TARGET PRODUCT PROFILES FOR ANTIBACTERIAL RESISTANCE DIAGNOSTICS

17 January 2020

World Health Organization

TARGET PRODUCT PROFILES FOR ANTIBACTERIAL RESISTANCE DIAGNOSTICS

17 January 2020

World Health Organization

Target product profiles for antibacterial resistance diagnostics
ISBN 978-92-4-000040-7

Acknowledgements

We are grateful to the individuals and institutions who provided feedback, including the ABR diagnostic TPP development group members, the individuals who attended the technical consultation held on 27–28 March 2019 and the other external stakeholders who provided comments.

WHO Secretariat

Francis Moussy and Maurine Murtagh (consultant).

Funding

This work was supported by the Wellcome Trust.

Table of Contents

Abbreviations and acronyms

ABR	antibacterial resistance
AC	alternating current
AMR	antimicrobial resistance
AST	antimicrobial susceptibility testing
CAI	community-acquired infection
CE-IVD	European Commission certification mark for in vitro diagnostic medical devices
CI	confidence interval
CLSI	Clinical and Laboratory Standards Institute
CSF	cerebrospinal fluid
CSV	comma-separated values file
DHCP	dynamic host configuration protocol
DNS	domain name system
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FDA	US Food and Drug Administration
GI	gastrointestinal infection
GMP	good manufacturing practices
GPS	global positioning system
GSM	global system for mobile communications
HAI	hospital-acquired infection
HTTPs	hypertext transfer protocol secure
IC	internal control
ID	identification
IP	Internet protocol
ISO	International Organization for Standardization
LAN	local area network
LMICs	low- and middle-income countries
MALDI-TOF-MS	matrix-assisted laser desorption/ ionization time-of-flight mass spectroscopy
MIC	minimum inhibitory concentration
NG	*Neisseria gonorrhoeae*
OEM	original equipment manufacturer
R&D	research and development
RFID	radio-frequency identification
SFTP	SSH file transfer protocol
SIR	susceptible, intermediate, resistance
SMS	short message service
TPP	target product profile
UPS	uninterruptable power supply
USB	universal serial bus
UTI	urinary tract infection
WHO	World Health Organization

Introduction

The increasing prevalence of antimicrobial resistance (AMR), which the World Health Organization (WHO) defines as the "ability of a microorganism – like bacteria, viruses and some parasites – to stop an antimicrobial (such as antibiotics, antivirals and antimalarials) from working against it" (*1*) is a serious threat to global public health and disproportionately burdens low-resource countries (*2*, *3*). The growing resistance to antibiotics of bacterial pathogens is recognized as the largest of these threats (*4*). The importance of diagnostics in efforts to combat AMR has also been recognized (*5*). In particular, there is a need to stimulate the development of, and access to, appropriate rapid diagnostic tools for bacterial pathogen identification (ID) as well as antimicrobial susceptibility testing (AST) at all levels of the healthcare system in low- and middle-income countries (LMICs).

In order to address these needs, WHO undertook an initiative to map available and pipeline diagnostics against antibacterial resistance (ABR), identify gaps in the availability of such diagnostics in LMICs, and establish a research and development (R&D) priority list of diagnostics against ABR for the next 3–5 years. This mapping and list of gaps and priorities provided the basis for developing consensus target product profiles (TPPs) for the highest-priority diagnostics on the R&D priority list. Details on the process used are provided in the next section.

A TPP is a planning tool for the development of health products, including diagnostics. Industry uses in-house TPPs as planning tools to strategically guide development towards desired product characteristics. In particular, TPPs specify the product's intended use, target populations and desired attributes, and guide product development programmes.

WHO develops TPPs that are intended to support the development of products needed for public health for which gaps have been identified. As a result, WHO TPPs are needs-based and focused on public health priorities. WHO TPPS also emphasize that access, equity and affordability are integral parts of the innovation process and need to be considered at all stages, not just after a product is developed.

The WHO TPP document informs product developers, regulatory agencies, procurement agencies and funders on R&D and public health priorities. It is intended to facilitate the most expeditious development of products addressing the greatest and most urgent public health needs.

The development of WHO TPPs follows a standardized procedure and includes a number of steps. These include (i) doing a needs assessment; (ii) constituting a scientific TPP development group (with standard WHO Declaration of Interest procedures); (iii) drafting and sharing an initial draft of the TPP with the development group; (iv) revising, posting and disseminating a new version of the TPP for public consultation for 28 days (with comment form); (v) revising and finalizing the TPP (an additional consultation step may be needed in case of significant disagreement); and (vi) posting and disseminating the final version of the TPP.

All WHO TPPs should be considered to be living documents that may require modification if the status of science or the pipeline in the area changes.

Process used for the development of TPPs for antibacterial resistance diagnostics

Needs assessment

- A mapping of commercially and available diagnostics against ABR was conducted from July 2018 to March 2019. The following key parameters were prioritized: (i) diagnostics to improve clinical/syndromic management of patients to reduce over prescription of antibiotics; (ii) antibiotics exhibiting the highest proportion of resistance; (iii) diagnostics that can be performed at primary and secondary care facilities in LMICs; (iv) diagnostics targeted at pathogens primarily related to community-acquired infections (CAIs) and secondarily at bacterial infections that are most frequently acquired in hospitals (HAIs); and (v) diagnostics to help distinguish bacterial from nonbacterial infections.
- This step resulted in a draft document mapping the diagnostics landscape against ABR with lists of gaps and R&D priorities. The draft document was sent to more than 40 external experts for comment during fall 2018 and was also posted on the WHO website for public consultation for 1 month in February 2019.
- The map, gaps and TPPs to be developed were discussed and agreed on during a technical consultation held on 27–28 March 2019 in Geneva. The standard WHO Declaration of Interest procedures were followed for the participants. The meeting report can be found at: https://apps.who.int/iris/bitstream/handle/10665/326481/WHO-MVP-EMP-IAU-2019.08-eng.pdf?ua=

detection of pathogens in syndromic diagnoses; for patient management, including prescription of appropriate antibiotics; and for surveillance. Six specific gaps in priority diagnostics to combat ABR in LMICs were identified:

  - improved near-patient testing for tuberculosis;
  - simplified phenotypic ID and AST;
  - host response tests;
  - improved diagnosis and AST for *Neisseria gonorrhoeae* (NG);
  - a multiplex diagnostic platform suitable for level 2 healthcare facilities to identify WHO prioritized bacterial pathogens associated with clinical syndromes and to ascertain genetic determinants of antibiotic resistance/susceptibility or phenotypic AST with respect to the pathogens identified; and
  - a simple, easy-to-use reflex test suitable for level 2 or level 1 healthcare facilities to detect AST of prioritized bacterial pathogens performed in parallel with, or following, confirmation or ID of bacterial pathogens on a separate test or test platform.

- For the first four gaps, TPPs have already been developed (and did not need to be revised at this time). The last two gaps did not have TPPs and thus are the focus of this document.

TPP development