GLI QUICK GUIDE TO TB DIAGNOSTICS CONNECTIVITY SOLUTIONS

global laboratory initiative
advancing TB diagnosis

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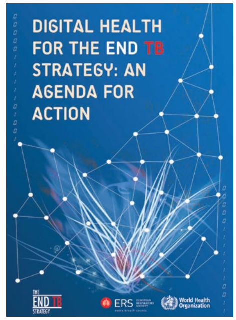
What are diagnostics connectivity solutions?

Traditional TB diagnostics methods, including smear microscopy and solid culture, typically require that a test result and associated patient details be manually written on paper, recorded in a register, and sent to the ordering clinician. These recording and reporting processes not only entail burdensome paperwork, but also human error can result in mistakes or omissions when handling these data. Furthermore, sending paper-based results can add a significant amount of time to the diagnostic process when the referring clinician is located at another site, and such data cannot be integrated automatically with patients' medical files. Paper-based data reporting for monitoring and evaluation (M&E) purposes often occurs on a quarterly basis, resulting in delay for a supervisor to recognize problems. Additionally, for practical purposes, such M&E data is usually aggregated or summarized when reported from facilities or different administrative levels, limiting the utility of these data for quality improvements and more advanced analysis.

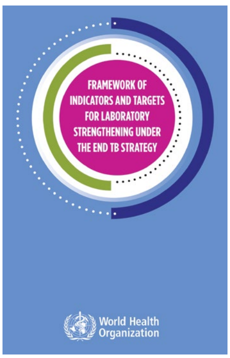
Newer diagnostics including Xpert® MTB/RIF (using the GeneXpert® platform), liquid culture (e.g., Bactec™ MGIT™), line probe assays (LPA) with automated readers, as well as HIV-related instrument-based diagnostics like Alere PIMA™ CD4 and Alere™ Q HIV-1/2 Detect, and Xpert® HIV-1 Qual, produce results data in digital format (also known

> Diagnostics connectivity solutions typically comprise: 1) a connectable diagnostic device that produces electronic data, 2) a software platform that receives and interprets data, and 3) a means to transmit data from the device to the software platform and to a server. The means of transmitting data consists of a modem that utilizes available networks such as mobile 3G, Wi-Fi or SMS. Connectivity solutions facilitate the automatic transmission of electronic data for a variety of uses, as described below, and some solutions allow for collection and use of data generated by different types of diagnostic devices. Connectivity solutions can provide a highly cost-effective way to ensure proper functioning of a diagnostic device network and improve linkage to care and patient management.

as electronic data). Unlike written data on paper, electronic data can be rapidly and accurately sent to different recipients according to relevance and utility and easily analysed.



As one of 9 priority digital health concepts identified by the *WHO Agenda for Action on Digital health for the End TB Strategy (1,2)* for target product profiles, the adoption and use of diagnostics connectivity solutions are also monitored as core indicators for laboratory strengthening under the End TB Strategy *(3)*. According to the *WHO Framework of indicators and targets for laboratory strengthening under the End TB Strategy*, all sites that use WHO-recommended rapid diagnostics should be transmitting results electronically to clinicians and to information management systems using data connectivity solutions no later than 2020 (*Indicator 4*). Furthermore, remote monitoring via data connectivity solutions should be used to monitor key performance indicators at all sites that use WHO-recommended rapid diagnostics no later than 2020 (*Indicator 9*).



How can diagnostics connectivity solutions be of use to your TB programme?

- **Remote monitoring and quality assurance:** With remote monitoring, designated persons can use any internet-enabled computer to access the software platform, providing them with an overview of the facilities, devices and commodities in their network. The head of a national reference laboratory or other authority can easily see how many tests are being performed and where, what are the results, and which sites are underperforming or experiencing abnormal results or errors, which may highlight a need for troubleshooting, device repairs, targeted on-site supervision, or retraining of technicians. Automated messages and warnings may be set and triggered when established thresholds are reached that require further investigation and follow-up.

- **Sending results automatically to clinicians:** Test results (or a subset of them; for example, rifampicin-resistant test results) can automatically and instantly upon result availability be sent to a clinician's phone or email, SMS printer or other clinical results reporting mechanism, allowing for faster patient follow-up. A text message could also be sent to a patient, informing when their test results are ready and instructing them to visit the clinician to receive them.

- **Sending results automatically to laboratory information management systems or electronic registers:** Test results can be automatically integrated into laboratory information management systems or electronic registers, reducing staff time and the chance of transcription errors, and greatly facilitating M&E processes. Some software can also be configured to allow for additional patient information to be entered; for example, a patient's HIV status or prior TB treatment history could be captured, aiding a programme to measure testing coverage and implementation of diagnostic algorithms. In the absence of an existing laboratory information management system or electronic register, some software may also be used to create the foundation for electronic patient medical records.

- **Inventory management:** Certain software can facilitate inventory management, by allowing stocks to be entered at site-level and forecasting the anticipated stock-out date or potential expiring cartridges based on the consumption rate. Replenishment of inventory can be managed before stock out, or potential expiring cartridges can be prioritized or moved to other sites. In addition, the tracking of lot numbers can identify poor performance and abnormal error rates for quality assurance purposes. Likewise certain software can track the status of warranties and when they approaching the time for renewal, as well as the need for upcoming calibration checks.

- **Surveillance:** real-time data and trends on disease or resistance patterns can be easily discerned using data from the network of devices. Software can avoid repeat enumeration of samples from the same patient and program performance can be shared with appropriate agencies and disease prevalence can help understand future care needs. Connected

diagnostics are expected to enhance the capacity of national TB programmes to generate performance indicators and to provide the data needed for several of the top 10 indicators of the End TB Strategy *(4)*.

- **Data Access:** Software can usually be configured so that subsets of data are made available to those that need it for maximum utilization whilst easing the burden of information overload for those who don't. Information can also be shared securely with partner organizations and manufacturers for support and product improvement purposes. Secure systems also protect the privacy of the patient.

The above usage scenarios are examples of how connectivity solutions can help with TB programmes. The list is not exhaustive and other scenarios are possible. Usage scenarios supported vary with the selection of connectivity software (see below).

What connectivity software is needed?

Connectivity software platforms have been developed by diagnostics manufacturers (for example, C360 by Cepheid, USA, for GeneXpert®) as well as by third-party companies and organizations, including GxAlert™/Aspect™ by SystemOne, DataToCare™ by Savics, and Connected Diagnostics Platform by FIND.

The selection of software depends on the preferences of the Ministry of Health and may depend on the offered functionalities, languages supported, requirements for internet connectivity, experience and capacity of the implementing provider, or data security measures and/or hosting arrangements in place (see below, *Data ownership and security*). The Ministry of Health may also want to select a software that is able to collect and use data from different diagnostic devices, e.g. GeneXperts® and Alere Pima™ analysers. Connectivity software platforms may have complementary functionalities, justifying implementation and use of more than one software platform in the same country. For example, a country might use a manufacturer's software so that the data can be sent directly for troubleshooting and maintenance purposes, while also using another software platform for supply management or remote monitoring.

An online up-to-date comparison of the varying connectivity software platforms available for GeneXpert can be found at: http://tinyurl.com/gliconnectivity

What hardware is needed?

Data from connected diagnostics must be stored on a **server**. These servers can be either hosted directly by a Ministry of Health or by a third party (see below, *Hosting Options*).

In order to send data from the diagnostic device to the server, the device will need access to the internet (see below, *Internet connectivity*). This capability is typically provided by a **modem**, which can be in various locations:

1. Some diagnostic devices have in-built modems, but this is an exception.
2. Modems may be present in the companion computer if the diagnostic device has one, such as in the desktop or laptop computer accompanying a GeneXpert. These computers often have Ethernet or Wi-Fi connection capabilities, however most laboratories lack an existing broadband internet connection that is needed in order to make use of the computer's Ethernet or Wi-Fi connection capabilities.

3. A 3G/2G modem in a USB internet dongle may be an option. These dongles contain SIM cards and access to the internet is provided by a cellular provider. Although they are relatively inexpensive, dongles carry a risk of being removed, misplaced and misused. Many countries that have relied on USB dongles have struggled to keep them present and functioning at the diagnostic device's computer for an extended period of time.

4. Standalone desktop modems (also known as smart routers) are generally the more reliable option but are more expensive. Desktop modems are separate from the diagnostic device and companion computer. The diagnostic device or computer will need to connect using Wi-Fi, Ethernet cable, RS-232 serial cable, or another connection to the modem, which then connects to the internet using cellular networks by way of SIM cards inserted into the modem. If the computer doesn't have Wi-Fi capability to connect to the modem, an Ethernet cable or Wi-Fi dongle will be required to connect the computer to the desktop modem.

   Some desktop modems provide the ability for dual- or quad-SIM deployments to leverage multiple mobile networks in a country, capacity for improved remote support, and internal security software to encrypt data and prevent unauthorized use of the data.

   However, desktop modems are not without their shortcomings. Many do not initiate retransmissions after network or power failures. Based on their experience in the field, CHAI has conceptualized the 'Node', a mini-server modem/router combination in a box which is described as a more robust and secure solution for automatic transmission in fragile connectivity environments, and is less vulnerable to unintended use compared to a PC with comparable software controlling the router.[1]

   Where cellular networks are used to connect devices it is advisable also to make use of private Access Point Names (APN) and Virtual Private Networks (VPN). In conjunction with desktop modems, these allow additional security and usage protection by limiting the use of data to the intended purpose, i.e. the SIM card cannot be used for general internet browsing as well as reducing the risk of acquiring a computer

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[1] At the time of publication in October 2016, the Node is under development.

virus. Private APNs are generally not available when using prepaid SIM cards (see below, *Internet connectivity*).

Additional hardware that is recommended for use with desktop modems are external antennas. These allow stronger and more stable connections if the modem is accessing the internet through the use of cellular networks.

Internet connectivity: SIM cards and data plans

In resource-limited settings, the modem as described above will usually need to access the internet via cellular networks such as 2G, 3G and 4G. In order for the modem to access the cellular network it will need a SIM card with an active data plan.

The data plan (measured in Megabytes-MB or Gigabytes-GB) should be sufficient to allow the transmission of data from all connected devices to the server. The data plan should also be sufficient to allow updates of anti-virus software and remote troubleshooting capabilities from the solution providers.

Data plans come in two variants:

1. **Prepaid** – Data are purchased in advance and once depleted will need to be topped up again. Generally these plans are not advisable: countries using them frequently struggle to keep SIM cards activated and topped up. The top-up process often requires the SIM to be removed from the modem, there is often a lack of visibility of the remaining credit available on the SIM cards, and the process requires human intervention.
2. **Postpaid** – Data are paid for on a monthly basis after use. This requires a contract to be in place with the network provider, and credit terms to be established in advance of launching the network.

SIM cards and data plans are often provided by the solution vendors but should be verified in the assessment, planning and budgeting stage of the connectivity project.

Hosting options

Hosting of the data collected as previously mentioned generally has two options.

1. Direct hosting using an in-country server: When the server is in-country, the Ministry of Health may have complete control over the data. This option requires adequate infrastructure, financial resources, and IT personnel to configure and maintain the server, including renewing software licenses and hardware upgrades. In-country servers will also need to budget for periodic offsite backups, a failover system, and feature upgrades. When hosting a connected diagnostic application within a Ministry of Health, a quarterly upgrade plan should be established to ensure the Ministry of Health can leverage all new features and security measures in place by the selected provider.
2. Third party hosting (also known as: virtual or cloud-based servers): Modern third party hosting platforms are highly secure, provide redundancy against data loss, are quickly scalable and are a good option when a country does not have the IT capacity to properly configure and maintain an in-country server. Third party hosting is

available for a monthly or annual hosting fee and is almost always cheaper than a dedicated in-country self-hosted server simply due to economies of scale of the business models of hosting companies. Some manufacturers offering a proprietary connectivity solution may require the testing and device data to be stored on a designated third party hosting platform.

Data ownership and security

If the chosen connectivity solution is being hosted by the connectivity software provider or on a third party hosting platform, a Data Use Agreement signed by the Ministry of Health and the connectivity software provider is recommended. Such an agreement should assign ownership of all data to the Ministry of Health, grant the Ministry of Health the decision to share access with selected parties, describe in detail the planned storage and security of the data, and any planned use of the data by the software provider, ensuring that patient data remains confidential and not disclosed to unauthorised users or used by the software provider outside of the terms of the agreement.

If the hosting and management of the servers is in-country then no Data Use Agreement would be needed with the software provider unless the provider has some form of remote connectivity to the servers for maintenance and troubleshooting purposes where access to data would be possible. A Data Use Agreement may nevertheless be beneficial to have with any in-country service providers or other selected parties to whom access to data would be granted.

Personnel needs during the operational phase

Allocation of in-country staff with designated mandates and responsibilities is required for the operational phase, i.e. post set-up of the connectivity solution. This team will be responsible for the continued operation, utilization and maintenance of connectivity solutions:

- **National, regional and local level data monitoring:** Persons should be assigned to systematically monitor data on a weekly or biweekly basis. Thresholds should be established related to error levels, underutilization of tests, under/oversupply of stock, or other metrics, and identified sites should be followed up according to a standard operating procedure (SOP). Quarterly review of data by an M&E team should review trends in device utilization and test results, and data related to patient access/coverage.

- **IT/network support:** Server maintenance will be required if data are hosted in-country. IT support is also required to troubleshoot connectivity issues that may arise at the site level.

- **Data connectivity administration:** Administrative support will be needed to ensure data invoices are paid or sim cards are topped up if applicable.

- **Training:** Continued training of existing users and training of new users will be required to ensure maximum benefit and minimum issues.

Budgeting

The costs required to set-up and operate a connectivity solution are highly country dependent, yet there are a number of common budget items. The following items should be budgeted to ensure a comprehensive solution:

Preparation phase

Landscape assessment: In-country assessment of existing systems and infrastructure (both laboratory and connectivity) by a diagnostics connectivity solutions provider, and sensitization of stakeholders. This assessment leads to recommendations on the utility applications of the planned diagnostic connectivity solution, data needs and a costed roadmap.

Set-up/installation phase

Hardware and equipment: Smart routers/modems, server, Wi-Fi dongles, antennas, SIM cards. All hardware should be suited for harsher environments.

Configuration and customization of connectivity solution: Configuration of server and customization of connectivity solution to collect country specific-indicators, create reports, web dashboards and/or notifications. Optional: development of API connections, for example with Laboratory Information Management Systems (LIMS), Electronic Medical Records (EMRs) or patient management tools

Implementation workshops/trainings: Workshops on data collection, data use and management, day-to-day operations of connectivity solution and installation/roll-out training

Installation and roll-out of connectivity solution: On-site installation of modems/routers and set-up of connectivity solution in laboratories, including in-country travel costs

Diagnostics connectivity solutions provider: Project management and consultancy to ensure proper roll-out

Operational phase

Running costs for connectivity: Monthly mobile data costs, server hosting, license costs for connectivity software (if any), and ancillary services including messaging, antivirus or updates

Remote or in-country technical support: Technical support from the implementing software service provider to users during daily use, user- and permission administration, platform development, IT-support and updates

In-country human resources: Data monitoring and supervision, IT/network support, administrative support, and programmatic support for follow-up trainings and capacity building to ensure programmatic impact

Depending on needs for software customization and variability in travel, training, personnel, consultancy, project management, hardware and data costs, the first-year preparation and set-up costs for a connectivity diagnostic solution for a network of approximately 10 GeneXperts may vary between 40,000 and 80,000 US dollars, and ongoing expenses in the operational phase may vary between 5,000 and 10,000 US dollars annually. For a network of approximately 100 GeneXperts, the first-year preparation and set-up costs may vary between 100,000 and 200,000 US dollars, and ongoing expenses may cost between 10,000 and 30,000 US dollars annually. Additionally, budget for in-country human resources should be included for data monitoring and supervision, IT/network support, data connectivity administration, refresher trainings and training of new users.

Donor agencies, including the United States Agency for International Development, the Global Fund, Global Affairs Canada (via the Stop TB Partnership's TB REACH initiative) and UNITAID, have provided support to countries for installation and implementation of diagnostics connectivity solutions.

A diagnostic connectivity budgeting tool has been developed by ChallengeTB/KNCV and will be available soon via:
http://www.challengetb.org

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