Unique Protocol ID: NOWDx COVID-19 Antibody POC

Brief Title: NOWDx Test for the Detection of Antibodies to COVID-19

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Study Title:	NOWDx COVID-19 EUA Blood Test CLIA Waiver Trial
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Reference:	None

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Abstract

This study is designed to test the performance and demonstrate effectiveness of the NOWDiagnostics, Inc. (NOWDx) COVID-19 Test for the detection of antibodies in response to SARS-CoV-2 infection. ADEXUSDx® is the registered brand of the COVID-19 antibody test intended for point of care (POC), also known as CLIA waived, use.

The study will be performed by CLIA waived site operators, representative of intended users of the ADEXUSDx® COVID-19 Test, to support U.S. Food and Drug Administration (FDA) Emergency Use Authorization (EUA) of the device. Site operators will perform tests on enrolled participants via finger stick method with capillary blood.

Venous whole blood samples will also be collected from participants per local standard phlebotomy procedures at the study sites and will be used by site operators to perform tests via transfer device method.

Background Information and Rationale

On February 4, 2020, the Secretary of Health and Human Services (HHS) determined that there is a public health emergency and that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the novel coronavirus (SARS-CoV-2). Rapid detection of coronavirus 2019 (COVID-19) cases in the United States requires wide availability of diagnostic testing to control the emergence of this rapidly spreading, severe illness. In light of this public health emergency, NOWDiagnostics Inc. elected to develop and manufacture a COVID-19 serological diagnostic test that identifies total immunoglobin (IgM, IgG, and IgA) to SARS-CoV-2. The FDA has issued guidance describing a policy for laboratories and commercial manufacturers to help accelerate the use of tests developed in order to achieve more rapid and widespread testing capacity in the United States. According to said FDA guidance, clinical accuracy should be established on human specimens from patients with microbiologically confirmed COVID-19 infection using an emergency use authorized assay in addition to human specimens from patients negative for COVID-19 using an emergency use authorized assay.

Study Objectives

The purpose of this study is to generate NOWDx COVID-19 Test performance data to support FDA POC EUA of the device with capillary blood from a finger stick, and POC EUA of the device with venous whole blood from a blood draw.

Study Duration, Planned Enrollment, and Number of Sites

Studies will be performed for the period July 20, 2020 through Aug 31, 2020. Total planned enrollment is 60 study participants. Studies will be performed at CLIA waived study sites. Participants will be varied in age, gender diverse, ethnically and racially diverse, economically diverse, and with different levels of education.

Study Population, Inclusion and Exclusion Criteria

The following cohorts will be prospectively recruited and enrolled in this study:

<u>Clinical Study Cohorts:</u>

- Cohort: Persons who have tested positive for COVID-19 with an emergency use authorized molecular (PCR) test and can furnish said test report; ≥ 7 days post emergency use authorized molecular (PCR) test
    - n=30

  - Inclusion criteria: Persons who have tested positive for COVID-19 with an emergency use authorized molecular (PCR) test and can furnish said test report; ≥ 7 days post emergency use authorized molecular (PCR) test
  - Exclusion criteria: persons <18 years old; persons with limited or no reading skills; persons who have previously participated in a NOWDx study; < 7 days post emergency use authorized molecular (PCR) test

- Cohort: Persons who have tested negative for COVID-19 with an emergency use authorized molecular (PCR) test and can furnish said test report; 0-6 days post emergency use authorized molecular (PCR) test
  - n=30
  - Inclusion criteria: Persons who have tested negative for COVID-19 with an emergency use authorized molecular (PCR) test and can furnish said test report; 0-6 days post emergency use authorized molecular (PCR) test
  - Exclusion criteria: persons <18 years old; persons with limited or no reading skills; persons who have previously participated in a NOWDx study; > 6 days post emergency use authorized molecular (PCR) test

Any person who does not meet inclusion criteria will be declined participation in the study. If a person is eligible for study participation in a cohort that has met the enrollment quota designated by NOWDx, he or she will be declined participation in the study.

Study Design

Recruitment, Screening, Consent, and Enrollment

Recruitment materials for this study (flyers, social media advertisements, and classified website advertisements) may be used to direct interested participants to the study sites for screening. See **Appendix A. Recruitment Materials**. Designated operators will screen each interested person via telephone for potential eligibility using a script. See **Appendix B. Phone Screening Script and FAQ.** Phone Screening Script responses will be recorded. If qualified, persons will be identified by designated operators as eligible for enrollment in a study cohort. Screened and eligible persons will be directed to a study site for enrollment. Enrollment eligibility information shared with site operators who will perform the study will be limited to general eligibility for the 'Clinical Study'. Specific cohort eligibility information will not be shared with site operators who will perform the study. At an active study site, a site operator will review the IRB-approved protocol and initiate the informed consent process. The formal consent of each participant, using the IRB-approved consent form, will be obtained before the participant engages in any study procedure. All prospective participants for the study will be provided with a consent form describing this study and will be given sufficient information in language suitable for persons to make an informed decision about their participation in the study. The site operator obtaining consent will thoroughly explain each element of the document including the purpose and requirements of the study. The consent process will take place in a quiet and private room or space, and persons may take as much time as needed to decide about their participation. Privacy will be maintained and questions regarding participation will be answered. No coercion or undue influence will be used in the consent process. The participant will be informed of any risks or discomforts he or she may experience during the study conduct. The consent form must be signed and dated by the participant. A copy of the signed and dated consent will be given to the participant, and the informed consent process will be documented in each participant's research record. A statement offering the participant the opportunity to withdraw from the study at any time without consequences will be provided. If the person declines consent, they will not be enrolled in the study. All consenting persons will be enrolled as participants.

Study Procedures

Herein, we present study procedures for the 'Clinical Study':

- Site operator 1 will create a participant ID.
  Note: Specific cohort assignment will not be made until study visit is complete.
- Site operator 1 will provide the participant with a demographic survey to complete (see **Appendix C. Demographic Survey of Participant**). Participant will complete the survey.
- Site operator 1 will read the Finger Stick Method (Waived) Instructions For Use and perform the ADEXUSDx® COVID-19 Test on the participant according to the instructions.
- Site operator 1 will complete a Case Report Form of Site Operator 1.
- Site operator 1 will complete a Post-Study Survey of Site Operator 1.
- A site operator will label one (1) EDTA/lavender-top tube with participant ID using labels printed in advance of study.
- A healthcare professional with appropriate phlebotomy training, using standard phlebotomy procedures, will collect one tube of blood from the participant (one EDTA/lavender-top tube), then gently invert the tube eight (8) times immediately to evenly distribute the additive.
- Site operator 2, blinded to the result of site operator 1, will read the Transfer Device Method (Waived) Instructions For Use and perform the ADEXUSDx® COVID-19 Test according to the instructions using blood from the EDTA/lavender-top tube.
- Site operator 2 will complete a Case Report Form of Site Operator 2.
- Site operator 2 will complete a Post-Study Survey of Site Operator 2.
- A trained laboratorian will prepare the sample for shipment according to the following specimen handling instructions:
  - For the EDTA/lavender-top tube:
    - *Note: Must be maintained at 2-8°C while handling.*
    - Centrifuge at high speed for 10-15 minutes, then immediately pipette the plasma into a transport tube.
    - Label the tube with subject ID, write 'Plasma' on the tube, ensure the cap is screwed on tight, and wrap in parafilm.
    - Store at -20°C for frozen shipment to NOWDx.
- The participant will return their demographic survey to a site operator.
- A site operator will complete a study visit checklist and incentive receipt form and obtain the signature of the participant.
- The participant will be compensated $50 by a site operator.
- A positive COVID-19 result with a NOWDx COVID-19 Test may be an indicator of an active or past SARS-CoV-2 infection. Participants with positive results will be referred for follow-up with their healthcare provider.
- All study forms will be sent to NOWDx daily.
- All remaining samples will be bulk shipped to NOWDx at the conclusion of the study for further testing as needed.

Statistical Considerations

The study is designed to support POC EUA of the ADEXUSDx® COVID-19 Test. Clinical study data will be analyzed to assess the performance of the NOWDx COVID-19 Test. Specifically, specificity and sensitivity of the NOWDx COVID-19 Test will be determined relative to an emergency use authorized molecular (PCR) assay. The data must demonstrate a minimum overall 90% positive percent agreement (PPA) and overall 95% negative percent agreement (NPA) with point estimates not lower than 90% for combined PPA and not lower than 93% for combined NPA.

All data will be subject to performance of routine interim analyses. Results from interim analyses will help determine if the clinical trial needs to be halted due to study performance problems.

Study Administration

Data Collection and Management

A data management plan (DMP) will serve as an outline for how data are to be handled during the study and after the study is completed.

Each study site PI will carefully monitor study procedures to protect the safety of study participants, the quality of the data, and the integrity of the study. All participant study materials will be assigned a unique identifying code called a Participant ID. The key to the code will be kept in a password protected file for the duration of the study. Only IRB approved study personnel at the Sponsor and the study site will have access to the code and information that identifies site specific study participants.

Paper or electronic study documents may be used in this study. Site operators will be given detailed operator instructions. All paper study documents must be scanned and emailed daily to clinicaltrials@nowdx.com. If internet connectivity is impaired, paper forms may be faxed to 479-927-6383 initially, then scanned and emailed upon reactivation of internet connection.

All paper study documents received from the sites will be stored on Microsoft SharePoint. Data will be entered into the database and are subject to independent data entry review at the time of data entry and during database audits. All EUA molecular (PCR) test reports received will be stored on Microsoft SharePoint. These data are also subject to independent data entry review at the time of data entry and during database audits.

Database audits will be performed bi-weekly and prior to performance of biweekly interim analyses to ensure reconciliation of relevant data (e.g. survey data, other relevant study forms).

The FDA and local regulatory authorities may inspect all study documents. If any results of the study are published, participant data will be de-identified.

Regulatory and Ethical Considerations

The study may be prematurely terminated due to the following events:

- Serious adverse event determined to be related to the NOWDx COVID-19 Test
- Interim analyses of study data show poor correlation of the NOWDx COVID-19 Test
- Any other unforeseen reasons

NOWDx will ultimately determine if the study or portions of the study need to be terminated prematurely. Study records will be made available for monitoring, auditing, IRB review, and regulatory inspection.

The protocol, informed consent document, and other relevant study documents will be submitted for IRB review and must be approved before the study is initiated. In addition, any subject recruitment materials must be approved by the IRB prior to being used.

Any changes to the protocol, informed consent form, or other relevant study documents will be submitted for IRB review and approval before implementation. A protocol change intended to eliminate an apparent immediate hazard to subjects may be implemented immediately provided the reviewing IRB is notified per their relevant policies.

This study will be conducted in accordance with all applicable government regulations and local institutional research policies and procedures.

Risks and Benefits

The possible risks associated with participating in this study are described in this section. The risks to a healthy person of donating small blood samples from a finger stick or venipuncture are very small. Possible risks include

bruising, pain, soreness, bleeding, infection, or inflammation of the puncture sites, and light-headedness or fainting. The discomfort of the procedure is the same or less as a routine blood draw. In addition to the risks listed above, participants may experience a previously unknown risk or side effect. This research project is not expected to present additional risk to the fetus for pregnant women as samples collected from pregnant women will be like those collected over the normal course of pregnancy. Risk for infection is minimized in the study design by providing instructions to use an alcohol swab on the area of specimen collection prior to finger stick to disinfect the puncture surface. The same risk is minimized by disinfection using alcohol swabs at the site of puncture prior to venipuncture, which is common practice in standard of care. Risk for pain during capillary blood collection is minimized through utilization of the Unistik Comfort Zone Technology®, technology inherent in lancets to be employed for all finger stick study procedures and designed to reduce pain for more comfortable sampling.

Possible Risk/Side Effect	**How often has it occurred?**	**How serious is it?**	**Can it be corrected?**
Infection	Extremely uncommon	Very serious	Report to a healthcare professional immediately for assessment and possible antibiotic treatment
Light-headedness	Common	Can be easily treated	If you feel dizzy, tell a healthcare professional. The feeling will pass after you rest and drink fluids.
Bruise on finger	About half of people	Can be easily treated	No long-term effects
Pain	Common	Mild	No treatment needed
Soreness	Uncommon	Mild	No treatment needed
Excessive Bleeding	Extremely uncommon	Can be easily treated	No long-term effects
Inflammation of site	Extremely uncommon	Can be easily treated	Usually goes away without treatment

There will be no direct benefits to the study participants; however, knowledge gained from the study could potentially benefit participants in the future.

Informed Consent and HIPAA Authorization

The Informed Consent will include HIPAA Authorization. Specifically, participants will provide explicit authorization to use or disclose their protected health information (PHI) required for study performance and prior to study enrollment.

The Informed Consent specifies PHI to be provided by participants during study conduct, specific information about who may use or disclose the PHI as a direct result of the participant providing authorization, and details of each use or disclosure that will be a result of the authorization. An individual providing authorization must understand any way that their information is planning to be used or disclosed. The Informed Consent also specifies the date of expiration where the authorization is no longer valid, and PHI can no longer be used or disclosed. Finally, all prospective participants must provide their authorization via signature on the Informed Consent.

Safety Monitoring

The study site PI or designated site operator at the study site will be responsible for monitoring the participant for any adverse event (AE) and/or serious adverse event (SAE). All AEs and SAEs will be recorded on the relevant participant case report form as well as an Adverse Event/Serious Adverse Event Report Form. All SAEs will be reported to NOWDx using the designated form within 24 hours of the site learning of the event. The study

site PI will be responsible for follow-up of any SAE until a final outcome is established and the outcome is recorded in the Adverse Event/Serious Adverse Event Report Form.

AEs will include any unfavorable and unintended sign, symptom, or disease temporarily associated with the use of a NOWDx COVID-19 Test.
SAEs will include any event that results in death, is life-threatening, requires hospitalization (admission for longer than 24 hours or prolongation of a current hospital stay), results in disability or permanent damage (substantial disruption of a person's ability to conduct normal life functions), or requires intervention to prevent permanent impairment or damage.

Retaining Samples

Following clinical study performance by site operator 2 of the ADEXUSDx® COVID-19 Test according to the Transfer Device Method (Waived) Instructions for Use, plasma sourced from EDTA/lavender-top tubes will be frozen and shipped to NOWDx.

Plasma may be used to perform necessary analytical or clinical tests to support FDA EUA or clearance of the NOWDx COVID-19 Test including, but not limited to, repeat testing in the event of invalid or discrepant test results or additional testing requested by the FDA following EUA or 510(k) CLIA Waiver submissions.

With participant consent, remaining plasma samples may be stored deidentified indefinitely following clearance of the NOWDx COVID-19 Test for future testing to support additional NOWDx COVID-19 Test indications for use, such as expanded use of the NOWDx COVID-19 Test with an analyzer. Remaining samples will not be shared with secondary researchers.

References

1. US Food and Drug Administration (FDA) Policy for Coronavirus Disease-2019 During the Public Health Emergency (Revised), Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff Document issued on the web on May 4, 2020.
2. Laboratory biosafety guidance related to coronavirus disease 2019 (COVID-19). World Health Organization. Interim guidance. 12 February 2020.

Appendices List

Appendix A. Recruitment Materials
Appendix B. Phone Screening Script and FAQ
Appendix C. Demographic Survey of Participant