JULY 6, 2020

Protocol for kit verification and quality control of Xpert® Xpress SARS-CoV-2 testing using GeneXpert Dx System in Nepal

VERSION 1 – JULY 2020

Joint collaboration with National Tuberculosis Control Center and National Public Health Laboratory

DEPARTMENT OF HEATH SERVICES

Ministry of Health and Population, Nepal

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1. BACKGROUND:

GeneXpert Dx System is a Cartridge-Based Nucleic Acid Amplification Testing (CB-NAAT) system which utilizes Xpert Xpress SARS-CoV-2 cartridges for detection of SARS-CoV-2 RNA in respiratory specimens including nasopharyngeal swab, nasal wash/aspirate, oropharyngeal swab, nasal swab and mid-turbinate swab. This technique has received WHO Emergency Use Listing for In-Vitro Diagnostics[1], US-FDA Emergency Use Authorization (EUA) and CE-IVD certification for diagnosis of COVID-19.[2] Some independent studies have demonstrated that the performance of Xpert Xpress SARS-CoV-2 testing is comparable with the performance of other RT-PCR techniques in detecting SARS-CoV-2 RNA in patient specimens.

The following sections outline the procedures for verification of Xpert Xpress SARS-CoV-2 testing for detection of SARS-CoV-2 RNA using GeneXpert Dx System in Nepal.

2. VERIFICATION AT NATIONAL LEVEL

A. Purpose: To perform verification of Xpert Xpress SARS-COV-2 testing in GeneXpert Dx system before its release at national level.

B. Responsibility: National Public Health Laboratory (NPHL) and National Tuberculosis Control Center (NTCC)

C. Site: NTCC

D. Personnel involved: From NTCC and NPHL

E. Requirements:

- Biosafety Level 2 laboratory
- Biosafety Cabinet Class II A2
- GeneXpert cartridges (Xpert Xpress SARS-CoV-2 cartridges) and accessories
- GeneXpert Dx System

F. Samples:

Either external reference materials (external QC materials) or known positive and negative patient samples can be used for kit verification purpose.

For determining accuracy of the Xpert® Xpress SARS-CoV-2 test, at least 10 known SARS-CoV-2 positive and 10 SARS-CoV-2 negative patient samples (total 20 samples) will be used. The samples which have been previously confirmed by other RT-PCR platforms will be used.

Of 10 positive samples, 5 will be strongly positive specimens (C_T value 15-24) and 5 will be moderately positive specimens (C_T value 25-30).[3]

[1] https://www.who.int/diagnostics_laboratory/200625_eul_sars_cov2_product_list.pdf

[2] https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas#cepdx

[3] Mitchell, S. L., George, K. S., Rhoads, D. D., Butler-Wu, S. M., Dharmarha, V., McNult, P., & Miller, M. B. (2020). Understanding, verifying and implementing Emergency Use Authorization molecular diagnostics for the detection of SARS-CoV-2 RNA. *Journal of Clinical Microbiology*.

For the purpose of determining precision of the test, triplicates of one strongly positive sample, one moderately positive sample and one negative sample will be tested i.e. the same sample will be tested three times. This process will require additional six tests i.e. each sample selected for precision testing will be tested two additional times as these will have been already tested once for determining accuracy as stated above.

H. Batch verification:

Each new batch/ lot of the Xpert Xpress SARS-CoV-2 cartridges arriving in the country in future will be verified using the confirmed SARS-CoV-2 positive and SARS-CoV-2 negative samples as stated above or using the commercially available standard positive and negative reference materials.

G. Report:

A standard verification report will be prepared to document results of the verification tests. Tables to be included in the report are provided in the Annex of this protocol. The verification report will provide appropriate recommendations for using Xpert Xpress SARS-CoV-2 test in Nepal. The test will be recommended for testing of patient samples according to the predetermined criteria if the test shows percentage agreement of $\geq 90\%$ with the results of the standard RT-PCR technique.

3. REQUIREMENTS FOR TESTING LABORATORIES

A. Verification at testing laboratories

Each laboratory designated to perform SARS-CoV-2 testing using the Xpert Xpress SARS-CoV-2 cartridges will receive one confirmed positive sample and one confirmed negative sample along with the first lot of the cartridges.

The laboratory will test these samples using the provided cartridges and communicate the results back to NPHL and NTCC in provided format.

After confirmation of successful testing, the designated laboratory will start testing the patient specimens and provide SARS-CoV-2 testing services according to the predetermined criteria.

B. External Quality Assessment

Each laboratory designated to perform SARS-CoV-2 testing using the Xpert Xpress SARS-CoV-2 cartridges will participate in the External Quality Assessment (EQA) of SARS-CoV-2 testing organized by the NPHL.

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ANNEX

Table 1: Comparison of SARS-CoV-2 RT-PCR Results between Xpert Xpress SARS-CoV-2 test and RT-PCR test using other platforms

Sample No.	RT-PCR results (Pos/Neg)	GeneXpert Results (Pos/Neg)	Agreement (Yes/No)
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
OVERALL AGREEMENT (%)			

Table 2: Cross-tabulation of SARS-CoV-2 RT-PCR Results between Xpert Xpress SARS-CoV-2 test and RT-PCR test using other platforms

		RT-PCR results from reference platform		Total
		Positive	Negative	
GeneXpert results	Positive			
	Negative			
Total				
Percentage agreement =				
Sensitivity =				
Specificity =				

Table 3: SARS-CoV-2 RT-PCR Results for samples run in triplicates

Sample	Test 1 Result	Test 2 Result	Test 3 Result
1. Strongly Positive			
2. Moderately Positive			
3. Negative			

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Acknowledgement of having read this SOP

№	Name	Position	Signature

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