

**Considerations for selection of SARS-CoV-2 diagnostics and potential multiplexing:
A perspective to ensure continuity of care for people with TB**

14 May 2020

Note: The original 14 April 2020 version of this document has been updated to reflect changes to WHO guidance on laboratory biosafety when testing for COVID-19: a BSL-2 laboratory with biosafety cabinet is no longer a prerequisite for use of the Xpert Xpress SARS-CoV-2 cartridge. The list of diagnostics on the WHO Emergency Use Listing has also been updated.

Significant efforts and investments have been made in recent years to develop extensive TB diagnostic networks in low- and middle-income countries, ensuring patients have access to the rapid molecular testing required to promptly start treatment on effective regimens.

Given the potential to leverage these networks and especially GeneXpert networks for SARS-CoV-2 detection, national TB programme and TB reference laboratory managers and staff are being engaged in development of COVID-19 case finding plans, including in selection of diagnostics and strategies to possibly multiplex existing instruments.

We must ensure continuity of TB patient care.

Therefore, the following points should be considered when selecting an appropriate SARS-CoV-2 diagnostic and deciding whether to multiplex instruments for detection of SARS-CoV-2:

A. APPROVAL STATUS OF SARS-CoV-2 DIAGNOSTICS

1. WHO maintains and regularly updates a list of SARS-CoV-2 diagnostics that have been assessed and accepted for procurement through its Emergency Use Listing (EUL) Procedure, or are on the pathway of assessment towards potential acceptance:

https://www.who.int/diagnostics_laboratory/EUL/en/

As of 14 May 2020, the following diagnostics for detecting SARS-CoV-2 nucleic acid have been approved for listing on the WHO EUL:

- Roche cobas SARS-CoV-2 Qualitative assay
- Primerdesign Ltd COVID-19 genesig Real-Time PCR assay
- Abbott Realtime SARS-CoV-2 assay
- PerkinElmer SARS-CoV-2 Real-time RT-PCR assay
- BGI Europe A/S Real-time fluorescent RT-PCR kit for detecting 2019-nCoV

Note that the review of the Cepheid Xpert Xpress SARS-CoV-2 cartridge is currently in process.

- a. Several of the diagnostics approved or under review are for use on automated real-time PCR instruments. Countries may already have these instruments for:
 1. TB case finding (e.g., Cepheid GeneXpert);
 2. HIV viral load monitoring or early infant diagnosis (e.g., Roche cobas 6800/8800 Systems, Abbott m2000 RealTime System); or
 3. Testing for other diseases.
- b. The above-referenced WHO website also includes links and lists of SARS-CoV-2 diagnostics that are approved by national regulatory authorities in countries that are members of the International Medical Device Regulators Forum (IMDRF).
 1. These are not endorsed by WHO, and the information is provided only to assist stakeholders with identifying the links to the various lists. The Cepheid Xpert Xpress SARS-CoV-2 cartridge received US FDA Emergency Use Authorization in March 2020.

B. DECIDING TO PROCURE SARS-CoV-2 DIAGNOSTICS:

1. If using donor funding, a country should ask for the donor's quality assurance policy around procurement of SARS-CoV-2 diagnostics. For example, a donor may only allow procurement of products that are on the WHO Emergency Use Listing or approved for emergency use by certain national regulatory authorities.
2. Several diagnostic manufacturers may need to prioritize domestic markets, which will have an impact on their ability to timely serve other countries. Manufacturer lead times between order placement and shipment readiness should be investigated to ensure that timelines in national COVID-19 response plans can be met or adjusted accordingly. Countries should also factor in potential delays due to lock downs and air traffic restrictions affecting international shipping.
3. Countries may need to plan for use of manual nucleic acid amplification tests while awaiting the possibility of automated tests to be delivered.
4. Because of the uncertainties mentioned above, it may be wise to consider multiple testing technology options rather than relying on one particular technology.
5. Specifically on the Cepheid Xpert Xpress SARS-CoV-2 cartridge, please be aware:
 - a. It is [now available](#) in the Stop TB Partnership Global Drug Facility (GDF) Catalog and orders placed for GDF clients have a manufacturer-committed lead time of **60 days**. Countries should also consider their own timelines required for order placement, payment approvals and import readiness. For more information on how to procure through GDF using donor or domestic funding, please contact: gdf@stoptb.org
 - b. Cepheid will be working with WHO and other partners on an allocation system given high demand from many countries for their test cartridge.

C. MULTIPLEXING SARS-CoV-2 AND TB TESTS ON EXISTING GENEXPERTS:

1. First and foremost, **TB testing must continue**: Xpert MTB/RIF is the only molecular test available for TB in most countries, and people with TB will suffer and TB-related deaths will increase if testing is stopped or reduced.
2. Countries should carefully estimate how much free capacity is available on instruments. In order to meet the required testing capacity, countries should always consider procuring additional machines and expanding working hours of staff with commensurate payment.
 - a. Countries deciding to make the significant capital investment to acquire more GeneXperts may consider procuring instruments with 10-color optic modules, as these instruments will allow for rapid second-line drug susceptibility testing with the Xpert XDR cartridge planned for release later in 2020.
 - i. Note that WHO has not yet released a performance report around use of 10-color optic modules for Xpert MTB/RIF testing, and the Xpert XDR cartridge will only be reviewed by WHO later in 2020. Please consult with Cepheid regarding availability of the modules for your country.
3. Considering that sample manipulation and the level of aerosol generation would be minimal, [WHO is no longer indicating](#) that a Biosafety Level 2 laboratory with biosafety cabinet is needed when preparing a specimen and loading a Cepheid Xpert Xpress SARS-CoV-2 cartridge “when the local risk assessment so dictates and the following conditions are fully met:
 - performed on a diaper or large paper towel **in a well-ventilated area** free of clutter, where there are no documents, computers or personal stuff
 - appropriate PPE worn similar to other manual testing, such as but not limited to a full-length long (elastic) sleeved lab coat, safety goggles or glasses, and suitable disposable gloves
 - risk assessment should inform the use of respiratory protection as a supplementary precaution
 - staff well trained in GMPP (Good microbiological practices and procedures)
 - no rush or increased pressure for test turnaround time
 - a validated infectious waste process including excess specimens”
4. Centralizing GeneXperts to facilitate SARS-CoV-2 testing should be avoided, as ensuring initiation of TB treatment requires minimizing turnaround times for testing.

For WHO technical guidance on laboratory testing for 2019-nCoV as well as on specimen collection, packaging and shipment, see resources at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance>

For WHO Global TB Programme’s *COVID-19: Considerations for TB care*, see: https://www.who.int/tb/COVID_19considerations_tuberculosis_services.pdf