin	Hospital origin	Community origin	Hospital origin	Community origin	Hospital origin	Community origin			
		S	I	R	S	I	R	S	I	R	S	I	R	S	I	R
<i>E. coli</i>	AST result															
<i>E. coli</i>	Co-trimoxazole															
<i>E. coli</i>	Fluoroquinolones R to any agent	No. of isolates tested:			No. of isolates tested:			No. of isolates tested:			No. of isolates tested:			No. of isolates tested:		
<i>E. coli</i>	Ciprofloxacin															
<i>E. coli</i>	Levofloxacin															
<i>E. coli</i>	Third-generation cephalosporins I+R to any agent	No. of isolates tested:			No. of isolates tested:			No. of isolates tested:			No. of isolates tested:			No. of isolates tested:		
<i>E. coli</i>	Ceftriaxone															
<i>E. coli</i>	Cefotaxime															
<i>E. coli</i>	Ceftazidime															
<i>E. coli</i>	Fourth-generation cephalosporins Cefepime															
<i>E. coli</i>	Carbapenems I+R to any agent	No. of isolates tested:			No. of isolates tested:			No. of isolates tested:			No. of isolates tested:			No. of isolates tested:		
<i>E. coli</i>	Imipenem															
<i>E. coli</i>	Meropenem															
<i>E. coli</i>	Ertapenem															
<i>E. coli</i>	Doripenem															
<i>E. coli</i>	Colistin															
<i>E. coli</i>	Ampicillin															



**Table A.3.3.** Surveillance of urinary tract infections

(Tables are not to be used as collection forms)

**Period**

yyyy/mm/dd to yyyy/mm/dd

**Number of surveillance sites**

Hospital(s): ..... Outpatient department(s): .....

**Data stratified by age and gender**

Age group (years)																					
0		1–4		5–14		15–24		25–34		35–44		45–54		55–64		65–80		≥ 81		Total	
F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M

Total number of patients from whom a urine sample was taken:

Hospital origin:\*

Community origin:\*\*

Total number of patients with positive urine culture, any species:

\* Hospital origin: hospitalized for > 2 calendar days when the specimen was taken:

- patient admitted to a health care facility for > 2 calendar days; or
- patient admitted to a health care facility for < 2 calendar days but transferred from another health care facility where admitted for ≥ 2 calendar days

\*\* Community origin:

- patient being cared for at an outpatient clinics when the specimen was taken; or
- patient hospitalized for ≤ 2 calendar days when the specimen was taken.

**Numbers of patients with positive and negative cultures, respectively, stratified according to individual case data**

This example covers reporting of aggregated data for only two of the ten age groups.

Species	Age group (years)							
	< 1				1–4			
	Female		Male		Female		Male	
	Hospital	Community	Hospital	Community	Hospital	Community	Hospital	Community
<i>E. coli</i>								
<i>K. pneumoniae</i>								
Other spp.								
Negative								

**Table A.3.3** (continued)

**Numbers of patients with susceptible, intermediate and resistant results for each priority pathogen and antibiotic**

This example covers only reporting of aggregated data for *E. coli* in two of the ten age groups. The listed drugs are priorities for surveillance of antibacterial resistance, although they may not be options for first-line treatment.

Antibiotic susceptibility testing (AST) guideline used:  CLSI  EUCAST Other: \_\_\_\_\_

Species	Antibiotics	Age group (years)															
		< 1						1-4									
		Female			Male			Female			Male						
Hospital origin		Community origin		Hospital origin		Community origin		Hospital origin		Community origin		Hospital origin		Community origin			
S		I		R		S		I		R		S		I		R	
<i>E. coli</i>	Co-trimoxazole																
<i>E. coli</i>	Fluoroquinolones R to any agent	No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:	
<i>E. coli</i>	Ciprofloxacin																
<i>E. coli</i>	Levofloxacin																
<i>E. coli</i>	Third-generation cephalosporins I+R to any agent	No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:	
<i>E. coli</i>	Ceftriaxone																
<i>E. coli</i>	Cefotaxime																
<i>E. coli</i>	Ceftazidime																
<i>E. coli</i>	Fourth-generation cephalosporins Cefepime																
<i>E. coli</i>	Carbapenems I+R to any agent	No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:		No. of isolates tested:	
<i>E. coli</i>	Imipenem																
<i>E. coli</i>	Meropenem																
<i>E. coli</i>	Ertapenem																
<i>E. coli</i>	Doripenem																
<i>E. coli</i>	Colistin																
<i>E. coli</i>	Ampicillin																

**Table A.3.4.** Surveillance of acute diarrhoea caused by *Salmonella* spp or *Shigella* spp.

(Tables are not to be used as collection forms)

**Period**

yyyy/mm/dd to yyyy/mm/dd

**Number of surveillance sites**

Hospital(s): ..... Outpatient department(s): .....

**Data stratified by age and gender**

Age group (years)																					
0		1–4		5–14		15–24		25–34		35–44		45–54		55–64		65–80		≥ 81		Total	
F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M

Total number of patients from whom a faecal sample was taken:

Hospital origin:\*

Community origin:\*\*

Total number of patients with stool culture positive for *Salmonella* spp. and *Shigella* spp.:

\* Hospital origin: hospitalized for > 2 calendar days when the specimen was taken:

- patient admitted to a health care facility for > 2 calendar days; or
- patient admitted to a health care facility for < 2 calendar days but transferred from another health care facility where admitted for ≥ 2 calendar days

\*\*Community origin:

- patient being cared for at an outpatient clinics when the specimen was taken; or
- patient hospitalized for ≤ 2 calendar days when the specimen was taken.

**Table A.3.4** (continued)  
**Numbers of patients with positive and negative cultures, respectively, stratified according to individual case data**

This example covers reporting of aggregated data for only two of the ten age groups.

Species	Age group (years)								
	< 1				1-4				
	Female		Male		Female		Male		
	Hospital origin	Community origin	Hospital origin	Community origin	Hospital origin	Community origin	Hospital origin	Community origin	
<i>Salmonella</i> spp.									
<i>Shigella</i> spp.									
Negative									



Table A.3.5. Surveillance of gonorrhoea

(Tables are not to be used as collection forms)

**Period**

yyyy/mm/dd to yyyy/mm/dd

**Data stratified by age and gender**

Age group (years)																					
0		1-4		5-14		15-24		25-34		35-44		45-54		55-64		65-80		≥ 81		Total	
F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M

**Numbers of patients with positive and negative cultures, respectively, stratified according to individual case data**

This example covers reporting of aggregated data for only two of the ten age groups for *N. gonorrhoeae*

Species	Age group (years)			
	15-24		25-34	
	Female	Male	Female	Male
<i>N. gonorrhoeae</i>				
Negative				

Table A.3.5 (continued)

**Numbers of patients with susceptible, intermediate and resistant results for each priority pathogen and antibiotic**

This example covers reporting of aggregated data for only two of the ten age groups. The listed drugs are priorities for surveillance of antibacterial resistance, although they may not be options for first-line treatment.

**Antibiotic susceptibility testing (AST) guideline used:**

CLSI  EUCAST  CDS<sub>a</sub> Other: \_\_\_\_\_

Species	Antibiotic	Age group (years)											
		15-24						25-34					
		Female			Male			Female			Male		
<i>N. gonorrhoeae</i>	AST result	S	I	R	S	I	R	S	I	R	S	I	R
<i>N. gonorrhoeae</i>	Cefixime												
<i>N. gonorrhoeae</i>	Ceftriaxone												
<i>N. gonorrhoeae</i>	Azithromycin												
<i>N. gonorrhoeae</i>	Spectinomycin												
<i>N. gonorrhoeae</i>	Ciprofloxacin												
<i>N. gonorrhoeae</i>	Gentamicin												

<sup>a</sup> Guidelines for calibrated dichotomous sensitivity disc diffusion are given in Unemo M, Ballard R, Ison C, Lewis D, Ndowa F, Peeling R, eds. Laboratory methods for sexually transmitted infections, including human immunodeficiency virus.

### Annex 4. Sample indicators for monitoring and evaluating implementation of GLASS

Indicator	Definition	Type and purpose	Value (national level)	Value (global level)	Frequency of data collection (global level)	Data source	Method
<b>Public health priorities targeted for surveillance</b>							
1. Priority specimens	Number of prioritized specimens included in GLASS targets	Output Monitoring	Absolute number	Countries with n out of N GLASS targets included (%)	With submission of GLASS data	Key informant	Informant or evaluation report. Could be derived from the surveillance data submission
2. Priority pathogens	Number of prioritized pathogens included in GLASS targets	Output Monitoring	Absolute number	Countries with n out of N GLASS targets included (%)	With submission of GLASS data	Key informant	Informant or evaluation report. Could be derived from the surveillance data submission
3. Priority pathogen-antimicrobial combinations	Number of prioritized pathogen-antimicrobial combinations included in GLASS targets	Output Monitoring	Absolute number	Countries with n out of N GLASS targets included (%)	With submission of GLASS data	Key informant	Informant or evaluation report. Could be derived from the surveillance data submission
<b>Surveillance structure</b>							
4. Presence of a national coordinating centre (NCC)	NCC with appropriate mandate, terms of reference and responsible person (focal point) is established	Input Evaluation	Yes / No	Countries with established NCCs meeting the GLASS requirements (%)	With submission of GLASS data	Key informant	Informant or evaluation report
5. Presence of a National Focal Point (NFP)	NFP is designated and communicating with GLASS	Input Evaluation	Yes / No	Countries with presence of a National Focal Point (%)	With submission of GLASS data	Key informant	Informant or evaluation report
6. Policy support for implementation of AMR surveillance	Authority both to implement national AMR surveillance and participate in GLASS has been delegated by the relevant institutional jurisdiction	Input Evaluation	Yes / No	Countries with NCCs having the mandate to participate in GLASS (%)	With submission of GLASS data	Key informant	Informant or evaluation report, existing regulation



Indicator	Definition	Type and purpose	Value (national level)	Value (global level)	Frequency of data collection (global level)	Data source	Method
<b>Public health priorities targeted for surveillance</b>							
7. National plan for AMR surveillance	Presence of strategic and budgeted operational plans for implementing and strengthening AMR surveillance, including participation in GLASS	Input Evaluation	Yes / No	Countries with AMR surveillance plans including participation in GLASS (%)	With submission of GLASS data	Key informant	Informant or evaluation report, existing plans
8. National reference laboratory (NRL)	At least one NRL that participates in an external quality assurance scheme is designated	Input Evaluation	Yes / No	Countries with NLR supporting GLASS (%)	With submission of GLASS data	Key informant	Informant or evaluation report
9. Number of AMR surveillance sites	Number of surveillance sites fulfilling requirements to collect and report data on patients and AST that can report to GLASS	Input Monitoring	Absolute number	Countries with $n_1, n_2, \dots, n_n$ surveillance sites (%)	With submission of GLASS data	Key informant	Informant or evaluation report
<b>Core functions</b>							
10. External quality assurance system	The national AMR programme organizes and runs external quality assurance for all laboratories sending data to GLASS, covering both bacterial identification and AST	Process Monitoring and evaluation	Yes / No	Countries participating in external quality assurance (%)	With submission of GLASS data	Key informant	Informant interview
<b>Support functions (guidelines and training)</b>							
11. AMR surveillance standards and guidelines	Availability of AMR surveillance standards and guidelines incorporating GLASS standards	Input Evaluation	Yes / No	Countries with national AMR surveillance standards and guidelines incorporating GLASS standards (%)	Annually	Informants, existing guidelines and standards	Informant interview, document review

Indicator	Definition	Type and purpose	Value (national level)	Value (global level)	Frequency of data collection (global level)	Data source	Method
<b>Public health priorities targeted for surveillance</b>							
12. Surveillance staff trained in AMR surveillance	Proportion of surveillance staff trained in AMR surveillance, including GLASS methods	Process Monitoring and evaluation	%	Distribution by country (%)	Annually	Informants, training reports	Informant interview
13. Clinical staff trained in AMR surveillance	Proportion of clinical staff trained in AMR surveillance, including GLASS methods	Process Monitoring and evaluation	%	Distribution by country (%)	Annually	Informants, training reports	Informant interview
14. Laboratory personnel trained in AMR surveillance and laboratory techniques	Proportion of laboratory personnel trained in AMR surveillance and laboratory techniques according to GLASS requirements	Process Monitoring and evaluation	%	Distribution by country (%)	Annually	Informants, training reports	Informant interview
<b>Quality and outputs of the surveillance system</b>							
15. Timeliness of submission of surveillance reports	Proportion of surveillance sites that submitted surveillance reports to the next level within the surveillance period	Output Monitoring and evaluation	%	Countries that submitted GLASS reports on time (%)	Annually	Reporting log	Review of documents Could be generated by IT platform
16. Completeness of reporting	Proportion of total expected surveillance reports received, regardless of timeliness of submission	Output Monitoring and evaluation	%	Countries that submitted the expected GLASS reports, regardless of timeliness of submission (%)	Annually	Reports	Review of documents Could be generated by IT platform
17. Completeness of data reported	Proportion of surveillance reports with no missing required information	Output Evaluation	%	Countries that submitted complete GLASS reports (%)	Annually	Reports	Review of documents Could be generated by IT platform

## Annex 5. Document review group

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