

Information note

Global TB Programme and HIV Department

CONSIDERATIONS FOR ADOPTION AND USE OF MULTIDISEASE TESTING DEVICES IN INTEGRATED LABORATORY NETWORKS

Background

Several new laboratory technologies are available or are being developed to allow for testing of different conditions using disease-specific tests on the same platform. For example, a single device may be able to test for the presence of tuberculosis (TB) and HIV, and quantitatively measure HIV and hepatitis C viral load by using disease-specific reagents or cartridges with self-contained nucleic acid testing technology. Some of these technologies are being designed for use at centralized reference laboratories while others may be positioned for use at or near to point of care. In settings where laboratory testing has been traditionally organized by disease programme, the introduction of multidisease testing devices (also known as polyvalent testing platforms or multianalyte analysers) brings new opportunities for collaboration and integration, which can provide significant system efficiencies and cost savings, increase patient access, and ultimately improve quality of care. Collaboration and integration should be a priority for both those countries with currently operational multidisease testing devices and those countries considering and planning for their introduction. This information note provides a strategic overview of key implementation considerations for diagnostic integration using these devices, and is primarily intended for use by national laboratory services and TB, HIV, and hepatitis programme managers. It may also be of interest to managers of maternal, newborn and child health programmes and sexual and reproductive health programmes, international and bilateral agencies, and organizations that provide financial and technical support to the relevant national health programmes.

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KEY CONSIDERATIONS FOR ADOPTION AND USE OF MULTIDISEASE TESTING DEVICES

1

Coordinated planning led by the ministry of health

- Essential to the adoption and use of multidisease testing devices is a country-led and country-coordinated process to develop a strategic country plan for multidisease testing, mapping of laboratory sites, specimen referral networks and a results reporting system.
- The ministry of health should establish internal coordinating mechanisms across all relevant disease programmes to support integrated planning and budgeting of all the activities mentioned below and to avoid creation of parallel systems.
- A technical working group comprising representatives from all relevant disease programmes, reference laboratories, procurement agencies and implementing partners should be established with a clear allocation of responsibilities. The group should convene periodically to review implementation and refine plans as needed.
- Funding streams for placement, use and maintenance of testing devices should be identified and, if needed, pooled to ensure complete implementation of plans and continuous service delivery.

2

Regulatory approval and validation

- When possible, streamlined regulatory approval processes should be considered and implemented for multidisease testing devices, particularly those having undergone a review by a stringent regulatory authority. For device-based technologies using one device for several different tests, full regulatory processes for each test may be unnecessary and burdensome, delaying implementation; abbreviated regulatory processes should be considered for each new test added to a device with existing approval for another assay when possible.
- In-country validation of multidisease testing devices, when necessary or required by national authorities, should be coordinated when possible among relevant disease programmes to avoid parallel efforts and reduce delay in introduction of new tests.

3

Product and site selection

- Selection of a multidisease testing device or devices, and the sites for deployment, should be a clear and transparent process led by the ministry of health that considers the needs of all relevant disease programmes, in combination with the functionalities and operating requirements of devices under consideration.
- Mapping of all sites for potential device placement in the country should be carried out based on target patient populations across diseases and testing volume needs for all tests to be used on the multidisease testing device. This should take into account expected device capacity in terms of specimen throughput (i.e., number of tests per day or per shift), and should consider any existing multidisease and single-disease testing devices to understand the needs for each facility, including whether some facilities may require a higher throughput device or additional devices once testing volumes are integrated.
- In some instances, devices may have been placed for a specific testing purpose and then later a new disease test is made available for use. Unused capacity of existing devices should be assessed before additional devices are procured. However, ongoing efforts to increase testing using existing devices for their original purposes should also be considered where necessary. For example, introduction of changes to diagnostic algorithms or activities to strengthen specimen referral systems may result in increased use of existing machines over time, and capacity for additional testing purposes may consequently be different than originally assessed. Programmes should work together to better understand the facility needs and demands in order to most appropriately ensure testing needs are met.
- Selection and placement of devices should take into consideration the infrastructure needs (space, electricity, temperature, etc.), specimen referral systems (see below), availability of patient access to treatment for each disease being tested, equipment, cartridge or reagent disposal requirements, biosafety requirements for handling of specimens for all planned test types, maintenance requirements, and human resources needed to ensure any and all supplemental equipment and infrastructure are in place or can be included in the planning process.

4

Integrated specimen referral systems

- Specimen referral systems for all specimens using multidisease testing devices should be established or integrated across test and specimen types when possible to optimize investment, impact and efficiency. This should be a key consideration in device placement. Specific requirements may be required for certain specimens, e.g. biosafety considerations for specimens for TB or Ebola testing.
- Any batching of specimen collection for transport should be properly planned so as not to overwhelm testing sites or transport personnel.



5

Standard operating procedures and trainings for end users

- Standard operating procedures should be developed for end users and must address instances of potential capacity shortfall at a given site, when prioritization of testing would be required based on specimen type, testing purpose or patient group. In such cases, priority specimens would be tested first, while remaining specimens would be referred to another site, subjected to an alternative test when applicable, or temporarily stored until testing capacity is available. Clinicians from all relevant disease programmes should be engaged in the consultative process for development of standard operating procedures with regard to prioritization of testing.
- All persons currently performing disease-specific tests should be considered for training on multidisease testing devices across all test types used in the setting.
- All persons directly using multidisease testing devices should have formal training to gain full proficiency in the following tasks for all test types used in the setting:
 - preparation of specimens for all test types following established standard operating procedures;
 - handling of specimens for all test types, including knowledge of proper biosafety precautions;
 - patient management and test counselling, if relevant (e.g. HIV viral load), as per national guidelines;
 - conducting testing for all test types;
 - following the nationally adopted testing algorithm for all assay types;
 - interpretation and reporting of results for all test types to referring clinicians;
 - device service and maintenance;
 - ensuring necessary waste disposal requirements are met, specific to each assay's reagents and cartridges.
- Training should be organized across all device uses with refresher training conducted at regular intervals according to national guidelines.
- Routine monitoring and supervision of facilities should be established and integrated across the different test types to maximize efficiency and provide adequate support to testing sites.

6

Ensuring capacity for supervision, monitoring and conducting trainings

- Individuals at national and regional levels should be selected and their proficiency established on use of the multidisease testing device for all test types, in order to be able to serve as master trainers, conduct supervisory visits and monitor performance indicators in their network for quality assurance purposes (see below), and troubleshoot across all test types. Advanced trainings on supervision, monitoring and conducting trainings may be required. The roles and responsibilities of selected individuals should be clearly defined across programmes.

7

Clinician training and demand generation

- Clinicians and primary care providers at testing sites and at any sites that refer specimens should be made aware of all types of tests available, the utility of each test in clinical management of patients, the established national testing algorithms for each disease, the procedures for requesting the tests, and the interpretation of results for all types of tests.
- Materials used for sensitization of clinicians and primary care providers should be developed collaboratively across disease programmes and with clinician and primary care provider input.
- Several of the tests being developed for multidisease testing devices can be used for co-infected patients and such use should be encouraged. For example, HIV/TB co-infected patients could hugely benefit from TB diagnosis and HIV viral load testing on the same device.

8

Inventory management, including procurement

- To support inventory management and facilitate timely ordering and cost-efficient distribution, integrated systems should be in place to monitor stocks and expiry dates of reagents, and a methodology to track consumption and wastage.
- Forecasting of orders should be integrated to account for all test types across disease programmes. Using multidisease testing devices and integrating forecasting and procurement¹ may allow for more regular and stable testing and potential cost savings with increased volumes and price negotiation with manufacturers.
- Supply chains should be coordinated and integrated as much as is feasible, in order to save costs on shipping, storage and domestic transport.

9

Quality management systems

- Quality management systems should be set up for any existing and new technologies to be implemented. These programmes should incorporate and span all test types to ensure more efficient, high-quality and cost-effective testing. Such programmes should include as many quality components as possible, including regular on-site supervision, quality indicator monitoring, calibration, service and maintenance, internal quality controls, external quality assessment and post-market surveillance.
- Service and maintenance systems should be developed or adapted and agreed upon within contracting processes with the manufacturer and integrated across test types, and budgeting coordinated across programmes. Roles, responsibilities and timelines for service

¹ More guidance on procurement of diagnostics and related laboratory items can be found at http://www.who.int/diagnostics_laboratory/procurement/131024_procurement_of_diagnostics_finalversion.pdf and http://apps.who.int/iris/bitstream/10665/44798/1/9789241503068_eng.pdf.



are critical to define in order to ensure uninterrupted, high-quality testing. Therefore, needs for scheduled routine service and maintenance should be well documented and monitored for each device, and coordinated nationally. When devices are already in place for one testing purpose, a careful analysis should be performed of the additional maintenance services required when other testing is performed; additional requirements and costs should be negotiated with the manufacturer in a way that creates efficiencies across programmes.

- Internal quality controls of each test and testing device should be reviewed with clear standard operating procedures developed to provide end users with clear guidance on how to resolve any issues and what to do in case of errors or other invalid results.
- To complement the internal quality controls of devices and automated or semi-automated test cartridges, the following five components of a quality assurance programme are recommended:
 - Device verification: Each device should be verified as being “fit for purpose” using known positive and negative material prior to implementation. All test types to be used on the device should be verified using corresponding positive and negative specimens. This can be done during end user training and certification processes.
 - Quality indicator monitoring and data management: Monitoring of quality indicators (also called performance indicators) should be carried out routinely. Monitoring testing volumes, numbers of positive and negative results, and error rates should be stratified by type of test performed. Monitoring should be carried out at site, regional and national levels. Routine, real-time review of data using diagnostics connectivity solutions² can allow for rapid response to device breakdowns, resolution of errors and improvement in testing quality, and review of internal quality control performance, and can ensure consistent stock management. Mechanisms for analysis of quality indicators, identification of nonconformities and implementation of corrective actions should be established.
 - Regular on-site supervision: Site visits should be planned at regular intervals to assess user practices for all test types, review quality indicators, assist with troubleshooting issues and conduct on-site refresher training as needed.
 - New lot quality control testing: Incoming batches of tests should be tested using a sample of cartridges to ensure expected performance.
 - External quality assessment: Blinded proficiency testing or another form of external quality assessment is recommended at least yearly, and distribution of panels for each test type should be organized and integrated for efficiency and cost savings.

2 Newer diagnostics produce electronic data that have the potential to be rapidly and accurately sent to different recipients and easily analysed. Diagnostics connectivity solutions (comprising computer software together with associated hardware and a data connectivity plan to send electronic data from diagnostic devices) facilitate the automatic transmission of electronic data for a variety of uses, including remote monitoring of performance indicators for quality assurance purposes, sending results automatically to clinicians or laboratory information management systems, and inventory management. For more information, see the *GLI quick guide to diagnostics connectivity solutions*: http://stoptb.org/wg/gli/assets/documents/gli_connectivity_guide.pdf.

10

Data management and integration

- Diagnostics connectivity software should be installed and adapted to accept and use data from all test types from a multidisease testing device. Connections should be established with laboratory information management systems and electronic registers to allow for automatic integration of data. During software set-up, its configuration should allow selected users across disease programmes to have access to relevant data as needed.
- In instances where patient information is transmitted and stored using diagnostics connectivity solutions, patient confidentiality rights and data use standards should be clearly defined across programmes. Negotiation of data use agreements with manufacturers and service providers may potentially be streamlined for multidisease testing devices.

Case study: adoption and use of GeneXpert® by TB and HIV programmes

Collaboration between national TB and HIV programmes should be a priority for countries using the GeneXpert® (Cepheid, Sunnyvale, United States of America) system, a fully automated multidisease testing device that uses disease-specific, self-contained cartridges and is able to be placed at lower levels of health systems given minimal biosafety and training requirements. GeneXperts have been procured by national TB programmes for detection of TB and rifampicin resistance using the Xpert® MTB/RIF assay, following an initial World Health Organization (WHO) recommendation for its use in December 2010.³ A test for early infant diagnosis of HIV, the Xpert® HIV-1 Qual assay received WHO prequalification in June 2016.⁴ A test for HIV viral load testing, the Xpert® HIV-1 Viral Load assay is currently undergoing WHO prequalification assessment.

While immediate collaboration between TB and HIV programmes and integration of testing would be invaluable, significant volumes of additional cartridges could overload current devices. Product and site mapping are critical to understand volume needs across test types and inform where new and additional devices are needed. Ongoing efforts by TB and HIV programmes to increase existing device usage, including strengthening specimen referral systems or widening the eligibility criteria for patient testing in national algorithms, must also be considered, and the expected increased volumes should be estimated.

Initially, prioritizing testing for critical populations, such as HIV-exposed infants, can support a phased approach to integration. For example, continuing current TB testing volumes on existing devices, while allowing for early infant HIV diagnosis testing and considering viral load testing for other priority populations, such as pregnant women or HIV/TB co-infected patients, will ensure critical testing needs are directed at those most in need (i.e., for whom a viral load test result could inform an important and urgent clinical decision), existing devices and staff are not overburdened, and efficiencies are gained.

3 http://apps.who.int/iris/bitstream/10665/112472/1/9789241506335_eng.pdf.

4 http://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-vrl/160613PQPublicReport_0259-0700-00_XpertQualHIV_v2.pdf.



Acknowledgements

Development of this information note was led by Wayne van Gemert (WHO Global TB Programme) and Lara Vojnov (WHO HIV Department). Technical inputs and review were provided by Olawale Ajose (UNITAID), Heidi Albert (FIND South Africa), Khalide Azam (National TB Reference Laboratory, Mozambique), Rebecca Bailey (Elizabeth Glaser Pediatric AIDS Foundation), Draurio Barreira (UNITAID), Eileen Burke (Global Fund to Fight AIDS, Tuberculosis and Malaria), Kaartikeya Chauhan (Clinton Health Access Initiative), Daniela Cirillo (San Raffaele Scientific Institute; SRL Milan), Jennifer Cohn (Elizabeth Glaser Pediatric AIDS Foundation), Stephanie Denamps (Clinton Health Access Initiative), Affolabi Dissou (National Hospital for Tuberculosis and Pulmonary Diseases, Benin), Lucilaine Ferrazoli (Adolfo Lutz Institute, Brazil), Mercedes Pérez González (WHO Department of Essential Medicines and Health Products), Martine Guillerm (Global Fund to Fight AIDS, Tuberculosis and Malaria), Victoria Harris (FIND South Africa), Chris Isaacs (FIND), Jeff Lemaire (Elizabeth Glaser Pediatric AIDS Foundation), Erica Lessem (Treatment Action Group), Marguerite Massinga Loembe (Centre de Recherches Médicales de Lambaréné and Université des Sciences de la Santé, Gabon), Smiljka de Lussigny (UNITAID), Paolo Maggiore (Clinton Health Access Initiative), Ivan Manhiça (National TB Programme, Mozambique), Charles Manyonge (Uganda National Reference Laboratory; SRL Kampala), Troy Murrell (Clinton Health Access Initiative), Alaine Nyaruhirira (Management Sciences for Health), Sara Padidar (UNITAID), Carmen Perez Casas (UNITAID), Maria Rosezoil Rioja (Clinton Health Access Initiative), Anita Sands (WHO Department of Essential Medicines and Health Products), Thomas Shinnick (TB laboratory consultant), Joseph Sitienei (Ministry of Health, Kenya), Alena Skrahina (Republican Research and Practical Centre for Pulmonology and Tuberculosis, Belarus), Khairunisa Suleiman (TB CAB), Catherina Timmermans (UNITAID), Dalila Zachary (Global Fund to Fight AIDS, Tuberculosis and Malaria), and colleagues of the WHO Global TB Programme (Fuad Mirzayev, Alexei Korobitsyn, Chris Gilpin, Avinash Kanchar, Yohhei Hamada, Annabel Baddeley, Karin Weyer, Mario Raviglione) and WHO HIV Department (Nathan Ford, Meg Doherty, Gottfried Hirnschall).

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WHO/HTM/TB/2017.06