



Rapid communication on the role of the GeneXpert[®] platform for rapid molecular testing for SARS-CoV-2 in the WHO European Region

**European Laboratory Initiative
on TB, HIV and Viral Hepatitis**

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Abstract

In view of the current COVID-19 pandemic and consequent need for automated rapid diagnostic technologies with a rapid turnaround time, the European Laboratory Initiative on TB, HIV and Viral Hepatitis (ELI) has developed this rapid communication to inform Member States of the WHO European Region on the potential use of the Xpert® Xpress SARS-CoV-2 cartridge (Cepheid, Sunnyvale, United States of America). These cartridges, which received Emergency Use Authorization from the United States Food and Drug Administration on 20 March 2020, can be run on GeneXpert® platforms that are already available in the Region and currently used for diagnosis of tuberculosis and rifampicin resistance (as recommended by WHO), hepatitis C and seasonal influenza, and for HIV viral load testing and early infant diagnosis of HIV infection. Based on the best available evidence and current knowledge, this rapid communication by ELI provides a short overview of (i) the major points when considering the use of GeneXpert machines for COVID-19 testing and (ii) the support that ELI is working to provide to Member States of the Region.

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Background

On 30 January 2020 WHO declared coronavirus disease 2019 (COVID-19) a public health emergency of international concern, and on 11 March declared it as a global pandemic. From the onset of this public health crisis, the need for rapid and accurate laboratory testing was highlighted, and laboratory scientists responded by developing the first diagnostic tests for COVID-19 within days of the release of the viral genome sequence.

The WHO European Region is currently the epicentre of the COVID-19 outbreak, with the disease reportedly most prevalent in the western part of the Region; however, this information needs to be carefully interpreted because countries are in different stages of disease transmission and the lower numbers reported in some eastern European countries may be due to the lack of available diagnostic services. All countries need to plan ahead to ensure sufficient diagnostic capacity, as outlined in the WHO guidance document, Laboratory testing strategy recommendations for COVID-19.¹

In this context, one of the key questions faced by countries is which diagnostic assay(s) to adopt to meet the demand for the four transmission scenarios identified by WHO (1,2). Serological or rapid antigen tests are currently not recommended by WHO for COVID-19 case detection: instead, nucleic acid amplification tests should be used. However, this guidance may change based on the availability of new serological tests (1). An overview of tests under development can be found on the FIND website (3). Some have already received Emergency Use Authorization by the United States Food and Drug Administration (FDA) and/or are CE-IVD marked² for diagnostic use in the European Union. WHO is continuously updating technical guidance for COVID-19, including recommendations on laboratory testing (2). No comprehensive comparison of the performance of rapid diagnostic has been performed to date, although several evaluations are ongoing or planned (5). For the time being, the following logistic and financial factors, among other factors, can be weighed to inform the choice of nucleic acid amplification test: turnaround time, throughput (i.e. number of tests that can be run simultaneously in one round), degree of automation, supply considerations and cost (list not exhaustive).

Key updates and considerations

COVID-19 testing with the Xpert® Xpress SARS-CoV-2 cartridge

In view of FDA Emergency Use Authorization of the Xpert® Xpress SARS-CoV-2 cartridge (Cepheid, Sunnyvale, United States of America) (6,7) on 20 March 2020, one option for COVID-19 testing may be to leverage the spare capacity of existing GeneXpert® machines. Possible advantages of this approach are that the assay is fully automated and provides results within

¹ For the latest update, please check the following version of the document, Laboratory testing strategy recommendations for COVID-19. Interim guidance: 22 March 2020 (1).

² CE marking is required for all in vitro diagnostic (IVD) devices sold in Europe. It indicates that an IVD device complies with the European In-Vitro Diagnostic Devices Directive (98/79/EC) and that the device may be legally commercialized in the European Union (4).

45 minutes. Laboratory staff may be already familiar with the GeneXpert® platform, given that the Xpert® MTB/RIF assay serves as the primary diagnostic assay for tuberculosis (TB) and its drug-resistant forms in eastern and central European countries in accordance with WHO recommendations (8). Therefore, the possibility of applying GeneXpert® platforms can be considered providing cartridge production capacity and cost are optimal. However, it is important to note that according to WHO guidelines and recommendations GeneXpert®-based COVID-19 testing should not be used outside of laboratories with adequate containment practices, which may diminish the value of the rapid turnaround time in the absence of efficient sample transport/logistics (9). Moreover, the WHO Emergency Use Listing procedure is ongoing (timeline for completion is not yet known) (10,11) and there is a possibility that the cartridge will not be endorsed or will be reserved only for narrow applications. Moreover, the throughput of Xpert® Xpress SARS-CoV-2 is limited (e.g. in a machine with four modules, only four tests can be done with a turnaround time of 45 minutes). Assuming one test is performed per module per hour and a 24-hour working pattern, the total theoretical capacity of 10 GeneXpert® machines with four modules would be approximately 960 samples per day. Crucially, however, the spare testing capacity is likely to be considerably lower.

Taken together, this means that although Xpert® Xpress SARS-CoV-2 is a potentially promising option for testing a limited number of samples (e.g. from patients in intensive care units or from health-care workers with the highest public health priority), it is probably not the optimal solution for the vast majority of samples, particularly in settings with large outbreaks. The Xpert® Xpress SARS-CoV-2 cartridge is probably best suited to complement a wider testing strategy that primarily relies on one or more higher throughput assays. Indeed, the latter strategy has been adopted by all countries that have or are currently experiencing large-scale disease transmission. In this context, it should be noted that no single high-throughput assay is considered optimal. Countries must assess the capacity of existing platforms, taking into account the aforementioned considerations for Xpert® Xpress SARS-CoV-2, to decide which assay(s) to select.

Testing for COVID-19 and TB

On 20 March 2020 the WHO Global TB Programme circulated an information note on TB and the COVID-19 response stating that, on a programmatic level, countries would need to develop targeted strategies for COVID-19 testing in TB patients, including those with previous disease (12). It also points out that testing for TB in individuals presenting for COVID-19 testing is becoming necessary, as is COVID-19 testing among individuals presenting to TB services with respiratory signs and symptoms.

Next steps

While awaiting additional regional and national approval for Xpert® Xpress SARS-CoV-2, as well as production of the first cartridges, core group members of the European Laboratory Initiative on TB, HIV and Viral Hepatitis (ELI) will focus on the following major areas to provide further

clarification and to support the WHO European Region with materials to be ready once this test becomes available in countries (in order of priority):

- identify and share the list of supplies that will be needed to run the test (e.g. viral transport tube, swabs);
- provide standard operating procedures in English and Russian;
- develop technical support materials to help countries rationalize their laboratory network and use the existing GeneXpert® machines for the maximal COVID-19 response without compromising their use for TB, HIV and viral hepatitis;
- provide remote or in-country support:
 - on necessary biosafety measures and considerations;
 - on workflow organization for GeneXpert® machines that will be used for several diseases (i.e. TB, HIV/viral hepatitis and COVID-19);
 - for sample transportation;
 - on data management tools (e.g. GxAlert) and laboratory record and report forms; and
 - for integration of rapid diagnostic tests into the overall diagnostic algorithms and testing strategies.

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