DRAFT

Global Antimicrobial Resistance and Use Surveillance System

GLASS-AMR manual

World Health Organization

Contents

Acknowledgements

Abbreviations and acronyms

AMC	antimicrobial consumption
AMR	antimicrobial resistance
AMU	antimicrobial use
AST	antimicrobial susceptibility testing
ATC	Anatomical Therapeutic Chemical (classification system)
AWaRe	WHO Access, Watch and Reserve antibiotic categorization
CAESAR	Central Asian and European Surveillance of Antimicrobial Resistance
CFU	colony-forming units
CLSI	Clinical and Laboratory Standards Institute
CSF	cerebrospinal fluid
EARS-Net	European Antimicrobial Resistance Surveillance Network
EGASP	WHO & CDC Enhanced Gonococcal AMR Surveillance Programme
ESBL	extended spectrum beta-lactamases
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organization of the United Nations
GAP-AMR	Global Action Plan on Antimicrobial Resistance
GLASS	Global Antimicrobial Resistance and Use Surveillance System
IACG	(United Nations) Interagency Coordination Group on Antimicrobial Resistance
ICU	intensive care unit
LQAS	lot quality assurance sampling
MIC	minimum inhibitory concentration
NCC	national coordinating centre
NFP	national focal point
NRL	national AMR reference laboratory
OIE	World Organisation for Animal Health
PBP	penicillin-binding protein
PCR	polymerase chain reaction
ReLAVRA	*Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos* (Latin American Network for Antimicrobial Resistance Surveillance)

UTI	urinary tract infection
WHO	World Health Organization
WHONET	Database software for the management and analysis of microbiology laboratory data developed by the World Health Organization
WGS	whole genome sequencing

1 Introduction

1.1 Background

Antimicrobial resistance (AMR) is the presence of resistance to antimicrobial medicines in infectious agents such as bacteria, viruses, fungi and parasites. This resistance can be intrinsic or acquired. AMR in a wide range of infectious agents is a growing public health threat of significant concern to countries and to many sectors across the One Health spectrum. Especially alarming is the rapid global spread of bacteria and fungi that cause common infections and are resistant against multiple or all treatment options.

In May 2015, the Sixty-eighth World Health Assembly adopted the Global Action Plan on Antimicrobial Resistance (GAP-AMR) (1) to reflect the worldwide consensus that AMR poses a profound threat to global health. One of the five strategic objectives of GAP-AMR 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 to support local, national and global strategies.

The first *Surveillance of antimicrobial resistance for local and global action* meeting (2) was hosted by the Swedish Ministry of Health and Social Affairs and the Public Health Agency of Sweden in 2014. At this event, representatives from 30 World Health Organization (WHO) Member States from all WHO regions reaffirmed the need for a global programme for the surveillance of AMR of relevance to human health to help form the basis for local, national and regional actions and to monitor the effectiveness of interventions. Participants agreed on the surveillance approach proposed by WHO and this informed the development of the first version of the Global Antimicrobial Resistance Surveillance System (GLASS) manual for early Implementation (3). They also agreed on a high-level road map for further development of GLASS and suggested that the initial five years of GLASS early implementation should be followed by a review and revision of the system.

In 2015, WHO launched GLASS in order to support the second objective of the GAP-AMR (4).

1.2 Early implementation and revision of GLASS

GLASS was designed to be implemented in five-year cycles followed by revision and further development based on the lessons learned and best practices identified during each of these periods. The first phase, defined as the early implementation of GLASS, covered the period 2015–2019. The key objectives of this phase have been to launch the global surveillance system and provide guidance and technical support to countries for the development of an effective national AMR surveillance system.

During the early implementation period, GLASS provided a standardized approach for the collection, analysis, and sharing of AMR data by countries. It also sought to document the implementation status of existing or newly developed national AMR surveillance systems. GLASS has promoted a shift from surveillance approaches based solely on laboratory data to a system that also includes epidemiological, clinical, and population-level data. It provides standards and tools for routine surveillance based on microbiological and clinical information on priority bacterial infections in humans. Country enrolment began in 2016. To date, GLASS has produced three global reports (5-7) on implementation progress and AMR surveillance data.

In alignment with the work on the GAP-AMR, GLASS also promotes integration with other surveillance programmes in public health, including the animal and plant production and environment sectors (8) in the context of its tripartite collaboration with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE). GLASS was designed to evolve continuously, and several new elements have been developed and added to the system, comprising different types of surveillance activities (Figure 1.1). A major step forward was the addition in 2019 of the global surveillance of antimicrobial consumption (AMC) in the human population[1] to be reported on an annual basis. In addition, focused AMR surveillance and surveys approaches have been developed and some of these are already in the initial phases of implementations.

Focused surveillance activities include the GLASS Emerging Antimicrobial Resistance Reporting (GLASS-EAR) component (9), the special project on AMR in *Neisseria gonorrhoeae* (Enhanced Gonococcal Antimicrobial Surveillance Programme [EGASP]), and the surveillance of AMR in bloodstream infections caused by *Candida* spp. The "One Health" AMR surveillance model assessing the occurrence of extended-spectrum beta-lactamase-producing *Escherichia coli* across human, environment and animal sectors (named the "Tricycle" project) (10) and point prevalence studies on antimicrobial use in humans (11) have been successfully applied in several countries. Application of the GLASS methodology for estimating attributable mortality due to selected types of AMR (12) has also begun in a few countries.

Hence, the original "routine" GLASS has already evolved during the early implementation phase into a much broader system (or rather "environment") of normative guidance and tools including antimicrobial consumption, focused surveillance, surveys and study protocols. This evolution should be seen in the context of different country needs and capacities, emerging AMR, and WHO's ambition to develop the evidence base in order to obtain reliable and representative data to inform national and global AMR burden estimates. However, revising GLASS is not just about adding activities, but also about recognizing that many countries do not yet have the capacity to produce reliable and representative surveillance data. GLASS-AMR offers a sample approach to generating (sub)national representative AMR data from patients seeking care (13).

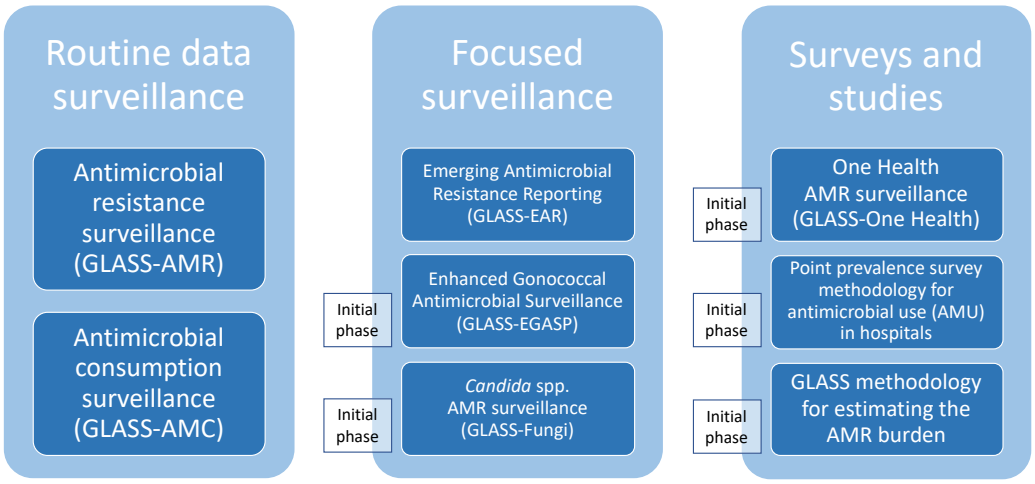

Figure 1.1. GLASS environment

[1] OIE, supported by FAO and WHO within the tripartite collaboration, has taken the lead to build a global database on antimicrobial agents intended for use in animals https://www.oie.int/en/scientific-expertise/veterinary-products/antimicrobials)

The GLASS revision took into consideration the lessons learned from GLASS early implementation, its current limitations and challenges, as well as suggestions and proposals for further development made by participating countries, WHO regional and country offices, and international partners. GLASS development and revision has been overseen by the WHO AMR Surveillance and Quality Assessment Collaborating Centres Network (14-15). The revision is based on formal and informal feedback from GLASS national focal points and implementing partners, assessment missions, special initiatives such as Northern GLASS (16), feedback from the United Nations Interagency Coordination Group on Antimicrobial Resistance (IACG) working paper on surveillance and monitoring for antimicrobial use and resistance (17), and published scientific papers (18-26).

1.3 Scope and purpose of the manual

This manual provides an update of the GLASS methods for AMR surveillance in humans and is part of a package of documents and tools designed to inform GLASS implementation. It describes the objectives and methodology of GLASS-AMR, the GLASS component dealing with the global surveillance of AMR in selected fast growing bacteria causing common infections in humans. It is important to note that this GLASS-AMR manual does not cover the other components of the "GLASS environment" shown in Figure 1.1.

The purpose of this manual is to provide guidance for countries on the GLASS-AMR methods and metrics. Development and implementation of AMR surveillance at national and local levels is addressed in more depth in a companion document (27)[2].

The intended readership of the manual includes national GLASS focal points, national public health professionals and national health authorities responsible for AMR surveillance in humans, and those contributing to national surveillance data collection. It may be useful for national professionals from other sectors supporting surveillance of AMR in the context of the "One Health" approach.

1.4 What is new in GLASS-AMR?

While the GLASS-AMR methodology has not been dramatically changed in the current revision, several modifications and additions have been made, including the following:

- cerebrospinal fluid (CSF), respiratory samples, and two additional specimen types (rectal and pharyngeal swabs) for the surveillance of AMR in gonococci have been added to the GLASS list of specimens;
- five new pathogens have been added, including *Pseudomonas aeruginosa*, *Neisseria meningitidis*, *Haemophilus influenzae*, *Salmonella enterica* serovar Typhi, and *Salmonella enterica* serovar Paratyphi A;
- several new antimicrobials have been included to describe the resistance of newly added target pathogens and to include both first- and second-line antimicrobials according to the WHO Access, Watch and Reserve (AWaRe) antibiotic categorization (28);
- a GLASS approach to assessing and improving the validity and representativeness of surveillance data has been introduced to guide interpretation of the data reported by countries and monitor development of the national surveillance systems and their quality;

[2] It will be revised and updated in 2021 based on the conclusion of the GLASS-AMR Manual .

- an option for submission of anonymized individual patient level data has been included, providing additional opportunities for AMR surveillance data validation and analysis
- an option for submission of data generated by molecular AMR diagnostics has been included to complement phenotypic AMR diagnostics data and improve understanding of the underlying mechanisms responsible for resistance.

In the next five years, GLASS will further consolidate the global surveillance of AMR by using the knowledge generated during early implementation to secure better quality, more robust and more representative collected data and generated results. This will permit a comparison of AMR patterns over time and generate reliable measures of the magnitude of the AMR problem provided by the routine surveillance and supported by additional special studies.

2 Objectives of GLASS-AMR

GLASS-AMR will continue to collect, analyse and report harmonized data on AMR in infected patients at the national level, following the standards described in this manual.

The objectives of GLASS-AMR are to:

- foster national surveillance systems and harmonize global standards;
- monitor global AMR trends in fast-growing bacteria causing common infections in humans and inform the WHO Model Lists of Essential Medicines (29) and WHO AWaRe classification of antibiotics;
- estimate the extent and burden of AMR globally by selected indicators;
- detect emerging resistance and its international spread;
- generate data to inform the implementation of prevention and control strategies and assess the impact of interventions; and
- inform research and development of new tools for the prevention, diagnosis and treatment of human infections caused by fast-growing bacteria.

3 Core components of a national AMR surveillance system

GLASS will continue supporting Member States in implementing national surveillance of AMR and collecting official AMR data through national focal points (NFPs) designated by ministries of health or national public health institutions responsible for national AMR surveillance. The functions and steps to establish or strengthen the core components of national surveillance systems are described in more detail elsewhere (27). The core components include a national coordinating centre (NCC), a national reference laboratory (NRL), and surveillance sites. A brief description is provided below.

3.1 National coordinating centre

The NCC establishes and oversees the national AMR surveillance programme, gathers national AMR data and ensures that the system is functional. Its mandate should include:

- defining national AMR surveillance objectives within the national AMR strategy;
- preparing and coordinating the dissemination of national protocols;
- coordinating data collection, analysis and reporting;

- sharing nationally-aggregated data with WHO (GLASS).

A national focal point is identified at the outset and serves as the central point of contact within the NCC for all parts of the national AMR surveillance system and GLASS. The NCC should continuously monitor and evaluate the national AMR 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 epidemiological expertise and appropriate capacities, work alongside the national reference laboratory for microbiology expertise, and have a defined structure for surveillance coordination and data management. The NCC should define a strategy for the implementation of surveillance standards and gradual expansion of the network to achieve national or subnational representativeness. It should promote links between AMR surveillance in humans, food, animal and plant production, as well as the environment, with the ultimate aim to ensure coordination for AMR surveillance across these sectors. Other essential tasks of the NCC are to be responsible for developing links and mechanisms for collaboration regarding the surveillance of AMC and AMU and other relevant types of public health surveillance both inside and outside of the country.

3.2 National reference laboratory

The national AMR reference laboratory promotes and facilitates good laboratory practice in the country and promotes the harmonization of methods and standards used in the national AMR surveillance system (30). It oversees antimicrobial susceptibility testing (AST) methods and quality performance of the laboratories supporting surveillance sites participating in the national AMR surveillance, and investigates unusual or anomalous test results and unusual resistance patterns before they are reported to the relevant national authority. The NRL has a key role in the confirmation and reporting of emerging resistance in accordance with the GLASS-EAR reporting framework (31). The NRL should work alongside the NCC in standardizing and verifying microbiological results. If the capacity to fulfil NRL tasks is not yet available within a country, collaboration can be temporarily established with another appropriate institute within the country or in another country. To this effect, the WHO AMR Surveillance and Quality Assessment Collaborating Centres Network (14) has been established to assist WHO in supporting Member States to build the capacity to develop and implement AMR surveillance, particularly in low- and lower-middle income countries. The network can also assist NRLs with confirmatory testing and further characterization if necessary.

3.3 Surveillance sites

The surveillance sites are the foundation of the surveillance system. The quality of data generated by the surveillance system is dependent on well-functioning surveillance sites capable of collecting the required patient information, together with performing appropriate microbiological testing, epidemiological analysis and timely reporting. Surveillance sites for AMR in humans are usually primary, secondary or tertiary care hospitals, or outpatient clinics with access to the relevant epidemiological and laboratory support. Participating sites should have access to appropriate data management systems, staff with clinical expertise, epidemiologists, and quality-assured bacteriology laboratory support to provide basic clinical, epidemiological and microbiological data from patients included in the surveillance system (32). The number of participating sites depends on the size of the country, its population distribution, and feasibility considerations in order to achieve a sustainable population coverage that is as representative as possible (13). Using a stepwise approach, participating countries are expected to establish a surveillance network, starting with at least one

surveillance site and then to extend the number progressively, with the aim to establish a high quality and representative surveillance network with balanced geographical, demographic and socio-economic sample characteristics. Both inpatient and outpatient health care facilities with access to epidemiological and microbiology laboratory support are usually appropriate surveillance sites and selecting both types is important for representative surveillance. The inclusion of specialty clinics may be considered for some priorities, such as sexually transmitted infection clinics for AMR surveillance in patients with gonorrhoea.

These core components link together through a constant flow of data and information exchange, building an effective network for the detection and monitoring of infections and AMR. The flow of information linking surveillance sites with the NRL and NCC should be aligned with existing national information systems to sustain data management processes.

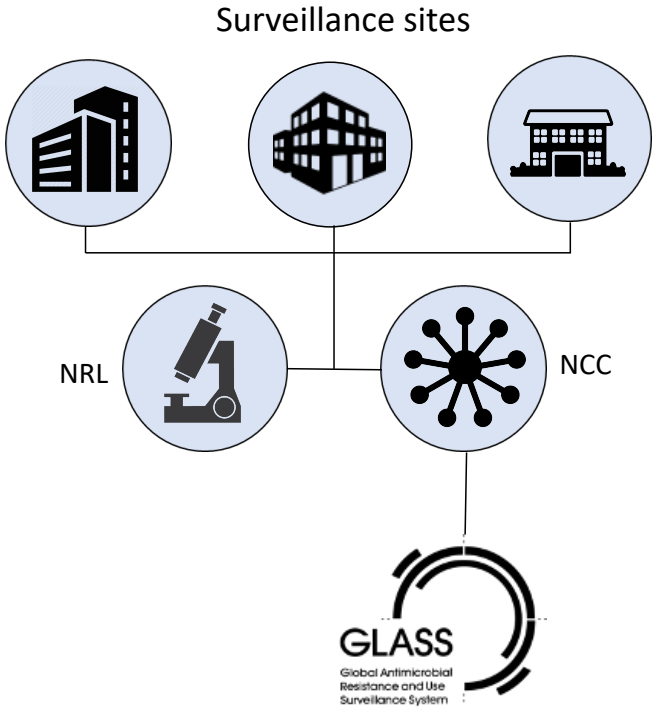

Figure 3.1.GLASS core components

4 GLASS-AMR surveillance approach

4.1 Population under surveillance

The population under surveillance is composed of patients seeking care in healthcare facilities for whom clinical samples are collected for routine microbiological investigations, including species identification and AST.

4.2 Surveillance method

GLASS requires AMR data to be collected through a surveillance system which gathers results from susceptibility testing for priority human bacterial pathogens isolated from clinical specimens sent routinely to laboratories for diagnostic purposes. Together with patients' microbiological results (species identification and AST), countries are also invited to report demographic and epidemiological variables (Section 7), either in aggregated or individual-level format.

For the purpose of this manual, the following terminology will be used to refer to the two types of AMR surveillance data currently collected by GLASS-AMR:

- **Isolate-based** data include information on the patient population with laboratory confirmed infections caused by the defined target pathogens under surveillance. They provide information on the proportion of patients with positive samples whose infections are caused by target pathogens resistant to specific antimicrobials (see Section 9.1).

- **Sample-based** data include information on the whole patient population with suspected infection from whom the clinical specimens have been collected. This population comprises patients with confirmed infection caused by the target pathogens, as well as patients with no microbial growth in collected specimens and those with positive samples with the growth of any other organisms, including other pathogens and commensal organisms. The sample-based approach allows to calculate the frequency of infections caused by antimicrobial drug-resistant pathogens in the patient population under surveillance (see Section 9.1).

Isolate-based data can be also seen as a subset of sample-based data (Figure 4.1). With the sample-based data approach, information is simply collected for a broader set of the same population. The patient population covered includes only those with a specific syndrome that seek care at a healthcare facility and from whom the clinical specimens have been collected in both isolate-based and sample-based approaches.

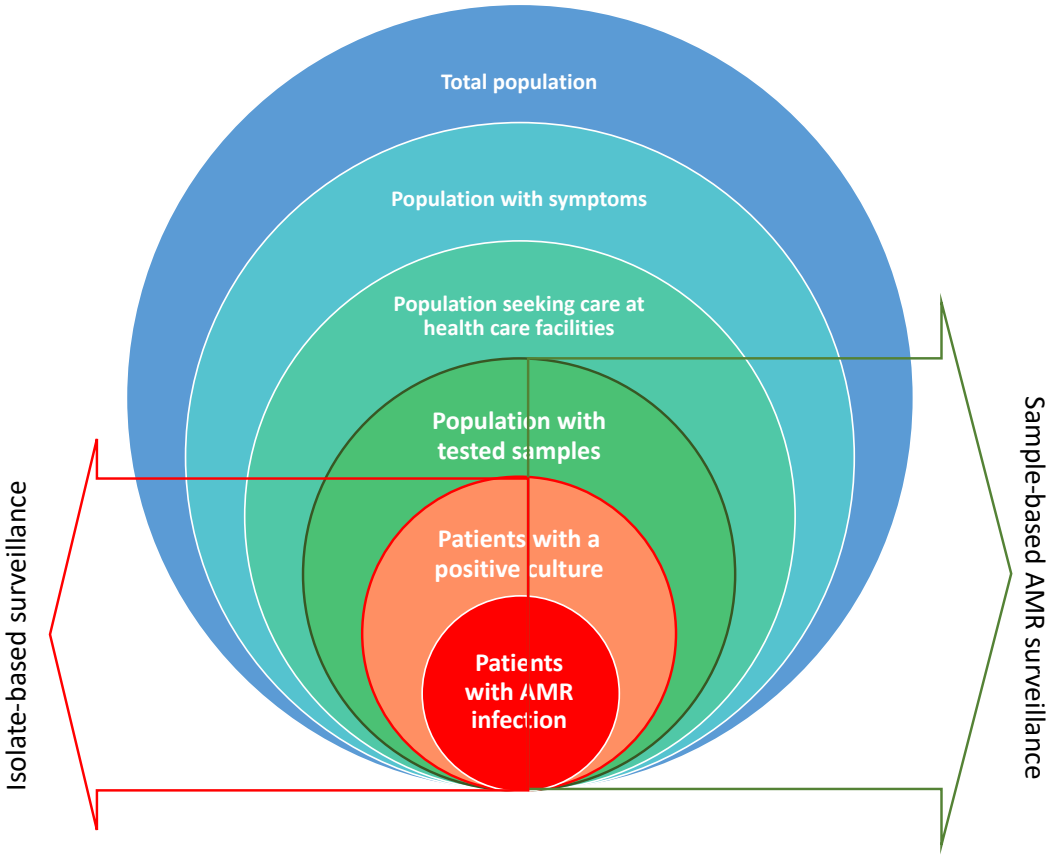

Figure 4.1. Patient populations in isolate-based and sample-based surveillance approaches

A comparison of types of data collected in isolate-based and sample-based surveillance approaches is shown in Table 4.1.

Table 4.1. Types of data collected in the two surveillance approaches

Type of data collected	AMR surveillance data	
	Isolate-based	Sample-based
Patients' AST results for bacterial pathogens and antibiotics under surveillance	●	●
Numbers of patients from whom samples have been collected for microbiological testing (both with and without growth of the bacterial pathogens under surveillance)		●

4.3 Considerations regarding GLASS-AMR surveillance approaches

There is no perfect surveillance system. Nevertheless, this does not disregard the importance and value of the information collected and reported. It is essential to identify and understand the limitations of the system and to take into account several considerations when interpreting data generated following the GLASS-AMR approach.

Both isolate-based and sample-based approaches are dependent on the following assumptions:

1. That patients with a specific syndrome who seek care at a health care facility will be assessed by a health care professional and sampled according to best clinical practice. The sample will then be transported to the laboratory for diagnostic microbiology investigations including culture and AST.
2. That the growth of a pathogen in selected specimens is a proxy for patient infection in the associated anatomical sites (for example, bloodstream infection, urinary tract infection, lower respiratory tract infection, enteric infection, urogenital infection). For this to be true, submitted microbiological data must relate to a true episode of illness in a patient which is dependent on the diagnostic criteria locally applied.
3. That the number of isolates with AST results can be used as a representation of the number of patients infected with the targeted susceptible or resistant bacteria in a specific anatomical site, after removal of repeated isolates of the same pathogen from the same specimen type from the same patient (see Section 8.4.2). Assuming also that routine microbiological testing is applied comprehensively and all patients with suspected infection will have a sample taken according to best clinical practices, and that all samples undergo bacterial identification and AST.

Although there are a number of limitations linked to these assumptions, they form the foundation for the applied method. Understanding the sources of bias and eventual flaws generated by each assumption is essential to interpret generated data, and to address the need for implementation of additional surveillance approaches.

4.3.1 Considerations when generating AMR estimates for the target population using data collected through surveillance

In any surveillance model the data collected and reported will often only represent the tip of the iceberg, frequently because of bias associated with the system design. In the case of AMR data, selection bias is the type of greatest concern (33). Selection bias leads to a distortion in the estimate of effect (that is, the percentage of isolates of a pathogen that are resistant to an antimicrobial agent), resulting from the way subjects (or isolates) are selected for the study population. For instance, data are often collected from a subset of health care facilities located in defined geographical areas (for example, main cities), or representing a selected type of care (for example, tertiary hospitals). In addition, patients in wards dedicated to certain medical specialities or the more critically ill might be more likely to be sampled for infection caused by resistant bacteria (for example, intensive care units or surgical wards) (34). However, it should be noted that the bias does not exactly come from the data directly, but rather in the generalizations, interpretations, and applications drawn from the data. If the data are collected predominantly from city hospitals for example, the national overview would not be complete, but the data will be representative of city hospitals. The error would be made if the estimates from the city hospitals are used to inform treatment guidelines for rural communities.

If a surveillance system reports on nearly all occurrences of a health event for the target population, then the system is by definition representative (35). By contrast, if it is known that the health care service coverage of the target population is not comprehensive, selection bias might cause the surveillance system to generate data that will over- or underestimate the true proportion of AMR in the target population and the obtained AMR rates will not be representative.

GLASS has developed a protocol (Section 5) that describes the minimum sampling criteria to be applied by countries when implementing surveillance. This is to assist countries that do not have the comprehensive health care service coverage necessary for the surveillance system to generate representative AMR rates at national and sub- national levels for the target population.

4.3.2 Considerations when relying on routine diagnostic results for surveillance purposes

It is important to highlight some of the disadvantages when relying only on diagnostic microbiological results for surveillance, particularly in countries with limited resources.

1. Lack of, or limited access to health care and microbiological testing could exclude a significant proportion of the population with infectious syndromes that should be under surveillance. This limitation will result in difficulty in obtaining a representative sample of the population with AMR infections.
2. Difficulties in obtaining a representative sample of the population seeking care, even when minimum sampling criteria are set.
3. Late microbiological testing can lead to distorted rates. For instance, in settings where microbiological sampling is not performed routinely, many patients may be tested only after antimicrobial treatment failures or when severely ill. This is likely to cause an ascertainment bias, with an over-estimation of the true resistance burden within that population.
4. Inaccurate microbiological methods will distort the estimation of the frequency of AMR which can lead to either over- or underestimation, depending on the direction of the inaccuracy.

To address the first issue, GLASS has developed a protocol (Section 5 and companion document (13)) to help achieve the representativeness of national or subnational data. Additionally, other surveillance approaches, together with data collected by periodical prevalence surveys, can be implemented to fulfil some of the remaining gaps (36-37). These additional surveillance approaches include syndrome-based (case-based) surveillance, and population-based surveillance using "lot quality assurance sampling" (LQAS). The use of complementary approaches should be based on countries' needs, constraints, and objectives to be achieved.

Syndrome-based AMR surveillance (3)**,** also known as case-based AMR surveillance (38-39), implies an active and systematic case-finding approach to identify patients with signs and symptoms that meet the case definitions for the specific syndromes. This active prospective surveillance approach can more accurately reflect the incidence of resistant infections in the population under surveillance and may provide more precise data about the burden of AMR in the chosen setting. However, it is laborious and requires additional resources because of the need for detailed clinical information in addition to the laboratory results. At the same time, the benefit of using this approach goes beyond the quality surveillance data as it promotes good diagnostic stewardship and may improve the quality of patient care.

Population-based surveillance using LQAS (40) combines surveillance of individuals in a defined population who present signs and symptoms that meet the case definitions for the specific syndrome with a sampling strategy to minimize logistic constraints. This approach yields a classification of the AMR prevalence as "high" or "low" by setting a threshold proportion of resistance and an appropriate sample size that will allow to define whether the target population is above or below the threshold. This approach might be sufficient to guide empirical treatment decisions and for estimates of AMR in infectious syndromes with low morbidity and mortality, but it does not accurately measure the real magnitude of AMR in the population.

4.3.3 Considerations when targeting the population of patients seeking care

It is paramount to highlight that the method described in this document aims to generate AMR estimates for the subset of the national population that seeks and has access to health care and laboratory tests. However, self-treatment at home or treatment at a local pharmacy or drug dispenser can be very frequent in certain settings and be a driver for AMR. Thus, additional studies must be designed and run in parallel to estimate AMR in the proportion of the population that cannot be captured by health care facility-based approaches. Community-based surveys, health care facility access behaviour surveys and patient-pathway analyses can help to fill this gap in essential information (41).

4.3.4 Considerations for reporting isolate-based versus sample-based data

Although both isolate-based and sample-based data can be reported to GLASS, it encourages countries to collect and report sample-based data. Isolate-based surveillance only provides data on resistance patterns within the bacterial population, as the information is only collected for patients infected by pathogens under surveillance. Sample-based surveillance can provide insight into patterns and the extent of AMR in the population undergoing testing according to specimen types. In settings where patients with suspected infections are systematically tested, the sample-based approach provides a proxy for all patients with the infection under surveillance. For example, using the tested population as the denominator allows an estimation of frequency of reported infectious syndromes associated

with a resistant pathogen, which can be stratified to identify prevalence of AMR by demographic or epidemiological categories, for example by age, gender, hospital or community infection onset.

4.3.5 Considerations when assuming the clinical significance of reported microbiological data

Some of the isolates identified may possibly represent cases of contamination of a specimen or colonization at a sampled site. Surveillance sites must take responsibility for assessing the clinical significance of positive cultures. However, some patients may have a combination of the bacteria causing infection and colonization and the laboratory may not be able to differentiate "true pathogens" from "colonizers". This is important to consider when interpreting the data, as the number of reported isolates might be higher than those causing infections. Therefore, the prevalence of AMR infections might also be over- or underestimated, depending on whether susceptibility rates among the colonizers differ from those among the infecting pathogens and, if so, by how much.

4.3.6 Considerations for the selective testing of pathogens and antimicrobial combinations under surveillance

The AST results for a specific antimicrobial could be missing due to selective testing. This includes second-line/cascade testing (that is, when second-line antimicrobials are tested only on isolates resistant to first-line antibiotics) and "prescribing-specific" testing (that is, when only those antimicrobials that are specifically requested or currently used for treatment are tested). In addition, some laboratories may selectively report only a subset of the AST results to clinicians, for example to encourage good antimicrobial stewardship. When selective reporting is applied in the context where most antimicrobials are routinely tested, surveillance reports should be generated from the full database of results for all antimicrobials that are routinely tested and not from the selectively reported data.

5 Bias mitigation to improve data representativeness

As mentioned previously, in the case of AMR, the type of bias of greatest concern is selection bias (see Section 4.3.1). In particular, for a system targeting the entire population of patients' seeking care and based on data collected through routine diagnostic testing, selection bias has a significant impact on the representativeness of collected data.

A surveillance system that is representative reflects the population characteristics related to time, place, and person. Thus, it accurately observes both the occurrence of the health event over time and the distribution by person and place of that event in the population at any point in time. Two main factors need to be considered by countries when implementing AMR surveillance:

1. **System capacity for generating results that represent the true proportion of AMR in a defined population**. When investigating a condition in a population, the ideal approach is to survey all the individuals within that population. For obvious reasons, this is very costly, time consuming, logistically demanding and almost impossible to implement in large populations. However, statistical methods allow us to identify a sample of individuals that is representative of the whole target population, so that the outcomes generated reflect occurrence in the larger entity.
2. **System capacity to capture all symptomatic patients constituting the defined population for which AMR rates are estimated**. Even when a clear case definition is available for a specific

syndrome, clinicians do not always take samples for microbiological culture and AST from all patients with suspected infection. Clinicians might only take samples from certain patients based on observed symptoms or risk factors, clinical perception, cultural belief or available resources. Such differences in individual clinical practice can lead to biased estimates of AMR occurrence as diagnostic results — both bacterial identification and AST — might not be available for all patients with suspected infection.

In order to help countries minimize biases associated with the capacity to generate representative results for a set population, GLASS has developed the *GLASS protocol for enhancing precision and representativeness of AMR routine surveillance* (13).The objective of this protocol is to provide national AMR focal points with defined criteria to be met retrospectively or set prospectively to ensure that generated estimates are representative of the national or subnational population of patients seeking care in health care facilities. This method is designed for countries that do not have data on health service delivery coverage, but do have available a comprehensive list of all national health care facilities with access to microbiological testing including AST and the number of patient admissions for each health care facility per year.

6 GLASS-AMR surveillance targets

6.1 Specimen types and target pathogens

6.1.1 Priority specimen types

During the early implementation of GLASS, blood, urine, faeces (stool), and urethral and cervical swabs were included as priority specimen types for global AMR reporting. The underlying assumption (see Section 4.3**Error! Reference source not found.**) was that isolation of a target pathogen from routine samples of one of these specimens would indicate the presence of infection in the bloodstream, urinary tract, gastrointestinal tract or urogenital tract (gonorrhoea), respectively. Infections in these anatomical sites are common, and an alarming increase has been observed in resistance to drugs of "last resort" used to treat infections in these sites in some countries.

Isolation of bacteria from blood specimens is usually indicative of a true infection, as long as no contamination occurs during the collection process, especially when focusing on specific pathogens, such as GLASS target pathogens for example. Some organisms can always be considered pathogens when isolated from certain sites, like *Salmonella* spp. from faeces or *N. gonorrhoeae* from urethral or cervical swabs. Since some associations between pathogen isolation and clinical infection are less clear cut (for example, in urine samples), GLASS relies on a clinical indication for sampling to reduce the number of false positives. While patients with uncomplicated urinary tract infection may not be routinely sampled, resulting in overestimated resistance rates, they can still provide an indication of emerging resistance in Gram-negative bacteria in the community.

To better address important public health threats, the next period of GLASS implementation has added additional specimen categories. These include cerebrospinal fluid (CSF) for the surveillance of AMR in bacterial meningitis pathogens, specimens from the lower respiratory tract for the surveillance of AMR in pathogens causing pneumonia, and non-urogenital samples (rectal and pharyngeal) for the surveillance of AMR in *N. gonorrhoeae*. The full list of selected specimen types and pathogens is shown in Table 6.1.

Other important sites of infection may be included in later stages. At the same time, it should be noted that **countries should include the sites of infection, pathogens and AST that are considered to be national priorities for surveillance**, **in addition to the specimens and pathogens targeted by GLASS**

6.1.1.1 Blood

Isolation of a pathogen from blood (as opposed to a contaminant) indicates the presence of a bloodstream infection, and is a diagnostic test recommended for every patient with sepsis, which is a life-threatening condition, even if treatment with appropriate antibiotics is initiated rapidly. Organisms typically considered as commensals may also cause bloodstream infections, but their significance can only be determined when two sets of blood cultures have been drawn from different sites within a specified timeframe and they are isolated from both sets. Ideally, routine blood culture should include two sets of cultures (each set consisting of an aerobic and anaerobic bottle if the laboratory is capable of isolating and identifying anaerobes) of cultures from two different venipuncture sites drawn five minutes apart after careful disinfection of the skin. If this is not possible, one set may be drawn from aspiration via an existing intravascular device, although this increases the risk for contamination. Isolation of a primary pathogen in a single set or of the same commensal in two culture sets does suggest a significant finding.

6.1.1.2 Cerebrospinal fluid (CSF)

CSF has been added as a priority specimen type in the second phase of GLASS in order to detect emerging resistance in primary pathogens causing bacterial meningitis (*N. meningitidis, Haemophilus influenzae, Streptococcus pneumoniae* and Gram-negative bacteria), another life-threatening disease. CSF cultures should ideally be combined with simultaneous blood cultures as the pathogenesis of the organisms causing primary meningitis is usually associated with bacteraemia. When the CSF punctate is collected (under aseptic conditions) into numbered tubes, the first tube should not be used for culture due to a higher probability of skin contaminants and tube no. 3 is frequently reserved for culture.

6.1.1.3 Urine

A midstream, clean catch sample of urine (MSU) is the specimen of choice to detect urinary tract infection, although poorly taken urine samples particularly from women and children can be prone to contamination with faecal, skin and normal vaginal microbiota. The laboratory should have standard algorithms in place to assess the likelihood of the clinical significance of contaminating organisms using purity of culture and colony counts. For example, a common approach to increase the clinical significance of urine samples is the exclusion of a sample with a growth of more than two pathogens in significant numbers, even if one of them is *E. coli* or *Klebsiella pneumoniae*.

Microbiology laboratories should have interpretation and reporting protocols for urinary tract infections in specific patient groups, including: children, pregnant women, the elderly, and those with an indwelling urinary catheter. In GLASS-AMR, only significant colony counts of the primary pathogens *E. coli* (10^5 colony-forming units [cfu]/mL) and *K. pneumoniae* (10^5 cfu/mL) should be included, although other pathogens may be relevant for patient management and local and national surveillance.

6.1.1.4 Stool

Diarrhoeal disease is a major cause of morbidity and mortality globally. *Shigella* spp. and non-typhoidal *Salmonella* are important bacterial causes of diarrhoeal disease, but these organisms are

not part of the normal stool microbiota. Growth of these pathogens in stool samples is therefore a diagnostic indicator of diarrhoeal disease. It should be noted that typhoidal salmonellae, although present and excreted in faeces, are most importantly detected in blood cultures as they cause systemic disease (fever and malaise) and may not be associated with diarrhoeal illness.

6.1.1.5 Specimens from the lower respiratory tract

Although bacterial respiratory tract infections are common, respiratory tract samples were not included in the early implementation of GLASS because of the difficulty in ascertaining the significance of pathogens when mixed with upper respiratory tract normal microbiota or other colonizers. This requires skill, experience, and a good liaison communication with the requesting clinicians.

Secondary bacterial pneumonia is well recognized as a complication in post-viral influenza-like illness. During the coronavirus disease (COVID-19) pandemic, a considerable number of hospitalized patients treated for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) respiratory illness, suffered morbidity and mortality associated with secondary bacterial infection (42-43). Therefore, respiratory samples have been included in the next phase of GLASS, despite difficulties in obtaining representative samples from the lower respiratory tract.

Recovery and recognition of organisms responsible for pneumonia depends on the following:

- adequacy of the lower respiratory tract specimen;
- avoidance of contamination by upper respiratory tract commensals;
- use of both microscopy techniques and culture methods;
- knowledge of current and recent antimicrobial treatment.

The distinction between tracheobronchial colonisation and true pulmonary infection can prove to be difficult.

Representative specimens from the lower respiratory tract include bronchial aspirate, transthoracic aspirate, bronchoalveolar lavage, transtracheal aspirate, bronchial brushings, protected catheter specimens, bronchial washings, endotracheal tube specimens in intubated patients (with the same contamination limitations as sputum specimens) (44), and expectorated sputum. Expectorated sputum samples are known to have significant issues with contamination. Early-morning sputum samples are preferred because they contain pooled overnight secretions in which pathogenic bacteria are more likely to be concentrated.

Gram stains on sputum specimens may be used for determining the quality of the specimen and for predicting likely pathogens by their characteristic appearance. Determining the quality of the specimen is based on the numbers of polymorphonuclear leucocytes and squamous epithelial cells present: purulent specimens may be selected for culture and non-purulent specimens or specimens contaminated with squamous epithelial cells may be rejected. The sensitivity of Gram stain can vary and is generally low and is often dependent on the individual reviewing the slide. Culture methods should follow standard protocols as defined by the local laboratory and should be performed only on representative samples.

If non-representative samples are cultured there is a risk that contaminants will be processed and reported – causing a major bias in the surveillance data collected. Furthermore, reporting of non-

significant (and potentially multiresistant) Gram-negative colonizers will drive the inappropriate use of broad-spectrum antibiotics and further promote selection of multi-drug resistant bacteria.

6.1.1.6 Specimen types for the surveillance of AMR in gonococci

N. gonorrhoeae is one of the pathogens in which antibacterial resistance has developed so extensively that there are very limited treatment options left in some places. Gonococcal infections can occur in different anatomical sites according to sexual practices. To align *N. gonorrhoeae* surveillance in GLASS with several already existing vertical programmes, microbiological reports from samples from two body sites other than urogenital specimens (urethral and cervical swabs) are now included in GLASS-AMR, that is, rectal and pharyngeal swabs.

6.1.2 Target pathogens

The pathogens initially selected for reporting to GLASS were chosen to cover common bacterial infections associated with health care as well as community-acquired infections. The selection covers pathogens causing a number of life-threatening infections, food-borne infections and infections where there are virtually no treatment options left. Pathogens were selected based on their public health burden, particularly if they develop multi-drug resistance. Multidrug-resistant organisms can result in significant harm to individuals and are a burden to health care systems and economies. Other pathogens (for example, *Salmonella* spp., *Shigella* spp.) were selected because they cause infections that lead to significant morbidity and mortality in low- and middle-income countries.

In this GLASS-AMR manual, additional pathogens have been included for surveillance. These include bacteria affecting vulnerable populations (for example, *H. influenzae* which can cause severe infections in children), and several of the GLASS target pathogens are included in the WHO *Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics* published in 2017 (45). According to the ranking applied in the prioritization process, four GLASS target pathogens are considered to be a critical priority, including *Acinetobacter* spp. and *Pseudomonas aeruginosa* resistant to carbapenems and *E. coli* and *K. pneumoniae* resistant to carbapenems or third-generation cephalosporins. A further three pathogens also belong to the high priority group (methicillin-resistant *Staphylococcus aureus*, fluoroquinolone-resistant *Salmonella* spp., and *N. gonorrhoeae* resistant to 3rd generation cephalosporins or azithromycin). Penicillin non-susceptible *S. pneumoniae* and fluoroquinolone-resistant *Shigella* spp. are medium priority according to the 2017 list.

GLASS focuses on some of the most important pathogens for surveillance at the global level, and during the next implementation stage the GLASS IT platform (a web-based platform for global data sharing on AMR) will only accept data from the specimen types and pathogens included in this manual. However, priorities for local and national surveillance may include other organisms and antimicrobial agents and should be addressed properly, even though they are not yet requested to be reported in GLASS.

The updated list of target pathogens and specimens selected by GLASS for the global reporting of AMR surveillance is shown in Table 6.1.

Table 6.1. GLASS target pathogens and specimen types

Target pathogens*	Specimens					
	Blood	CSF	Urine	Stool	**Lower respiratory tract**	Urethral, cervical, **rectal, pharyngeal** swabs
Acinetobacter spp.	●	○			●	
E. coli	●	○	●		○	
K. pneumoniae	●	○	●		●	
P. aeruginosa	●	○			●	
S. aureus	●	○			●	
S. pneumoniae	●	●			●	
N. meningitidis	●	●				
H. influenzae	○	●			●	
Salmonella spp. (non-typhoidal)	●	○		●		
***S. enterica* serovar Typhi**	●			○		
***S. enterica* serovar Paratyphi A**	●			○		
Shigella spp.				●		
N. gonorrhoeae						●

● Data collected and included in the official GLASS report when available
○ Included in the GLASS database to accommodate data when submitted, but not necessarily included in the official GLASS report

*New target pathogens and specimens are marked in bold font

6.2 Antimicrobial-pathogen combinations

Antimicrobials have been selected to allow for detection of the possible presence of the most important antibiotic resistance mechanisms for each target pathogen. While a relatively limited number of antimicrobial agents is included, information gleaned from the surveillance data can be interpreted (based on known resistance mechanisms) to other classes of antimicrobials. Consideration was given also to antimicrobials that are commonly used and available locally and nationally in participating countries. Among 32 antimicrobial drugs selected for global surveillance purposes, 11 are classified as “Access”, 18 belong to the “Watch” group, and 3 are “Reserve” antibiotics, according to the WHO AWaRe classification of antibiotics (46). Eighteen of the selected antibiotics are included in the current WHO Model Lists of Essential Medicines (29). The full list of the antimicrobial-pathogen combinations covered by GLASS is provided in Table 6.2.

When using Table 6.2, it is important to clearly understand the following:

- Table 6.2 provides the list of target antimicrobial-pathogen combinations selected by GLASS-AMR for global surveillance purposes. **The list is not intended to guide testing or prescribing practices.**

- The list does **not** imply that all of the included antimicrobials should be routinely included in AST by clinical laboratories. However, if susceptibility testing to any of these antimicrobials is performed, the results should be reported to GLASS. Similarly, the list does **not** mean that these are the only antimicrobials recommended for routine AST for the organism/body site

combination. Please refer to your local guidelines and international standards for recommendations.

- While an attempt was made to select a small number of representative drugs for each antimicrobial group, there are similar drugs in the same categories (for example, multiple third-generation cephalosporins or carbapenems). This was done on purpose, as different laboratories in different countries will often test just one of the drugs in a group, and a laboratory may change which drug is tested over time. This approach allows users and GLASS to meaningfully combine data from different laboratories that test different drugs within each antimicrobial group.

6.2.1 Subgroups of antimicrobials

AMR may need to be analysed both for a single antimicrobial and for a group of similar antimicrobial drugs. Grouping can be done with antimicrobials from the same class to better detect important resistance phenotypes, or with antimicrobials from different classes to recognize and track multidrug-resistant phenotypes (39). Collection of individual-level data (Section 7.2) allows for both grouping options.

Aggregation of data for individual antimicrobials reported by countries makes the subsequent grouping of results from similar or different antimicrobials at the global level technically impossible. That is why, in addition to the data on specific individual antimicrobial-pathogen combinations, GLASS requests countries to submit data on the priority subgroups of similar antimicrobials for the antimicrobial-pathogen combinations as presented in Table 6.2 using the Anatomical Therapeutic Chemical (ATC) classification system (47) to define and code the subgroups. Use of this classification will also facilitate the integrated analysis of AMR data and data on national antimicrobial drug consumption as the consumption data are often reported using ATC subgroups only.

6.3 Molecular targets

During the next implementation period, GLASS will continue to collect phenotypic test results, gradually introducing molecular methods (48) including whole-genome sequence (WGS) (49) results and planning their implementation on a systematic basis for the mid- and long-term GLASS development stages. For the next implementation period an option for submission of data generated by molecular AMR diagnostics has been included to complement phenotypic AMR diagnostics data and improve understanding of the underlying mechanisms responsible for resistance. The selected molecular surveillance targets are listed in Annex 8.

Table 6.2. Specimens, pathogens, and antimicrobial drugs selected for the global surveillance of AMR

Specimen	Laboratory case definition	Pathogens under surveillance	Antimicrobial group (ATC)	Antimicrobials to report to GLASS if tested [a]
Blood	Isolation of pathogen from blood [b]	*Acinetobacter* spp.	Tetracyclines Aminoglycosides Carbapenems [c] Polymyxins	Tigecycline, minocycline Gentamicin, amikacin Imipenem, meropenem, doripenem Colistin
		E. coli and *K. pneumoniae*	Sulfonamides and trimethoprim Fluoroquinolones Third-generation cephalosporins Fourth-generation cephalosporins Carbapenems [c] Polymyxins	Co-trimoxazole Ciprofloxacin, levofloxacin Ceftriaxone, cefotaxime, ceftazidime Cefepime Imipenem, meropenem, ertapenem, doripenem Colistin
		P. aeruginosa	Third-generation cephalosporins Combinations of penicillins, including beta-lactamase inhibitors Aminoglycosides Carbapenems [c] Polymyxins	Ceftazidime Piperacillin/tazobactam Gentamicin, amikacin, tobramycin Imipenem, meropenem, doripenem Colistin
		S. aureus	Beta-lactamase resistant penicillins Second-generation cephalosporins	Oxacillin Cefoxitin [d]
		S. pneumoniae	Beta-lactamase sensitive penicillins Beta-lactamase resistant penicillins Third-generation cephalosporins Sulfonamides and trimethoprim Macrolides	Penicillin G Oxacillin [e] Ceftriaxone, cefotaxime Co-trimoxazole Erythromycin
		Salmonella spp.[f]	Fluoroquinolones Third-generation cephalosporins Carbapenems [c]	Ciprofloxacin, levofloxacin Ceftriaxone, cefotaxime, ceftazidime Imipenem, meropenem, ertapenem, doripenem
		Salmonella enterica serovar Typhi and *Salmonella enterica* serovar Paratyphi A	Amphenicols Penicillins with extended spectrum Sulfonamides and trimethoprim Fluoroquinolones Third-generation cephalosporins Macrolides	Chloramphenicol Ampicillin Co-trimoxazole Ciprofloxacin, levofloxacin Ceftriaxone, cefotaxime, ceftazidime Azithromycin
		S. pneumoniae	Beta-lactamase sensitive penicillins	Penicillin G

Specimen	Laboratory case definition	Pathogens under surveillance	Antimicrobial group (ATC)	Antimicrobials to report to GLASS if tested [a]
Cerebrospinal fluid (CSF)	Isolation of pathogen from cerebrospinal fluid		Beta-lactamase resistant penicillins Third-generation cephalosporins Sulfonamides and trimethoprim	Oxacillin [e] Ceftriaxone, cefotaxime Co-trimoxazole
		N. meningitidis	Beta-lactamase sensitive penicillins Rifamycins Fluoroquinolones Third-generation cephalosporins	Penicillin G Rifampicin Ciprofloxacin Ceftriaxone, cefotaxime
		H. influenzae	Penicillins with extended spectrum Combinations of penicillins, including beta-lactamase inhibitors Third-generation cephalosporins Sulfonamides and trimethoprim	Ampicillin Amoxicillin-clavulanic acid Ceftriaxone, cefotaxime Co-trimoxazole
Urine	Significant growth in urine specimen [g]	*E. coli* and *K. pneumoniae*	Nitrofuran derivatives Penicillins with extended spectrum Sulfonamides and trimethoprim Fluoroquinolones Third-generation cephalosporins Fourth-generation cephalosporins Carbapenems [c] Polymyxins	Nitrofurantoin (for *E. coli*) Mecillinam Co-trimoxazole Ciprofloxacin, levofloxacin Ceftriaxone, cefotaxime, ceftazidime Cefepime Imipenem, meropenem, ertapenem, doripenem Colistin
Stool	Isolation of *Salmonella* spp.[h] or *Shigella* spp. from stool	*Salmonella* spp.	Sulfonamides and trimethoprim Fluoroquinolones Third-generation cephalosporins Carbapenems [c]	Co-trimoxazole Ciprofloxacin, levofloxacin Ceftriaxone, cefotaxime, ceftazidime Imipenem, meropenem, ertapenem, doripenem
		Shigella spp.	Sulfonamides and trimethoprim Fluoroquinolones Third-generation cephalosporins Macrolides	Co-trimoxazole Ciprofloxacin, levofloxacin Ceftriaxone, cefotaxime, ceftazidime Azithromycin

Specimen	Laboratory case definition	Pathogens under surveillance	Antimicrobial group (ATC)	Antimicrobials to report to GLASS if tested [a]
Lower respiratory tract	Significant growth in representative sputum samples or in material obtained from lower respiratory tract by the procedures listed in Section 6.1.1.5	*S. pneumoniae*	Beta-lactamase sensitive penicillins Beta-lactamase resistant penicillins Third-generation cephalosporins Sulfonamides and trimethoprim	Penicillin G Oxacillin[e] Ceftriaxone, cefotaxime Co-trimoxazole
		H. influenzae	Penicillins with extended spectrum Combinations of penicillins, including beta-lactamase inhibitors Third-generation cephalosporins Fluoroquinolones Sulfonamides and trimethoprim	Ampicillin Amoxicillin-clavulanic acid Ceftriaxone, cefotaxime Ciprofloxacin, levofloxacin Co-trimoxazole
		S. aureus	Beta-lactamase resistant penicillins Second-generation cephalosporins	Oxacillin Cefoxitin [d]
		Acinetobacter spp.	Tetracyclines Aminoglycosides Carbapenems [c] Polymyxins	Tigecycline, minocycline Gentamicin, amikacin Imipenem, meropenem, doripenem Colistin
		E. coli and *K. pneumoniae*	Sulfonamides and trimethoprim Fluoroquinolones Third-generation cephalosporins Fourth-generation cephalosporins Carbapenems [c] Polymyxins	Co-trimoxazole Ciprofloxacin, levofloxacin Ceftriaxone, cefotaxime, ceftazidime Cefepime Imipenem, meropenem, ertapenem, doripenem Colistin
		P. aeruginosa	Third-generation cephalosporins Combinations of penicillins, including beta-lactamase inhibitors Aminoglycosides Carbapenems [c] Polymyxins	Ceftazidime Piperacillin/tazobactam Gentamicin, amikacin, tobramycin Imipenem, meropenem, doripenem Colistin

Specimen	Laboratory case definition	Pathogens under surveillance	Antimicrobial group (ATC)	Antimicrobials to report to GLASS if tested [a]
Urethral, cervical, rectal, pharyngeal swabs	Isolation of *Neisseria gonorrhoeae*	*N. gonorrhoeae*	Third-generation cephalosporins Macrolides Aminocyclitol Fluoroquinolones Aminoglycosides	Ceftriaxone, cefixime Azithromycin Spectinomycin Ciprofloxacin Gentamicin

[a] The listed substances are priorities for the 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. AST results and numerator and denominator data for each drug will be reported separately

[b] Any pathogen isolated from a blood culture may be significant for local and national surveillance; only the pathogens selected for global surveillance are listed here

[c] Imipenem or meropenem is preferred to represent the group when available

[d] Recommended for the detection of methicillin resistance in *Staphylococcus aureus* (MRSA) when using disk diffusion testing.

[e] Oxacillin disk testing is a screening for reduced susceptibility or resistance to penicillin

[f] Not serovar Typhi or Paratyphi A

[g] Urinary catheter samples should be excluded if possible

[h] Discriminate serovar Typhi or Paratyphi A whenever possible

7 GLASS-AMR data submission

GLASS-AMR accepts the submission of both aggregated and individual level data.

7.1 Aggregated data

Two datasets are requested to be submitted to GLASS (see *Table 7.1*).

1. **RIS dataset** with susceptibility testing results. These are data (aggregated from all participating national surveillance sites submissions) on the number of **R**[3], **I**[4], **S**[5] isolates for each target antimicrobial detected in GLASS priority specimens, stratified by gender, age group and infection origin.
2. **SAMPLE dataset** with the number of tested patients. These are the numbers of patients from whom specimens have been taken and sent to the laboratory for bacterial isolation purposes, stratified by gender, age group and infection origin (as in the RIS dataset).

Both *RIS* and *SAMPLE* datasets should be generated from the same source database. Countries can submit a *SAMPLE* dataset with a *RIS* dataset, or a *RIS* dataset alone.

For GLASS reporting purposes all variables in the datasets are mandatory and they should always be present. When patient demographic and epidemiological data are not available (gender, age or infection origin), an "UNK" value must be entered. Users can manually input "UNK" values, or use applications for data management and analysis, such as WHONET, which automatically generate the "UNK" values for missing data.

With reference to previously mentioned isolate-based and sample-based data approaches (Section 4.2), *Table 7.1* describes how the two datasets provide the needed information. All patients included in the *RIS* dataset must be also represented in the *SAMPLE* dataset, as the latter includes the information on the whole target population. Conversely, as the *SAMPLE* dataset includes also information on patients with no bacterial growth, the *RIS* dataset will always include a lower number of patient data.

Table 7.1. Datasets reported using the two surveillance approaches

Data collected	AMR surveillance approach	
	Isolate-based	Sample-based
Patients AST results for bacterial pathogens and antibiotics under surveillance	RIS dataset	RIS dataset
Numbers of patients from whom samples have been collected for microbiological testing (both with and without growth of the bacterial pathogens under surveillance) according to specimen type		*SAMPLE* dataset

[3] **R** = **R**esistant
[4] **I** = Susceptible, **I**ncreased exposure (EUCAST) or **I**ntermediate (CLSI)
[5] **S** = **S**usceptible

7.1.1 *RIS* dataset

Data included in the *RIS* dataset are listed below:

- reporting country
- year of data collection
- specimen type
- pathogen
- gender
- infection origin (community versus hospital as proxy for infection onset)
- age group
- antimicrobial used for AST
- number of R isolates
- number of I isolates
- number of S isolates
- number of isolates with AST results not reported (not performed) for a specific antibiotic
- number of isolates with AST performed but no interpretation of results available
- subset of national aggregated data

A detailed description of the variables in the RIS dataset is available in the Annex 1.

7.1.2 *SAMPLE* dataset

The *SAMPLE* dataset is collected to generate sample-based data and it contains denominator data organized using the same aggregation and stratification approaches as for the *RIS* file. To create a stratified *SAMPLE* file, the source database needs to contain the number of patients with all positive (that is, both with growth of GLASS and non-GLASS pathogens) and negative (no growth) results and with all GLASS variables present (gender, age and infection origin). The *SAMPLE* dataset **cannot** be generated if only the number of patients with positive species identification results is available, without the number of negative tests.

Note that the dataset contains only the number of patients for which samples were sent to the laboratory for bacterial isolation purposes, and not for other reasons. For example, stool specimens are often taken for "ova and parasites". Similarly, many genital samples are collected for the diagnosis of vaginosis/vaginitis by microscopy, not for the culture of *N. gonorrhoeae*, which requires special media and growth conditions. Therefore, if these patients were to be included in the dataset, they would incorrectly increase the denominator of cultured patients, which is a proxy for patients showing symptoms of a bacterial infection, as mentioned in Section 4.3.4.

Data included in the *SAMPLE* dataset are listed below:

- reporting country
- year of data collection

- specimen type
- gender
- infection origin (community vs. hospital as proxy for infection onset)
- age group
- number of tested patients
- subset of national aggregated data

A detailed description of the variables in the *SAMPLE* dataset is available in the Annex 2.

7.2 Individual-level data

GLASS-AMR offers the option of submitting individual, line-listed anonymized AMR data to participating countries. Apart from allowing for better data validation and management, the huge benefit associated with individual data is their analytical potential. Specifically, individual-level data can allow to:

- monitor the occurrence of multidrug resistance, critical for informing research and development of new therapeutic and diagnostic tools;
- explore additional data analyses and stratifications;
- generate state/province or regional statistics by including facility identifiers to support an analysis of data by national surveillance systems
- analyse drivers and risk factors linked to resistance
- enhance the ability to study the evolution of resistance during the year
- improve capacity for outbreak detection
- generate transmission trends, using both spatial and genetic information
- provide several additional ways to assess data quality

At the same time, GLASS-AMR will continue collecting national aggregated data, which will still offer a valuable set of information regarding the proportion and frequency of AMR within a given population. In addition, once its limitations are understood, data can be used to obtain meaningful insight into the development of resistance in enrolled countries. However, the aggregation of AMR data at national levels poses a major challenge for accurate data analysis and interpretation of results.

A number of countries are already submitting individual level data to several international networks supporting GLASS such as the Central Asian and European Surveillance of Antimicrobial Resistance Network (CAESAR) (50), the European Antimicrobial Resistance Surveillance Network (EARS-Net) (51), and the Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos (ReLAVRA; Latin American Network for Antimicrobial Resistance Surveillance) (52). The individual data module has been developed in the GLASS IT platform and is available to all countries that wish to explore the benefits of individual data submission, including the validation and analytical tools built into the platform.

7.2.1 Individual-level dataset

The individual level dataset includes both the AST interpretations (R, I, S) and "raw" AST measurements (disk zone diameters or minimum inhibitory concentration [MIC] values) and has all the variables required to generate the GLASS aggregated dataset, as well as additional technical and epidemiological variables.

All patient-specific identifiers in the individual-level data set are anonymized to avoid identification of individual patients. Data included in the individual-level dataset are as follows:

- reporting country
- laboratory identifier (will be encrypted by the NCC before reporting to GLASS)
- healthcare facility identifier (will be encrypted by the NCC before reporting to GLASS)
- hospital department
- anonymised patient identifier
- gender
- age
- patient location type (inpatient vs. outpatient)
- date of admission
- date of specimen collection
- specimen type
- isolate identifier
- pathogen
- antimicrobial used for AST
- AST results (zone diameters and interpretations, MICs and interpretations, gradient strip testing results and interpretations)
- final interpretation of AST results (R, I, S, etc.)
- guidelines used for susceptibility testing (CLSI, EUCAST, etc.)

A detailed description of the variables (including several technical variables and variables specific for the WHO regional networks' data collection not listed above) is available in Annex 3.

7.2.2 Collection of additional denominators for the individual-level dataset

In addition to the variables listed in Section 7.2.1, countries reporting individual data are requested to also submit data on population denominators and characteristics of the participating surveillance sites, including the following information:

At the national level:

- total national population in the reporting year (based on the United Nations Population Division estimates)

Per surveillance site:

- numbers of patients seeking care during the reporting year at surveillance sites;
- number of consultations in outpatient clinics for the reporting year;
- total number of patient admissions for inpatient facilities for the reporting year;
- type of the facility (hospital versus outpatient clinic);
- level of care for the hospitals (primary, secondary, tertiary) (see Annex 6. Types of care);
- best estimate of the catchment population of the healthcare facility in the reporting year;
- hospital size in beds in the reporting year;
- number of intensive care beds in the reporting year;
- total number of patient days in the hospital in the reporting year;
- total number of blood culture requests (sets)[6] per year;
- total number of patients with suspected bloodstream infection for which blood culture was requested per year;
- total number of blood specimens received by the laboratories per year.

7.3 Collection of data on the status of national surveillance system

GLASS will continue to collect data on the status of national AMR surveillance systems using the GLASS implementation questionnaire (see Annex 7), together with the collection of indicators to define the representativeness and quality of the AMR surveillance data.

8 Collection, management, analysis and reporting of data

8.1 GLASS data flow

A schematic view of the AMR data flow is shown in Figure 8.1 and described below.

[6] One request/set consists of any number of blood culture bottles that are taken from one patient on a single occasion for diagnostic purposes

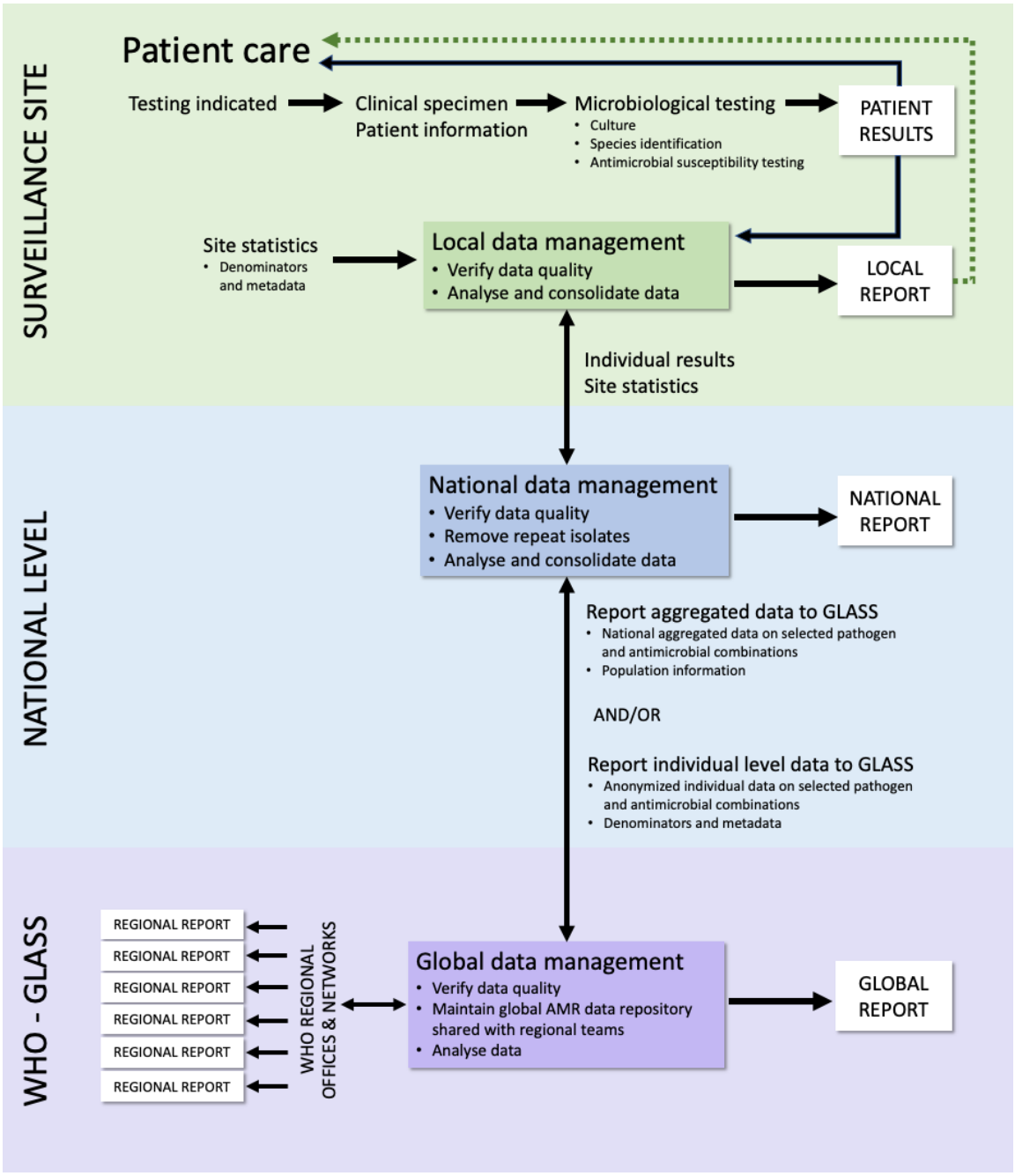

Figure 8.1. GLASS data flow

8.2 Collection and management of data at surveillance sites

Clinicians at the participating health care facilities should be trained and encouraged to send samples for culture and AST from patients with suspected infection to the laboratory serving the health care facility/surveillance site. GLASS methodology is based on the assumption that all patients with suspected infection will be sampled. While this is not yet the case in many places, an effort should be made to introduce health care facilities to the concept of diagnostic stewardship, which comprises coordinated guidance and interventions to improve the use of microbiological diagnostics to guide therapeutic decisions (32). Appropriate and timely diagnostic testing, including specimen collection, pathogen identification and AST, including the accurate and timely reporting of clinically relevant results must be promoted in all health care facilities. The underutilization and incorrect use of

microbiological tests and diagnostic tools has a negative effect on the management and outcome for individual patients. It may also lead to a selection bias and result in a lack of representative and reliable surveillance data for empiric treatment recommendations and AMR control strategies.

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 informatics tool, and to produce timely reports and feedback on a regular basis.

The very minimum core patient data required by GLASS that should accompany any request for AST are as follows: unique identifier; age; gender; specimen type; date of specimen collection; date of admission; and patient location type status (inpatient versus outpatient). The last two are important to define the origin of the infection. Additional information may be requested according to local and national protocols and when reporting individual-level data to GLASS (for example, hospital name, ward or department, patient diagnosis, medical history, referral, antimicrobial therapy, etc.).

To implement the sample-based approach (see Section 4.2), data associated with the sample should be registered (added where hospital information systems are in use) using data management software as soon as the request is generated and before the species identification and AST results are available, independent of these results being negative or positive. These results should be added to the database serving as a repository for surveillance data for all specimen types and all pathogens and antimicrobials relevant for the surveillance site, without limiting the list by the GLASS targets or the targets defined by a national programme.

For sites that do not yet have suitable software for efficient data management and reporting in place, the freely available WHONET software (53) is recommended. WHONET can be used on stand-alone computers or be linked to existing information systems and includes a feature for exporting AMR statistics into the format required for producing local and national reports and for uploading to the GLASS IT platform.

8.3 Laboratory procedures at surveillance sites

On-site laboratory capability and capacity for testing specimens facilitates surveillance, but is not essential if the site can store and transport samples rapidly to another testing facility serving the site. All surveillance sites must be linked to at least one laboratory that can identify the pathogens and perform AST in time according to appropriate standards. Sampling, culture and species identification must be performed according to good laboratory practice, as described in WHO manuals (54-55) and textbooks and as recommended by the NRL. For AST, the disk diffusion methods recommended by the CLSI (56) or EUCAST (57), or automated, semi-automated or manual testing for MICs and gradient diffusion can be used. The latest published clinical breakpoints should be applied. All methods should be internationally recognized and selected based on the available resources and sustainability considerations. With the aggregated data collection, GLASS will collect only susceptibility data interpretations categorized as “R”, “I” and “S”. However, it recommends that MICs and inhibition zone diameters are also collected and reported at national level whenever possible, to allow quality control of data, comparison of old and new results, and to track microbiological subpopulations in outbreak investigations, etc. The information on which interpretive criteria are being applied is collected by

GLASS-AMR for the reporting country (aggregated data) and for the participating surveillance sites (individual-level data).

Staff should be trained to recognize any unusual or unexpected findings from routine microbiology species identification and AST results, and raise alerts if necessary. When a new drug is introduced into clinical practice, laboratories should routinely test susceptibility to the drug in order to identify emerging resistance.

Some of the isolates identified, particularly mixed flora, may represent cases of contamination of specimens or colonization at the sampled body site. Surveillance sites are responsible for assessing the clinical significance of positive cultures and to identify and exclude contaminants from their data. Therefore, positive cultures reported are considered a proxy for infection.

Laboratories serving participating surveillance sites should use a quality management system recognized by the NRL to assure 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 the appropriate WHO manuals (58-59) and CLSI (60) or EUCAST (61) guidelines. All laboratories that provide data to an AMR surveillance system must participate in at least one proficiency testing scheme that is recognized by the NRL and covering AST. Corrective actions should be promoted by the NRL based on the findings from external quality assessment programmes.

8.4 Collection and management of data at the national level

The NCC receives standardized datasets from the local surveillance sites and reports the data to GLASS. In addition to the datasets required by GLASS, a more comprehensive approach is recommended at the national level, including other species and specimen types according to national policy.

The most common surveillance period and also recommended by GLASS is one year. Collecting the data over one year provides a more representative sample and decreases the impact of outbreaks or seasonal variations on the observed AMR rates.

In particular, management of data at the national level includes quality checks, removal of duplicated results, encryption, generation of aggregated data files and submission of the data to GLASS.

8.4.1 Checking quality of data at the local level

It is expected that the local surveillance sites will perform quality checks on collected data before submitting them to the national level. The data will need to be assessed for completeness including 100% completeness of mandatory variables, and checked for consistency and plausibility, as well as adherence to national standards for microbiological species identification and AST. At the national level, data should be validated using a similar approach and corrections may need to be requested through communications with participating surveillance sites.

8.4.2 Removal of duplicate results

Individual patients are often sampled repeatedly for diagnostic purposes or to assess the therapeutic response. Patients with infections caused by resistant microorganisms are more likely to be sampled repeatedly. When several cultures are collected during patient management, duplicate findings for

the same patient and the same microorganism (more precisely, repeat isolates of the same species, even if the resistance characteristics differ) should be excluded from the source database (de-duplication), keeping the first sample to ensure that data are not biased by repeated measurements.

Before starting the de-duplication process, it is advisable to review variables containing information about the patient and to particularly check whether the database contains patient identifiers or unique counters. If they are missing, a variable with a unique patient identifier or counter should be generated. When there are missing values, a unique identifier could be created, for example, from the patient's personal information data for each missing value.

While the local surveillance sites could apply different de-duplication algorithms, depending on a specific purpose (for example, informing infection prevention and control) and when preparing the hospital antibiograms and local surveillance reports, it is expected that the NCC will take the responsibility of de-duplication according to the national protocol and GLASS recommendations. All consecutive isolates (and negative samples) should be submitted to the NCC, which will remove duplicate results (ideally, with the participation of the surveillance site to build the local capacity).

When reporting to GLASS, for each surveillance period (for example, 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 isolate should be included in the report; if growth of *E. coli* is 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 included. The only exception is when on one and the same day, the same pathogen is isolated from both blood and CSF from a single patient. In this case, only data on the CSF isolate are included in analyses.

If two records for the same patient show the same pathogen in the same specimen type, but the infection origin has changed from hospital to community, both samples should be included. Repeated negative results for the same specimen type in the same patient should also be de-duplicated in the generation of the *SAMPLE* file where the interest is "number of tests performed" and not the results of those tests.

In the example below[7] three patients have several samples taken during the reporting year. Duplicated records to be removed are marked in red:

Sample ID	Patient ID	SPECIMEN	PATHOGEN	ORIGIN
27	A	BLOOD	ESCCOL	HO
~~244~~	~~A~~	~~BLOOD~~	~~ESCCOL~~	~~HO~~
369	B	BLOOD	KLEPNE	HO
~~394~~	~~B~~	~~BLOOD~~	~~NEGATIVE~~	~~HO~~
~~438~~	~~B~~	~~BLOOD~~	~~NEGATIVE~~	~~HO~~
626	A	BLOOD	ESCCOL	CO
627	C	BLOOD	NEGATIVE	HO
~~760~~	~~A~~	~~BLOOD~~	~~ESCCOL~~	~~HO~~
792	B	URINE	NEGATIVE	HO
801	A	URINE	KLEPNE	HO
~~805~~	~~A~~	~~URINE~~	~~KLEPNE~~	~~HO~~
~~900~~	~~C~~	~~BLOOD~~	~~NEGATIVE~~	~~HO~~

[7] This is a simplified view of the database, not all variables that should be part of the source database are shown here

De-duplication promotes standardization and comparison of the data at the local, national, regional and global levels.

8.4.3 Data encryption

WHO is committed to data protection and privacy for patients and healthcare facilities. For that reason, the patient identification (ID) number and the sample ID available at the local surveillance sites and NCC should be encrypted in accordance with country legislation before the data are shared with GLASS. Encryption of the patient ID can be accomplished using the standard function available in WHONET or using other encryption tools available. At the national level, laboratory and hospital codes should be generated. The hospital and laboratory names will only be available at the national level and will not be shared with GLASS.

8.4.4 Data anonymization

Laboratory data may contain personal information. It is important that all information that may lead to the identification of a patient is removed before data are sent to a national or international surveillance network. Examples of identifying information are names, birth dates, home addresses, and national identifiers, such as social security numbers. Such information should not be used as a patient identifier. The unique identifier should not be traceable to the patient and has to be encrypted if the original one is an identifying element.

8.4.5 Grouping antimicrobials

Grouping of antimicrobials is needed when aggregated data are reported to GLASS (see Section 6.2.1). The priority sequence R $\rightarrow$ I $\rightarrow$ S is used to classify AST results in a pathogen. When combining the results for the antimicrobial representing the group or class, the outcome is based on the most resistant result and so it is important to note that the resulting data may not indicate resistance to all antimicrobials in the group. For example, if a pathogen's susceptibility to imipenem is "I" and susceptibility to meropenem is "R", then the susceptibility to carbapenems is set to "R". Of note, this approach should be applied with caution as such an extrapolation could lead to over-reporting of resistance for some classes where different resistance mechanisms are present, for example, aminoglycosides or fluoroquinolones.

8.4.6 Data aggregation and submission to GLASS

8.4.6.1 Submission of aggregated data

The NCC is responsible for preparing the aggregated GLASS *RIS* and *SAMPLE* datasets from data collected at the surveillance sites. The first step for the data manager at the NCC is to combine the datasets from all local surveillance sites into one dataset. The resulting data should be aggregated according to specifications detailed in Annexes 1 and 2. The WHONET software has automated export functions that include the generation of the *RIS* and *SAMPLE* files. If relevant microbiology test results are stored within a laboratory information system (LIS), the data can be imported into WHONET using the BacLink data import utility (bundled with WHONET); which can then produce the *RIS* and *SAMPLE* datasets using the automated export functions. When the *RIS* and *SAMPLE* files are generated, they can be uploaded to the GLASS IT platform (62) as described in the *Guide to use of the GLASS IT platform*[8].

[8] *User guide to the GLASS IT platform: submission and analysis of AMR data* (tentative title, work in progress)

8.4.6.2 Submission of individual level data

Preparation of the individual level GLASS dataset also starts with combining the datasets from all local surveillance sites into one national dataset. The resulting data should be exported in the GLASS individual file format described in Annex 3. It is important to ensure that the data are properly anonymized and encrypted before submission. The WHONET software has automated export function that include generation of the GLASS individual dataset compatible with the datasets collected by the WHO regional networks. When the GLASS individual level dataset is generated, it can be uploaded via the individual data module in the GLASS IT platform as described in the *Guide to the use of the GLASS IT platform*.

8.4.7 Global and regional management of GLASS-AMR data

GLASS has developed an IT platform for global data sharing on AMR. Launched in 2016, the platform is hosted on a WHO server and serves as a common environment for standardized data submission, validation, analysis, reporting and data-sharing with countries and WHO regional and country offices.

The GLASS-IT-platform is a secure web-based platform with user-specific roles and access rights. The platform accepts data in a number of formats, thus allowing for flexibility and tailored approaches to the needs of individual countries, and WHO teams from the regional and country offices. This shared ownership of the global AMR data repository allows collaborative work with countries, and the generation of different analyses and reports at the global, regional and country levels.

All GLASS databases are accessed with unique authentication and rights management processes. Users of the GLASS-IT platform can upload, manage and submit data, access upload history, access and download previously submitted data and generate customised data reports. Users can also access statistical information and dashboards based on data provided. All databases have common data workflows (enrolment, data upload, data validation, import, and report publication).

9 Analysis and reporting of data

A global report on AMR surveillance is produced every year and includes progress in establishing surveillance capacity, quality and reporting at national and regional levels. Data showing the progress of countries and AMR data will be published and made available on the GLASS (63) and WHO Global Health Observatory (64) websites.

Currently GLASS reports both the:

- proportion of drug-resistant infections among all patients with a microbiologically-confirmed infection for each specimen-pathogen-antibiotic combination; and
- frequency of infection caused by resistant pathogens among the population of patients who sought medical care and from whom samples have been collected for microbiological testing in the reporting period

In its next implementation phase GLASS is collecting a larger amount of information, particularly through the individual-level module. 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 the target population (denominator). Stratification and risk factor analysis can help

associate AMR with a group of patients, or clinical drivers. New analytical approaches will be developed according to the availability and nature of collected data.

9.1 Key GLASS-AMR metrics for global reporting

Proportion of drug-resistance. For each specimen type, pathogen and antimicrobial drug under surveillance, the proportions of patients with growth of resistant strains are calculated using the following formula and presented graphically:

$$\frac{\text{Number of patients, per specimen type, with infection by pathogen}_x \text{ resistant to antibiotic}_y \text{ under surveillance}}{\text{Total number of patients, per specimen type, with infection by pathogen}_x \text{ susceptible, I, and resistant to antibiotic}_y \text{ under sureveillance)}} * 100\%$$

Note that due to selective testing, although the infected population for a specific pathogen under surveillance does not change, the denominator will change based on the antibiotic under surveillance, as the actual number of patients comprising the denominator is based on the availability of AST results for that antibiotic.

Example:

Number of patients with bloodstream infections caused by E. coli resistant to cefotaxime / number of patients with bloodstream infection caused by E. coli with AST results (susceptible, I, resistant) for cefotaxime.

Frequency of infections and drug-resistant infections. For countries that submitted sample-based data, a further analysis is performed. It is important to note that as countries are asked to provide only clinically significant results, positive cultures reported are considered to be a proxy for infection. In addition, data de-duplication only allows new cases to be reported. Thus, the frequency of infection with pathogens under surveillance and the frequency of infection with pathogens resistant to specific antibiotics are calculated for the tested population, defined as the total number of symptomatic patients that sought medical care and from which samples of different specimen types where taken.

For each specimen type, infection origin and pathogen, rates of patients with new infections are calculated per 100,000 tested patients using the following formula and presented graphically:

$$\frac{\text{Number of patients, per specimen type, with infection by pathogen}_x \text{ under surveillance}}{\text{Population tested during the reporting period per specimen type and infection origin}} * 100000$$

Example:

Number of patients with bloodstream infection of community origin caused by E. coli / number of patients with suspected infection of community origin from which a blood sample was taken

Subsequently, for each specimen type, infection origin, pathogen, and antibiotic under surveillance, rates of patients with a new growth of resistant strains, are calculated per 100,000 tested patients, using the following formula and presented graphically:

$$\frac{\text{Number of patients, per specimen type, with infection by pathogen}_x \text{ resistant to antibiotic}_y \text{ under surveillance}}{\text{Population tested during the reporting period per specimen type and infection origin}} * 100000$$

Example:

Number of patients with bloodstream infection of community origin caused by E. coli resistant to cefotaxime / number of patients with suspected infection of community origin from which a blood sample was taken

Note that in this case it is not assumed that the absence of AST results should be interpreted as having a susceptible result, but that patients with no bacterial growth cannot influence the magnitude of resistance patterns in the target population

Glossary

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Annex 1. *RIS* dataset variables

The RIS variables are shown in the Table A.*1* below:

Table A.1. Variables in the RIS dataset

Variables in *RIS* dataset	Type of variable	Example
COUNTRY	Coded value*	*AFG*
YEAR	Coded value	*2015*
SPECIMEN	Coded value	*BLOOD*
PATHOGEN	Coded value	*ACISPP*
GENDER	Coded value	*M*
ORIGIN	Coded value	*HO*
AGEGROUP	Coded value	*01<04*
ANTIBIOTIC	Coded value	*AMK*
R_CATEGORY	Integer (≥0)	*15*
I_CATEGORY	Integer (≥0)	*10*
S_CATEGORY	Integer (≥0)	*30*
UNKNOWN_NO_AST	Integer (≥0)	*5*
UNKNOWN_NO_BREAKPOINTS	Integer (≥0)	*0*
BATCHID	Coded value	DS1

* Coded values lists for all coded value variables are available in Annex 4

*Variable **COUNTRY***

COUNTRY is a mandatory coded value variable with three-letter country codes based on ISO 3166-1 (for example, AFG = Afghanistan). The list of country codes with both full and short country (territory) names is available in Annex 4.

*Variable **YEAR***

YEAR is a mandatory coded value variable. The value in the *RIS* file shows the year represented by the data collection, typically using specimen collection date in the source database.

*Variable **SPECIMEN***

SPECIMEN is a mandatory coded value variable. The coded value list for the GLASS specimens is available in Annex 4.

*Variable **PATHOGEN***

PATHOGEN is a mandatory coded value variable. The coded value list for the GLASS target pathogens is available in Annex 4.

*Variable **GENDER***

GENDER is a mandatory coded value variable. The coded value list is available in Annex 4. Please use the *UNK* value when the data are not stratified by gender.

*Variable **ORIGIN***

ORIGIN is a mandatory coded value variable. The coded value list is available in Annex 4.

Please note that infections are considered to be of "hospital origin" if patients had been hospitalized for > 2 calendar days when the specimen was taken. This includes the following:

- 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

Infections are considered to be of "community origin" for patients seeking care at an outpatient clinic when the specimen was taken or patients hospitalized for ≤ 2 calendar days when the specimen was taken.

If the data on the patient origin are not entered directly at the surveillance site using the above-mentioned case definitions, the variable ORIGIN could be calculated using the variables with the data on the date of admission, date of sample, and patient location type (outpatient versus inpatient locations).

Please use the *UNK* value when the data are not stratified by infection origin.

*Variable **AGEGROUP***

AGEGROUP is a mandatory coded value variable. The coded value list is available in Annex 4. Please note that the sign "<" is used in the AGEGROUP codes instead of the sign "-": this is to avoid re-formatting issues in Microsoft Excel. Please use the UNK value when the data are not stratified by age.

*Variable **ANTIBIOTIC***

ANTIBIOTIC is a mandatory coded value variable. The coded value list is available in Annex 4 and includes both codes for individual antimicrobials and ATC codes for the sub-groups of antibiotics.

Numeric variables in the RIS file: overview

Numeric variables in the *RIS* file include AST interpretation results, based on definitions and standards used in the reporting country. They also include data on the identified pathogens (isolates) where AST was not performed or could not be interpreted.

*Variable **R_CATEGORY***

R_CATEGORY is a mandatory integer (≥0) variable representing the number of isolates resistant to a specific antibiotic. This includes AST results interpreted as **resistant ("R")**, according to EUCAST(65) or CLSI(56) (and including a nonsusceptible [NS] category according to CLSI) definitions of susceptibility categories.

*Variable **I_CATEGORY***

I_CATEGORY is a mandatory integer (≥0) variable representing the number of isolates with AST results interpreted as **susceptible, increased exposure** according to EUCAST or **intermediate** (including susceptible-dose dependent [SDD]) according to CLSI.

*Variable **S_CATEGORY***

S_CATEGORY is a mandatory integer (≥0) variable representing the number of isolates with AST results interpreted as **susceptible, standard dosing regimen**, according to EUCAST or **susceptible** according to CLSI.

*Variable **UNKNOWN_NO_AST***

UNKNOWN_NO_AST is a mandatory integer (≥0) variable representing the number of isolates with AST results not reported (not performed) for a specific antibiotic.

*Variable **UNKNOWN_NO_BREAKPOINTS***

UNKNOWN_NO_BREAKPOINTS is a mandatory integer (≥0) variable representing the number of isolates with AST performed but no interpretation of results available for a specific antibiotic.

Both UNKNOWN_NO_AST and UNKNOWN_NO_BREAKPOINTS are very important for assessing the selection bias and countries are encouraged to always report missing AST results. When the data show a high percentage of unknown AST results for specific antimicrobials, the level of uncertainty on the generated AMR rates could be very high[9].

*Variable **BATCHID***

BATCHID is a mandatory coded value variable. It is introduced to distinguish subsets of national aggregated data provided by a country where it is not possible to aggregate national data in the same way for some reason, or when dividing the national data set has an important added value. For example, this may be needed if the country has different surveillance systems or there is a need to report data from different parts of the country separately. BATCHID may also be needed if, for example, the sample statistics (needed for generating a *SAMPLE* file) are missing for a large part of the country.

Table A.2. Using BATCHID: an example of country A

Data set	*RIS* file	*SAMPLE* file	Comments
Dataset 1 from surveillance sites A, B, F (BATCHID=DS1)	Available	Available	Data will be used to calculate both proportions and AMR rates per 100,000 sampled patients for the dataset 1
Dataset 2 from surveillance sites C, D, E, G (BATCHID=DS2)	Available	Not available	Data will be used in reports displaying proportions only (%) for the dataset 2
National dataset (total)	Dataset 1 + Dataset 2	ND*	Data will be used in reports displaying proportions only (%) for the country A

* ND = no data

Countries are free to choose up to five datasets (dataset 1, dataset 2, dataset 3, dataset 4, and dataset 5). The dataset 1 (DS1) value is used by definition when the data are reported as a single set.

[9] Currently GLASS applies 30% unknown AST results cut-off value when reporting different outcomes. This value was selected as giving a reasonable balance in terms of results inclusion and proportion of isolates with data available

Annex 2. *SAMPLE* dataset variables

The *SAMPLE* dataset variables are shown in the Table A.3 below:

Table A.3. Variables in the SAMPLE dataset

Variables in *SAMPLE* dataset	Type of variable	Example
COUNTRY	Coded value	*AFG*
YEAR	Coded value	*2015*
SPECIMEN	Coded value	*BLOOD*
GENDER	Coded value	*M*
ORIGIN	Coded value	*HO*
AGEGROUP	Coded value	*01<04*
NUMINFECTED	Integer (≥0)	1000
NUMSAMPLEDPATIENTS	Integer (≥0)	*1000*
BATCHID	Coded value	DS1

The variables COUNTRY, YEAR, SPECIMEN, GENDER, ORIGIN, AGEGROUP, and BATCHID in the SAMPLE file have the same specifications as those in the RIS file and the same coded values (see Annex 4).

*Variable **NUMINFECTED***

NUMINFECTED is a mandatory integer variable. It represents the number of patients with laboratory results indicating the growth of pathogens under surveillance included in the GLASS dataset.

*Variable **NUMSAMPLEDPATIENTS***

NUMSAMPLEDPATIENTS is a mandatory integer variable. It represents the number of patients with samples collected for bacteriological testing and includes all positive samples (both isolates of the GLASS target pathogens and other bacteria) as well as negative (no growth) samples.

For the BLOOD specimens, all blood samples taken for bacteriological testing are included. All URINE specimens should be counted, independently of the type of collection. For the STOOL specimens, all faecal samples from patients collected for bacteriological testing should be counted, excluding samples sent specifically for the detection of *Clostridium difficile* and samples taken to detect viruses and parasites.

Annex 3. Individual level variables

Table A.4. Variables in the individual level dataset[10,11]

Variable name[a]	Type of variable	Description
RecordID	String	Technical variable (primary key) Unique anonymized identifier for each record within and across the national surveillance system and subject – Member State selected and generated. Recommended format: "[ReportingCountry] [LaboratoryCode] [Patient Counter] [Pathogen] [Specimen] [Antibiotic] [DateUsedForStatistics]"
RecordType	Coded value	Technical variable describing the structure and format of the data. CAESAR uses the fixed value: AMRTEST. Coded values for other countries are available from the GLASS secretariat
RecordTypeVersion	Numeric	Technical variable: version number of the variable set
Subject	Coded value	Technical variable: CAESAR uses the fixed value: AMR
DataSource	Coded value	Technical variable, uses coded name for local surveillance system
ReportingCountry	Coded value	Country code. The coded values used by GLASS are the same as for the variable COUNTRY in the aggregated dataset, they are available in the *Annex 4.* The CAESAR protocol requires two letter country codes, same as the internet suffix
Status	Coded value	Technical variable to describe status of reporting: NEW/UPDATE or DELETE
LaboratoryCode	Coded value	Laboratory code unique for each laboratory within the country. Recommended format: [ReportingCountry]-[code of three characters]
PatientCounter	Integer (numeric)	Anonymized patient ID
Gender	Coded value	Gender of the patient. The coded values are the same as for the variable GENDER in the aggregated dataset and are available in Annex 4
Age	Numeric	Age of the patient in years when the sample was taken
PatientType	Coded value	Patient location type: INPAT/OUTPAT/O/UNK
DateUsedForStatistics	Date	Date of sample collection
Specimen	Coded value	Specimen type. The coded values are the same as for the variable SPECIMEN in the aggregated dataset and are available in Annex 4
IsolateId	Text	Isolate sample identifier
HospitalId	Text	Hospital code.
HospitalUnitType	Coded value	Hospital department. The coded values are available in Annex 5
DateOfHospitalisation	Date	Date of admission

[10] More detailed specifications for the variables included in the data file are available in the *CAESAR Manual Version 3, 2019*, and the details of the file structure, data preparation and uploading to the GLASS IT platform are provided in the *User guide to the GLASS IT platform: submission and analysis of AMR data* (in preparation)

[11] The GLASS-AMR individual level dataset was initially developed to accommodate submission of individual AMR surveillance data from CAESAR countries via the GLASS IT platform and built around the TESSY format initially used by EARS-Net and then adopted also by CAESAR

Variable name[a]	Type of variable	Description
Pathogen	Coded value	Pathogen code. The coded values are the same as for the variable PATHOGEN in the aggregated dataset and are available in Annex 4
ResultPCRmec	Coded value	Detection of polymerase chain reaction (PCR) mecA-gene: POS/NEG/UNK
ResultPbp2aAggl	Coded value	Detection of penicillin-binding protein (PBP)2a-agglutination: POS/NEG/UNK
Serotype	Coded value	Serotype/group of the pathogen isolated from the sample. Reference: Danish Kauffman-Lund scheme from the former WHO Collaborating Centre for Reference and Research on Pneumococci at Statens Serum Institute in Denmark[12] The values are serotypes coded as a number, for example, 1, or a number + letter e.g. 6A. This variable is to be reported only if Pathogen = STRPNE
ESBL	Coded value	ESBL present: POS/NEG/UNK
ResultCarbapenemases	Coded value	Carbapenemase detected: POS/NEG/UNK
Antibiotic	Coded value	Antibiotic code The coded values are the same as for the variable ANTIBIOTIC in the aggregated dataset and are available in the *Annex 4*
SIR	Coded value	Final interpretation result of all different susceptibility tests performed: S/I/R
ResultZoneSign	Coded value	Sign used in the zone diameter (> < =)
ResultZoneValue	Numeric	Zone value (mm)
ResultZoneSIR	Coded value	Interpretation of susceptibility from the zone: S/I/R
ResultMICSign	Coded value	Sign used in the MIC (> < =)
ResultMICValue	Numeric	MIC (mg/L)
ResultMICSIR	Coded value	Interpretation of susceptibility from the MIC: S/I/R
ResultEtestSign	Coded value	Sign used in the MIC from a gradient strip test (> < =)
ResultEtestValue	Numeric	MIC value from gradient strip test (mg/L)
ResultEtestSIR	Coded value	Interpretation of susceptibility from the gradient strip test: S/I/R
DiskLoad	Text	Disk load (text)
ReferenceGuidelinesSIR	Coded value	The guideline used (EUCAST = European Committee on Antimicrobial Susceptibility Testing CLSI = Clinical and Laboratory Standards Institute, NAT = National O = Other)

[a] Variables used to generate aggregated datasets are set in bold type

[12] Geno KA, Gilbert GL, Song JY, Skovsted IC, Klugman KP, Jones C, et al. Pneumococcal capsules and their types: past, present, and future. Clin Microbiol Rev. 2015 Jul 1;28(3):871–99

Annex 4. Coded values for variables collected with national aggregated data

Variable ***COUNTRY***

Code	Label	Country (territory, area)
AFG	Afghanistan	Islamic Republic of Afghanistan
ALB	Albania	Republic of Albania
DZA	Algeria	People's Democratic Republic of Algeria
AND	Andorra	Principality of Andorra
AGO	Angola	Republic of Angola
ATG	Antigua and Barbuda	Antigua and Barbuda
ARG	Argentina	Argentine Republic
ARM	Armenia	Republic of Armenia
AUS	Australia	Australia
AUT	Austria	Republic of Austria
AZE	Azerbaijan	Republic of Azerbaijan
BHS	Bahamas	Commonwealth of the Bahamas
BHR	Bahrain	Kingdom of Bahrain
BGD	Bangladesh	People's Republic of Bangladesh
BRB	Barbados	Barbados
BLR	Belarus	Republic of Belarus
BEL	Belgium	Kingdom of Belgium
BLZ	Belize	Belize
BEN	Benin	Republic of Benin
BTN	Bhutan	Kingdom of Bhutan
BOL	Bolivia (Plurinational State of)	Plurinational State of Bolivia
BIH	Bosnia and Herzegovina	Bosnia and Herzegovina
BWA	Botswana	Republic of Botswana
BRA	Brazil	Federative Republic of Brazil
BRN	Brunei Darussalam	Brunei Darussalam
BGR	Bulgaria	Republic of Bulgaria
BFA	Burkina Faso	Burkina Faso
BDI	Burundi	Republic of Burundi
CPV	Cabo Verde	Republic of Cabo Verde
KHM	Cambodia	Kingdom of Cambodia
CMR	Cameroon	Republic of Cameroon
CAN	Canada	Canada
CAF	Central African Republic	Central African Republic
TCD	Chad	Republic of Chad
CHL	Chile	Republic of Chile
CHN	China	People's Republic of China
COL	Colombia	Republic of Colombia
COM	Comoros	Union of the Comoros
COG	Congo	Republic of the Congo
COK	Cook Islands	Cook Islands

Code	Label	Country (territory, area)
CRI	Costa Rica	Republic of Costa Rica
CIV	Côte d'Ivoire	Republic of Côte d'Ivoire
HRV	Croatia	Republic of Croatia
CUB	Cuba	Republic of Cuba
CYP	Cyprus	Republic of Cyprus
CZE	Czech Republic	Czech Republic
PRK	Democratic People's Republic of Korea	Democratic People's Republic of Korea
COD	Democratic Republic of the Congo	Democratic Republic of the Congo
DNK	Denmark	Kingdom of Denmark
DJI	Djibouti	Republic of Djibouti
DMA	Dominica	Commonwealth of Dominica
DOM	Dominican Republic	Dominican Republic
ECU	Ecuador	Republic of Ecuador
EGY	Egypt	Arab Republic of Egypt
SLV	El Salvador	Republic of El Salvador
GNQ	Equatorial Guinea	Republic of Equatorial Guinea
ERI	Eritrea	State of Eritrea
EST	Estonia	Republic of Estonia
ETH	Ethiopia	Federal Democratic Republic of Ethiopia
FJI	Fiji	Republic of Fiji
FIN	Finland	Republic of Finland
FRA	France	French Republic
GAB	Gabon	Gabonese Republic
GMB	Gambia	Islamic Republic of the Gambia
GEO	Georgia	Georgia
DEU	Germany	Federal Republic of Germany
GHA	Ghana	Republic of Ghana
GRC	Greece	Hellenic Republic
GRD	Grenada	Grenada
GTM	Guatemala	Republic of Guatemala
GIN	Guinea	Republic of Guinea
GNB	Guinea-Bissau	Republic of Guinea-Bissau
GUY	Guyana	Republic of Guyana
HTI	Haiti	Republic of Haiti
HND	Honduras	Republic of Honduras
HUN	Hungary	Hungary
ISL	Iceland	Republic of Iceland
IND	India	Republic of India
IDN	Indonesia	Republic of Indonesia
IRN	Iran (Islamic Republic)	Islamic Republic of Iran
IRQ	Iraq	Republic of Iraq
IRL	Ireland	Ireland
ISR	Israel	State of Israel

Code	Label	Country (territory, area)
ITA	Italy	Republic of Italy
JAM	Jamaica	Jamaica
JPN	Japan	Japan
JOR	Jordan	Hashemite Kingdom of Jordan
KAZ	Kazakhstan	Republic of Kazakhstan
KEN	Kenya	Republic of Kenya
KIR	Kiribati	Republic of Kiribati
KOS	Kosovo[13]	Kosovo
KWT	Kuwait	State of Kuwait
KGZ	Kyrgyzstan	Kyrgyz Republic
LAO	Lao People's Democratic Republic	Lao People's Democratic Republic
LVA	Latvia	Republic of Latvia
LBN	Lebanon	Lebanese Republic
LSO	Lesotho	Kingdom of Lesotho
LBR	Liberia	Republic of Liberia
LBY	Libya	Libya
LTU	Lithuania	Republic of Lithuania
LUX	Luxembourg	Grand Duchy of Luxembourg
MDG	Madagascar	Republic of Madagascar
MWI	Malawi	Republic of Malawi
MYS	Malaysia	Malaysia
MDV	Maldives	Republic of Maldives
MLI	Mali	Republic of Mali
MLT	Malta	Republic of Malta
MHL	Marshall Islands	Republic of the Marshall Islands
MRT	Mauritania	Islamic Republic of Mauritania
MUS	Mauritius	Republic of Mauritius
MEX	Mexico	United Mexican States
FSM	Micronesia (Federated States of)	Federated States of Micronesia
MCO	Monaco	Principality of Monaco
MNG	Mongolia	Mongolia
MNE	Montenegro	Montenegro
MAR	Morocco	Kingdom of Morocco
MOZ	Mozambique	Republic of Mozambique
MMR	Myanmar	Republic of the Union of Myanmar
NAM	Namibia	Republic of Namibia
NRU	Nauru	Republic of Nauru
NPL	Nepal	Federal Democratic
NLD	Netherlands	Kingdom of the Netherlands
NZL	New Zealand	New Zealand
NIC	Nicaragua	Republic of Nicaragua

[13] All references to Kosovo should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)

Code	Label	Country (territory, area)
NER	Niger	Republic of the Niger
NGA	Nigeria	Federal Republic of Nigeria
NIU	Niue	Republic of Niue
NOR	Norway	Kingdom of Norway
OMN	Oman	Sultanate of Oman
PAK	Pakistan	Islamic Republic of Pakistan
PLW	Palau	Republic of Palau
PSE	Palestine	Occupied Palestinian territory
PAN	Panama	Republic of Panama
PNG	Papua New Guinea	Independent State of Papua New Guinea
PRY	Paraguay	Republic of Paraguay
PER	Peru	Republic of Peru
PHL	Philippines	Republic of the Philippines
POL	Poland	Republic of Poland
PRT	Portugal	Portuguese Republic
QAT	Qatar	State of Qatar
KOR	Republic of Korea	Republic of Korea
MDA	Republic of Moldova	Republic of Moldova
ROU	Romania	Romania
RUS	Russian Federation	Russian Federation
RWA	Rwanda	Republic of Rwanda
KNA	Saint Kitts and Nevis	Saint Kitts and Nevis
LCA	Saint Lucia	Saint Lucia
VCT	Saint Vincent and the Grenadines	Saint Vincent and the Grenadines
WSM	Samoa	Independent State of Samoa
SMR	San Marino	Republic of San Marino
STP	Sao Tome and Principe	Democratic Republic of Sao Tome and Principe
SAU	Saudi Arabia	Kingdom of Saudi Arabia
SEN	Senegal	Republic of Senegal
SRB	Serbia	Republic of Serbia
SYC	Seychelles	Republic of Seychelles
SLE	Sierra Leone	Republic of Sierra Leone
SGP	Singapore	Republic of Singapore
SVK	Slovakia	Slovak Republic
SVN	Slovenia	Republic of Slovenia
SLB	Solomon Islands	Solomon Islands
SOM	Somalia	Federal Republic of Somalia
ZAF	South Africa	Republic of South Africa
SSD	South Sudan	Republic of South Sudan
ESP	Spain	Kingdom of Spain
LKA	Sri Lanka	Democratic Socialist Republic of Sri Lanka
SDN	Sudan	Republic of the Sudan

Code	Label	Country (territory, area)
SUR	Suriname	Republic of Suriname
SWZ	Swaziland	Kingdom of Swaziland
SWE	Sweden	Kingdom of Sweden
CHE	Switzerland	Swiss Confederation
SYR	Syrian Arab Republic	Syrian Arab Republic
TJK	Tajikistan	Republic of Tajikistan
THA	Thailand	Kingdom of Thailand
MKD	North Macedonia	North Macedonia
TLS	Timor-Leste	Democratic Republic of Timor-Leste
TGO	Togo	Togolese Republic
TON	Tonga	Kingdom of Tonga
TTO	Trinidad and Tobago	Republic of Trinidad and Tobago
TUN	Tunisia	Republic of Tunisia
TUR	Turkey	Republic of Turkey
TKM	Turkmenistan	Turkmenistan
TUV	Tuvalu	Tuvalu
UGA	Uganda	Republic of Uganda
UKR	Ukraine	Ukraine
ARE	United Arab Emirates	United Arab Emirates
GBR	United Kingdom of Great Britain and Northern Ireland	United Kingdom of Great Britain and Northern Ireland
TZA	United Republic of Tanzania	United Republic of Tanzania
USA	United States of America	United States of America
URY	Uruguay	Eastern Republic of Uruguay
UZB	Uzbekistan	Republic of Uzbekistan
VUT	Vanuatu	Republic of Vanuatu
VEN	Venezuela (Bolivarian Republic of)	Bolivarian Republic of Venezuela
VNM	Viet Nam	Socialist Republic of Viet Nam
YEM	Yemen	Republic of Yemen
ZMB	Zambia	Republic of Zambia
ZWE	Zimbabwe	Republic of Zimbabwe

*Variable **BATCHID***

Code	BatchID	Label
DS1	Data Set 1	Data Set 1
DS2	Data Set 2	Data Set 2
DS3	Data Set 3	Data Set 3
DS4	Data Set 4	Data Set 4
DS5	Data Set 5	Data Set 5
EGASP	EGASP	EGASP

*Variable **SPECIMEN***

Code	Specimen	Label
BLOOD	Blood	BLOOD
CSF	Cerebrospinal fluid	CSF
URINE	Urine	URINE
STOOL	Stool	STOOL
LOWRESP	Lower respiratory tract	LOWRESP
UROGENITAL	Urethral and cervical swabs	UROGENITAL
ANORECTAL	Anorectal swabs	ANORECTAL
PHARYNGEAL	Pharyngeal swabs	PHARYNGEAL

*Variable **PATHOGEN***

Code	Pathogen	Label
ACISPP	*Acinetobacter* spp.	*Acinetobacter* spp.
ESCCOL	*Escherichia coli*	*Escherichia coli*
HAEINF	*Haemophilus influenzae*	*Haemophilus influenzae*
KLEPNE	*Klebsiella pneumoniae*	*Klebsiella pneumoniae*
NEIGON	*Neisseria gonorrhoeae*	*Neisseria gonorrhoeae*
NEIMEN	*Neisseria meningitidis*	*Neisseria meningitidis*
PSEAER	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa*
SALSPP	*Salmonella* spp.	*Salmonella* spp.
SALPAR	*Salmonella enterica* serovar Paratyphi A	*Salmonella enterica* serovar Paratyphi A
SALTYP	*Salmonella enterica* serovar Typhi	*Salmonella enterica* serovar Typhi
SHISPP	*Shigella* spp.	*Shigella* spp.
STAAUR	*Staphylococcus aureus*	*Staphylococcus aureus*
STRPNE	*Streptococcus pneumoniae*	*Streptococcus pneumoniae*

*Variable **GENDER***

Code	Gender	Label
M	Male	Male
F	Female	Female
O	Other	Other
UNK	Unknown	Unknown

*Variable **ORIGIN***

Code	Origin	Label
HO	Hospital origin	Hospital origin
CO	Community origin	Community origin
UNK	Unknown	Unknown

*Variable **AGEGROUP***

Code	Age groups	Label
<1	<1	<1
01<04	1-4	1-4
05<14	5-14	5-14
15<24	15-24	15-24
25<34	25-34	25-34
35<44	35-44	35-44
45<54	45-54	45-54
55<64	55-64	55-64
65<74	65-74	65-74
75<84	75-84	75-84
85<	85+	85+
UNK	Unknown	Unknown

*Variable **ANTIBIOTIC***

Code	Antimicrobial agent	Label
AMK	Amikacin	Amikacin
AMC	Amoxicillin-clavulanic acid	Amoxicillin-clavulanic acid
AMP	Ampicillin	Ampicillin
AZM	Azithromycin	Azithromycin
FEP	Cefepime	Cefepime
CFM	Cefixime	Cefixime
CTX	Cefotaxime	Cefotaxime
FOX	Cefoxitin	Cefoxitin
CAZ	Ceftazidime	Ceftazidime
CRO	Ceftriaxone	Ceftriaxone
CXM	Cefuroxime	Cefuroxime
CHL	Chloramphenicol	Chloramphenicol
CIP	Ciprofloxacin	Ciprofloxacin
CLR	Clarithromycin	Clarithromycin
COL	Colistin	Colistin
SXT	Co-trimoxazole	Co-trimoxazole
DOR	Doripenem	Doripenem
ERY	Erythromycin	Erythromycin
ETP	Ertapenem	Ertapenem
GEN	Gentamicin	Gentamicin
IPM	Imipenem	Imipenem
LVX	Levofloxacin	Levofloxacin
MEC	Mecillinam	Mecillinam
MEM	Meropenem	Meropenem
MNO	Minocycline	Minocycline
NIT	Nitrofurantoin	Nitrofurantoin
OXA	Oxacillin	Oxacillin

Code	Antimicrobial agent	Label
PEN	Penicillin G	Penicillin G
TZP	Piperacillin/tazobactam	Piperacillin/tazobactam
RIF	Rifampicin	Rifampicin
SPT	Spectinomycin	Spectinomycin
TGC	Tigecycline	Tigecycline
TOB	Tobramycin	Tobramycin
ATC Code[14]	Antibiotic sub-group	Label
J01GB	Aminoglycosides	Aminoglycosides
J01BA	Amphenicols	Amphenicols
J01CF	Beta-lactamase resistant penicillins	Beta-lactamase resistant penicillins
J01CE	Beta-lactamase sensitive penicillins	Beta-lactamase sensitive penicillins
J01DH	Carbapenems	Carbapenems
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	Combinations of penicillins, incl. beta-lactamase inhibitors
J01MA	Fluoroquinolones	Fluoroquinolones
J01DE	Fourth-generation cephalosporins	Fourth-generation cephalosporins
J01FA	Macrolides	Macrolides
J01XE	Nitrofuran derivatives	Nitrofuran derivatives
J01XX	Other antibacterials	Other antibacterials
J01CA	Penicillins with extended spectrum	Penicillins with extended spectrum
J01XB	Polymyxins	Polymyxins
J01DC	Second-generation cephalosporines	Second-generation cephalosporines
J01EE	Sulfonamides and trimethoprim	Sulfonamides and trimethoprim
J01AA	Tetracyclines	Tetracyclines
J01DD	Third-generation cephalosporins	Third-generation cephalosporins

[14] *ATC/DDD Index 2020* (https://www.whocc.no/atc_ddd_index/)

Annex 5. Coded values for variables collected with individual data

Variable ***HospitalUnitType***

Code	Department	Label
INTMED	Internal medicine	Internal medicine
PEDS	Paediatrics/neonatal	Paediatrics/neonatal
PEDSICU	Paediatrics/neonatal ICU	Paediatrics/neonatal ICU
SURG	Surgery	Surgery
ONCOL	Haematology/oncology	Haematology/oncology
OBGYN	Obstetrics/gynaecology	Obstetrics/gynaecology
ICU	ICU = Intensive Care Unit	ICU = Intensive Care Unit
ED	Emergency department	Emergency Department
URO	Urology	Urology
INFECT	Infectious disease	Infectious disease
O	Other	Other
UNK	Unknown	Unknown

Annex 6. Types of care

For the purpose of individual-level data submission, health care facilities will be categorized based on the type of care[15], that is, primary, secondary, and tertiary health care facilities (*Table A.5*). The choice of stratifying by type of care is important in order to take into account the different types of patients and complexity of procedures that can be associated with an increase in risk for AMR.

Table A.5. Types of care

Type of care	Criteria
Primary care (typically 30-250 beds)	• Few specialties (mainly internal medicine, obstetrics-gynaecology, paediatrics, general surgery or only general practice); • Limited laboratory services are available for general, but not for specialised pathological analysis; • Commonly referred to as a "district hospital", "rural hospital", "community hospital" or "general hospital"
Secondary care (typically 200-800 beds)	• Hospital is highly differentiated by function with 5 to 10 clinical specialities, such as haematology, oncology, nephrology, intensive care unit (ICU); • Takes some referrals from other (primary) hospitals; • May have teaching activities; • Commonly referred to as a "regional hospital", "provincial (county) hospital" or "general hospital"
Tertiary care (typically 300-1500 beds)	• Highly specialised staff and technical equipment (ICU, haematology, transplantation, cardio-thoracic surgery, neurosurgery); • Clinical services are highly differentiated by function. • Specialized imaging units; • Regularly takes referrals from other (primary and secondary) hospitals; • Often a university hospital or associated with a university; • Commonly referred to as a "national hospital", "central hospital" or "academic or university hospital"

When a hospital has facilities with different levels of care, then the highest hospital category should be reported. For example, if one facility of the hospital belongs to the primary level and another facility belongs to the tertiary level, then the reported category should be the tertiary hospital.

[15] WHO methodology for point prevalence survey on antibiotic use in hospitals, version 1.1. Geneva: World Health Organization ; 2018 (https://apps.who.int/iris/handle/10665/280063)

Annex 7. Implementation questionnaire

This is an updated version of the GLASS implementation questionnaire used during the early implementation phase.

WHO Region

Country	
Year	

1. **Has a national coordination centre (NCC) been established?**
   - ☐ Yes, with a mandate and terms of reference in line with the GLASS manual
   - ☐ In progress
   - ☐ No
2. **Have plans been agreed to implement and strengthen antimicrobial resistance surveillance (AMR) surveillance, including participation in GLASS?**
   - ☐ Yes
   - ☐ No
   - ☐ Unknown
3. **Have one or more national reference laboratory(s) been designated to support national AMR surveillance in humans?**
   - ☐ Yes
   - ☐ No
   - ☐ Unknown
4. **Does the national reference laboratory(s) participate in an external quality assurance (EQA) scheme?**
   - ☐ Yes
   - ☐ No
   - ☐ Unknown
5. **Which antimicrobial susceptibility testing (AST) standards are applied in your country?**
   - ☐ CLSI (Clinical and Laboratory Standards Institute)
   - ☐ EUCAST (European Committee on Antimicrobial Susceptibility Testing)
   - ☐ Other
     - If other, please specify: _____
   - ☐ Unknown

6. **How many surveillance sites (or laboratories if number of sites not available) provide data to the national AMR surveillance system?**

   6a. Number of hospitals/inpatients facilities (overnight hospitalization): _____

   6b. Number of outpatient facilities (no overnight hospitalization capacity): _____

   6c. Number of in-out patient facilities**:** _____

   6d. Number of laboratories (answer if the identification of the number of surveillance sites submitting AMR data is not possible due to the setup of your national surveillance system)**:** ____

   ☐ Unknown

7. **How many local clinical laboratories provide clinical microbiology service to surveillance sites reporting AMR data to the national AMR surveillance system?**

   Number of laboratories: _____

   ☐ Unknown

8. **Does the national AMR programme organize and run EQA for local clinical microbiology laboratories supporting the national AMR surveillance system?**

   ☐ Yes

   ☐ No

9. **If yes, does this EQA cover both bacterial identification and AST?**

   ☐ Yes

   ☐ No

Please fill the information below ONLY for surveillance sites and the laboratories providing data to GLASS during the current data call.

10. **How many surveillance sites (or laboratories if number of sites not available) provided AMR surveillance data to GLASS during this data call?**

    10a. Number of hospitals/inpatients facilities (overnight hospitalization): _____

    10b. Number of outpatient facilities (no overnight hospitalization capacity): _____

    10c. Number of in-out patient facilities**:** _____

    10d. Number of laboratories (answer if the identification of the number of surveillance sites submitting AMR data is not possible due to the setup of your national surveillance system)**:** ____

    ☐ Unknown

11. **How many laboratories provided clinical microbiology service to surveillance sites reporting AMR surveillance data to GLASS during this data call?**

    Number of laboratories: _____

    ☐ Unknown

12. How many of them (see Q11) participate in EQA programme for bacterial identification and AST?

Number of laboratories: _____

☐ Unknown

13. Could you please provide a brief introduction to the current country AMR surveillance structure and/or activities (maximum length 1500 character)

Annex 8. Molecular indicators

GLASS target pathogens	**Mechanisms of resistance**	Molecular targets
Acinetobacter spp. *P. aeruginosa*	Carbapenem resistance	NDM, OXA, VIM, IMP, GES, KPC
	Colistin resistance	mcr 1-10
E. coli *K. pneumoniae* *Salmonella* spp. *Shigella* spp.	Extended spectrum beta-lactamases	CTX-M, TEM, SHV
	Carbapenem resistance	NDM, OXA, VIM, IMP, GES, KPC
	Colistin resistance	mcr 1-10
S. aureus	Methicillin resistance	mecA/mecC
	Linezolid resistance	cfr