Annex 5e

PROTOCOL ON COVID-19 RAPID MOLECULAR TESTING FOR THE HEALTH FACILITIES, MINISTRY OF HEALTH MALAYSIA VERSION 1.0

1. OBJECTIVE

This document provides brief protocol for rapid molecular testing available in Ministry of Health, Malaysia for the detection of SARS-CoV-2.

2. BACKGROUND

2.1 All COVID-19 laboratories in MOH are using real time Reverse Transcriptase Polymerase Chain Reaction (RT- qPCR) as a confirmatory test for COVID-19 infection which may takes several hours of 6 to 8 hours for a completion.

2.2 With the advancement of technology, research and development, real Rapid PCR platforms are being introduced recently. These platforms enable results to be provided within 1 – 2 hours and are now available in hospital's laboratories in MOH. Rapid PCR allow faster case detection, diagnosis and management of COVID-19 patients.

2.3 Two rapid PCR tests available in MOH facilities are:

2.3.1 GeneXpert - Xpert Xpress SARS-CoV-2 test

i. The Xpert Xpress SARS-CoV-2 test is an automated in vitro diagnostic test for qualitative detection of nucleic acid from SARSCoV-2 which is performed on GeneXpert Instrument Systems.

ii. The GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequences in simple or complex samples using real-time PCR assays and the results is ready within 1 hour.

iii. The Xpert Xpress SARS-CoV-2 test provides test results based on the detection of two gene targets, N2 and E gene and Internal Control (IC). A correlation study between two targets and one target (N2 only) has been carried out in Institute Medical Research (IMR), Ministry of Health and showed a sufficient correlation.

iv. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge utilized by the GeneXpert instrument.

2.3.2 QIAstat -Dx Respiratory SARS-CoV-2 Panel

i. This is a multiplexed nucleic acid real-time PCR test which can detect nucleic acid from 22 respiratory viral and bacterial organisms, including the SARS-CoV-2 virus.

ii. The SARS-CoV-2 in this panel targets two genes of the virus genome, Rdrp and E gene, detected with the same fluorescence channel. The two targets are not differentiated, and amplification of either or both regions leads to a fluorescence signal.

iii. The QIAstat-Dx Respiratory SARS-CoV-2 Panel Cartridge includes a full process IC, which verifies all steps of the analysis process, including sample resuspension/homogenization, lysis, nucleic acid purification, reverse transcription and PCR.

2.4 This document therefore is aimed as guidance protocol for the health facilities in MOH with access to these two rapid molecular testing platforms for the usage of SARS-CoV-2 detection.

2.5 This protocol shall be refined based on the latest available evidence from time to time.

3. IMPLEMENTATION

3.1 Indication

Rapid SARS-CoV-2 PCR testing should only be considered in high risk patients where an urgent result is required within one to four hours.

Testing can only be requested by a Specialist, preferably following discussion with the Medical Microbiologist or Infectious Disease Physician.

3.2 Testing criteria:

i. **Critically ill patients** with recent onset of respiratory symptoms/pneumonia (SARI) following the updated existing Guidelines of Infection Prevention and Control (IPC) in Clinical Management of Severe Acute Respiratory Infections (SARI/Pneumonia TRO Covid-19

ii. **Urgent transplant cases**

iii. Brought in dead (BID) cases with **high probability or high suspicion of Covid-19.** Testing can only be requested by Forensic Pathologist and/or Emergency Physician, preferably following discussion with the Medical Microbiologist or Infectious Disease Physician.

iv. **Urgent cases other than above, upon consultation with Medical Microbiologist or Infectious Disease Physician.**

In urgent cases, the choice of test between these rapid molecular platforms and RTK Antigen depends on the indication and availability of the test.

3.3 Specimen requirement:

i. Specimen collections should be done by trained personnel and the usage of appropriate PPE shall be ensured.

ii. Types of Specimen:

Table 1. Types of specimen and transportation

	GENEXPERT	QIASTAT
Type of Specimen	Nasopharyngeal swab Nasal wash / aspirate	Nasopharyngeal swab
Transport Media	Nasopharyngeal swab in Viral Transport Media (VTM) Nasal wash/aspirate in sterile container	Nasopharyngeal swab in Universal Transport Media (UTM)
Packaging	Triple Packaging	Triple Packaging
Transportation	Maintain 2-8^{o}C up to 72 hours	Maintain 2-8^{o}C up to 72 hours

iii. Test procedure to be done as per manufacturer's recommendation

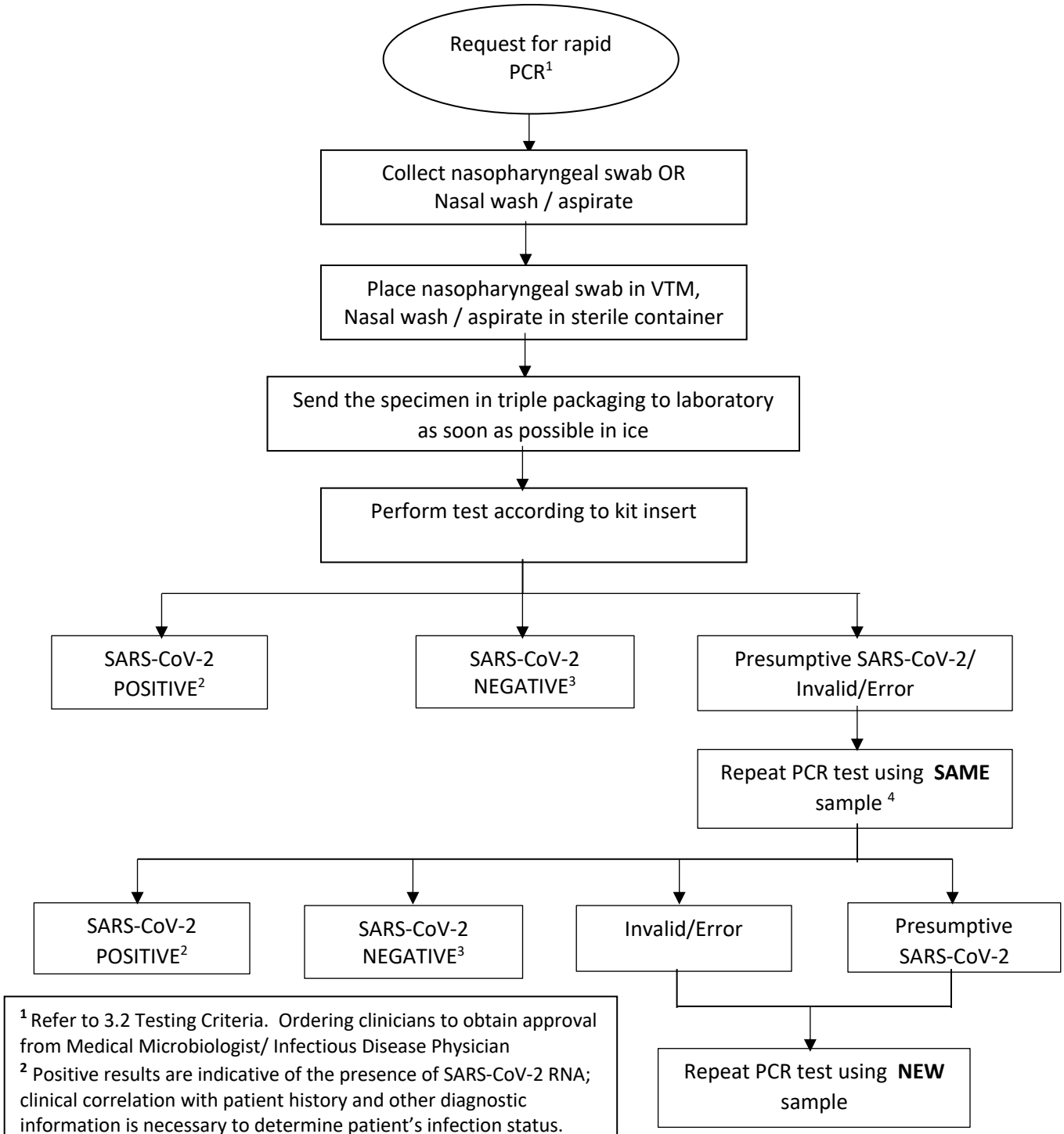
3.4 **Waste management:**

All clinical samples and consumables used shall be autoclaved or incinerated.

4. FLOWCHART AND RESULT INTERPRETATION

4.1 Xpert Xpress SARS-CoV-2

Diagram 1. Flowchart using Xpert Xpress SARS-CoV-2



[1] Refer to 3.2 Testing Criteria. Ordering clinicians to obtain approval from Medical Microbiologist/ Infectious Disease Physician

[2] Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient's infection status.

[3] Negative results do not preclude SARS-CoV-2 infection. If clinically indicated, repeat PCR after 48 hours – 72 hours.

[4] Repeat PCR test using other RT-PCR or rapid PCR platform, based on local setting.

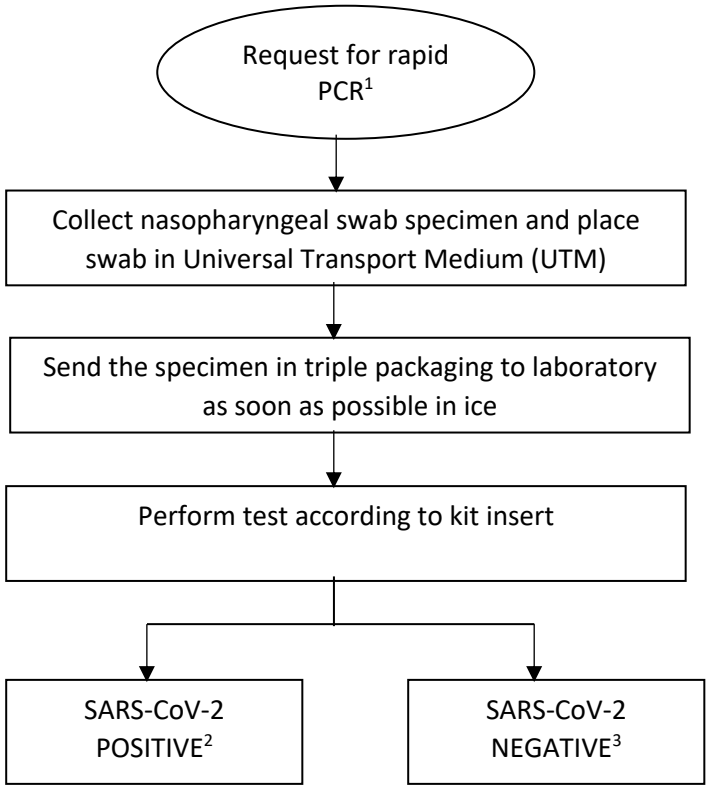
Table 2. Xpert Xpress SARS-Co-V-2 Possible results

Result Text	N2	E	SPC
SARS-CoV-2 POSITIVE	+	+	+/-
	+	-	+/-
SARS-CoV-2 PRESUMPTIVE POSITIVE	-	+	+/-
SARS-CoV-2 NEGATIVE	-	-	-
INVALID	-	-	-

Note: A correlation study between two targets (N2 and E) and one target (N2 only) done in Institute of Medical Research showed sufficient correlation for the detection of SARS-CoV-2.

4.2 QIAstat-Dx Respiratory SARS-CoV-2 Panel

Diagram 2: Flowchart using QIAstat-Dx Respiratory SARS-CoV-2 Panel



[1] Refer to 3.2 Testing Criteria. Ordering clinicians to obtain approval from Medical Microbiologist/ Infectious Disease Physician

[2]Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Repeat testing with other PCR platform if indicated.

[3] Negative results do not preclude SARS-CoV-2 infection. If clinically indicated, repeat PCR after 48 hours – 72 hours.

5. REPORTING OF RESULT

All results must be reported in SIMKA OUTBREAK. All positive results shall be informed to Infectious Disease Physician and the State CPRC.

6. QUALITY CONTROL

Verification shall be done by all centers providing these rapid molecular tests.

i. For labs with multiplex PCR onsite:
   - Test one known positive sample on GeneXpert or Qiastat Respiratory SARS-CoV-2 Panel.
   - Confirm the first 9 patient samples against multiplex PCR.

ii. For labs without multiplex PCR onsite:
   - Test one known positive sample (from referral lab) on GeneXpert or Qiastat .
   - Send the first 9 patient samples to referral lab for confirmation.

7. REFERENCES:

i. Annex 1 – Case definition of Covid-19 (updated 5 October 2020), Guideline Covid-19 Management in Malaysia No. 5/2020

ii. Annex 2 b – Management of Suspected Case required admission (updated 5 October 2020), Guideline Covid-19 Management in Malaysia No. 5/2020

iii. Xpert Xpress SARS-CoV-2 - Instructions for use

iv. QIAstat-Dx® Respiratory SARS-CoV-2 Panel Instructions for Use (Handbook)