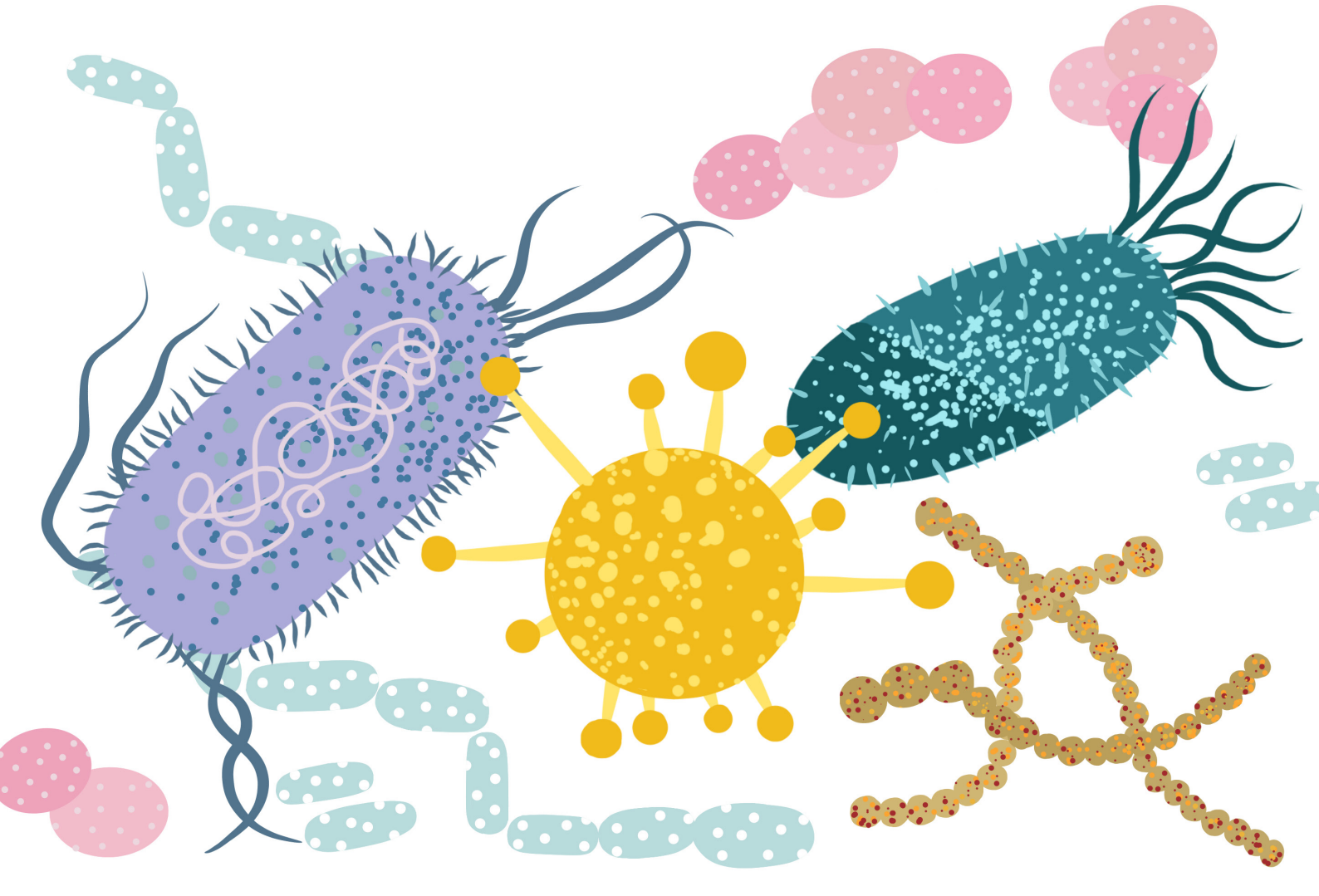
PAHO Pan American Health Organization

World Health Organization Regional Office for the Americas

Protocol for Enhanced Isolate-Level Antimicrobial Resistance Surveillance in the Americas

Primary Phase: Bloodstream Infections



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Primary Phase: Bloodstream Infections

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Contents

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The Pan American Health Organization (PAHO) thanks the following authors and contributors:

Agustina Forastiero (Argentina), Chen-Ling Hsieh (Taiwan), Uzo Chukwuma (United States of America), John Stelling (United States of America), Alejandra Corso (Argentina), Celeste Lucero (Argentina), Ezequiel Tuduri (Argentina), Carolina Duarte (Colombia), Maria Victoria Ovalle (Colombia), Antonieta Jimenez (Costa Rica), Esmeralda Villatoro (El Salvador), Teresa Camou (Uruguay), Vishwanath Partapsingh (Trinidad and Tobago), Aldo Sosa (Belize), Lorna Perez (Belize), Juan Carlos Hormazabal (Chile), Fernando Villavicencio (Ecuador), Yolanda Narvaez (Ecuador), Norma Mones Colima (Mexico), Nancy Melgarejo Touchet (Paraguay), Ronnie Gavilan (Peru), Rosa Sacsaquispe (Peru) and Loida Gonzalez (Dominican Republic),

Contributions by PAHO staff: Marcelo Galas, Hatim Sati, Pilar Ramon-Pardo, and Nienke Bruinsma.

Abbreviations

AMR	antimicrobial resistance
AMS	antimicrobial stewardship
AST	antimicrobial susceptibility testing
ATM	antimicrobial
BSI	bloodstream infection
CAESAR	Central Asian and Eastern European Surveillance of Antimicrobial Resistance
CC	collaborating center
CLSI	Clinical and Laboratory Standards Institute
CSF	cerebrospinal fluid
ECDC	European Centre for Disease Prevention and Control
EQA	external quality assessment
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GLASS	Global Antimicrobial Resistance Surveillance System
ICU	intensive care unit
IPC	infection prevention and control
LIS	laboratory information system
LSS	local surveillance site
MDR	multidrug-resistant
MIC	minimum inhibitory concentration
MOH	ministry of health
NAP	national action plan
NCC	national coordinating center
NRL	national reference laboratory
PAHO	Pan American Health Organization
PDR	pandrug-resistant
ReLAVRA	Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos
RRL	regional reference laboratory
S/I/R	sensitive/intermediate/resistant breakpoint category
SOP	standard operating procedure
UN	United Nations
WHO	World Health Organization
WHONET	database software for microbiology laboratories
XDR	extensively drug-resistant

Scope and purpose of this protocol

The purpose of this protocol is to describe the procedures for enhancing antimicrobial resistance (AMR) surveillance in Latin America (through the Red Latinoamericana de Vigilancia de la Resistencia a los Antimicrobianos [ReLAVRA] network) and the Caribbean. Its main objective is to combine patient data with laboratory and epidemiological surveillance data to provide an improved understanding of the scope and effects of AMR in populations. The protocol includes practical guidance and technical support for countries to participate in early implementation of enhanced isolate-level data collection that is focused on blood isolates. Implementation of the protocol will enable uniform data collection and standardization of data collection processes, methods, and tools to ensure and support data comparability within the Region of the Americas. It is important to note that countries in the Region can have different levels of national AMR surveillance systems in place. For this reason, the protocol aims to support countries in further strengthening their national AMR surveillance systems but also provides guidance in developing and setting up a surveillance system for those countries that do not yet have a system in place.

The methodology described in the manual builds on the ReLAVRA methodology and aligns with the Global Antimicrobial Resistance Surveillance System (GLASS) methodology, enabling countries to participate in GLASS[1]. Parts of the manual are adapted from the WHO Europe Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) manual[2], and reference is made to the GLASS early implementation manual[3].

[1] World Health Organization. Global Antimicrobial Resistance Surveillance System (GLASS). World Health Organization. 2019. Available from: https://www.who.int/glass/en/

[2] Central Asian and Eastern European Surveillance of Antimicrobial Resistance. CAESAR manual, Version 2, 2015. Available from: http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/publications/2015/central-asian-and-eastern-european-surveillance-of-antimicrobial-resistance.-caesar-manual,-version-2,-2015

[3] World Health Organization. Global Antimicrobial Resistance Surveillance System: manual for early implementation. 2015. Available from: HYPERLINK "https://www.who.int/antimicrobial-resistance/publications/surveillance-system-manual/en/%20"https://www.who.int/antimicrobial-resistance/publications/surveillance-system-manual/en/

Introduction

Background

The discovery of antibiotics and other antimicrobial agents in 1928 by Alexander Fleming has dramatically changed human and veterinary medicine, preventing and curing infections and saving millions of lives. Ever since this discovery, resistance to antimicrobial treatment through the natural process of adaptation has been on the rise. Antimicrobial resistance (AMR) was documented well before the discovery of penicillin has become widespread over time and has risen to alarming levels. Multiple interplaying factors may have resulted in the rapid emergence and propagation of AMR [1, 2]. Overuse and misuse of antimicrobial agents, unsafe disposal of these agents, poor hygiene, and lack of infection prevention measures are some of these factors, and they greatly accelerate the rate at which resistance emerges through increased selection pressures.

Almost all countries in the PAHO region have reported resistance rates against one or more of the commonly used antibiotics. In some cases, the nonsusceptibility rates reported are as high as 50% or even higher. Furthermore, there have been reports of rapidly emerging and spreading AMR mechanisms in the case of common and last-resort antibiotics [3-6].

During the 67th session of the WHO Regional Committee for the Americas in Washington, D.C., in October 2015, the strategic action plan on antibiotic resistance for the Americas was adopted by all Member States in the Region [7]. This agreement is aligned with the global action plan on AMR that was adopted at the World Health Assembly in the same year [8]. The end goal of both plans is to ensure, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them.

The growing awareness among national leaders was also demonstrated at the United Nations (UN) General Assembly High-Level Meeting on Antimicrobial Resistance in September 2016. In a political declaration, all 193 UN Member States committed themselves to developing multisectoral national action plans in line with the World Health Assembly Global Action Plan on Antimicrobial Resistance, including its second strategic objective: to strengthen the knowledge and evidence base through surveillance and research [9].

One of the main pillars of the Global Action Plan is the implementation of AMR surveillance. This is the systematic, ongoing process of data collection, analysis, and reporting that quantitatively monitors spatial and temporal trends in the occurrence and distribution of susceptibility and resistance to antimicrobial agents.

AMR surveillance provides essential information needed to guide medical practice, including therapeutics and disease control activities. Antimicrobial susceptibility information plays a major role in improving the quality, safety, and cost of health care through informing individual patient care, guiding empirical therapy, and supporting infection prevention and control (IPC) and antibiotic stewardship programs. Appropriate and targeted use of antimicrobials improves patient outcomes and reduces the rate at which resistance emerges and spreads. Regular analysis and feedback on surveillance data to health care workers allow timely adjustment of antimicrobial therapy guidelines and initiation of measures to control hospital and community outbreaks of multidrug-resistant bacteria.

Antimicrobial resistance surveillance in the Americas

PAHO has supported AMR laboratory surveillance activities through several regional surveillance networks, based on cooperation between participating countries. The Latin American Surveillance Network of Antimicrobial Resistance (ReLAVRA by its Spanish acronym) was created in 1996 and is supported and coordinated by PAHO. Currently, the following 19 countries take part in ReLAVRA: Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, the Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay, and Venezuela (Figure 1). Each country is represented by an officially designated national reference laboratory (NRL) that also coordinates the national external quality assurance program for AMR surveillance. The NRLs, in coordination with PAHO, provide technical support, protocols, training, and manuals to the participating laboratories within the national AMR surveillance network. The AMR data entered into the laboratory information system (LIS) (WHONET 5.6 or similar) are processed by the participating laboratories of the national networks and analyzed at the local level, and periodic reports are prepared for health personnel to contribute to adjustment of empirical treatments and appropriate use of antimicrobials (ATMs) in health institutions. Sensitivity data are compiled and analyzed by the NRLs, which then publish them in different modalities at the local level and distribute them at the central level (ministry of health) to be used in the design of AMR control strategies. Subsequently, the data are sent by the ministry of health to PAHO, through the PLISA Health Information Platform for the Americas, where the data is published in a regional conglomerate [10]. At each level, quality information is reviewed comprehensively, and if error or bias is detected, this information is fed back to the previous level for review. In this way, we work to continuously improve the quality of databases. See paragraph 3.3 'Data submission to and feedback from PAHO', for more information on the process.

PAHO and other national and regional partners are working with the Caribbean region, through collaborative initiatives, focusing mostly on building laboratory capacity for AMR surveillance. In 2018, during the Multi-Country Workshop to Strengthen Antimicrobial Resistance Surveillance in the Caribbean, 21 countries and territories stated the need for increased collaboration in and coordination of AMR activities in the Caribbean region (Figure 1). During the workshop, the establishment of an AMR surveillance network in the Caribbean was recommended, and the development of an AMR surveillance protocol was identified as an initial step to ensure standardization of information and procedures.

Goals of AMR isolate-level surveillance

One of the most important benefits of AMR surveillance at the isolation level is to achieve a standardized, comparable, and easily validated data collection method at the national, regional, and global levels. The data obtained will optimize patient care by adapting treatment guidelines according to type of patient and type of infection, with consideration of circulating pathogens and local and national resistance levels. Through this protocol, PAHO aims to provide support to national AMR surveillance systems in their continuous efforts to improve the accuracy and quality of diagnosis at all levels of the

Figure 1.
Regional AMR surveillance in Latin America (ReLAVRA) and the Caribbean

surveillance chain. The implementation is based on a standardized and progressive approach, starting with bloodstream infections (BSI).

The protocol acknowledges that countries in the Region are at different levels of progress in terms of isolate-level AMR surveillance, especially regarding the integration of the clinical/epidemiological data of patients with laboratory results. Therefore, the goal of the protocol is to facilitate the implementation of this type of surveillance from different starting points:

i. when no national AMR surveillance system is in place as of yet;

ii. to enable the collection of additional patient and population data in already-existing surveillance systems; and

iii. to further improve the quality of data being collected by those countries that already perform surveillance with this modality.

Furthermore, the standard operating procedures (SOPs) and defined standardized data fields will allow countries in the Region to participate in the Global Antimicrobial Resistance Surveillance System (GLASS). The scope of GLASS in terms of species and specimen types is wider than the methodology described in this manual.[1] Nevertheless, the design of this document keeps in mind a stepwise approach to implementation of enhanced isolate-level surveillance starting with BSIs, with the possibility of expanding to more species and specimen types.[2] This approach will also allow for effective implementation of AMR surveillance in a manner that will streamline reporting to GLASS and

[1] In addition to the ReLAVRA data on pathogens in blood, GLASS also collects data on *Escherichia coli* and *Klebsiella pneumoniae* in urine, *Shigella* spp. in stools and blood, *Salmonella* spp. in stools, and *Neisseria gonorrhoeae* in urethral and cervical swabs.

[2] In many countries, national AMR surveillance systems already include additional pathogens, antimicrobials, and other types of clinical specimen cultures (e.g., urine, pus) of local or national importance.

reduce additional burden on GLASS reporting countries in the Region.

Objectives of AMR isolate-level surveillance

The objectives of AMR isolate-level surveillance are as follows:

i. To institute a systematic approach towards isolate-level data collection and analysis of antimicrobial susceptibility information on 9 pathogens identified from BSIs (as a starter).

ii. To establish timely reporting of information on pathogens of interest and their antimicrobial susceptibility profiles; determine trends, distributions, and etiologies of the most prevalent AMR infections among BSIs; and determine newly emerging resistance.

iii. To analyze and quantify trends, magnitudes, distributions, and impacts of AMR on disease epidemiology.

iv. To facilitate patient management through informing empiric treatment guidelines and to ensure quality/cost-effective care and patient safety through optimal antimicrobial therapy.

v. To inform local, regional, and global actions and interventions for AMR prevention and control.

vi. To provide data to monitor and evaluate the impact of interventions and to identify needs.

The objectives have a regional scope with a global projection through GLASS (Box 1). Most importantly, the implementation of these objectives in the countries will contribute to monitoring local and national AMR performed by national coordinating centers (NCCs), NRLs, and the laboratories and hospitals that are part of national surveillance networks.

Manual development

This manual was developed by the PAHO AMR Special Program, in collaboration with the AMR technical focal points in countries, to facilitate the implementation and strengthening of AMR enhanced isolate-level surveillance in the Region. The idea for the early implementation of isolate-level AMR surveillance in the Region was introduced and discussed during the biannual ReLAVRA meeting in Montevideo, Uruguay, in November 2017 and during the Multi-Country Workshop to Strengthen Antimicrobial Resistance Surveillance in the Caribbean, which took place in Barbados in June 2018.

After these initial discussions, all countries in the Region were formally invited to participate in the early implementation. The objectives of the early implementation were as follows:

i. To strengthen or establish national AMR surveillance systems through standardization of enhanced isolate-level AMR data collection, starting with blood isolates.

ii. To develop a joint protocol for isolate-level AMR surveillance in Latin America and the Caribbean.

iii. To develop a standard WHONET configuration for data collection, including a back link that allows easy export of data from laboratory information systems to WHONET. Once available in WHONET, the data can be transferred to the regional base.

iv. To develop an automated database review system that allows rapid feedback on data quality and potential errors or biases in the information reported for country review.

v. To develop an interactive database (dashboard) to show AMR maps and trends in the Region.

vi. To enable a stepwise approach for participation in GLASS.

Box 1.
Global Antimicrobial Resistance Surveillance System (GLASS)

Launched in October 2015, the Global Antimicrobial Resistance Surveillance System (GLASS) supports the Global Action Plan on Antimicrobial Resistance. Its aim is to support global surveillance and research in order to strengthen the evidence base on antimicrobial resistance (AMR), help inform decision making, and drive national, regional, and global actions.

GLASS promotes and supports a standardized approach to the collection, analysis, and sharing of AMR data at the global level by encouraging and facilitating the establishment of national AMR surveillance systems that are capable of monitoring AMR trends and producing reliable and comparable data.

The GLASS objectives are to:

- Foster national surveillance systems and harmonized global standards;
- Estimate the extent and burden of AMR globally according to selected indicators;
- Analyze and report global data on AMR on a regular basis;
- Detect emerging resistance and its international spread;
- Inform the implementation of targeted prevention and control programs; and
- Assess the impact of interventions.

The first GLASS Report: Early Implementation 2017-18 presents information from GLASS enrolled countries on the status of their AMR surveillance systems and AMR data for selected bacteria that cause infections in humans. The aims of the report are to document participation efforts and outcomes across countries and highlight differences and constraints identified to date. The most recent GLASS report was published in May 2020 and also includes data on Antimicrobial Use Surveillance.

Source: World Health Organization. Global Antimicrobial Resistance Surveillance System (GLASS). World Health Organization. 2019. Available from: https://www.who.int/glass/en/

1. Organization of a national AMR surveillance system

There are three core components that are essential for the overall set up of a national AMR surveillance system:

i. AMR surveillance national coordinating center (NCC);

ii. AMR national reference laboratory (NRL); and

iii. AMR local surveillance sites (LSSs) (clinics, hospitals, and laboratories).

The LSSs are responsible for collecting AMR data at the local level and reporting these data (directly or through the subnational level) to the NCC and/or the NRL. The functions and roles of the three core components of the national AMR surveillance system can differ between countries in terms of structure as well as number of participating LSSs. Nevertheless, the overall roles and responsibilities of these three levels remain the same and are described below in more detail.

For additional details about the core components described in this chapter, please refer to the WHO report "National antimicrobial resistance surveillance systems and participation in the Global Antimicrobial Resistance Surveillance System" (GLASS): a guide to planning, implementation, and monitoring and evaluation [11].

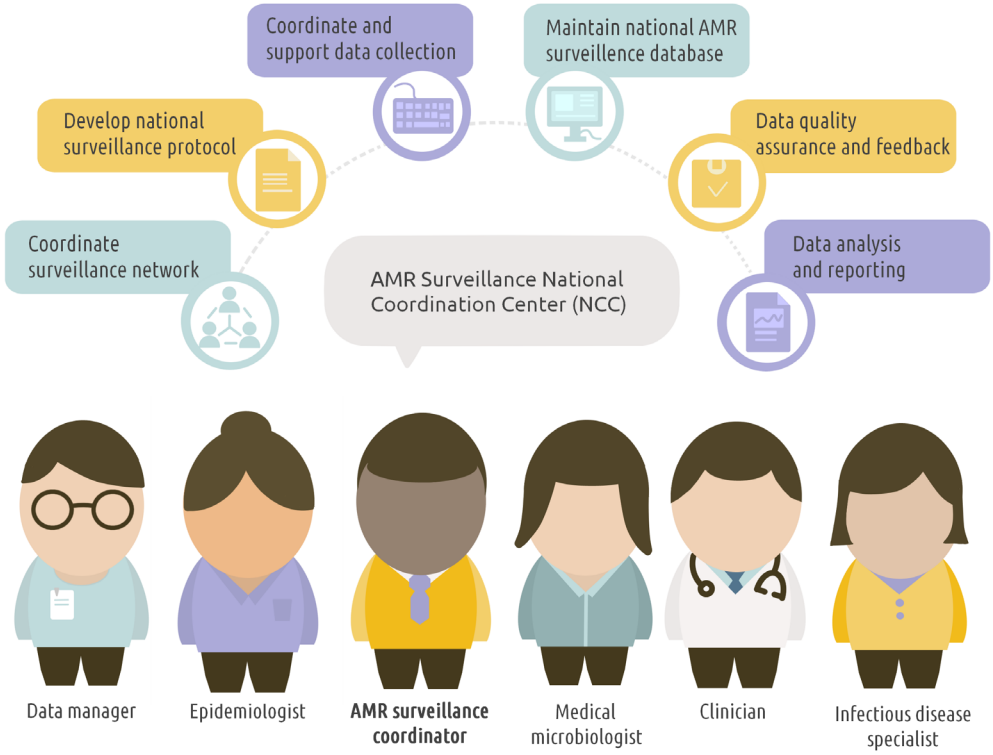
1.1 AMR national coordinating center (NCC)

The NCC is responsible for overseeing and coordinating the national AMR surveillance system. Ideally, the NCC is run by a multidisciplinary team consisting of a specialized epidemiologist (or a professional with expertise in data analysis and interpretation), a medical microbiology specialist, an infectious disease specialist, a clinician and a data management specialist. This structure ensures a multidisciplinary approach to AMR surveillance (Figure 2). The suggested roles and responsibilities of the NCC are described in Box 2. In many countries in Latin America, laboratory AMR surveillance has historically been the responsibility of the NRLs. As a result, some or all of the functions of the NCC are currently being performed by the NRL. Each country, according to its organization and structure of the surveillance system, should define whether there is a need for an NCC or whether its functions will be assumed by the NRL. In the latter case, it is essential that the different functions of an NCC (Figure 2) are covered by the NRL to ensure fulfillment of NCC roles and responsibilities (Box 2).

1.2 AMR national reference laboratory (NRL)

Every participating country should have a NRL for AMR surveillance. The primary functions of the NRL within the AMR surveillance system are to promote good microbiological laboratory practices, including adapting and disseminating up-to-date microbiological methods, standards, and protocols; to serve as a resource and coordination point for quality assessment in laboratories; and to facilitate collaboration with AMR surveillance sites on all technical laboratory matters relating to

Figure 2.
AMR surveillance national coordinating center (NCC): Professionals and functions



AMR (see Box 3 and Figure 3). If no laboratory within the country qualifies for the functions of an NRL, regional collaboration can be established with an appropriate institute in a neighboring country or with the regional reference laboratory (RRL). As described above, an NRL can also function as the NCC.

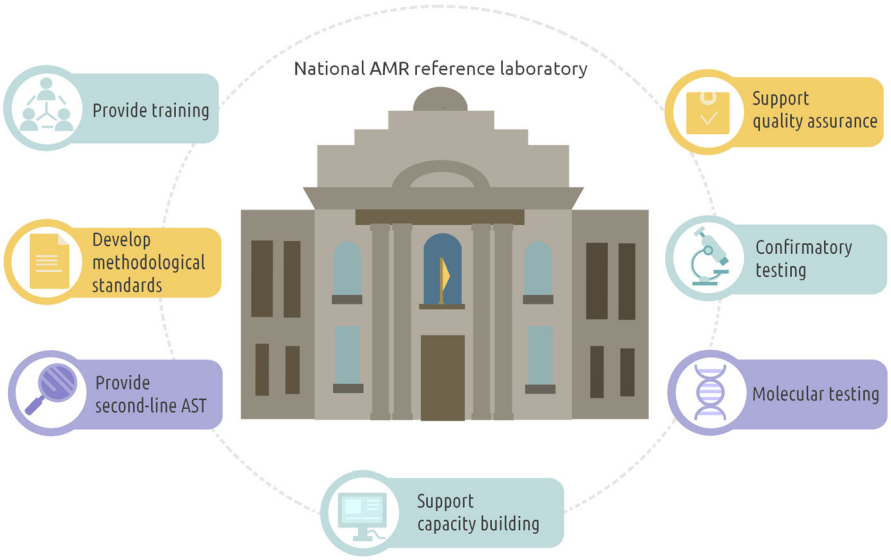
In the Region of the Americas, NRLs collaborate closely with the RRL in Argentina (Antimicrobial Agents Service, Bacteriology Department of the Instituto Nacional de Enfermedades Infecciosas ANLIS "Dr. C. G. Malbrán"). This WHO collaborating center (CC) is assisting PAHO/WHO by providing reference laboratory services and training on antimicrobial susceptibility testing (AST), resistance mechanisms, quality assurance, and surveillance. An important role of the WHO CC is the external quality assessment (EQA) that is carried out in the Region through the Programa Latinoamericano de Control de Calidad en Bacteriología y Resistencia a los Antimicrobianos, which currently includes 20 countries, 17 from Latin America, and 3 from The Caribbean. This EQA program was implemented in 2000 to evaluate and improve the capacities for identification, sensitivity testing, and detection of resistance mechanisms in the NRLs within the Region.

Box 2.

Roles and Responsibilities of the National Coordinating Center (NCC)

- Define AMR surveillance objectives within the national AMR strategy and facilitate linkages with AMR surveillance across human health, animal health, plant health, food, and environmental sectors.
- Coordinate the surveillance network and monitor and evaluate the AMR surveillance system on an ongoing basis. Select and facilitate enrollment of surveillance sites (Chapter 2).
- National surveillance protocol: develop or adapt national AMR surveillance standards, protocols, and tools in all sectors involved and coordinate their dissemination.
- Coordinate and support data collection: provide guidance and information on data collection and reporting to the AMR surveillance sites and the NRL.
- Maintain the national AMR surveillance database: Ensure the quality of the data management structure and format and information technology solutions.
- Data quality assurance and feedback: this includes performing regular checks of data completeness and data quality and providing feedback to hospitals and laboratories within the network in collaboration with the NRL.
- Data analysis and reporting: analyze national surveillance data and disseminate the results to relevant stakeholders, including the ministry of health and directors of the participating hospitals, ideally through the yearly production of a national surveillance report and the organization of a yearly AMR surveillance meeting. Coordinate collection and compilation of national AMR data.
- Data for action: facilitate and ensure discussion of surveillance results with all stakeholders, thereby improving the network's awareness of the national situation, leading to better use of surveillance data in hospitals, for the development of guidelines, and at the political level. Discussion of results also provides an opportunity to improve data collection.
- Provide scientific and managerial leadership to develop public health policy around AMR surveillance and stewardship.
- Collaboration and participation in international networks, such as GLASS, ReLAVRA, Caribbean, etc. Carry out, together with the NRL, specific data management processes. Among them, quality controls, data cleaning, encryption and export of data to PAHO and other organizations. In addition, this includes provision of information on the population representativeness of AMR surveillance sites participating in the national AMR network.

Figure 3.
Roles and responsibilities of the AMR national reference laboratory



1.3 Local AMR surveillance sites

The national AMR surveillance system consists of a network of clinical laboratories (AMR LSSs) performing AST of the priority microorganisms responsible for infections (blood infections initially) and periodically submitting these data to the national data manager at the NCC. For a laboratory to be eligible for participation in the national AMR surveillance system, it must be able to process and share the AST results of routinely collected clinical samples. The laboratory may be directly associated (on site) with a hospital where (blood) samples are collected as part of the standard care for patients with infections. Alternatively, the laboratory may serve several health care facilities, thereby performing the role of a central testing facility (off site). The commitment and active support of the clinical staff, administration, and management at the AMR LSS are essential in order to conduct AMR surveillance according to the requirements and standards of the national system and to maintain long-term sustainability. The different roles and responsibilities of the AMR LSS are described in Box 4.

Box 3.

Roles and Responsibilities of the National Reference Laboratory (NRL)

- Serve as a resource and coordination point for laboratory expertise and share information and advice with relevant stakeholders.
- Serve as a link between the LSS and the NCC.
- Liaise with the NCC.
- Develop, maintain, and share relevant reference materials.
- Promote good laboratory practices and provide guidance and technical support for quality management, pathogen isolation and identification, and AST methodologies.
- Support capacity building of laboratories through oversight of and training on microbiology laboratory techniques, equipment, and appropriate and safe specimen management.
- Organize or facilitate participation in EQA schemes for laboratories serving AMR surveillance sites, review the EQA performance of participating laboratories, offer feedback on EQA results to laboratories, and provide training and consultation.
- Participate in the yearly EQA exercise provided by the RRL or in a similar international EQA.
- Provide guidance on isolates to be sent for confirmatory testing to the NRL and establish national alert rules for strain confirmation and performance of specialized testing (see Chapter 2 for a list of resistant patterns recommended for confirmation).
- Perform timely confirmatory testing (e.g., testing of isolates with rare and unusual resistance patterns and resistance mechanisms, including phenotypic and genotypic characterization).
- Strengthen rapid response to outbreaks through timely testing and identification of causal agents and provide laboratory support during outbreak investigations, including epidemic alerts, response and prevention, and monitoring.
- Collaborate and conduct research in the field of microbiology.
- Participate in subregional, regional, and global antimicrobial resistance networks for research and development.
- Carry out specific data management processes together with the NCC before sending the data to PAHO. The management process can include, among others, quality control, data cleaning, encryption and export of data to PAHO.

At the AMR LSS, AST data (antibiograms) are crucial to inform patient care, clinical decisions, and treatment selection. In addition, accumulative AST data (accumulative antibiograms) inform local antibiotic treatment guidelines and antimicrobial stewardship programs and interventions that support appropriate use of antimicrobials, all of which reduce the further development of antimicrobial resistance (see Box 4 and the manual Recommendations for Implementing Antimicrobial Stewardship Programs in Latin America and the Caribbean) [12].

1.4 Selection of AMR surveillance sites

An important step in setting up a national AMR surveillance system is the selection of representative surveillance sites that meet the minimal criteria for AMR isolate-level surveillance. While it is ideal to collect data from all facilities in the country, this is often not feasible for obvious and practical reasons.

Hence, national AMR surveillance is often based on a subset of participating health care facilities and laboratories (AMR surveillance sites). While there is no restriction on the number of sites participating in AMR surveillance, several criteria are recommended for inclusion of the sites, the most important of which is achieving national representation. Criteria for surveillance sites are detailed below:

i. **Geographical representativeness:** To yield geographically representative data, selection of AMR surveillance sites from different geographical and demographic area (e.g., rural and urban areas) is recommended.

ii. **Types of health care facilities:** A combination of public community health clinics/laboratories, public hospitals/ laboratories, and private hospitals/ laboratories is ideal. The participating health care/laboratory facilities should also reflect a mix of levels of care (e.g., tertiary, general, and pediatric hospitals) within the country/area. The proportion of each facility type depends on population size, the proportion of BSI patients the facility sees on average, location (e.g., urban vs. semi-urban), and willingness and capacity for surveillance (see below).

iii. **Technical capacity:** The participating sites should have the resources and technical diagnostic capacity to characterize and report cases. A "case" is defined as any patient with a proven health care-associated or community-acquired blood infection confirmed by a blood culture.

iv. **Quality laboratory capacity:** This refers to capacity for diagnostics, characterization, confirmation, and antimicrobial susceptibility testing for BSIs, applying appropriate procedures and under quality principles. Sites that lack the laboratory capacity for BSI AST must at least have the capacity for proper specimen management, storage, and transportation (to a secondary laboratory facility or a national laboratory).

v. **Willingness for participation:** The engagement and responsibility of all of the actors involved is a fundamental requirement for the quality and integrity of the data collected.

vi. **Continuity of reporting from the selected sites:** Countries at the beginning stages of establishing enhanced isolate-level AMR surveillance system may start with a few

Box 4.

Roles and Responsibilities of AMR Local Surveillance Sites

- Promote diagnostic stewardship activities on site. Diagnostic stewardship is defined as "coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate, timely diagnostic testing, including specimen collection, pathogen identification and accurate, timely reporting of results to guide patient treatment." For more details, see Diagnostic stewardship: a guide to implementation in antimicrobial resistance surveillance sites [13].
- Collect clinical specimens and work in collaboration with the other health personnel in the institution to obtain clinical, demographic, and epidemiological data following standard protocols.
- The microbiology laboratory providing support to the surveillance site should:
  - Isolate and identify pathogens, perform AST according to national standards, and report microbiological information derived from the tested clinical specimen
  - Participate in a proficiency testing scheme/EQA coordinated by the NRL
- Compile and manage basic clinical, demographic, and epidemiological information derived from tested clinical specimens.
- Analyze the AMR information obtained and prepare reports for health personnel in charge of patient care.
- Provide feedback on and discuss locally generated surveillance data to inform local treatment guidelines, AMR control strategies, and use of accumulative AST data (antibiograms).
- Report quality-assured AST results and relevant core patient data to the NCC in a standardized format; further details on data collection and submission to the national AMR surveillance group are provided in Chapter 2.

sites and gradually increase the number of sites to ensure population coverage and representativeness [14].

1.5 National AMR surveillance as part of the overall governance and national coordination of AMR

To establish a successful and sustainable national AMR surveillance system in human health, support from the government is essential, including support with respect to legal, technical, and financial aspects. Implementation of AMR surveillance activities will require long-term investment, for instance in operational research, laboratories, human health surveillance systems, competent regulatory capacities, and professional education and training.

To enable the three core components (NCC, NRL, and AMR LSS) needed for national AMR surveillance described in this chapter, the ministry of health is responsible for mandating a national institution to function as the NCC and a national laboratory to function as the NRL. The function of the NCC is usually assumed by the national public health institute, by the epidemiology unit of the ministry of health, or by other nationally designated institutes (e.g., research institutes) when they are considered more suitable. Suitability is determined on the basis of the institute's access to laboratory, clinical, and epidemiological expertise and the presence of a defined structure for surveillance coordination and data management. As mentioned previously, in some countries the functions of the NCC and the NRL are based at the same institute. In addition, the ministry of health is responsible for providing a legal basis for centralized collection of patient data at the national level.

1.6 National AMR surveillance: An essential part of AMR national action plans

Establishing sound national AMR surveillance (in both human and animal health) is an essential objective of any AMR national action plan (NAP) developed by a country. Hence, the development and strengthening of national AMR surveillance systems must be prioritized, monitored, and evaluated regularly. The results of such monitoring and evaluation should be used to advocate for mobilization of resources needed for a sustainable system.

In addition, the information obtained from national AMR surveillance is essential for promoting awareness of AMR and is a fundamental tool for measuring the impact of interventions and AMR strategies defined in NAPs (e.g., antimicrobial stewardship and IPC programs). For more guidance on the implementation of NAPs, please refer to *Turning plans into action for antimicrobial resistance (AMR): Working Paper 2.0: Implementation and coordination [15]*.

2. Methodology

2.1 Pathogens identified from bloodstream infections (BSIs)

For the early implementation of isolate-level surveillance in BSIs, nine pathogens/groups were selected. These pathogens were prioritized because they are common causative agents of invasive infections, with a high risk for AMR and limited therapeutic options (Table 1). In addition, these pathogens have the potential to spread both in the community and between health care settings, which highlights their importance in public health. It is important to note that countries in the Latin American region have been collecting and reporting aggregate-level AMR data on these pathogens through the PAHO-coordinated ReLAVRA network since 1996.

Many of these pathogens are also included in the WHO priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. In addition, some of the pathogens prioritized in this protocol are included in the GLASS pathogen list for blood infections.[16] Table 1 shows the list of pathogens included in this protocol relative to their level of prioritization by WHO for research and development of new antimicrobials and whether they are included in GLASS.

Since the focus of this manual is on blood isolates, *Neisseria gonorrhoeae* and *Shigella* spp. are not included. Important to note is that separate guidance on AMR surveillance has recently been published for *N. gonorrhoeae*. [17] Special guidance on *Candida* spp. AMR surveillance (Global Antimicrobial Resistance Surveillance System (GLASS) early implementation protocol for the inclusion of *Candida* spp) is available online in both English and Spanish at https://www.who.int/glass/resources/publications/early-implementation-protocol-for-the-inclusion-of-candida-spp/en/.

Annex B shows all of the antimicrobial agents that can be reported per pathogen. Countries are strongly recommended to report the required antimicrobial agents for each of the pathogens (marked with an asterisk) for standardization and comparability within and between countries.

2.2 Data collection at the local surveillance sites

At the local surveillance sites (LSSs), isolate-level AST results should be recorded, managed, and collected systematically using a standardized system. The data collection process at this level should capture individual isolate-level information including specific patient, specimen, and hospital data.

Data can be collected using the WHONET software or through any other reliable laboratory information system (LIS). WHONET is a free Windows-based database program that was developed specifically for the management and analysis of microbiology laboratory data, with a special focus on analysis of AST data at the institutional level. The software can be downloaded from the WHONET website (https://whonet.org/) and serves as a starting point for routine electronic collection of AST data at surveillance sites. A standard configuration for data collection is available in WHONET, as well as an export function to send the data from the national level to the regional or global level. The WHONET configuration for this protocol is integrated with the *Candida* spp. AMR surveillance protocol, which enables countries to use one standard configuration for both initiatives, also minimizing any duplication of work.

A series of explanatory videos describing the steps to implement the WHONET

Table 1.
Pathogens under surveillance

Pathogen	WHO priority pathogen list	Pathogen included in GLASS
Acinetobacter baumannii	Priority 1: critical (carbapenem-resistant)	Yes
Escherichia coli	Priority 1: critical (carbapenem-resistant and third-generation cephalosporin-resistant)	Yes
Enterococcus spp.	Priority 2: high (vancomycin-resistant)	No
Klebsiella pneumoniae	Priority 1: critical (carbapenem-resistant and third-generation cephalosporin-resistant)	Yes
Enterobacteriaceae (other)	Priority 1: critical (carbapenem-resistant and third-generation cephalosporin-resistant)	No
Pseudomonas aeruginosa	Priority 1: critical (carbapenem-resistant)	No
Salmonella spp.	Priority 2: high (fluoroquinolone-resistant)	Yes
Staphylococcus spp.	Priority 2: high (methicillin-resistant, vancomycin intermediate and resistant)	Yes
Streptococcus pneumoniae	Priority 3: medium (penicillin-nonsusceptible)	Yes

configuration at the local or national level are available on the PAHO/AMR website.

PAHO recommends collecting AST data throughout the year to avoid the influence of outbreaks involving antibiotic-resistant bacteria, disease seasonality, or seasonal variations in hospital visits on the observed resistance proportions. Additionally, all consecutive isolates should be collected as part of routine laboratory practice and submitted to the NCC (or NRL) without deduplication on a quarterly basis (as a minimum).

Table 2 displays the recommended list of data fields that should be collected for each specimen. The mandatory fields are indicated with the letter a; without these data, the results will be excluded from the database. **The required fields**, indicated with the letter b, will be used as an indicator of the quality of the database and will help in measuring the evolution in the quality of information provided by the country. Further explanations and definitions of the data fields are provided in Annex C.

Table 2.
Defined set of data fields

1.	Country[a]
2.	Laboratory ID[a]
3.	Patient ID (Identification number)[a]
4.	Sex[b]
5.	Date of birth
6.	Age[b]
7.	Institution (hospital ID)
8.	Date of admission
9.	Ward
10.	Department
11.	Type of patient/patient origin (Location type)
12.	Type of infection/hospital-associated infection (HAI) or community-acquired infection (CAI)[b]
13.	Specimen number
14.	Isolate number
15.	Specimen date[a]
16.	Specimen type[a]
17.	Organism[a]
18.	ESBL present
19.	Carbapenemase results
20.	Inducible clindamycin
21.	Antibiotic[a]
22.	Interpretation of susceptibility[a]
23.	Zone value (mm)
24.	MIC (mg/l)

[a] Mandatory field: If a mandatory variable is missing, the record will not be exported to the regional level.

[b] Required field: Required variables are important variables and essential for correct analysis of the data. If a required variable contains missing data, the record will still be exported to the regional level.

Use of date of admission to distinguish between health care-associated infections (HAIs) and community-acquired infections (CAIs)

Reporting the date of admission is important as it will enable distinction between health care-associated infections (HAIs) and community-acquired infections (CAIs) using globally standardized definitions. For BSIs, these definitions (also described in the GLASS early implementation manual [16]) are as follows:

- Hospital-origin (health care-associated) bloodstream infections (BSIs): patients admitted for >2 calendar days when the specimen was obtained or admitted to the health care facility for <2 calendar days but transferred from another health care facility where they were admitted for ≥2 calendar days.
- Community-origin (community-acquired) BSIs: patients in the hospital for ≤ 2 calendar days when the specimen was taken.

It is important to point out that some countries may use other strategies for the application of these international definitions such as the patient sample referral form, which contains information about the origin of the infection (HAI or CAI) provided by the medical staff. In this case, an additional data field is available to indicate whether the isolates originated from the hospital (health care-associated) or the community (community-acquired).

PAHO recognizes the existing barriers in acquiring date of admission, as this information is often not gathered as part of routine data collection in laboratories. However, we strongly encourage countries to invest in connecting data from laboratory information systems and hospital information systems to enable more detailed analyses combining clinical, laboratory, and patient information.

2.3 Procedures at the AMR local surveillance site

As described in Chapter 1, each AMR LSS must be able to process and share the results of routinely collected clinical samples. To ensure good quality of AST results, each LSS needs to follow SOPs and guidelines, have a laboratory quality management system, participate in an external quality assessment program, and have adequately trained laboratory personnel.

i. AST guidelines. Use of international guidelines for susceptibility testing, including harmonized breakpoints, is essential to ensure comparability between AST in different laboratories and countries. The CLSI (Clinical Laboratory and Standards Institute) [18-20] provides comprehensive methodological standards guidance for routine AST, confirmatory testing, and their interpretation and is used by most countries in the Americas. ReLAVRA recommends that countries use CLSI standards with the exception of those rare antimicrobial-microorganism combinations for which the RRL (in consensus with the NRLs in the Region) has recommended other EUCAST cut-off points [21] or local studies. A uniform test panel for AST including indicators of susceptibility to all antimicrobial groups should be tested and analyzed for all bacterial isolates, as listed on the minimum reporting panel (see Annex B).

ii. Quality assurance. A laboratory quality management system and regular application of internal quality assurance procedures allow for timely detection and correction

of errors in laboratory procedures. National auditing and accreditation schemes in conjunction with external quality assurance programs ensure that laboratories conform to international quality standards.

2.4 AMR surveillance procedure at the national level

The NCC (or NRL) receives standardized data sets from the AMR LSS, analyzes them, and subsequently reports the data to PAHO, through the PLISA platform. To ensure standardization and validity and to maintain the quality of the data, specific data management processes are carried out by the NCC and the NRL before the data are submitted to PAHO. These data management processes include but are not limited to data quality checks, deduplication, encryption, and export of the data to PAHO (Figure 4). Part of these processes are performed automatically by the export module provided by PAHO.

i. **Quality check:** Data quality checks are a necessity to ensure the accuracy, completeness, consistency, reliability, and timeliness of data reported at the local, national, and regional levels. The NCC, together with the NRL, should perform quality checks on data collected from the local surveillance site. At a minimum, assessment of the data for completeness should be performed; this includes ensuring 100% completeness of the required and mandatory variables, which consist of patient, specimen, and hospital information (Annex C). The NCC should check the microbiology results for consistency and plausibility.

The following is a list of recommend quality checks that should be performed:

1. Assess submitted data for completeness and missing required and mandatory values;
2. Evaluate the microbiological results for consistency and plausibility of the submitted data;
3. Ensure that pathogens and resistance patterns of interest are confirmed;
4. Adherence to local and national standards for bacterial culturing, species identification, and AST; and
5. Ensure that the clinical susceptible/intermediate/resistant (S/I/R) breakpoints used are appropriate and in line with the relevant guidelines (CLSI or EUCAST).

ii. **Deduplication:** Individual patients are often sampled repeatedly as part of their care, either for diagnostic purposes or to assess their response to treatment. This is usually the case for patients with infections caused by resistant microorganisms, who are more likely to be sampled more than once. To ensure the representativeness of the AST data reported and to reduce bias, the national surveillance sites (NCC or NRL) must **report only the first isolate per microorganism per person per year to the regional level**. For the countries which use WHONET, and apply the standardized WHONET export module to transfer the information to PAHO, the deduplication is done automatically by the modul.

At the regional level (PAHO), the submitted data are also checked to ensure

deduplication. The standardized process for deduplicating the data will allow only one isolate, representing one patient, to be included in the analysis per year (**only the first isolate per microorganism per person per year will be included in the analysis**). This minimizes bias associated with reporting of repeated cultures and allows standardization and comparability of data at the national, regional, and global levels.

To facilitate deduplication, sites should collect a unique patient identifier so that specimens from the same patient can be identified and repeated samples can be removed. Deduplication can be achieved through the WHONET deduplication feature when exporting the data.

iii. **Data encryption:** PAHO is committed to privacy rights of patients and health care facilities alike. For that reason, the patient identification (ID) number available at the AMR LSS and the NCC must be used by one of these levels to encrypt individual patient data (in accordance with the country's legislation) before the data are shared with PAHO. Encryption of data using the patient ID can be accomplished using the standard configuration and export function available in WHONET. At the national level, an AMR LSS code composed of the country code (e.g., ARG) must be generated. In WHONET, the country code is automatically registered when any AMR LSS is configured. In WHONET, the hospital code (e.g., numbers such as 001 or letters such as ABC) should be a three-character code defined by the network coordinator. Full hospital/health care facility names will be available only at the national level and will not be shared with PAHO.

iv. **Collection of population denominators:** Details on population denominators (an estimate of the catchment population of the hospital) and characteristics of participating laboratories and hospitals (e.g., number of blood culture requests, total number of patients, number of beds, level of care) are collected as well through a separate short survey coordinated by the NCC (see Chapter 4 and Annex A). This information facilitates interpretation of the data and assessments of their accuracy and representativeness. Also, collecting data on the total number of hospitalized patients seeking care in the hospitals participating in the surveillance network will enable estimation of the number of bloodstream infections per 1,000 patients per year that are caused by, for example, carbapenem-resistant organisms.

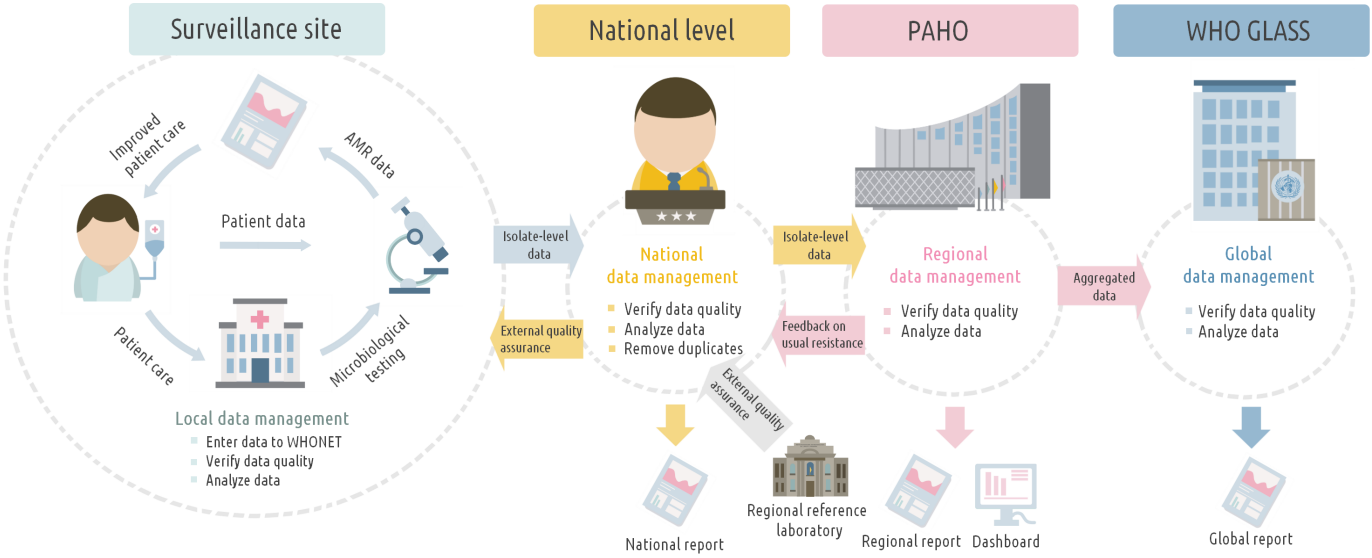
2.5 Feedback from the NCC to the AMR local surveillance sites

Upon completion of quality checks on the data, the NCC and NRL should provide feedback to the AMR LSS for correction. It is recommended that data not passing quality checks not be submitted to the national surveillance system database without the LSS in question addressing the errors in the data. Timely feedback on any problems with the data provides an opportunity for improvements in data quality to be made; the NCC should request an improved file that addresses the data quality checks. Data quality checks align with the frequency of data submission; quarterly frequency is recommended. Further details about the role of the NCC were provided in Chapter 1.

2.6 AMR surveillance procedure at the national reference laboratory (NRL)

The NRL provides countries with the capacity for confirmatory testing of antimicrobial-resistant pathogens and molecular characterization. For the purpose of confirmatory testing of multidrug-resistant organisms or exceptional antimicrobial-resistant phenotypes, local surveillance sites should send bacterial isolates to the NRL. This protocol includes a list of pathogens and resistance patterns of interest that require characterization and confirmatory testing by the national reference laboratory (Annex D). The resistance phenotype list was adopted from CLSI guidelines [18-20], but each country should adapt the category to which each microorganism/resistance mechanism combination belongs according to local epidemiology and the operational capacity of the NRL. It will be necessary to send to the NRL only those resistance phenotypes that correspond to category 1. This list should be reviewed and updated periodically, as national epidemiology or the ability to detect resistance mechanisms in LSS changes. As with the LSS, recording of AST results at the NRL can be done either through a laboratory information system or through direct entry into WHONET, capturing patient, specimen, and hospital information. Results of AST performed at the NRL should be sent back to the LSS for corrections or updates. Further details about the role of the NRL were provided in Chapter 1.

Figure 4.
Data flow between the surveillance sites, the national , regional (PAHO), and global level (WHO HQ)



3. Preparation and submission of national data sets to PAHO

Technical requirements for the data set to be submitted to PAHO and feedback procedures are described below, including data security and anonymization.

3.1 Structural and technical requirements of the PAHO data set

The NCC is responsible for the preparation of the PAHO data set from data collected at the LSSs. As described in Chapter 2 and Table 1, all AST and epidemiological data for BSI samples involving an identified pathogen of interest should be submitted to PAHO. **Annex C contains a complete overview of the variables/data fields.**

The first step for the data manager at the NCC is to review the information (as described in Chapter 2). Next, the data sets from all participating AMR LSSs are combined into one general (national) data set. To ensure standardization and integration of national data into a regional database, PAHO recommends using the WHONET software to generate the national data submitted to PAHO. This is because the WHONET software has a designated automated export function that includes all of the required variables for this PAHO protocol, organized in the correct format. If the surveillance data are managed using the LIS, the data can be imported into the BACKLINK software (bundled with WHONET), which can then produce a PAHO standardized data set using the automated export function.

3.2 Data security and data anonymization

3.2.1 Data security

To guarantee continuous surveillance, it is important to safeguard data against computer malfunction, theft, or human errors. Therefore, it is strongly recommended that data files be backed up regularly and saved in a safe place such as network storage or a local computer. In addition, prior to editing a data set/file, it is recommended that a copy of the original data set/file be made so that it is possible to return to the original file if any mistakes are made during editing.

3.2.2 Data anonymization

Laboratory data may contain personal information. Therefore, it is important that **all information that may lead to the identification of a patient is removed before data are sent to any surveillance network, national or international.** Examples of identifying information are **names, birth dates, home addresses, and national identifiers such as social security numbers**. This information can be used as a patient identifier at the LSS level; however, according to the legislation of each country, data must be anonymized when they are sent outside the institution using an identifier (patient ID) that is unique to that patient but not traceable to the patient. To ensure comparability of data reported at the regional level, PAHO provides an export module in WHONET to automatically anonymize patients when the database is transferred to PLISA.

3.3 Data submission and feedback from PAHO

The anonymized data set should be transferred by the NCC to PAHO on a yearly basis. The data are uploaded through the AMR country collaboration site at the PLISA Health Information Platform for the Americas. The national AMR focal points have a password to login on their specific AMR country collaboration site to securely upload the dataset.

Once the data set has been successfully uploaded the data validation process will start. A notification will be sent to the national AMR focal points when the validation results are available for review. The country is then requested to provide feedback and revise the data (if needed) and upload the updated data. The validation steps contain the following elements.

- Technical details on the number of records received, rejected, and accepted.
- An overview of unusual results. These could be rare or unusual resistance phenotypes, or results that may indicate errors in AST or species identification.
- The number of isolates reported per pathogen, per laboratory, and in total. This overview may identify missing data for specific laboratories.
- Demographic and clinical patient information, by pathogen and in total. The distribution (percentage%) by origin of infection (HAI or CAI), gender, age category, and hospital department of patients should be displayed. This gives an indication of the characteristics of patients that are selected for sampling and may identify missing data on these characteristics.
- Resistance percentages for the pathogen-antibiotic combinations and multidrug resistance divided into multidrug-resistant (MDR); extensively drug-resistant (XDR); and pan-resistant (PDR) [22].

The validation process is also reviewed by the specialists of the AMR Special Program at PAHO, and additional comments or questions that may arise from the data are shared with the NCC for review. Once the national data set has been checked and, if needed, corrected in accordance with the feedback report, the NCC officially confirms the accuracy of the AMR data submitted to PAHO. After the country data accuracy confirmation, the data are used for regional data analysis and reporting.

3.3.1 Timelines for data submission to PAHO

i. PAHO will invite countries to submit their annual AMR data set files between May 1 and June 30 of the next year (data call). During this same period, PAHO will also request the yearly hospital/laboratory questionnaire results (Chapter 4 and Annex A).

ii. Countries will receive their feedback report for quality control and confirmation of the data before August 31.

iii. Countries are requested to make the necessary corrections, resend their data file if needed, and confirm their data by October 15.

iv. Data confirmed by the country will be made available through the interactive website before November 15.

v. During World Antibiotic Awareness Week (the third week of November), a summary report of the submitted data will be published by PAHO.

3.4 Reporting AMR data to GLASS

At WHO Headquarters, aggregated AMR data from countries are collected globally in GLASS. To avoid discrepancies, double reporting, and additional burden on its members, PAHO, with the approval from the participating countries, can provide aggregated AMR data to GLASS on behalf of countries that are enrolled in GLASS. This way, PAHO can facilitate the process and ensure quality and consistency of the data before sharing them with GLASS, with limited impact on timeliness.

4. Data analysis and reporting

Analysis of regional AMR data and preparation of summary statistics for reporting are performed at PAHO. This chapter describes the methodology used for analysis and reporting.

4.1 Definitions and methods for AMR data analysis

- Only the first isolate per microorganism per person per year is included in analyses at the regional and global levels.
- In terms of analysis, an isolate is considered resistant to an antimicrobial agent when it is tested and interpreted as resistant (R) as defined by the clinical breakpoint criteria used by the local laboratory and the specific recommendations regarding AMR mechanisms that have an impact on patient treatment and lead to the conclusion that the ATM is not appropriate despite showing sensitivity results. An isolate is considered nonsusceptible to an antimicrobial agent when tested and interpreted as either resistant (R) or intermediately susceptible (I) using the same local clinical breakpoint criteria.
- Descriptive analyses are conducted to describe the demographic population impacted by the pathogens and resistance patterns identified. National percentage results are reported as a resistance percentage, that is, the percentage of resistant (R) isolates out of all isolates with AST information for that specific species/antimicrobial group.
- Trend analyses are conducted to explore temporal trends in resistance percentages by country. Countries reporting fewer than 30 isolates per year per pathogen and/or not providing data for the surveillance period will not be included in the trend analysis. The Cochran-Armitage test will be used to assess the statistical significance of trends; a p-value of ≤0.05 is considered statistically significant.

4.1.1 Grouping of antibiotics

In some instances, resistance percentages are presented for a single antibiotic, and and in others, for a group of antibiotics. Resistance or nonsusceptibility to an antibiotic group is defined as resistance or nonsusceptibility to at least one of the antibiotics in the group, using the priority sequence R → I → S. See Annex B for the list of pathogen-antibiotic combinations under surveillance, including the grouping of antibiotics for analyses. Grouping of antibiotics is done when the test characteristics for detecting resistance to all drugs within the group are comparable.

4.1.2 Calculating multidrug resistance

In addition to resistance percentages for individual antibiotics and antibiotic groups, resistance percentages for MDR, XDR, and PDR are calculated in accordance with the regional consensus published in the Pan American Journal of Public Health in 2019. Isolates with missing data on one or more of the required antibiotic groups are excluded from the analysis [21].

4.2 Laboratory and hospital questionnaires

When analyzing AMR surveillance data, it is important to have background information on the patient population and on sampling practices in the hospitals. This information provides a better understanding of resistance proportions within the local context and enables calculation of resistance incidence. Additionally, this information allows assessments of the representativeness of the national AMR surveillance system.

When a country starts to submit data to PAHO, the NCC is asked to complete a small questionnaire for each participating hospital and laboratory. Every year, a request will be sent out to update the information provided (Annex A). Details on population denominators (an estimate of the catchment population of the hospital) and characteristics of participating laboratories and hospitals (e.g., number of blood culture requests, total number of patients, number of beds, and level of care) are included in this information request (Annex A). These details facilitate interpretation of the data and assessments of their accuracy and representativeness. Collecting data on the total number of hospitalized patients seeking care in the hospitals participating in the surveillance network will enable estimation of the number of bloodstream infections per 1,000 patients per year that are caused by, for example, carbapenem-resistant organisms.

4.3 Data and validity

The following factors may affect the data quality and validity during each of the phases in the data generation process: i) representativeness (selection of surveillance sites participating in the surveillance program), ii) sampling habits (selection of patients for blood culturing in the hospital), iii) laboratory quality assurance (processing of samples in the laboratory), and iv) interpretation and data analysis (aggregation and analysis of the data).

Error and bias: Deviations from true values may be due to either random or systematic errors. Both types of errors affect data accuracy. Random deviation results from chance variation occurring during sampling or measurement. Systematic deviation is caused by systematic errors in collecting, processing, and analyzing data. Systematic deviation is also called bias. In particular, systematic deviation may occur because of choices made when taking patient samples (sampling bias), when processing samples in the laboratory (measurement error), or when aggregating data for analysis (such as including multiple isolates from the same species in the same patient in the same calendar year). Random error will always occur and can be reduced to a certain extent. In contrast, systematic error can be significantly reduced by paying attention to details and improving the data generation process.

Several sources of error and bias in AMR surveillance data, as well as possible strategies to prevent error or bias, are summarized in Table 3.

4.4 Publication of AMR data

On a yearly basis, PAHO will publish a regional summary report displaying results for all countries within the network that provided validated and approved data in tables, maps, and bar charts. Also, an interactive database

Table 3.
Sources of error and bias in AMR surveillance data

Type of error/bias		Mechanism	Solution
Random error	Sampling variation	Chance	• Increase sample size
	Measurement variation	Test-to-test variation in application of laboratory procedures	• Increase sample size • Standardize procedures • Provide continuous training of laboratory staff • Set up quality assurance systems
	Bias due to sampling procedures		
Systematic error	Selection of participating sites	Sampling specific patient populations only, such as tertiary hospitals, ICUs, urban centers	• Select a mixture of hospital types and departments from different geographical regions, different medical specialties, and different patient populations
	Selection of patients	Sampling only severe cases or after treatment failure	• Improve case ascertainment; i.e., promote sampling of all cases with signs of bloodstream infection prior to treatment initiation (active case finding)
	Laboratory standards	• Use of nonuniform or nonstandardized AST methods or out-of-date standards • Sequential testing, such as testing susceptibility for carbapenems only if isolate is resistant to third-generation cephalosporins	• Use national standards based on international standards for AST methodology (e.g., CLSI) • Test susceptibility to all indicator antimicrobials (uniform test panel) on all microorganisms
	Measurement error	• Improper application of laboratory methods, such as use of nonstandard inoculum • Inadequate laboratory materials, such as use of expired or non-quality-controlled antimicrobial disks • Damaged and/or poorly calibrated equipment, such as out-of-date firmware used with automated systems	• Provide continuous training of laboratory staff • Set up laboratory quality assurance systems • Perform confirmatory testing of multidrug-resistant microorganisms or exceptional antimicrobial-resistant phenotypes • Procure high-quality/quality-controlled materials
	Bias from data aggregation and analysis procedures		
		• Inclusion of repeat isolates from individual patients • Use of varying expert rules, such as different rules for deriving resistance used in each laboratory	• Collect non-aggregated (raw) data • Use standardized data aggregation and analysis methods

data will be available online at https://www.paho.org/en/topics/antimicrobial-resistance

The dashboards provide regional maps and general trends in antibiotic susceptibility (S, I, R) for selected priority pathogen-drug combinations in the Latin American and the Caribbean region. The dashboards are aimed at improving the knowledge and increasing the interest of end users by displaying regional and national trends in an interactive and user-friendly fashion, using outputs that will allow better understanding and interaction with the data.

Countries are strongly encouraged to use the regional AMR database for additional research, analysis, and publications. In the case of publications in scientific journals, the following agreements should be followed:

i. For publications on behalf of the network, the network name will be included as an author, and the institution names of each of the countries leading the national AMR surveillance will be mentioned either in a footnote or the acknowledgment, depending on the rules of the journal.

ii. PAHO will use the data only as per the protocol objectives and obtain country approval for additional data use, including use of anonymized hospital- or lab-level data. This also accounts for countries that would like to use data from the regional AMR database for additional analysis and research purposes and publications.

iii. On the website, a suggested reference for use of data displayed on the interactive website will be available, including a link to the interactive database website where all institutions and links to their respective websites are listed.

5. Challenges for national AMR surveillance

Technical capacity: Countries with limited capacity for AMR surveillance can designate a few sites during the early stages of implementation of enhanced AMR surveillance. One approach is to start stepwise with sites that have the greatest technical laboratory diagnostic/surveillance capacity and interest with respect to AMR surveillance. Once the site starts to collect and report data regularly, the scope of surveillance activities can be expanded. To better understand whether a potential site is suitable for surveillance, an initial qualitative questionnaire can be used to provide additional insight on the characteristics of sentinel sites (e.g., number of patients, number and type of staff, types of patients, services provided, capacity for laboratory surveillance and sample management).

Sample representativeness: Achieving adequate representation often depends on several factors, such as the size of the country, the complexity of demographic and geographic strata, levels of care, and/or the surveillance capacity of institutes and available resources.

- **Selective inclusion of patients:** Selective inclusion of patients from certain hospital departments (e.g., intensive care units [ICUs]) or institution types (e.g., tertiary care institutions), patients with certain types of infections (e.g., community-acquired urosepsis or health care-associated bloodstream infections), patients with chronic or recurring infections, or patients with relapses or treatment failure will likely overestimate the resistance proportion because these patients may have been subjected to the selective pressure of antimicrobials.
- **Overrepresentation of specific patient groups:** Severely ill patients, patients with certain treatment contraindications, and patients with a high suspicion of AMR infections will likely be overrepresented when surveillance data are collected through routine practices. Sampling from these special patient categories will allow for an understanding of the occurrence in that specific population, but the results will not necessarily generalizable to the overall patient population (population at risk). This is especially true in limited resource settings where empirical treatment of BSI is frequent and sampling for identification and AST is reserved for severe cases (due to limited resources).
- **Sampling habits and self-treatment:** If possible, samples should always be taken prior to initiation of antimicrobial therapy. Sampling after self-treatment in settings where over-the-counter sale of antibiotics is common will likely result in overestimates of resistance proportions.

6. PAHO technical support: AMR surveillance

PAHO supports setting up and strengthening national AMR surveillance networks through consultations, activities, and training that improve laboratory quality, data management, analysis, and reporting. Support is provided in collaboration with partners, WHO CCs, and experts in the field.

Areas of technical support include:

- Assessments of national AMR surveillance sites
- Training courses on laboratory quality management
- Support in setting up laboratory quality assurance systems
- Provision of annual external quality assessment (EQA) exercises through the Malbrán Institute (WHO CC)
- Support to laboratory networks making the transition to CLSI methodology
- Training for AMR national reference laboratories
- Support in setting up and improving standardized (electronic) data collection (WHONET), data management, and data quality assurance procedures
- Support national AMR surveillance network meetings to discuss surveillance data, EQA results, and improvements in surveillance and to assess capacity-building needs
- Support regional/multi-country network meetings to discuss AMR trends, network progress, EQA results, and specific issues and challenges related to AMR surveillance

Additional PAHO activities closely related to AMR surveillance:

- Support of NAP stakeholder meetings
- Review of AMR NAPs
- Point prevalence surveys on antibiotic use in hospitals
- Support in outbreak investigations

Technical support is provided through:

- Regional, multi-country, or national workshops/training
- Laboratory assessments
- Virtual training sessions
- Ad hoc desktop support
- Development of manuals and protocols

For more information and questions about the technical support provided by PAHO, please contact AMRHQ@PAHO.ORG.

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Annexes

Annex A. Laboratory and hospital questionnaires

The NCC/NRL is requested to collect the information below from the laboratories and hospitals that are part of the surveillance network on a yearly basis, during the same frame as the AMR data file is collected (between May 1 and June 30 of the next year; see Chapter 3). The laboratory questionnaire results should be provided/uploaded in a separate file. The file template will be available through the AMR country collaboration sites in PLISA.

Laboratory questionnaire

(please complete the questionnaire for each laboratory participating in the national AMR surveillance system)

1	Laboratory code:	
2	Total number of blood culture requests (sets) per year [1,2]:	

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

[2] If not available, please calculate by dividing the total number of blood culture bottles processed by the total number of bottles per blood culture requested.

Hospital questionnaire

(please complete the questionnaire for each hospital participating in the national AMR surveillance system)

1	Hospital code:	
2	Laboratory code:	
3	The level of care of the hospital (Important: check definitions below):	❏ Primary level [1] ❏ Secondary level [2] ❏ Tertiary level [3] ❏ If different, please specify: _____
4	Best estimate of catchment population of your hospital in the reporting year [4] (contact hospital administration):	
5	Hospital size in beds in the reporting year:	
6	Number of intensive care beds in the reporting year:	
7	Total number of patient admissions for the reporting year:	
8	Total number of patient days [5] in the hospital in the reporting year:	
9	The average occupancy rate in the reporting year (%) (if 8 not available):	

[1] Primary level, often referred to as a district hospital or first-level referral. The hospital has few specialties, mainly internal medicine, obstetrics-gynecology, pediatrics, and general surgery, or only general practice; limited laboratory services are available for general but not for specialized pathological analysis; bed capacity ranges from 30 to 200 beds.

[2] Secondary level, often referred to as a provincial hospital. Highly differentiated by function with five to 10 clinical specialties; bed capacity ranges from 200 to 800 beds.

[3] Tertiary level, often referred to as a central or regional hospital. Highly specialized staff and technical equipment (e.g., cardiology, ICU, and specialized imaging units); clinical services are highly differentiated by function; may have teaching activities; bed capacity ranges from 300 to 1,500 beds.

[4] University/teaching hospitals may also function as district hospitals, thereby actually serving two different populations. If this is the case for your hospital, please provide the catchment population for the tertiary care service.

[5] Patient days: the number of patient days is the number of days spent in the institution for all patients occupying a bed. A day is measured at midnight, and the day of discharge is not counted as an extra day. This means that a patient admitted today and discharged tomorrow will have one patient day. Day patients will have zero patient days as they do not stay past midnight and must not be included in the total count.

Annex B. Pathogen-antibiotic combinations under surveillance

*(*minimum required variable)*

Pathogen	Class of antibiotics	Antibiotics	Abbreviation
Escherichia coli	Aminoglycosides	Amikacin*	AMK
	Aminoglycosides	Gentamicin*	GEN
	Penicillins	Ampicillin	AMP
	Penicillins + beta-lactamase inhibitors	Amoxicillin-clavulanate*	AMC
	Penicillins + beta-lactamase inhibitors	Piperacillin-tazobactam*	TZP
	Carbapenems	Imipenem*	IPM
	Carbapenems	Meropenem*	MEM
	Carbapenems	Ertapenem	ETP
	First-generation cephalospo-rins	Cefazolin	CZO
	Cephamicyns	Cefoxitin	FOX
	Third-generation cephalos-porins	Ceftazidime*	CAZ
	Third-generation cephalos-porins	Ceftriaxone OR cefotaxime*	CRO or CTX
	Fourth-generation cephalos-porins	Cefepime*	FEP
	Polypeptides	Colistin	COL
	Folate pathway antagonists	Trimethoprim-sulfamethoxazole	SXT
	Quinolones	Ciprofloxacin*	CIP
	Fosfomycins	Fosfomycin	FOS
	Nitroheterocyclics	Nitrofurantoin	NIT
	Quinolones	Nalidixic acid	NAL
	Tetracyclines	Tetracycline	TCY
	Tetracyclines	Tigecycline	TGC
Klebsiella pneumoniae	Aminoglycosides	Amikacin*	AMK
	Aminoglycosides	Gentamicin*	GEN
	Penicillins + beta-lactamase inhibitors	Amoxicillin-clavulanate	AMC
	Penicillins + beta-lactamase inhibitors	Piperacillin-tazobactam*	TZP
	Carbapenems	Imipenem*	IPM

Pathogen	Class of antibiotics	Antibiotics	Abbreviation
	Carbapenems	Meropenem*	MEM
	Carbapenems	Ertapenem	ETP
	First-generation cephalosporins	Cefazolin	CZO
	Cephamicyns	Cefoxitin	FOX
	Third-generation cephalosporins	Ceftazidime*	CAZ
	Third-generation cephalosporins	Ceftriaxone or cefotaxime*	CRO or CTX
	Fourth-generation cephalosporins	Cefepime*	FEP
	Polypeptides	Colistin	COL
	Folate pathway antagonists	Trimethoprim-sulfamethoxa-zole	SXT
	Quinolones	Ciprofloxacin*	CIP
	Fosfomycins	Fosfomycin	FOS
	Nitroheterocyclics	Nitrofurantoin	NIT
	Quinolones	Nalidixic acid	NAL
	Tetracyclines	Tetracycline	TCY
	Tetracyclines	Tigecycline	TGC
***Salmonella* spp.**	Penicillins	Ampicillin*	AMP
	Penicillins + beta-lactamase inhibitors	Amoxicillin-clavulanate	AMC
	Cephamycins	Cefoxitin	FOX
	Third-generation cephalosporins	Ceftazidime	CAZ
	Third-generation cephalosporins	Ceftriaxone OR cefotaxime*	CRO or CTX
	Third-generation cephalosporins	Cefpodoxime	POD
	Phenicols	Chloramphenicol*	CHL
	Polypeptides	Colistin	COL
	Folate pathway antagonists	Trimethoprim-sulfamethoxa-zole*	SXT
	Quinolones	Ciprofloxacin*	CIP
	Fosfomycins	Fosfomycin	FOS

Pathogen	Class of antibiotics	Antibiotics	Abbreviation
	Macrolides	Azithromycin*	AZM
	Nitroheterocyclics	Nitrofurantoin*	NIT
	Quinolones	Nalidixic acid	NAL
	Tetracyclines	Tetracycline	TCY
	Tetracyclines	Tigecycline	TGC
Other *Enterobacteriaceae*	Aminoglycosides	Amikacin*	AMK
	Aminoglycosides	Gentamicin*	GEN
	Penicillins	Ampicillin	AMP
	Penicillins + beta-lactamase inhibitors	Amoxicillin-clavulanate	AMC
	Penicillins + beta-lactamase inhibitors	Piperacillin-tazobactam*	TZP
	Carbapenems	Imipenem*	IPM
	Carbapenems	Meropenem*	MEM
	Carbapenems	Ertapenem	ETP
	First-generation cephalosporins	Cefazolin	CZO
	Cephamycins	Cefoxitin	FOX
	Third-generation cephalosporins	Ceftazidime*	CAZ
	Third-generation cephalosporins	Ceftriaxone OR cefotaxime*	CRO or CTX
	Fourth-generation cephalosporins	Cefepime*	FEP
	Polypeptides	Colistin	COL
	Folate pathway antagonists	Trimethoprim-sulfamethoxazole	SXT
	Quinolones	Ciprofloxacin*	CIP
	Fosfomycins	Fosfomycin	FOS
	Nitroheterocyclics	Nitrofurantoin	NIT
	Quinolones	Nalidixic acid	NAL
	Tetracyclines	Tetracycline	TCY
	Tetracyclines	Tigecycline	TGC
Acinetobacter baumannii	Aminoglycosides	Amikacin*	AMK
	Aminoglycosides	Gentamicin*	GEN
	Penicillins + beta-lactamase inhibitors	Ampicillin-sulbactam*	SAM
	Penicillins + beta-lactamase inhibitors	Piperacillin-tazobactam*	TZP
	Carbapenems	Imipenem*	IPM
	Carbapenems	Meropenem*	MEM

Pathogen	Class of antibiotics	Antibiotics	Abbreviation
	Third-generation cephalosporins	Ceftazidime*	CAZ
	Fourth-generation cephalosporins	Cefepime*	FEP
	Polypeptides	Colistin	COL
	Folate pathway antagonists	Trimethoprim-sulfamethoxazole	SXT
	Quinolones	Ciprofloxacin*	CIP
	Tetracyclines	Doxycycline	DOX
	Tetracyclines	Minocycline	MNO
	Tetracyclines	Tetracycline	TCY
	Tetracyclines	Tigecycline	TGC
***Staphylococcus* spp.**	Aminoglycosides	Gentamicin*	GEN
	Penicillins	Oxacillin*	OXA
	Cephamycins	Cefoxitin*	FOX
	Folate pathway antagonists	Trimethoprim-sulfamethoxazole*	SXT
	Quinolones	Levofloxacin	LVX
	Quinolones	Ciprofloxacin*	CIP
	Glycopeptides	Teicoplanin	TEC
	Glycopeptides	Vancomycin*	VAN
	Lincosamides	Clindamycin*	CLI
	Oxazolidinones	Linezolid*	LNZ
	Macrolides	Erythromycin	ERI
	Rifamycins	Rifampicin*	RIF
	Tetracyclines	Doxycycline	DOX
	Tetracyclines	Minocycline*	MNO
	Tetracyclines	Tetracycline*	TCY
	Aminocoumarins	Novobiocin	NOV
	Lipopeptides	Daptomycin	DAP
Streptococcus pneumoniae	Penicillins	Oxacillin*	OXA
	Penicillins	Penicillin*	PEN
	Carbapenems	Imipenem	IPM
	Carbapenems	Meropenem	MEM
	Third-generation cephalosporins	Ceftriaxone	CRO
	Third-generation cephalosporins	Cefotaxime*	CTX
	Phenicols	Chloramphenicol	CHL

Pathogen	Class of antibiotics	Antibiotics	Abbreviation
	Folate pathway antagonists	Trimethoprim-sulfamethoxazole	SXT
	Quinolones	Levofloxacin*	LVX
	Glycopeptides	Vancomycin*	VAN
	Lincosamides	Clindamycin	CLI
	Macrolides	Erythromycin	ERI
	Rifamycins	Rifampicin*	RIF
	Tetracyclines	Tetracycline	TCY
Pseudomonas aeruginosa	Aminoglycosides	Amikacin*	AMK
	Aminoglycosides	Gentamicin*	GEN
	Penicillins + beta-lactamase inhibitors	Piperacillin-tazobactam*	TZP
	Carbapenems	Imipenem*	IPM
	Carbapenems	Meropenem*	MEM
	Monobactams	Aztreonam*	ATM
	Third-generation cephalosporins	Ceftazidime*	CAZ
	Third-generation cephalosporins	Cefoperazone	CFP
	Fourth-generation cephalosporins	Cefepime*	FEP
	Polipeptides	Colistin	COL
	Quinolones	Ciprofloxacin*	CIP
***Enterococcus* spp.**	Aminoglycosides	High-dose gentamicin*	GEH
	Aminoglycosides	High-dose streptomycin*	STH
	Penicillins	Ampicillin*	AMP
	Glycopeptides	Teicoplanin	TEC
	Glycopeptides	Vancomycin*	VAN
	Oxazolidinones	Linezolid	LNZ
	Lipopeptides	Daptomycin	DAP

Annex C. Detailed data fields

The table below includes the 24 data fields as defined for the current enhanced isolate-level AMR surveillance. The fields in bold will be transferred to PLISA through an export module available in WHONET. The fields in italics (in WHONET by default) are for use by the LSS and NRL/NCC and will not be transferred to the regional base. The data fields below and the related WHONET configuration include the needed data fields and standard codes for inclusion of *Candida* spp. in GLASS.

IMPORTANT (!) (#) There are differences between the names and codes of the early implementation protocol variables for inclusion of *Candida* spp. in GLASS and the WHONET program. With the intention of being able to use a single WHONET configuration for the protocols currently carried out in the Americas and the Caribbean region, those that involve differences are detailed in the table.

[1] Mandatory field: If a mandatory variable is missing, the record will not be exported to the regional level.

[2] Required field: Required variables are important variables and essential for correct analysis of the data. If a required variable contains missing data, the record will be exported anyway to the regional level.

Variable name	Type	Variable	Description	Coded value	In the protocol for inclusion of *Candida* spp. in GLASS, this field is called (#):
1. Country[1]	**Text**	**COUNTRY_A**	**Country name**		
This field is part of the laboratory configuration. It is not necessary to enter for each sample; the system always places it. Country name is collected to analyze the number of isolates reported by country. It also allows analyzing spatial trends or distributions of AMR regionally and provides information on regional coverage of surveillance to ensure representative data.					
2. Laboratory ID[1]	**Text**	**LABORATORY**	**Unique identifier for laboratories**		**Hospital code**
This field is part of the laboratory configuration. It is not necessary to load it for each sample; the system always places it. Anonymized laboratory ID provides information on the source of data submitted to the national surveillance system. This information allows data quality assurance.					
3. Identification number[1]	**Text**	**PATIENT_ID**	**Unique identifier for patients within hospital**		**Patient identification / code**
Patient ID is collected to identify duplicated data entry at the national level to ensure overall data quality. This information is anonymized to preserve data privacy before data are sent to PAHO.					
First name	***Text***	***FIRST_NAME***	***Patient identifier***		
The patient's first name is collected as the identifier of the patient and is important in making reports of individual results and differentiating patients in case there is no unique identifier of the patient in the institution. WHONET uses it for data encryption.					

Variable name	Type	Variable	Description	Coded value	In the protocol for inclusion of *Candida* spp. in GLASS, this field is called (#):
Last name	***Text***	***LAST_NAME***	***Patient identifier***		
The patient's last name is collected as the identifier of the patient and is important in making reports of individual results and differentiating patients in case there is no unique identifier of the patient in the institution. WHONET uses it for data encryption.					
4. Sex[2]	**Text**	**SEX**	**Patient gender**	**m: male f: female o: other u: unknown**	**Gender**
Sex is collected to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations between gender groups and to identify potential risk factors for resistance.					
5. Date of birth	**Date**	**DATE_BIRTH**	**Date of birth**	**For example: MON-DD-YYYY**	**Date of birth (or age)**
Date of birth is collected to obtain age information for subgroup analysis; to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations across different age groups; and to identify potential risk factors for resistance.					
6. Age[2]	**Text**	**AGE**	**Patient's age at the time of sampling**	**Years: 1,2,3... Months: 1m,2m,... 11m... Days: 1d,-2d,...,30d Weeks: 1w,2w,... 51w**	**Date of birth (or age)**
Age is collected in case date of birth is not available; otherwise, age is generated: [Age] = [Specimen Date] – [Date of Birth]					
Age category	*Text*	*PAT_TYPE*	*Patient age group*	*new: newborn ped: pediatric adu: adult ger: geriatric unk: unknown oth: other*	
The age category is an important field (especially if the patient's age is not known exactly) to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations in different age groups and to identify possible risk factors for resistance.					
7. Institution	**Text**	**INSTITU**	**Hospital name**		
The anonymized institution provides information on the source of the data sent to the national surveillance system and ensures the quality of the data. It also provides information on national coverage of the surveillance system to guarantee representative data. **ONLY COMPLETE THIS FIELD WHEN THE LOADED ISOLATE DOES NOT BELONG TO YOUR HOSPITAL.**					
8. Date of admission	**Date**	**DATE_ADMIS**	**Date of admission in hospital**	**MON-DD-YYYY**	
Date of admission is collected to identify whether the infection of a patient is a hospital-associated infection or community-acquired infection, using the definition from GLASS (provided in the manual).					
9. Ward	**Text**	**WARD**	**Name of the ward**	**(Depends on the hospital)**	
Ward is collected to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations across different ward types and to identify potential risk factors for resistance. It is also useful in identifying the spread of strains in different areas of the hospital and suspected outbreaks. This field is very useful for management of information internally in the hospital and has no greater utility at the NCC or PAHO level.					

Variable name	Type	Variable	Description	Coded value	In the protocol for inclusion of *Candida* spp. in GLASS, this field is called (#):
10. Department	Text	DEPARTMENT	Service where the patient is admitted when the sample is taken		Hospital department/unit
				med: medicine	Medical adults
				sur: surgery	i
				icu: intensive care unit	
				int: intermediate care unit	
				obg: obstetrics/ gynecology	obstretics
				ped: pediatrics	i
				neo: neonatology	i
				inf: infectious disease	HIV or other immunodeficiency diseases
				hao: hematology/ oncology	hematological/ oncology
				psy: psychiatry	
				eme: emergency	
				out: outpatient	
				lab: laboratory	
				cli: other clinic	
				hos: other hospital	
				com: community	
				mix: mixed	
				oth: other	
				unk: unknown	
				aicu: Adult ICU	i
				picu: pediatric ICU	i
				nicu: neonatal ICU	i
				ccu: coronary care unit	i
				trm: traumatology	Trauma
				tran: trasplant service	Transplant
				burn: burn	i
				nur: nursing home	Geriatric

Variable name	Type	Variable	Description	Coded value	In the protocol for inclusion of *Candida* spp. in GLASS, this field is called (#):
The department where the patient is hospitalized is very important to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations in different types of hospital departments and to identify possible risk factors for resistance. This parameter allows an independent codification of rooms that is specific to each institution and a grouping of patient origin into distinct categories that provide useful epidemiological information for the analysis.					
11. Location type	Text	WARD_TYPE	Patient origin/ patient type	out: outpatient in: inpatient inx: inpatient (non-ICU) icu: intensive care unit int: intermediate CU eme: emergency nur: nursing home com: community lab: laboratory oth: other unk: unknown mix: mixed	Patient type
Location type is collected to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations across different ward types and to identify potential risk factors for resistance.					
12. Origen infección[2]	Text	INFECT_TYP	Hospital origin (health care-associated) Community origin (community-acquired)	ho: hospital origin co: community origin unk: unknown	Community- or hospital-acquired
Hospital-associated infection or community-acquired infection is collected in case date of admission or specimen date is not available. Currently codes and descriptions are available only in Spanish. Please see Annex 2 for more information.					
13. Specimen number	Text	SPEC_NUM	Unique identifier for each specimen		Isolate number/code
Specimen number is collected to identify duplicated data entry and to ensure data quality.					
14. Isolate number	Text	ISOL_NUM	Identify each isolation within the same sample		
Isolate number is collected to identify duplicated data entry and to ensure data quality. It is important when different microorganisms are isolated from the same sample.					
15. Specimen date[1]	Date	SPEC_DATE	Date of sample collection	For example: MON-DD-YYYY	Date of isolate collection
Specimen date is collected to identify whether the infection of a patient is a hospital-associated infection or community-acquired, using the definition from GLASS (provided in the manual).					

Variable name	Type	Variable	Description	Coded value	In the protocol for inclusion of *Candida* spp. in GLASS, this field is called (#):
16. Specimen type[1]	Text	SPEC_TYPE	Source of the isolate	bl: Blood	Specimen
Specimen type is collected to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations across different types of specimens and to analyze the source of isolates. Only the results of blood samples in this first stage will be transferred regionally.					
17. Organism[1]	Text	ORGANISM	Pathogen species and genus of the pathogen that has been isolated from the sample		Isolate identification
Organism is collected to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations across different types of pathogens.					
18. ESBL	Categorical	ESBL	Detection of ESBL	+: positive -: negative	
ESBL is collected for confirmation of resistance to gram-negative bacteria.					
19. Carbapenemase	Categorical	CARBAPENEM	Carbapenemase detection; refers to the phenotypic test for carbapenemase activity (for example, colorimetric methods, MIC, immunochromatography)	+: positive -: negative	
Carbapenemase results are collected for resistance confirmation. The modified Hodge test (MHT) and especially the Triton Hodge test (recommended by the RRL) have a high sensitivity for detection of carbapenemases but little specificity, so their results should not be included in this field.					
20. Inducible clindamycin	Categorical	INDUC_CLI	Inducible clindamycin resistance	+: positive -: negative	
Inducible clindamycin is collected to report resistance to macrolides and lincomycins in gram-positive bacteria.					
21. Antibiotic panel[1]	Text		Name of the antimicrobial agent		Code of antifungals tested
Antimicrobial agent is collected to analyze the percentages of susceptible, intermediate, susceptible-dose dependent, and resistance for drug-microorganism combinations across different antimicrobial groups.					
22. Interpretation of susceptibility testing[1]	Categorical		Final interpretation results of all different susceptibility tests performed	S: susceptible I: intermediate R: resistant NS: nonsusceptible	
Interpretation of susceptibility is collected to analyze the final interpretation results confirmed at the country level. IMPORTANT: WHONET currently does not include the Susceptible Dependent Dose (SDD) classification. It will be interpreted as Intermediate (I) in those drug-microorganism combinations for which such a classification exists: ***Enterobacteriaceae***: cefepime ***Enterococcus*** spp.: daptomicyn ***Candida albicans, C. glabrata, C. parapsilosis,*** and ***C. tropicalis***: fluconazole					

Variable name	Type	Variable	Description	Coded value	In the protocol for inclusion of *Candida* spp. in GLASS, this field is called (#):
23. Zone value (mm)	**Number**		**Zone (value in mm)**		
Zone value is collected to determine whether an isolate is susceptible, intermediate, susceptible-dose dependent, or resistant to an antimicrobial according to the CLSI standard (recommended) or to the interpretation guide used.					
24. MIC (mg/l)	**Number**		**MIC (value in mg/l)**		
MIC value is collected to determine whether an isolate is susceptible, intermediate, susceptible-dose dependent, or resistant to an antimicrobial according to the CLSI standard (recommended) or to the interpretation guide used.					

The following fields and variables are specific to mycology. Please see Annex 2 in the WHONET manual for more information.					
Método de identificación (ID)[2]	Texto	ID_METHOD	Method used to identify *Candida* species	co: conventional ap: API 20 o 32 C ph: BD Phoenix vi: Vitek mi: MicroScan to: MALDI-TOF mo: molecular se: sequencing ot: other re: Remel	
The identification method is important at the national level to guarantee data quality.					
Versión del software del método de ID[2]	Texto	SOFT_VER	Software version of the automated method used for the identification of *Candida* species	Free text	
The software version of the identification method is important at the national level to ensure data quality.					
Gen amplificado para la ID[2]	Texto	GENE_TARGE	Gene amplified for the ID of *Candida* species	Free text	
The name of the amplified gene for the identification of *Candida* species is important at the national level to guarantee data quality.					
Método de sensibilidad[2]	Texto	ASTF_METHO	Susceptibility method used to determine MICs	bmdc: broth microdilution CLSI bmde: broth microdilution EUCAST syo: Sensititre YeastOne vi: Vitek mi: MicroScan atbf: ATBFungus ot: otro	
The method used to determine the MIC is important at the national level to ensure data quality.					

Annex D. Resistant phenotypes recommended for characterization

The following table represents an example of a form model with the AMR phenotypes that can be presented according to the microorganism-ATM combinations and their stratification into categories according to epidemiological relevance. NRLs should assign a category to each resistance phenotype based on frequency of occurrence and the ability of laboratories to detect the mechanism at the local level. Only phenotypes assigned to category 1 need to be referred to the NRL for confirmation. Any of the pathogens in the table that exhibit PDR should be sent to the NRL for confirmation, characterization, and special tests to provide treatment alternatives.

Definitions of Categories

Category 1 - Occurrence of resistance phenotypes is not reported or has been only rarely reported to date

Category 2 - Occurrence of resistance phenotypes is uncommon in most institutions

Category 3 - Occurrence of resistance phenotypes may be common but is generally considered of epidemiological concern

Organism or Group Organism	Resistance Phenotype Detected	Category 1	Category 2	Category 3
Any *Enterobacteriaceae*	Colistin/polymyxin - NWT		x	
	Carbapenemase +[a]	x[b]		
	Ceftazidima/avibactam NS[c] wild type	x		
Salmonella and *Shigella* spp.	Cephalosporin III - I or R		x	
	Fluoroquinolone - I or R		x	
Acinetobacter baumannii	Colistin/polymyxin - R	x		
Psedomonas aeruginosa	Colistin - R	x		
	Polymyxin I or R			
Enterococcus spp.	Daptomycin - R		x	
	Vancomycin - R			x
	Linezolid - NS	x		
	Tedizolid - NS	x		
Staphylococcus aureus	Vancomycin - MIC ≥ 16 (VRSA)	x		
	Vancomycin = 4 - 8 (VISA)	x		
	Ceftaroline - R		x	
	Daptomycin - R	x		
	Linezolid - R	x		
	Tedizolid - NS	x		
Coagulase-negative *staphylococci*	Daptomycin - R	x		
	Linezolid - R	x		
	Vancomycin - I or R		x	
Streptococcus pneumoniae	Fluroquinolone - I or R		x	
	Imipenem - I or R		x	
	Linezolid - NS	x		
	Vancomycin - NS	x		
	Ceftaroline - NS	x		
	Using nonmeningitis breakpoints			
	Amoxicillin or penicillin - R			x
	Extended spectrum cephalosporin - R			x

[a] Send the first isolation of enterobacteria suspected of producing carbapenemase when carbapenems NS and with one or more positive confirmatory phenotypic tests (synergy with phenylboronic ac./EDTA and/or Bluecarba test/Carba NP Direct and/or immunochromatography).

[b] PDR (pandrug resistance): resistance to all ATMs listed in Annex B [24]

[c] Isolates of *Enterobacteriaceae* ceftazidime/avibactam (CZA) NS that are not producers of metallo-beta-lactamases (MBL). CZA is a new active drug against enterobacteria and *Pseudomonas* spp. producers of serin-carbapenemases and carbapenemases of class D, but it is inactive against producers of MBL.

Reference: Clinical and Laboratory Standard Institute - M100, Appendix A.

Antimicrobial resistance (AMR) surveillance plays an important role in the early detection of resistant strains of public health importance and prompt response to outbreaks in hospitals and the community. Surveillance findings are needed to inform medical practice, antibiotic stewardship, and policy and interventions to combat AMR. Appropriate use of antimicrobials, informed by surveillance, improves patients' treatment outcomes and reduces the emergence and spread of AMR.

This protocol describes the steps and procedures to establish/enhance AMR surveillance in Latin America and the Caribbean. It provides technical guidance to integrate patient, laboratory, and epidemiological data to monitor AMR emergence, trends, and effects in the population. It also provides the necessary elements to move from aggregated data to isolate-level data surveillance starting with blood isolates. It facilitates uniform data collection processes, methods, and tools to ensure data comparability within the Region of the Americas. Finally, it builds on over a decade of experience of the regional AMR surveillance network—ReLAVRA by its Spanish acronym—and its procedures are aligned with the Global Antimicrobial Resistance Surveillance System (GLASS) methodology, enabling countries to participate in the global GLASS AMR surveillance.

PAHO
Pan American Health Organization
World Health Organization Americas

525 Twenty-third Street, NW
Washington, D.C., 20037
United States of America
Tel.: +1 (202) 974-3000
www.paho.org

9 789275 122686