Clinical Performance of INDICAID COVID-19 Rapid Antigen Test

Sponsor:
Phase Diagnostics, Inc
(PHASE)

10527 Garden Grove Boulevard
Garden Grove, CA 92843

EFFECTIVE DATE: November 6, 2020

For Investigational Use Only:
The performance characteristics of this product have not been established.

STATEMENT OF INVESTIGATOR In signing this page, the Principle Investigator (PI) agrees to accept this protocol and conduct this study in compliance with the protocol, applicable regulations, and institutional policy; maintain confidentiality of protocol and investigational materials; and discontinue the study at Phase's request.	
Investigator's Signature	Date
Investigator's Printed Name	Title, Institution

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STUDY DEFINITIONS

Abbreviations	***Definition***
AE	Adverse Event
BSL	Biosafety Level
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
FP	False Positive
FN	False Negative
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
ICU	Intensive Care Unit
ID	Identification
IUO	Investigational Use Only
IFU	Instructions for Use
IRB	Institutional Review Board
LFA	Lateral-Flow Immunoassay
LoD	Limit of Detection
LOS	Length of Stay
MERS	Middle East Respiratory Syndrome
NPA	Negative Percent Agreement
PHEIC	Public Health Emergency of International Concern
PHI	Protected Health Information
PI	Principle Investigator
POC	Point of Care
PPA	Positive Percent Agreement
RNA	Ribonucleic Acid
RT-PCR	Reverse Transcription Polymerase Chain Reaction
SARS-CoV	Severe Acute Respiratory Syndrome Coronavirus
sFTP	Secure File Transfer Protocol
TP	True Positive
TN	True Negative
UADE	Unanticipated Adverse Device Effect
US	United States
WHO	World Health Organization

RESPONSIBILITIES

This section details the responsibilities of the PI, the Sponsor, and the study monitors.

Role	Responsibilities

Investigator	• Obtain IRB approval for protocol prior to study initiation, if needed. • Conduct study in accordance with signed Statement of Investigator, study protocol, GCP, GLP, other applicable country specific regulations. • Submit proposed protocol amendments or deviations to IRB and sponsor and obtain approval. • Submit progress reports, final reports, and special reports to IRB, when applicable. • Supervise the use of the IUO device. • Permit country specific regulatory agency and Sponsor's Clinical Affairs Staff to inspect facilities and records or delinked records as applicable. • Refrain from promoting investigational materials. • Retain study records according to Phase Diagnostics and country specific regulations.
Sponsor (Phase Diagnostic Inc.)	• Provide approved Study Protocol. • Verify investigators are qualified by training and experience. • Verify IRB approval of protocol has been obtained prior to study initiation. • Verify Clinical Trial Agreement has been fully executed prior to study initiation. • Select qualified monitors. Provide all testing materials needed for the study. Provide Study Protocol, testing instructions and selection criteria for testing sites, operators and participants. Approve selected testing sites and operators. Data review and analysis. • Assign a Monitor to conduct periodic monitoring visits which include, but are not limited to: o Audit case report forms against source documents as appropriate and verify accuracy and completeness. o Document and investigate missing data. o Review investigator files for completeness and compliance with the protocol and other appropriate regulations. o Review adverse events/serious adverse events reports and comply with country specific reporting legislation, if applicable. o Prepare written reports of each visit which include but are not limited to: visit date; monitor name; site name; PI name; findings; and actions taken if any. o Provide consolation at Investigator's request.

BACKGROUND / RATIONALE

Coronaviruses are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as MERS and SARS-CoV. A novel coronavirus (SARS-CoV-2) was discovered in December 2019 and has resulted in millions of confirmed human infections worldwide[1]. COVID-19, the disease brought on by the virus, produces symptoms in infected patients that are similar to the other viral respiratory diseases including fever, cough, and shortness of breath[2]. The median incubation time is estimated to be approximately 5 days with symptoms estimated to be present within 12 days of infection[3]. As the number of SARS-CoV-2 infections continues to increase, there is growing demand for diagnostic tests that can produce rapid, accurate and accessible results.

To help address this need, the goal of the project is to develop a low-cost, non-invasive rapid point-of-care diagnostic test for the qualitative detection of SARS-CoV-2 in respiratory specimens. Current methodology for detecting SARS-CoV-2 is a molecular-based test that utilizes RT-PCR. This is a laborious process that requires expensive equipment and reagents, special training, and can take hours until test results are available. The PHASE Diagnostics rapid test is a qualitative lateral-flow immunoassay to determine the presence of SARS-CoV-2 in respiratory samples in a single hand-held device, with a time-to-result of 15 minutes.

PRODUCT DESCRIPTION AND INTENDED USE

The INDICAID Rapid Antigen Test Kit includes 25 individually sealed single-use Test Devices, 25 Buffer Solution Vials, and 25 sterile Nasal Swabs. A Quick Reference Instruction Sheet is provided with each test kit.

The INDICAID COVID-19 Rapid Antigen Test (INDICAID Rapid Test) is a lateral flow immunoassay (LFA) intended for the qualitative detection of nucleocapsid protein antigen from SARS-CoV-2 in direct nasal swabs from individuals suspected of COVID-19 by their healthcare provider within the first 7 days of symptom onset.

In the USA, testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform moderate, high, or waived complexity tests. The INDICAID Rapid Test)is intended for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation. The test is intended for use by medical professionals or trained personnel specifically instructed and trained in the techniques of in vitro diagnostic procedures and proper infection control procedures, and individuals similarly trained in point of care settings but who are not laboratory professionals.

Positive results are for the identification of SARS-CoV-2 nucleocapsid antigen. This antigen is generally detectable in upper respiratory samples during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

Negative results should be treated as presumptive, do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19, and confirmed with a molecular assay, if necessary, for patient management.

PRINCIPLE OF TEST

The INDICAID Rapid Test is a chromatographic rapid test (approximately 20 minutes) that uses a sandwich immunoassay design to directly and qualitatively detect the presence or absence of SARS-CoV-2 nucleocapsid protein. The results of the test are visually interpreted.

After collecting the swab, the patient's sample is placed in the Buffer Solution Vial containing an extraction buffer. The sample is dispensed into the sample well of the test device and migrates through the test strip that contains antibodies conjugated to a chromophore (detector particle). This antibody-chromophore conjugate will bind to the nucleocapsid protein of the SARS-CoV-2 virus if present in the sample. The sample continues to flow through the test strip and is trapped by capture antibodies, which can be visually observed by the presence of the test line ("T").

STUDY OVERVIEW

The purpose of this study is to evaluate the clinical performance of the INDICAID Rapid Test. This will be established by determining the positive percent agreement (PPA), negative percent agreement (NPA), and overall percent agreement (OPA) between the results of the test under investigation and an EUA-approved RT-PCR test, using clinical samples collected from COVID-19 symptomatic individuals. A minimum of 30 RT-PCR SARS-CoV-2 positive and 30 negative patients are required to assess the clinical performance.

STUDY OBJECTIVE

The objective of this study is to assess the clinical performance of the INDICAID Rapid Test device in the hands of the intended user at the point-of-care (POC) setting.

SITE REQUIREMENTS

Target sites include point-of-care clinic and testing settings with non-laboratory healthcare professionals located in the US.

Study sites agrees to the following:

- Strictly adhere to the testing procedures outlined in this study protocol.
- Obtain informed consent for each patient (participant) enrolled.
- Provide complete and legible data and information.
- Adhere to applicable rules of human subject protection when collect patient specimens (21 CFR Part 50 and 56.103(a).
- Collect specimens in accordance with the collection method needed for the comparator method (RT-PCR test)

STUDY DESIGN

Study Duration

This study will take place across 2 testing sites for 60 days or until patient enrollment targets are met (minimum of 30 RT-PCR SARS-CoV-2 positive and 30 negative patients).

Sample Enrichment

In order to enrich for positive patient samples, we will be enrolling patients who have previously been tested with an FDA EUA approved Antigen Test until we obtain the required 30 positive and 30 negative specimens (as tested by the comparator RT-PCR test).

STUDY MATERIALS

Provided to each site

- INDICAID COVID-19 Rapid Antigen Test kits labeled “For Investigative Use Only”.
- INDICAID COVID-19 Rapid Antigen Test Quick Reference Guide
- Contrived samples for testing (10 positive and 10 negative)
- Clinical study materials, forms, and templates

Materials Needed (at each site)

- Sample collection kit (comparator FDA EUA RT-PCR test)

STUDY PROCEDURES

Informed Consent

In order to protect the rights, safety, and welfare of subjects, the study is conducted in accordance with the 21 CFR 50, Protection of Human Subjects. Prior to study enrollment, each subject will be asked to voluntarily provide his or her oral consent after being provided the IRB-approved Research Information Sheet. The Investigator or designee will explain the nature, purpose, expected duration, and risks of study participation. Each potential subject will have the opportunity to ask questions and receive answers from personnel conducting the study. All subjects will be provided a copy of the Research Information Sheet.

Study Participant Enrollment and Eligibility Criteria

Study participants must meet the eligibility criteria listed below in order to be enrolled in the study.

Inclusion Criteria

- Study participant has provided verbal informed consent as required by reviewing institutional review board (IRB). The Experimental Bill of Rights will also be provided for all study participants enrolled in applicable states.
- Study participant is at least 5 years of age. Participants under 18 years old requires parental/legal care provider consent.
- Study participant reports at least 2 of the following COVID-19 symptoms:
    - Fever or chills
    - Fatigue
    - Sore throat
    - Congestion or runny nose
    - Cough
    - Headache
    - Diarrhea
    - Shortness of breath or difficulty breathing
    - Muscle or body aches
    - New loss of taste or smell
    - Nausea or vomiting
- On-set of symptoms must be within 7 days.
- Study participant has been previously tested with an FDA EUA SARS-CoV-2 Antigen test as part of the clinic site standard of care and with test results known.
- Study participant agrees to provide the following specimens for this study:
    - Three (3) clinician-collected nasal swabs (two swabs to perform sequential INDICAID Rapid Tests and a third to perform the comparator FDA EUA RT-PCR test. See below for sample collection instructions)

Exclusion Criteria

- The study participant has been previously enrolled to the study
- Participant is under the age of 5 years
- Participant does not consent
- Participant cannot provide the required samples
- Patient is asymptomatic

Specimen De-Identification

Study specimens will be identified by a study-specific ID number and will not contain any additional protected health information (PHI).

Study Participant Withdrawn or Excluded After Enrollment

If, after enrollment, a study participant is found to have not met an inclusion criterion, the study participant will be withdrawn from the study and any completed test results will be excluded from data analyses.

Operator Background

All study operators are to be non-laboratory, healthcare professional personnel. Between the 2 sites a minimum of 5 operators shall be enrolled to perform the testing.

Order of Specimen Collection

Specimen collection for testing with the INDICAID Rapid Test and the comparator RT-PCR test will take place after standard of care and will be randomly assigned.

INDICAID Specimen Collection and Testing Procedure

- INDICAID Rapid Test specimens will be collected and tested according to the INDICAID COVID-19 Rapid Antigen Test Quick Reference Guide.
- Each operator shall test a minimum of 3 positives and 3 negatives
- Operator ID, Patient ID, Date of Collection and test results (presence or absence of Control Line and Test Line and positive or negative results interpretation) are to be recorded on the Data Collection Form provided.
- INDICAID Rapid Test results will not be disclosed to the patient. COVID-19 disease state will be based on the Standard of Care procedures at the clinical site.

Comparator Test Specimen Collection and Testing Procedure

- Comparator FDA EUA RT-PCR test specimens will be collected and shipped to a CLIA certified laboratory, Warrior Diagnostics, Loveland Colorado (or equivalent site and method to be approved by Phase Diagnostics) according to the sites' Standard of Care procedures for RT-PCR Testing.
- Operator ID, Patient ID, Date of Collection and results from the laboratory testing service provider are to be recorded on the Data Collection Form.

- Comparator test results will not be disclosed to the patient. COVID-19 disease state will be based on the Standard of Care procedures at the clinical site.

Bias Minimization and Elimination

To minimize bias in specimen analysis by the INDICAID Rapid test, the following practices will be employed:

- Each site will be identified with a numerical ID code
- Patients eligible for the study will be screened by a separate clinic personnel not involved in collecting patient samples or performing the INDICAID Rapid Test.
- Operators collecting the patient samples and performing the INDICAID Rapid Test shall be blinded to the result of any prior rapid antigen test or comparator RT-PCR test.

Storage Handling and Shipment

The specimens to be tested on the INDICAID Rapid test shall be tested immediately upon sample collection at the testing site with no storage of the sample. Specimens collected to be tested using the RT-PCR test shall be stored in the following manner:

Temperature Storage	Time Stored
2-8°C	Samples shipped overnight on ice packs within 24 hours of collection

Shipping of biological samples should be done to IATA standards using the appropriate packing materials.

INVESTIGATIONAL DEVICE STORAGE AND DISPOSITION

Each site will be responsible for documenting the receipt, maintain proper storage and proper use of the INDICAID Rapid Test kits as prescribed. Any discarded test device shall be documented and remaining test devices returned to Phase Diagnostics.

RISK / BENEFIT ANALYSIS

Potential Risks Associated with the Study

There is potential risk of exposure to the Coronavirus Disease 2019 and other pathogen to the site operator. The selected site ensures that associated risks are mitigated by employing appropriate state and local safety measures. Refer to the CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Covid-19, https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

Reporting Adverse Events

No adverse events (AEs) are anticipated for this study. The study is performed entirely *in vitro*. The INDICAID Rapid Test is for investigative use only and labeled accordingly. Test results obtained with the INDICAID Rapid Test are not reported to the appropriate health authorities or used as a diagnosis or determine a treatment method.

If an AE or unanticipated adverse device effect (UADE) occurs during a study, the PI shall report the occurrence to Phase Diagnostics Clinical Affairs within 24 hours of the PI first learning of the event. Phase Diagnostics Clinical Affairs will evaluate the AE of the UADE as soon as it is received. Phase Diagnostics will report the AE or UADE according to local and country specific reporting requirements, all governing institutional review boards (IRBs), and all participating PIs.

DATA AND RECORDS MANAGEMENT

Study Data and Records Maintenance

According to 21 CFR 812.140(d), Investigators are required to maintain records for a period of two years after the later of the following two dates: (1) the date on which the investigation is terminated or completed or (2) the date that the records are no longer required for purposes of supporting a premarket approval application, a notice of completion of a protocol development protocol, a humanitarian device exemption application, a premarket notification submission, or a request for De Novo classification. Study binders will be provided to each site to organize the required study records and documentation. Each site will be directly responsible for the maintenance and organization of the study documentation. During and after the study, all the information will be submitted to reviewed by Phase Diagnostics to ensure that any missing information is obtained or that any conflicting documentation is resolved.

MONITORING PLAN

Contact with the PI and study personnel will be maintained by Phase Diagnostic Clinical Affairs representatives primarily the Phase Diagnostic Clinical Study Monitor through periodic site visits, telephone calls, and e-mail. The purpose of site visits will be, verify adherence to the study protocol, and review all study-related documentation and records. A site initiation visit will be conducted to confirm preparedness for protocol execution, confirm satisfactory site facilities, review and clarify regulations and protocol requirements, and train the site personnel prior to activating the site for enrollment. On-site and remote interim monitoring visits will be conducted as needed. A close-out visit will be conducted to ensure all study data and documentation is complete and accurate.

STATISTICAL METHODS

This section describes the overall approach to data analysis. This proposed design enables evaluation of variance over various factors. All data analysis will be performed in accordance with general principles espoused in CLSI EP12[4].

Statistical Analysis Plan

		Reference Test RT-PCR		
INDICAID COVID-19 Rapid Antigen Test		Infected	Not Infected	Total
	Positive	TP	FP	TP+FP
	Negative	FN	TN	FN+TN
	Total	TP+FN	FP+TN	TP+FP+FN+TN

TP = true positive
TN = true negative
FP = false positive
FN = false negative
PPA = TP/(TP+FN)
NPA = TN/(TN+FP)
OPA = (TP+TN)/Total Samples

The following performance characteristics will be computed: PPA, NPA, OPA and accuracy. The 95% confidence interval for these performance characteristics will be computed using Wilson-Score method.

ADMINISTRATION

Site Qualification

All sites will be assessed and approved by PHASE staff prior to the start of the study to ensure that each site has the proper procedures, equipment, and personnel in place to conduct the trial in accordance with the approved protocol and to abide by the principles of Good Clinical Practice (GCP), Good Laboratory Practice (GLP), and applicable United States Food and Drug Administration (FDA) regulations. The sponsor reserves the right to disqualify any site for failure to follow the study protocol, and substitute with a new site that meets these and other study protocol requirements.

IRB Review and Approval

Institutional Review Board approval will be obtained for the study protocol.

Training

Site personnel shall be trained prior to performing any study procedures. Training shall include, but is not limited to, the study protocol, personnel responsibilities, specimen documentation, data recording and reporting, specimen handling and shipping, and transmission of the data to Phase Diagnostics.

Protocol Deviations

Deviations from the study protocol is not allowed. Any proposed (planned) deviation will be documented by the Site Administrator or PI. PHASE will review and assess the proposed deviation prior to approving/rejecting the deviation. Unplanned deviation will be documented and reported to the PI and Phase. Phases will determine whether or not the deviation has affected the validity of any associated results.

REFERENCES

1. Johns Hopkins University, Coronavirus Resource Center. https://coronavirus.jhu.edu/. Accessed October 3, 2020.
2. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-2019). https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html.
3. Lauer SA, Grantz KH, Bi Q, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med*. 2020;172(9):577-582. doi:10.7326/M20-0504
4. NCCLS. *User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline*. NCCLS Document EP12-A [ISBN 1-56238-468-6]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA; 2002.

REVISION HISTORY

Revision Number	Effective Date	Summary of Changes	Author
1.0	November 6, 2020	New protocol	