Global Antimicrobial Resistance Surveillance System (GLASS)

Molecular methods for antimicrobial resistance (AMR) diagnostics to enhance the Global Antimicrobial Resistance Surveillance System

World Health Organization

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Disclaimer

The information on individual diagnostic tests in this document is publicly available and was obtained by searching PubMed for relevant publications on molecular AMR diagnostics for GLASS priority pathogens and Google searches for diagnostic companies that offer molecular AMR tests (see Annex 1 for search terms). All searches were conducted between 13 October 2017 and 4 December 2017.

WHO has not validated and does not endorse the use of any of the commercial tests mentioned in this document. The molecular diagnostic tests listed in Table A1.1 are approved by the United States Food and Drug Administration or marked conformité Européenne (conforming to the standards of the European Union and European Economic Area). As more molecular diagnostic tests are developed and validated, the table will be updated to include validated tests approved by other regulatory agencies.

Contents

Executive summary

Antimicrobial resistance (AMR) is a serious threat to global public health. In 2015, WHO launched the Global Antimicrobial Resistance Surveillance System (GLASS) in order to standardize the collection of data on AMR in Member States, for planning, prevention and intervention programmes. Reports to GLASS currently rely on detection of phenotypic resistance, which requires bacteria to be cultured and tested for growth in the presence of antimicrobial agents. In future, GLASS may incorporate the results of molecular testing for AMR detection by appropriate methods. Molecular diagnostic methods can be used at the same time as phenotypic testing to yield additional information, such as the exact gene or mutation underlying a resistance phenotype. This information can be used to interpret AMR profiles at surveillance sites and better understand the global occurrence of certain resistance mechanisms.

Different laboratory settings have different requirements for molecular methods for AMR diagnostics. This technical note addresses three generic laboratory settings with different capacity for molecular AMR testing: those with no prior experience in molecular AMR surveillance; newly established national reference laboratories (NRLs) with some experience in molecular methods; and fully established NRLs with experience in molecular AMR surveillance. Molecular diagnostic methods are graded according to their complexity of use, setup cost and cost per tested specimen. This technical note provides guidance to people involved at various levels of AMR surveillance in choosing the most appropriate molecular AMR test for their setting, including clinical and reference laboratories. The document also provides a review of available methods and how they could be used in national surveillance.

Of the available molecular methods, fully automated, integrated, cartridge-operated polymerase chain reaction (PCR) or loop-mediated isothermal amplification (LAMP) devices and lateral flow assays are the most suitable for laboratories with no previous experience in molecular testing in AMR surveillance. It is difficult to determine the cost per tested specimen, especially for low- and middle- income countries (LMICs), because pricing models are specific to regions and suppliers; uncertainty about the cost of molecular testing is a major barrier to its use for AMR surveillance in LMICs. The WHO catalogue ordering system, which includes pre-negotiation of prices and optimizing the flow of supplies, could lower the cost per test. Moreover, harmonization and standardization of clinical laboratory testing within national laboratory systems in LMICs could result in pooled procurement, which would be useful for negotiating prices with manufacturers.

Although molecular AMR diagnostics for known resistance markers are highly sensitive, there is no firm evidence of their cost-effectiveness or affordability in all settings. Poor understanding of resistance mechanisms may impede use of effective molecular diagnostics for some disease organisms. For example, there is currently no validated molecular diagnostic test for AMR in gonorrhoea or pneumococcal infections. Nevertheless, as costs for molecular diagnostics fall and knowledge about the genetic mechanisms of AMR increases, molecular tests are likely to become valuable tools available for AMR surveillance in all settings. Proof-of-principle studies can be conducted to demonstrate the added value of molecular AMR diagnostics to supplement phenotypic testing. A future document will outline plans and guidance on conducting proof-of-principle studies.

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