Diagnostic stewardship

A guide to implementation in antimicrobial resistance surveillance sites

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World Health Organization

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This guide has been developed to support the practice of robust microbiological diagnosis, including antimicrobial susceptibility testing (AST), in patients presenting with clinical symptoms compatible with infectious diseases; a concept known as “diagnostic stewardship”. It is of particular relevance to health-care workers and laboratory and surveillance staff working in settings in which microbiological diagnosis is not systematically part of patient management or treatment decisions.

Staff at health facilities that conduct surveillance as part of the national antimicrobial resistance (AMR) surveillance programme and contribute data to the Global Antimicrobial Resistance Surveillance System (GLASS) are strongly encouraged to use this guide to adapt practices, systems and organizational structures to enhance diagnostic stewardship. Patient management and use of antimicrobial medicines will improve, and accurate and representative AMR surveillance data will be generated to inform treatment guidelines and AMR control strategies.

Health administrators and policy makers who are responsible for the organizational and administrative structure at AMR surveillance sites will also find this guide of interest and assistance.

Main reference material

The diagnostic stewardship concept refers to the Global Antimicrobial Resistance Surveillance System: Manual for Early Implementation, Geneva: World Health Organization (2015); Leenstra T, Tambic A, van de Sande-Bruinsma N, Nahrgang S. Proof-of-Principle antimicrobial resistance routine diagnostics study (PoP-study) Protocol, Version 1.1 (April 2016); and Dik JW, Poelman R, Friedrich AW, Panday PN, Lo-Ten-Foe JR, van Assen S, van Gemert-Pijnen J Julia EWC, Niesters HGM, Hendrix R, Sinha B. An integrated stewardship model: antimicrobial, infection prevention and diagnostic (AID). Future Microbiology, 2015 Sep 1.

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Acronyms

AMR	antimicrobial resistance
AST	antimicrobial susceptibility testing
CLSI	Clinical and Laboratory Standards Institute
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GLASS	Global Antimicrobial Resistance Surveillance System
SOPs	Standard operating procedures
WHO	World Health Organization

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Introduction

The World Health Organization (WHO) has developed the Global Antimicrobial Resistance Surveillance System (GLASS) to support the implementation of the Global Action Plan on antimicrobial resistance (AMR). GLASS promotes and facilitates standardized antimicrobial resistance (AMR) surveillance worldwide. Whilst different types and sources of data are important to guide AMR control strategies (e.g. in humans, animals, food, plants, environment), in this early stage of development GLASS is focusing on bacterial resistance in humans. The WHO *GLASS Manual for Early Implementation*[1] provides details of the proposed approach and defines targets for the surveillance of resistance in common bacterial pathogens. One of the main objectives of GLASS is to encourage and facilitate the establishment of national AMR surveillance systems that are capable of monitoring AMR trends and producing reliable and comparable data on a regular basis, to contribute data to the global system in order to monitor AMR trends. A national AMR surveillance system comprises three core components, namely, a national coordinating centre, a national reference laboratory and one or more AMR surveillance sites. Surveillance sites are responsible for collecting data on AMR at the local level and reporting these data to the central level – the national coordinating centre.

A detailed description of the functions and roles and responsibilities of the national coordinating centre, the national reference laboratory and the surveillance sites, including sample terms of reference for each can be found in "National antimicrobial resistance surveillance systems and participation in the Global Antimicrobial Resistance Surveillance System (GLASS) – A guide to planning, implementation, and monitoring and evaluation".[2]

The concept of "diagnostic stewardship" at surveillance sites is an important component of AMR surveillance in humans as well as in the overall AMR control strategy. It is referred to in the *GLASS Manual for Early Implementation* but it does not contain a detailed explanation or guidance on successful implementation. This guide has been developed as an accompaniment to the manual, to elaborate on this concept and to provide practical support to surveillance sites participating in GLASS.

The guide is divided into two chapters:

The first chapter is aimed primarily at clinicians and other front-line health-care workers including laboratory and surveillance staff on site. It describes the "diagnostic pathway", outlining the steps to be taken that are directly related to specimen management for patient care.

The second chapter is aimed at health-care managers, administrators and policy makers. It addresses the organizational and structural elements that must be in place to facilitate successful diagnostic stewardship in health-care facilities and surveillance sites.

[1] Global Antimicrobial Resistance Surveillance System: Manual for Early Implementation. Geneva: World Health Organization; 2015 at http://www.who.int/antimicrobial-resistance/publications/surveillance-system-manual/en/

[2] Available at http://www.who.int/antimicrobial-resistance/global-action-plan/surveillance/supporting-documents-tools/en/ or from the GLASS secretariat (glass@who.int)

What is “diagnostic stewardship”?

Diagnostic stewardship is defined in the GLASS Manual 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, and pathogen identification and accurate, timely reporting of results to guide patient treatment*.”

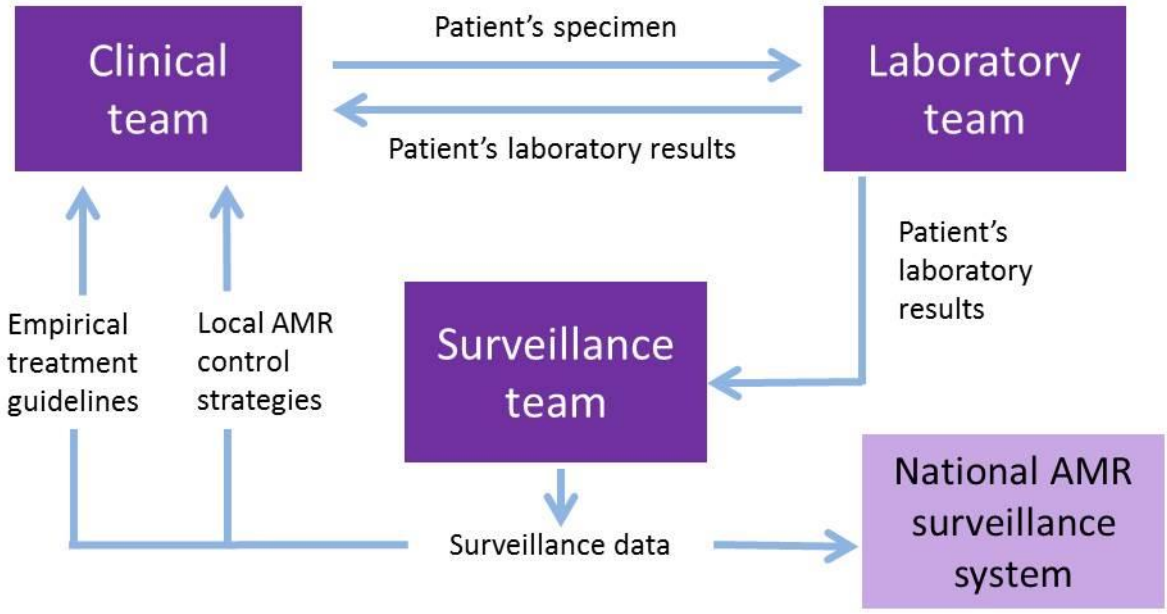
The main objective of microbiological diagnostic stewardship is to deliver:

- patient management guided by timely microbiological data to deliver safer and more effective and efficient patient care; and
- accurate and representative AMR surveillance data to inform treatment guidelines, and AMR control strategies.

Patient management comprises several aspects, including diagnosis, treatment, and infection and prevention control. The underutilization and incorrect use of microbiological tests and diagnostic tools can have a negative effect on the management and outcome for individual patients. It also results in a lack of representative surveillance data for empiric treatment recommendations and AMR control strategies.

Figure 1 illustrates the relationship between laboratory results generated for individual patient care and surveillance data which are used to inform empirical treatment recommendations and AMR control strategies, including infection prevention and control.

Figure 1: Relationship between individual care and surveillance data



Diagnostic stewardship is an integral part of antibiotic stewardship programmes and is also essential for infection prevention and control activities in health-care facilities. Timely and accurate microbiological results help clinicians to select the most appropriate antibiotics or antibiotic combinations for their patients, as well as to implement the necessary precautions to reduce the risk of transmission and prevent outbreaks due to bacterial pathogens in health-care facilities.[3]

But to achieve this, good laboratory practices and affordable access to laboratories with good quality management, as well as the capacity and capability to perform timely and reliable microbiological diagnostics are essential. Although microbiological testing is common in health-care facilities in well-resourced settings, in many parts of the world the concept of diagnostic stewardship is yet to be fully recognized and embedded within regular clinical practice. Furthermore, a number of barriers have been identified that impede the implementation of diagnostic stewardship, some within the health-care system as a whole, others at the level of the health-care facility. Even in settings with sufficient laboratory capacity, economic and logistic constraints, as well as lack of understanding and training, can hinder successful implementation of diagnostic stewardship.

Diagnostic stewardship embraces all stages of the diagnostic process in clinical microbiology and laboratory management: it begins with the practice and procedures that guide specimen selection, collection and the completion of clinical, demographic and epidemiological data that must accompany each specimen; it includes the correct storage and transportation of specimens to the laboratory; it covers how laboratories receive, register and process specimens, including how appropriate tests are selected and performed; and it extends subsequently to how results are reported and interpreted and then used to guide patient management. The success of each stage in this process is dependent upon the quality and effective use of available resources.

Diagnostic stewardship is an effective and important mechanism in the capacity building and quality improvement process in the health-care system. It also helps to optimize resource utilization and to improve surveillance data.

Clinicians and other front-line health-care workers who provide care for patients presenting with infectious diseases syndromes at surveillance sites, as well as laboratory staff who provide microbiological diagnostic services to those health-care facilities, will find this guide of use in helping them to integrate diagnostic stewardship into their routine work.

It will also be of interest to surveillance staff responsible for generating local statistics based on results from routine clinical testing to inform empirical treatment guidelines and AMR control strategies. However, implementation of diagnostic stewardship within health-care facilities cannot succeed without institutional commitment and so this document is also relevant to health administrators and other relevant stakeholders responsible for the organizational and administrative structures at surveillance sites.

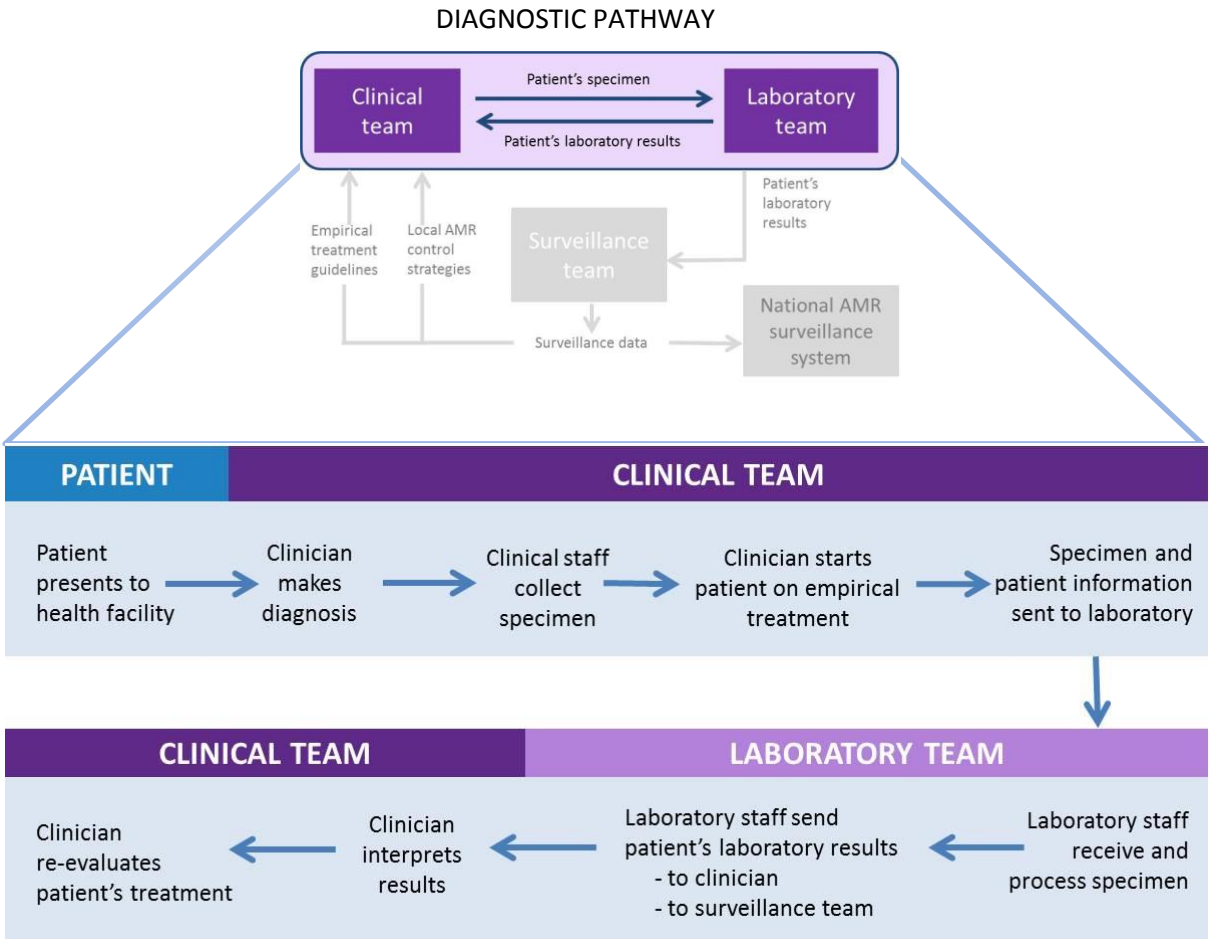
The guide has been developed as part of the implementation of GLASS and is aimed specifically at health-care facilities that are participating in the system as designated surveillance sites. However, as it describes a generic concept, it may also be useful for health-care facilities that are not yet participating in national AMR surveillance and GLASS.

[3] Dik JW, Poelman R, Friedrich AW, Panday PN, Lo-Ten-Foe JR, van Assen S et al. An integrated stewardship model: antimicrobial, infection prevention and diagnostic (AID). Future Microbiology 2015 Sep 1

1. The diagnostic pathway

The diagnostic pathway begins when the patient presents at the health-care facility. It covers the initial interaction between the patient and clinicians and other frontline health-care workers providing care and responsible for diagnostic sampling, through to the role of the laboratory staff responsible for processing the sample and reporting the results back to the clinician. The different steps along this workflow are displayed in Figure 2.

Figure 2: Steps along the diagnostic pathway



1.1. Specimen selection and collection

When a patient presents with a suspected infectious disease, the clinician must decide on the appropriate diagnostic tool(s) to be used, including which specimen(s) to collect for analysis, and be aware of correct handling procedures. Local guidelines and standard operating procedures (SOPs) must include clear case definitions for sampling. Specimen collection should take place before initiating any empiric treatment.

In the case of a serious or life-threatening infection, microbiological sampling should be done before initiating treatment whenever possible, but treatment should not be delayed while waiting for the diagnostic procedure to be performed or for the laboratory results.

Clinical diagnosis of infectious disease is based not only on the patient's history, including underlying risk factors, exposure, symptoms and clinical signs, but also the results from laboratory tests, including microbiological results. The local epidemiological situation and the antimicrobial susceptibility profile will also have an influence on the appropriate empiric treatment of a patient with an infectious disease. In settings with limited access to microbiological diagnostics, the empiric treatment is a common approach. The empiric treatment is also used for early initiation of therapy in severe infections. Surveillance data will be key in guiding the empiric treatment and successful patient outcome.

It is of critical importance that each specimen is accompanied by complete and accurate clinical, demographic and epidemiological patient information. Core patient information according to the *GLASS Manual for Early Implementation* (see Figure 3) includes, at a minimum, a unique identifier, name, date of birth, gender, specimen type, date of specimen collection, and hospital or community origin (see sample request form; to determine hospital or community origin the date of admission would be required from the source data). Additional information may be requested according to local and national protocols (e.g. hospital name, ward or department, patient diagnosis, medical history, referral, antimicrobial therapy etc.).

Figure 3: Sample request form from GLASS Manual for Early Implementation, Annex 2

Patient identification

a. Unique identification number _____

b. Name: (family name, given name(s)) _____

_____

Gender:

Male ❒

Female ❒

Date of birth: (yyyy/mm/dd) _____

Years _____ Months (if < 1 year) _____

Specimen information:

❒ Blood ❒ Urine ❒ Faeces ❒ Urethral secretion ❒ Cervical secretion

❒ Other

Date of specimen collection:

(yyyy/mm/dd)

_____

Had the patient been hospitalized for more than 2 calendar days at the time for sampling?

❒ Yes ❒ No

The early implementation of GLASS is based on case-finding by routine sampling strategies according to local practices and guidelines. Specimens from patients with a suspected bacterial infection are submitted to laboratories for pathogen isolation, identification and antimicrobial susceptibility testing according to SOPs and local guidelines. In the early implementation phase, GLASS is targeting data from four priority specimen types and eight priority bacterial pathogens. The four specimen types have been chosen because they represent infections in the bloodstream, urinary tract, gastrointestinal tract and genital tract and so cover infections in both the hospital and community settings (see the *GLASS Manual for Early Implementation* for more information).

Specimens from patients presenting with respiratory tract infections are not targeted in the early implementation phase of GLASS. The process of collecting sputum requires a patient to produce an adequate specimen and is prone to contamination by oropharyngeal flora. In addition, interpretation of the clinical significance of identified microorganisms may be challenging, and furthermore, respiratory specimens must be processed under appropriate biosafety conditions because of the risk of transmission of certain viruses and tuberculosis. Respiratory specimens other than sputum may depend on sampling techniques which are indicated only in certain circumstances and not widely available, such as broncheoalveolar lavage.

Local guidelines and SOPs normally specify how different specimens should be collected, including the appropriate material to be used (e. g. blood culture bottle, urine container, swabs), the required amount of specimen and technique for clean and safe sampling (e. g. sterile venepuncture for blood specimen) and the appropriate precautions, including use of personal protective equipment such as gloves, that must be adhered to. See below for general information relating to the collection and transportation of specimens included in GLASS. More detailed descriptions and recommendations for specimen management can be found elsewhere.

1.1.1. Blood specimen [4, 5, 6,]

For adults 20 to 30 mL of blood per culture set is recommended (for children a smaller amount is required, adjusted to age and weight accordingly). For automated systems with commercial blood culture bottles, the volume withdrawn should follow the manufacturer's instructions. Whenever possible more than one set of blood cultures from different venepuncture sites should be collected. Optimal volume for blood cultures will yield a higher recovery rate of microorganisms in the bloodstream and help to determine the clinical relevance of identified isolates. Blood culture contamination can be minimized by strict adherence to the aseptic collection technique and collection of peripheral blood via a venepuncture with proper antiseptic skin preparation. Catheter-drawn blood cultures have a higher risk of contamination. Strict adherence to sampling techniques is also critical for patient safety and to minimize occupational hazards, such as needle stick injuries. For

[4] Basic Laboratory procedures in clinical bacteriology, 2nd edition. Geneva: World Health Organization; 2003 at http://apps.who.int/iris/handle/10665/42696

[5] Baron EJ, Miller JM, Weinstein MP, Richter SS, Gilligan PH, Thomson RB Jr et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2013 recommendations by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM). Clin Infect Dis, 2013. 57(4): p e22-e121

[6] Proof-of-Principle antimicrobial resistance routine diagnostics study (PoP-study) Protocol, Version 1.1 – April 2016, Annex B; SOP for sampling BCs; available from the WHO Regional Office for Europe upon request, Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) network at http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/antimicrobial-resistance/central-asian-and-eastern-european-surveillance-of-antimicrobial-resistance-caesar

automated systems, blood culture bottles should be kept at room temperature when transport is delayed. For manual processing, blood culture bottles should be kept at 37°C in the event of a transport delay. Blood culture bottles should not be refrigerated.

1.1.2. Stool specimen [4,5]

Stool specimens should be collected in clean specimen containers and should be transported at room temperature to the microbiological laboratory, ideally within 2 hours. Local SOPs for stool specimen collection and transport may recommend an appropriate transport medium when transport is delayed to enhance recovery of bacterial pathogens, such as placing the specimen in a vial containing Cary-Blair transport medium.

1.1.3. Urine specimen [4,5]

Urine is prone to contamination by commensal flora. Patients should be instructed in how to collect midstream urine ("clean-catch" urine) in a sterile container in order to minimize contamination. If any delay is likely in transporting the specimen to the laboratory, the specimen should be refrigerated immediately after collection to reduce the risk of overgrowth by contaminating organisms. Alternatively urine may be collected in containers with boric acid, when transport delay is anticipated.

1.1.4. Genital specimen [7]

Appropriate urethral and cervical discharge collection is essential to ensure that *N. gonorrhoeae* can be isolated successfully in order to support the diagnosis of gonorrhoea and determine antimicrobial susceptibility. Each specimen should be correctly inoculated in a culture or placed in the appropriate transport medium. If culture media is directly inoculated at the clinic, or bedside, the plates are placed in an atmosphere containing 5% CO_2-enriched humid atmosphere (or candle jar) at 35°C to 36°C and transferred to the laboratory as soon as possible. If the specimen cannot be inoculated immediately onto the culture medium, the swabs should be inserted into a non-nutrient transport medium such as Stuart or Amies. These can be left at room temperature and transported as soon as possible to the laboratory. The isolation rate after transport of specimens in a non-nutrient transport medium at room temperature (25°C) is decreased after 24 hours.

1.2. Turn-around time

Once the specimen has reached the laboratory, the turn-around time to the release of the results will depend upon the diagnostic tools used and the processing procedures. Clinicians should be kept informed of when they can expect to receive the results of the tests on the submitted specimens from the laboratory. This applies to preliminary results, such as gram-stain results, initial growth on plates and final results e. g. species identification and antimicrobial susceptibility. They should be made aware that the final results from culture-based species identification and antimicrobial susceptibility testing may take several days at which point empiric treatment should be reviewed and

[7] Laboratory diagnosis of sexually transmitted infections, including human immunodeficiency virus. Geneva: World Health Organization; 2013 at http://apps.who.int/iris/bitstream/10665/85343/1/9789241505840_eng.pdf

may need to be adapted accordingly, although with the use of new automated diagnostic systems for identification and antimicrobial susceptibility the turn-around time is substantially reduced. Any unnecessary delay in obtaining results from the laboratory will diminish the benefits of conducting diagnostic tests, particularly if the results are released too late to help guide decisions on appropriate treatment for the patient. Rapid diagnostic tests are a useful tool in supporting stewardship activities. However, reliable rapid tests or point-of-care tests to identify bacterial pathogens and provide the susceptibility profile of the identified pathogen are rarely available.

1.3. Storage and transport

Correct handling and management of specimens prior to analysis is essential in order to be confident that the results provided by the microbiology laboratory are accurate, significant, and clinically relevant. Much depends on the quality of the specimen sent to the laboratory for analysis. Specimens must be labelled correctly and must be accompanied by a standard form completed by the attending clinical staff that provides core patient information (see sample request form, Figure 3). SOPs should be available with instructions for appropriate storage of the specimens at the health-care facility, as well as requirements for transportation to the laboratory. Transport logistics and mechanisms must be operating reliably.

Correct management of specimens at the health-care facility and during transport to the laboratory is critical in ensuring accurate laboratory results that influence treatment decisions and impact on patient care and outcome. It also has an impact on the quality of surveillance data, on infection prevention and control, on health-care facility and laboratory costs, and on the efficiency of the laboratory.[8]

1.4. Summary of pre-analytical specimen management at point-of-care

The following table provides a summary of key aspects of clinical specimen management for bacterial culture. Each should be addressed within local SOPs and local guidelines for clinicians and other health-care workers responsible for collection of specimens.

[8] Dik JW, Poelman R, Friedrich AW, Panday PN, Lo-Ten-Foe JR, van Assen S et al. An integrated stewardship model: antimicrobial, infection prevention and diagnostic (AID). Future Microbiology 2015 Sep 1

Table: Summary of key aspects of clinical specimen management for bacterial culture

When should a specimen be collected for bacterial culture?	✓ Case definition fulfilled ✓ Prior to antimicrobial therapy whenever possible
What kind of specimen should be selected for bacterial culture?	✓ Appropriate specimen from suspected site of infection according to case definition
How should a specimen be collected for bacterial culture?	✓ By trained staff ✓ With strict adherence to precautions ✓ Using appropriate technique ✓ Using correct material and container ✓ Ensuring adequate amount of specimen ✓ Using appropriate transport medium ✓ Ensuring correct labelling
How should a specimen be transported to laboratory?	✓ In the correct package for safe transport ✓ Within 2 hours after collection, at room temperature (around 20 to 25°C) ✓ In correct storage at the health-care facility if necessary ✓ Accompanied by a request form with complete clinical, demographic and epidemiological information

1.5. Laboratory processing and procedures

Microbiology laboratories play a critical role in the successful management of patients with infectious diseases by providing reliable, timely, and relevant results.[9] The results from diagnostic tests should help to differentiate between diseases caused by pathogens, and noncommunicable conditions. Microbiological results should identify the disease-causing organism and describe the susceptibility profile of the organism. Microbiological results optimize patient management by enabling targeted antimicrobial therapy when indicated. However, laboratories are dependent upon appropriate specimen management by the clinical team.

The laboratory is responsible for proper documentation of specimen processing and reporting of results to clinicians. The laboratory may have an internal electronic information system to facilitate this documentation, but if not, thorough paper documentation should be used. Laboratory staff record receipt of the specimen, including time of arrival at the laboratory, and should then verify that the specimen has been managed correctly prior to analysis whenever possible and that all labelling and supplementary information is complete and in line with requirements.

Each laboratory should have a set of agreed criteria for specimen rejection to ensure results are consistently reliable and accurate. Criteria for rejection may include broken containers, poorly sealed

[9] Guide for establishing laboratory-based surveillance for antimicrobial resistance. Brazzaville: WHO Regional Office for Africa; 2013 at http://apps.who.int/medicinedocs/documents/s20135en/s20135en.pdf

and leaking specimens, all of which put laboratory staff at risk, unlabelled specimens, unacceptable delay between specimen collection and arrival at laboratory, incorrect storage conditions, incorrect container or transport medium, or inadequate quantity of specimen. Whenever a specimen is rejected, the reasons for rejection should be documented at the laboratory and the clinical team who submitted the specimen should be informed immediately.

Each laboratory should develop, implement and regularly update SOPs that cover processing and storage, pathogen isolation, species identification and antimicrobial susceptibility testing (AST). AST should be conducted according to good laboratory practice including quality control at each stage and should meet an internationally-recognized performance and interpretive standard, such as those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST)[10] and the Clinical and Laboratory Standards Institute (CLSI).[11]

It is essential that laboratory reagents for culture and AST testing are of sufficient quality. Laboratories should have a comprehensive quality management system in place which would include routine internal quality control and quality assurance and they should participate in an external quality assessment scheme, which may be organized by the national reference laboratory.

Appropriate biosafety practices should be observed throughout the entire process of specimen handling and laboratory procedures.[12]

1.6. Feedback and reporting of results

Optimal patient care depends on good communication between clinical staff at point-of-care, microbiology laboratories and surveillance staff. Clear procedures should be in place for communication between clinical, laboratory and surveillance staff. Procedures should state, for example, how rapidly provisional results will be communicated, the on-call availability of laboratory staff, and include provision for regular meetings to discuss results for individual care, to facilitate the development and adaptation of local treatment guidelines, and to address performance and challenges. Clinicians should expect to receive reports in a timely manner, including interpretive statements that enable the results to be easily and effectively applied for patient management. Reports should be stored and be accessible in patient files, ideally also electronically. Laboratories must also report negative results from specimens.

A microbiology laboratory may choose different approaches, such as selective reporting using the cascade method when reporting antimicrobial susceptibility results to clinicians. Selective or cascade reporting means that antimicrobial susceptibility results for second-line antibacterial agents, such as those with broader spectrum, are only reported to clinicians if organisms are resistant to first-line agents thereby helping clinicians to select appropriate antibacterial agents.[13] The surveillance team, however, should receive the full antimicrobial susceptibility report whenever possible, including results for all antimicrobial agents tested (irrespective of whether the results were reported to

[10] European Committee on Antimicrobial Susceptibility Testing – EUCAST (http://www.eucast.org/)

[11] Clinical and Laboratory Standards Institute - CLSI: Performance Standards for Antimicrobial Susceptibility Testing M100-S26:2016 read-only web version (http://em100.edaptivedocs.net/Login.aspx)

[12] Laboratory Biosafety Manual - Third Edition. Geneva: World Health Organization; 2004 at http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/

[13] Clinical and Laboratory Standards Institute - CLSI: Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline – Fourth Edition; M39-A4

clinicians). The full report is particularly important in compiling the overall AMR profile at the surveillance site and informing treatment guidelines at both the local and national levels, as well as in identifying particular resistance mechanisms and monitoring multidrug resistance profiles.

A clear and well-understood process should be put in place for the communication of preliminary results as soon as they are available, as well as results that are critical for patient management. This could include a defined list of "alert results" which laboratory staff would immediately communicate to the clinical team on-call, and should also comprise preliminary results, e.g. gram stain and initial growth of bacteria. Laboratory staff should also be available to respond to any queries or requests for verification of questionable results from the clinical team or from the surveillance team.

2. Organizational aspects of diagnostic stewardship

This section describes the organizational and administrative aspects that should be considered when planning activities to support the implementation of diagnostic stewardship at surveillance sites.

2.1. Pre-requisites for diagnostic stewardship

Surveillance sites must have the relevant clinical, laboratory, epidemiological and data management capacity. A more detailed description of requirements of surveillance sites can be found in "National antimicrobial resistance surveillance systems and participation in the Global Antimicrobial Surveillance System (GLASS) – A guide to planning, implementation, and monitoring and evaluation".[14]

Access to a laboratory with good quality management,[15] capacity and capability to perform microbiological diagnostics according to recognized standards is essential in order to implement diagnostic stewardship activities.

The laboratory may be part of the surveillance site or be located outside of the health-care facility. In either case, the logistics, transportation of specimens and communication between the surveillance site and the laboratory must be organized to ensure that specimens can be processed without delay and that results can be reported back to clinicians and surveillance staff. A courier system to transport the specimens from the surveillance site to the laboratory may be needed, particularly if the laboratory is not located at the surveillance site, and transport conditions must be carefully controlled.

Any material and infrastructure needs must be met. A transparent procurement policy must be put in place, and tender documents, for diagnostic and laboratory materials, must be available.

[14] Available at http://www.who.int/antimicrobial-resistance/global-action-plan/surveillance/supporting-documents-tools/en/ or from the GLASS secretariat (glass@who.int)
[15] WHO (2011) Laboratory quality management system: handbook at http://www.who.int/ihr/publications/lqms/en/

2.2. Assessment of conditions for implementation of diagnostic stewardship at the surveillance site

An initial review of existing SOPs, guidelines, human, material and financial resources, and outstanding needs, should be conducted prior to planning and implementing diagnostic stewardship activities at a surveillance site. The review should consider clinical, laboratory and surveillance capacity, including quality management, procurement needs and transportation and courier systems.

Any potential barriers and constraints that would impede the use of microbiological diagnostics should be identified and documented. These constraints might include costs, reimbursement of microbiological diagnostic testing, supply chain for consumables, transportation of samples, lack of staff awareness, training needs, quality assurance, among other issues. Based on the findings of the review, a realistic plan for the gradual implementation of diagnostic stewardship should be developed. The extent to which diagnostic stewardship plans can be implemented is likely to depend upon the priorities of the national surveillance system and the surveillance site as well as on the resources available and number of patients presenting at the surveillance site. Diagnostic stewardship may be introduced initially only for more severe infections such as bloodstream infections or only for specific infectious diseases, according to the surveillance site priorities, capacities and resources.

2.3. Resources and budget

A budget for the implementation of diagnostic stewardship activities at the surveillance site should be formulated and approved by the senior management of the surveillance site. The budget for diagnostic stewardship should be part of the overall budget of the surveillance site. Cost estimations should consider the requirements at each stage of the diagnostic pathway, including the costs of developing and adapting local guidelines and SOPs, and the costs of developing and implementing training material.

Reimbursement for microbiological diagnostics differs depending on the structure of the health-care system and health coverage and may have a negative impact on sampling. In this context it may be important to increase knowledge among funders of the benefits for individual patient care and for healthcare as a whole. Actual implementation costs and outcome parameters could inform cost-effectiveness studies and policy.

2.4. Roles and responsibilities

The responsibility for delivering good microbiological diagnostic services is shared equally across clinical and laboratory staff at the surveillance site. Both teams have key roles to play in the process. The successful implementation of diagnostic stewardship at surveillance sites requires a multidisciplinary team approach as well as institutional commitment including the allocation of appropriate human, financial and logistic resources. The multidisciplinary team should be mandated by the senior management to implement diagnostic stewardship activities at the surveillance site and should report back on a regular basis.

The composition of the multidisciplinary team at the surveillance site should reflect the existing organizational and administrative structures, but should aim to include the representation of:

- Clinical staff
- Microbiology laboratory staff
- Surveillance/epidemiological staff

The scope of work of the multidisciplinary team could include:

- development, adoption and implementation of quality management practices including local guidelines and SOPs for specimen selection, collection, transport, laboratory testing and reporting;
- review and oversight of training needs and activities, including supportive supervision for diagnostic stewardship at the surveillance site;
- promotion of good diagnostic stewardship at referral sites (particular if one laboratory in one facility serves several surveillance sites);
- monitoring of progress of the diagnostic stewardship activities;
- convening of regular team meetings to (i) present and discuss laboratory results and related issues, (ii) present progress in implementation, (iii) identify and address administrative, technical, operational and logistic issues;
- establishment of links with the antibiotic stewardship programme, infection and prevention programme, and drug committee;
- participation in local surveillance data management for reporting and development of local treatment guidelines.

Key areas of responsibility for each of the different professionals involved in diagnostic stewardship at surveillance sites include:

- Clinicians (i) ensure correct indication for sampling and sample selection, (ii) ensure complete and correct clinical, demographic and epidemiological patient information is provided for each specimen, and (iii) interpret and act on laboratory results to optimize patient management;
- Clinical staff (i) collect specimens using the appropriate techniques, (ii) label specimens appropriately and complete all accompanying documentation accurately, and (iii) ensure transportation and, if indicated, appropriate storage while awaiting transportation;
- Laboratory staff (i) record receipt of specimens upon arrival, (ii) ensure processing of specimens according to SOPs, (iii) read and record results, including interpretation and confirmation by the respective laboratory staff, (iv) provide clinicians with timely results and patient management advice, (v) provide on-call services for follow-up requests, queries from clinical team, and urgent testing requests beyond working hours, (vi) provide accurate and timely data to surveillance staff, and (vii) implement and enforce quality control procedures;
- Surveillance staff (i) ensure appropriate compilation and analysis of patient clinical, demographic, epidemiological and microbiological data, (ii) ensure dissemination of

compiled and analysed results to all health-care workers and laboratory staff at the facility, (iii) ensure the reports are transmitted to staff responsible for developing treatment guidelines, and (iv) ensure transmission of regular reports and alerts to the national surveillance coordinating centre.

2.5. Communication

Good communication between the different professionals involved, namely the laboratory, clinical, and surveillance teams, plays a critical role in successful diagnostic stewardship. In some circumstances the laboratory will be located in the surveillance site, in others the surveillance site may have a link to an external laboratory providing the services. Either way, the clinical and surveillance team and the laboratory must agree on the communication mechanism and channels. This should extend to communication of unusual or unexpected signals and suspected outbreaks. Clinical staff should be aware of the working hours for specimen reception and processing and the availability of on-call laboratory services for requests related to microbiological diagnostics, such as microbiologist consultation services.

Joint ward rounds, with the presence of both clinicians and microbiologists, provide further opportunities for improving communication and patient management. Regular multidisciplinary team meetings facilitate and improve collaboration and foster mutual understanding between clinical, laboratory and surveillance staff.

2.6. Training

It is vital that all professionals at each stage of the diagnostic workflow are fully aware of their respective roles and responsibilities and are able to perform their activities appropriately. Training should be conducted for clinical, laboratory and surveillance staff on case finding and relevant diagnostic activities at surveillance sites. Local guidelines and SOPs should be developed and/or adapted by clinical, laboratory and surveillance staff and disseminated through tailored training.

Specific areas of training needs include:

- Introductory training for all staff involved in diagnostic stewardship at surveillance sites with clear definitions of the different roles and responsibilities; additional training for multidisciplinary team members in relevant communication skills, including clear instructions on the coordination and tasks of the multidisciplinary team.

- Training for clinical staff in conducting relevant diagnostic activities, such as case finding, criteria and indications for specimen collection, providing correct and complete information in request forms, and on transportation and storage at the surveillance site before transport; additional training needs include the interpretation of laboratory results and choice of best therapeutic option based on laboratory results, and effective communication with the microbiologist. Any changes to the surveillance approach should be accompanied by appropriate training.

- Training for laboratory staff on SOPs for pathogen detection, and for bacterial species identification and antimicrobial susceptibility testing, including effective communication with the clinical staff; the national reference laboratory which serves as a resource and coordination point for laboratory expertise could support the laboratories serving surveillance sites by developing, maintaining, and sharing relevant reference material for good laboratory practice. The national reference laboratory should also facilitate participation in an external quality assessment scheme.

- Training in data management at surveillance sites as a component of the diagnostic feedback process.

2.7. Monitoring and evaluation of the diagnostic stewardship programme

The two overriding objectives of diagnostic stewardship at the surveillance sites are (i) to reach decisions on treatment that are guided by accurate and timely diagnostic results including antimicrobial susceptibility data, and (ii) to contribute accurate AMR surveillance data to inform empiric treatment guidelines and to develop control strategies, including infection prevention and control. Progress in implementing diagnostic stewardship at the surveillance site must be monitored and evaluated, and adjustments made as needed to achieve these objectives.

The initial assessment will provide the baseline upon which steps and targets for each element of diagnostic stewardship can be built in order to achieve the expected outcomes. The targets should be defined by the surveillance site, together with a core set of indicators (i.e. input, process, output and outcome indicators) to assist in monitoring towards the progress for each element.

Figure 4 below illustrates the process of monitoring and evaluation of the diagnostic stewardship programme at the surveillance site. It provides examples of the resources that would be needed ("input") and activities ("process") required to achieve the desired target and result ("output") that will eventually lead to the expected outcomes. The baseline assessment should help in defining realistic and measurable targets as part of the planning process together with their respective input, process, output and outcome indicators.

An example on monitoring one aspect of the implementation of the diagnostic stewardship programme is provided in Annex 1.

Figure 4: Steps in monitoring and evaluation of diagnostic stewardship at AMR surveillance sites

STEPS	EXAMPLES
PLANNING (baseline)	• Situation analysis, resources and needs assessment conducted
INPUT (needed resources)	• Funding for diagnostic stewardship activities in the surveillance site • Local guidelines and SOPs for diagnostic stewardship • Trained and capacitated staff on local diagnostic stewardship guidelines • Microbiological laboratory facilities with equipment and consumables • Communication protocols and facilities
PROCESS (activities)	• Mobilization and management of funds • Development or adaptation of SOPs • Development and implementation of training materials for diagnostic stewardship • Implementation of training courses • Internal and external quality assurance, regular procurement & maintenance of equipment and consumables • Agreed means and frequency of communication among clinical, laboratory and surveillance staff
OUTPUT (results)	• Sustainable financing and resources available on regular basis • Common understanding of protocols for diagnostic stewardship • Staff trained and capacitated leading to compliance with local diagnostic stewardship protocols and steps • Increase in specimens submitted to the laboratory according to SOPs • Good laboratory practices in place resulting in reliable and timely results • Patient treatment and surveillance actions are informed in a timely manner
OUTCOME	• Patient treatment guided by timely microbiological data resulting in safer and more efficient patient care • Accurate and representative AMR surveillance data to inform treatment guidelines and AMR control strategies

Annex 1: Example of monitoring staff capacity building

Below is an example of one type of indicator to measure progress in building staff capacity in "the proper use of available laboratory diagnostic tools, completion of patient information according to local SOPs and submission of patient specimens to the laboratory by clinical staff".

- **Target**: to reach 80% of clinical staff trained in the proper use of available laboratory diagnostic tools, completion of patient information according to local SOPs and submission of patient specimens to the laboratory (baseline e.g. 10% staff already trained) in a defined time period.
- **Input indicator**: availability of guidelines and SOPs on proper use of available laboratory diagnostic tools, completion of patient information and submission of patient specimens to the laboratory.
- **Process indicator**: development of training materials and training of clinical staff on proper use of available laboratory tools, completion of patient information and submission of patient specimens to the laboratory.
- **Output indicator/Result: a**fter implementation, 60% of staff trained within the defined time period ➔ the target (in this example, 80%) could not be achieved. The next step would be to assess and to identify the reasons why the target had not been met, and identify how to reach the remaining staff.

Potential obstacles in the process should be identified early in order to implement mitigation measures, such as the procurement of materials and consumables, additional costs related to the appropriate use of microbiological diagnostics, available resources and budget, revision of guidelines and processes, and modification of training. Results of findings should be reported back to the clinical, laboratory and surveillance staff and communicated to the senior management of the surveillance sites.