Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

March 31, 2021

DEPARTMENT MEMORANDUM
No. 2021 - 0161

TO: **ALL UNDERSECRETARIES AND ASSISTANT SECRETARIES; DIRECTORS OF BUREAUS AND CENTERS FOR HEALTH DEVELOPMENT; MINISTER OF HEALTH – BANGSAMORO AUTONOMOUS REGION IN MUSLIM MINDANAO; EXECUTIVE DIRECTORS OF SPECIALTY HOSPITALS AND NATIONAL NUTRITION COUNCIL; CHIEFS OF MEDICAL CENTERS, HOSPITALS, SANITARIA AND INSTITUTES; PRESIDENT OF THE PHILIPPINE HEALTH INSURANCE CORPORATION; DIRECTORS OF PHILIPPINE NATIONAL AIDS COUNCIL AND TREATMENT AND REHABILITATION CENTERS AND ALL OTHERS CONCERNED**

SUBJECT: **Interim Guidelines for the Conduct of Saliva-Based RT-PCR Testing for the Detection of SARS-CoV-2**

I. BACKGROUND

The impact of the ongoing COVID-19 pandemic to the healthcare system and the economy of the country is overwhelming. With over 677,653 cases and 12,992 deaths as of March 23,2021, widespread testing to rapidly identify SARS-COV-2 infected individuals is important to ensure proper treatment and implementation of public health measures, isolation measures and contact tracing activities are early conducted to contain the COVID-19 disease.

Nasopharyngeal swab (NPS) and oropharyngeal swab (OPS) remain the gold standard respiratory specimens for SARS-COV-2 reverse transcription polymerase reaction (RT-PCR) test. Nevertheless, the collection of NPS and OPS specimens is technically demanding, invasive, and requires close contact between swabbers and patients posing risk of transmission to healthcare workers (HCWs). The use of personal protective equipment (PPE) during specimen collection protects the healthcare workers. However, PPE is an added cost to the overall procedure of testing making it more costly to patients. The collection of swab specimens also brings discomfort to patients especially to children and the elderly when a series of samples is required. Thus, the need for a non-invasive specimen collection procedure with supervision of a trained healthcare worker becomes evident.

Evidence shows that saliva specimens can be used as an alternative to NPS and OPS specimens for RT-PCR testing. Collection of saliva specimens has several advantages over NPS and OPS such as convenience to patients, ease of collection, and economical and non-invasive nature of collection. The use of saliva can potentially reduce the time and cost for testing, and also minimizing the risk of exposure and transmission of the virus to healthcare workers. However, shifting from the present standard specimens to saliva specimen requires validation due to large variation of different types of specimen collection kits, methods of processing saliva, and oral collection procedures such as spitting or drooling, using pipette or special sponges, and etc. The WHO Guidelines on Diagnostic Testing for SARS-COV-2 emphasized that the

sensitivity of oral fluids such as saliva has a wide performance range compared to NPS and OPS due to a large variety of collection methods and processing steps. Thus, laboratories must collect their own performance data linked to the local method of collection and in the relevant population for testing. At this time, WHO "does not recommend the use of saliva as the *sole* specimen type for routine clinical diagnostics". If nonstandard collection methods are intended to be used to diagnose other respiratory pathogens, the detection of these pathogens needs to be part of the validation procedure."[1]

In view of the foregoing and based on latest evidence, these interim guidelines aim to provide guidance for the conduct of saliva-based RT-PCR testing for the detection of SARS-COV-2 virus.

II. GENERAL GUIDELINES

A. The choice of the most optimal specimen for RT-PCR test shall be dependent on the clinical presentation, timing of onset of symptoms or exposure. Clinical and epidemiological correlation shall be considered prior to specimen collection.

B. NPS and OPS **shall remain as the standard specimens** for the diagnosis of SARS-COV-2 virus using reverse transcription polymerase chain reaction (RT-PCR) test.

C. Saliva specimens shall **ONLY** be allowed for nucleic acid amplification (NAAT) based tests and **ARE NOT ALLOWED** for antigen or antibody-based tests.

D. COVID 19 laboratories shall use FDA registered RT PCR kits with atleast 95% sensitivity and 99% specificity.

E. The Food and Drug Administration (FDA) shall issue **special certification** to RT PCR detection kits with validation results for saliva use conducted by RITM or its recognized testing laboratories.

F. The Research Institute for Tropical Medicine (RITM) and its recognized laboratories shall perform kit validation in compliance with FDA requirements for issuance of **special certification.**

G. Saliva-based RT-PCR test shall only be performed by licensed COVID-19 laboratories using RT-PCR detection kits issued with special certification by FDA.

H. RITM shall publish the results of its evaluation of diagnostic test kits and other laboratory commodities and make this information available in its website.

I. COVID-19 laboratories that intend to offer saliva-based RT-PCR test shall conduct in-house verification of the new saliva-based RT-PCR methods prior to performance of actual testing.

J. The Quality Assurance System shall be in-place for saliva-based RT-PCR test.

K. COVID 19 laboratories shall provide training and/or orientation to saliva specimen collectors as the accuracy of the laboratory test is greatly influenced by the method and timing of specimen collection.

L. Reporting of confirmed cases shall be in accordance with Administrative Order 2020-0013, entitled "Revised AO 2020-0012 Guidelines for the Inclusion of COVID-19 in

the List of Notifiable Diseases for Mandatory Reporting to the Department of Health dated 17 March 2020", and its amendments AO 2020-0013-A and B.

M. All testing facilities shall utilize the appropriate PhilHealth benefit and/or any benefit provided by health maintenance organizations (HMOs) or private health insurance providers for reimbursement.

III. SPECIFIC GUIDELINES

A. Standard Specimens for RT-PCR Test

1. Upper respiratory specimens namely NPS and OPS during the early stage of infections, especially in asymptomatic or mild cases, collected by trained healthcare workers.
2. Lower respiratory specimens, such as sputum, endotracheal aspirate, or bronchoalveolar lavage, collected later in the course of disease or in patients with more severe respiratory disease.

B. Regulatory Requirements

1. Manufacturers, through their local distributors, shall apply to FDA for local authorization of RT-PCR kits using saliva as specimen.
2. Local distributors of brands without FDA Special Certification for saliva shall not be allowed to sell products for saliva use.
3. List of RT PCR kits with Special Certification for saliva shall be published by FDA.
4. RITM, together with other RITM recognized laboratories, shall perform kit validation in compliance with FDA requirements for the issuance of special certification.
5. Validation reports shall be consolidated and evaluated by RITM, and directory of validated brands shall be posted in the RITM website.

C. In House Verification by COVID-19 Laboratories

1. The COVID 19 laboratories shall perform in-house verification of the new RT-PCR methods using FDA registered RNA extraction kit and RT-PCR detection kit validated for saliva specimens. (See Annex A- Standard Method for Verification of Saliva as Alternative Specimen for SARS-COV-2 Realtime PCR Testing: Interim Guidance for Laboratories in the COVID-19 Laboratory Network).
2. The COVID 19 laboratories shall submit the saliva-based RT-PCR verification report to RITM.
3. RITM shall issue certification to the COVID 19 laboratory for saliva-based RT-PCR testing.
4. RITM shall endorse to HFSRB the copy of certification of COVID 19 laboratories capable of performing saliva-based RT PCR testing.
5. HFSRB shall regularly provide a census of COVID-19 laboratories certified to perform saliva-based RT-PCR testing.

D. Implementation Arrangement

1. The use of saliva-based RT-PCR testing shall be in accordance with HTAC recommendations. The laboratories shall develop their laboratory Standard Operating Procedures for proper collection, handling, storage and testing of saliva

specimens adopted from the national standard operating procedures (See Annex B) or using their own in-house validated protocol.

2. Saliva specimen collectors shall be trained by the receiving laboratory and the conduct of training shall be supported and regularly monitored the DOH Centers for Health Development.
3. COVID 19 laboratories performing saliva-based RT-PCR test shall clearly communicate to saliva specimen collectors the type of saliva specimen collection kit and the method of specimen collection depending on validated protocol and/or manufacturer's product insert.
4. A full line list of positive and negative specimens shall be reported through the COVID-19 Document Repository System (CDRS).
5. The Philippine Health Insurance Corporation (PhilHealth) shall develop the appropriate payment and provider engagement mechanisms for saliva-based PCR testing in accordance with details set forth in these guidelines.
6. No additional payment shall be charged to patients beyond the PhilHealth coverage for the conduct of saliva-based RT-PCR testing.

For strict compliance.

FRANCISCO T. DUQUE III, MD, MSc
Secretary of Health

ANNEX A. Standard Method for Verification of Saliva as Alternative Specimen for SARS-CoV-2 Realtime PCR Testing: Interim Guidance for Laboratories in the COVID-19 Laboratory Network

Research Institute for Tropical Medicine - Department of Health
9002 Research Drive, Filinvest Corporate City, Alabang, Muntinlupa City, 1781 Philippines
Tel Nos.: (632) 809-7599 / 807-2631/32/37 • Fax: (632) 842-2245 • Website: www.ritm.gov.ph

Standard Method for Verification of Saliva as Alternative Specimen for SARS-CoV-2 Real Time PCR Testing: Interim Guidance for Laboratories in the COVID-19 Laboratory Network

As of 7 February 2021

Introduction

There is a growing body of evidence that saliva may be used, in addition to nasopharyngeal and oropharyngeal swabs (NPS and OPS), as an alternative specimen for PCR testing. Collection of saliva specimens has several advantages over NPS and OPS: the manner of collection is more convenient to patients; it is non-invasive and economical; collection does not require special swabs, and patients can be instructed to produce the specimen themselves without the use of a special facility.

The use of saliva as an alternative specimen for the detection of SARS CoV 2 would significantly reduce the time and cost of collection, minimize the risk of exposure and viral transmission to healthcare personnel and lessen the demand for PPE. Ultimately, this would make high volume testing feasible if enhanced surveillance is to be implemented. It must be noted, however, that saliva as a specimen for PCR, provides an alternative, especially if NPS and OPS are difficult to perform or contraindicated, or when there are no swab supplies, transport media and/or trained personnel are available.

Target Performance

At least 90% positive percent agreement (95% CI) or concordance for paired saliva and NPS/OPS samples tested by PCR.
At least 90% negative percent agreement (95% CI) or concordance for paired saliva and NPS/OPS samples tested by PCR.

Rationale

In keeping with international standards of good laboratory practice, any new method introduced by the laboratory shall be subject to verification prior to regular performance.

Scope

The following contains guidance for the standard method for verification of saliva as alternative specimen for SARS-CoV-2 RT- PCR.

Objective
To determine the suitability of saliva as an alternative specimen in a laboratory's particular set-up using its specific PCR reagents, supplies, and laboratory equipment prior to adoption of the procedure in the laboratory.

Method

1. **Parallel collection of specimens**
    a. Subjects shall be provided standard instructions for self-collection of saliva. *
        i. Provide the detailed and step-by-step saliva collection method and sample pre-treatment procedure employed by the laboratory.
        ii. Provide a photo of the saliva collection materials used for the verification.
        iii. If commercial saliva collection materials are used, provide also specific brand details and instructions for use.

    *As a good practice, inform and obtain consent of subjects that additional saliva shall be taken along with NPS/OPS for laboratory verification purposes.

    b. Self-collection of saliva shall be observed by a healthcare staff.
    c. Within 10 minutes, the healthcare staff shall subsequently collect a nasopharyngeal/oropharyngeal swab from each patient for parallel testing.
    d. NPS/OPS shall be placed in viral transport medium as part of standard specimen collection and transported to the testing laboratory.
    e. Parallel collection shall be performed until at least 30 PCR positive NPS/OPS and 30 PCR negative NPS/OPS have been completed.

2. **Nucleic acid extraction and PCR Testing**
    a. Nucleic acid extraction and PCR testing of both saliva and NPS/OPS shall be performed within 48 hours of collection, using the laboratory's extraction procedure and PCR assay, following the manufacturer's instructions, with recording of Ct values for each gene target for each specimen type.

3. **Analysis of data**
4.
    a. **Data tables**
        i. Data shall be summarized following the table below, showing the Ct values, interpretation of individual results using NPS/OPS with corresponding results for saliva.

NPS/OPS			**Saliva**		
Lab ID	**Ct Value per gene target**	**Result Interpretation**	**Lab ID**	**Ct Value per gene target**	**Result Interpretation**
NPS/OPS Lab ID-001			Saliva-Lab ID-001		
NPS/OPS Lab ID-002			Saliva-Lab ID-002		
…			….		

NPS/OPS Lab ID-XX			Saliva-Lab ID-XX		

b. **Compute for Percent Agreement**
Calculate the over-all percent agreement of the PCR test using saliva samples with respect to the results for NPS/OPS

Saliva	**NPS/OPS**	
Test Result Interpretation	Positive	Negative
Positive		
Negative		

Positive Percent Agreement = _____

Formula:

$$\frac{\text{No. of positive results in agreement (NPS/OPS)}}{\text{Total number of results}} \times 100$$

Negative Percent Agreement = _____

Formula:

$$\frac{\text{No. of negative results in agreement (NPS/OPS)}}{\text{Total number of results}} \times 100$$

c. **Compute for Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value with the parallel NPS-OPS PCR as reference test**

Record Keeping
The laboratory shall maintain information on the verification. These records shall be made available for review and inspection upon request.

Submission of Verification Documents
The accomplished method verification report shall be submitted to the Research Institute for Tropical Medicine for review.

Issuance of Certification
After review, RITM shall issue a certification to the laboratory for it to proceed with the use of saliva as an alternative specimen for SARS-CoV-2 PCR if it passes the verification.

Method Verification Report for Saliva as Alternative Specimen for SARS-CoV-2 RT PCR

Date of verification:			
Name of Laboratory:			
Complete Address:			
Laboratory head (Pathologist):			
Chief medical technologist:			
Contact information:	E-mail address:	Landline No.	Mobile No.

Part 1: Saliva Collection and Sample Pre-Treatment Procedure

- Provide the detailed and step-by-step saliva collection method and sample pre-treatment procedure employed by the laboratory
- Provide a photo of the saliva collection materials verified for this procedure
- If a commercial saliva collection material is used, provide also specific brand details and instructions for use

Part 2: PCR Assay Intended to be used for Verification of Saliva as Alternative Specimen

Nucleic Acid Extraction kit (Manual or automated)	• *Brand/manufacturer*
Automated Extraction machine (if applicable)	• *Brand/manufacturer*
PCR detection kit	• *Brand/manufacturer*
PCR machine	• *Brand/manufacturer*

Part 3. Results

NPS/OPS			Saliva		
Lab ID	**Ct Value per gene target**	**Result Interpretation**	**Lab ID**	**Ct Value per gene target**	**Result Interpretation**
NPS/OPS Lab ID-001			Saliva-Lab ID-001		
NPS/OPS Lab ID-002			Saliva-Lab ID-002		
NPS/OPS Lab ID-003			Saliva-Lab ID-003		
NPS/OPS Lab ID-004			Saliva-Lab ID-004		
NPS/OPS Lab ID-005			Saliva-Lab ID-005		
...			....		
NPS/OPS Lab ID-XX			Saliva-Lab ID-XX		

Percent Agreement

Saliva Test Result Interpretation	**NPS/OPS** Positive	Negative
Positive		
Negative		

Positive Percent Agreement = _____

Formula:

$$\frac{\text{No. of positive results in agreement (NPS/OPS)}}{\text{Total number of results}} \times 100$$

Negative Percent Agreement = _____

Formula:

$$\frac{\text{No. of negative results in agreement (NPS/OPS)}}{\text{Total number of results}} \times 100$$

Sensitivity: _____ **% (** _____ **/** _____ **) CI:** _____
Specificity: _____ **% (** _____ **/** _____ **) CI:** _____
Positive Predictive Value: _____ **% (** _____ **/** _____ **) CI:** _____
Negative Predictive Value: _____ **% (** _____ **/** _____ **) CI:** _____

Report prepared by:

_____
Technical Staff
Signature over printed name

Approved by:

_____
Head of Laboratory
Signature over printed name

ANNEX B. Laboratory Standard Operating Procedures (SOP) for the Conduct of RT-PCR Testing Using Saliva Specimen

1. **Specimen collection**
    a. Completely accomplished Case Investigation Form (CIF)
        i. Use the latest COVID-19 CIF for all patients.
        ii. Ensure that the CIF is completely accomplished with all data, including the demographic information, presence of symptoms, exposure and travel history, and details on the day of collection (i.e., day of illness at time of collection, if applicable).

    b. Timing of collection
        i. Morning saliva is the preferable sample as it contains greater viral load. However, this should not preclude collection at any other time as needed or as applicable, provided that proper collection procedure is strictly followed.

    c. Specimen collection supplies
        i. Wide-mouth sterile container with screw-cap or pop-top cover*
        ii. Specimen labeling materials

        **NOTE: There may be other commercial devices or containers for saliva collection available. These should be verified by the laboratory prior to routine use.*

    d. Method of collection
        i. Advise patients to avoid eating, drinking, brushing teeth, using mouthwash, and smoking for at least 30 minutes prior to sample collection
        ii. Provide patients with a properly labeled, graduated, sterile, wide-mouth container, along with instructions on how to provide saliva sample
            1. Advise patient to pool his/her saliva in the mouth.
            2. Ask the patient to spit at least 2-3 ml of saliva to the container.

2. **Biosafety considerations**
    a. Conduct specimen collection in an open/well-ventilated area.

b. Proper distance (at least 1 meter) should be maintained when healthcare workers instruct and directly observe the specimen collection procedure.
c. The laboratory staff should wear the following minimum PPE: face mask, eye-protection/face shield.
d. In addition to face mask, eye-protection/face shield, wear gloves when handling the specimens after submission by the patient.

3. **Required personnel**
   a. Ensure that there are healthcare workers assigned who shall provide instructions and directly observe patients on the proper collection of saliva specimen.
   b. Ensure only trained technical staff in biosafety and molecular detection of SARS-CoV-2 shall perform the test.

4. **Specimen transport**
   a. Transport conditions
      i. Ensure that all specimen containers are closed tightly to prevent leakage and perform a triple packaging system in accordance with the International Air Transport Association (IATA) guidelines.
      ii. Keep the samples at 2-8°C prior to testing.
      iii. Transport the samples to the laboratory and test within 48 hours of collection.

5. **Sample Treatment**
   a. The sample treatment method to be used shall follow the validated laboratory protocol.
   b. For commercial extraction kits that are already optimized for processing saliva, refer to the manufacturer's guidelines regarding sample treatment (e.g., using VTM or PBS) in recommended dilutions.
   c. Aliquot the necessary volume for testing from the resulting supernatant (according to the manufacturer's recommended sample volume).

6. **RT-PCR testing**
   a. Only FDA-authorized SARS-CoV-2 PCR kits verified for the purpose shall be used;
   b. The laboratory's standard procedures for PCR testing shall be strictly followed;
   c. Interpretation and analysis shall follow the instructions in the PCR kit insert provided by the manufacturer.

   **NOTE: Manufacturers are recommended to secure emergency use authorization for PCR kits using saliva as specimen at the Food and Drug Administration.*

7. **Quality Assurance**
   a. Once a laboratory's methods for specimen extraction and Real-Time PCR detection protocols are verified and certified to have acceptable performance in detection of SARS-CoV-2 viral RNA, the laboratory is responsible for ensuring that any deviations/changes in the methodology also undergoes verification procedures, prior to routine adoption for diagnostics.
   b. The laboratory shall continue to participate in the Quality Assurance Program implemented by the RITM as National Reference Laboratory.

8. **Waste disposal**
   Disposal of all generated waste such as discarded collection supplies, personal protective equipment, consumables, and other materials used in testing shall adhere to the 4th Edition of the DOH Health Care Waste Management Manual.