Title:	Performance Evaluation of the Lucira COVID-19 & Flu Test versus FDA cleared/authorized SARS-CoV-2 and Influenza A&B Assays
Protocol Number: **Date:**	09A-CLI-001 Rev. B 01 Aug 2022
Sponsor:	Lucira Health 1412 62nd Street Emeryville, CA 94608
Department:	Clinical Affairs (510) 350-8071
Primary Contact:	PPD
Secondary Contact:	PPD

FOR INVESTIGATIONAL USE ONLY

The use of this device is limited by Federal law to investigational use. The performance characteristics of this device have not been established.

Protocol Signature Page

Study Acknowledgement/Confidentiality

By signing this protocol, the Investigator(s) acknowledges and agrees:

The protocol contains all necessary details for conducting the study. The Investigator shall conduct this study as detailed herein, in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirements. In addition, the Investigator shall make every reasonable effort to complete the study within the time designated.

This Protocol is designed to meet the regulatory requirements for COVID-19/Influenza Molecular Tests designed for the qualitative detection of SARS-CoV-2 and Influenza A & B. This Protocol, furnished by the Sponsor, Lucira Health, will be made available to all physicians, nurses, and other personnel who participate in the conducting of this study. The Investigator shall discuss this material with them to assure that they are fully informed regarding the conduct of the study.

This document contains information that is privileged or confidential. As such, it may only be disclosed in accordance with the clinical trial agreement, or disclosures required by federal laws or other regulations. Persons to whom any of this information is to be disclosed must first be informed that the information is confidential. These restrictions on disclosure will apply equally to all future information supplied, which is indicated as privileged or confidential.

The Sponsor anticipates utilizing the data from this study for submission to government regulatory authorities and possibly in publication of the results of the study.

The conduct and results of this study shall be kept confidential.

Where it is the intention of the Sponsor to file for patent or other intellectual property right protection, publication may be deferred at the opinion of the Sponsor for up to eighteen months from the date of completion of the proposed joint publication to allow the Sponsor to make all filings it deems appropriate.

Investigator Details & Signatory

Protocol Number	09A-CLI-001 Rev. B	
Title	Performance Evaluation of the Lucira COVID-19 & Flu Test versus FDA cleared/authorized SARS-CoV-2 and Influenza A&B Assays	
Site Name/ Address		
Principal Investigator Name	Principal Investigator Signature	Date

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) and the following:

United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 812)

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

1 ABBREVIATIONS AND DEFINITIONS

Abbreviation	Description
AE	Adverse Event
CFR	Code of Federal Regulations
CRF	Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IRB	Institutional Review Board
ISO	International Organization for Standardization
NA	Not Applicable
NAV	Not Available
ND	Not Done
PHI	Protected Health Information
PI	Principal Investigator
QRI	Quick Reference Instructions
SAE	Serious Adverse Event
UADE	Unanticipated Adverse Device Events
UNK	Unknown

Abbreviation/Term	Description
Adverse Event (AE)	Any untoward medical event that occurs to a subject during a study (with onset after first study-specific procedure), whether or not that event is considered study-related
Case Report Form (CRF)	A printed, optical, or electronic document designed to record all the information required by the protocol to be reported to the Sponsor on each study subject
Food and Drug Administration (FDA)	An agency of the US government responsible for promulgating regulations and guidelines that further define how to comply with the Food, Drug and Cosmetics Act of Congress. The FDA is authorized to grant marketing approval to new drugs and devices.
Good Clinical Practice (GCP)	A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of the trial subjects are protected
Health Care Professional (HCP)	Person responsible for performing critical study-related procedures
Informed Consent (IC)	A process by which a subject voluntarily confirms his/her willingness to participate in a trial, after having been informed of all aspects of the trial relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.
Informed Consent Form (ICF)	The form prepared by the Investigator/Sponsor and approved by the IRB, which must be signed by a subject before entry in a clinical trial. It is the legal written record that the subject, or his/her representative, agrees to voluntarily participate in the investigation.
Institutional Review Board (IRB)	Any board, committee, or other group formally designated by an institution to review biomedical research involving subjects and established, operated, and functioning in conformance with 21 CFR Part 56
International Conference on Harmonization (ICH)	A committee consisting of US, EU, and Japanese members organized to develop guidelines for the conduct of clinical studies
Investigator	One or more persons responsible for the practical performance of a trial and for the integrity, health, and welfare of the subjects during the clinical study

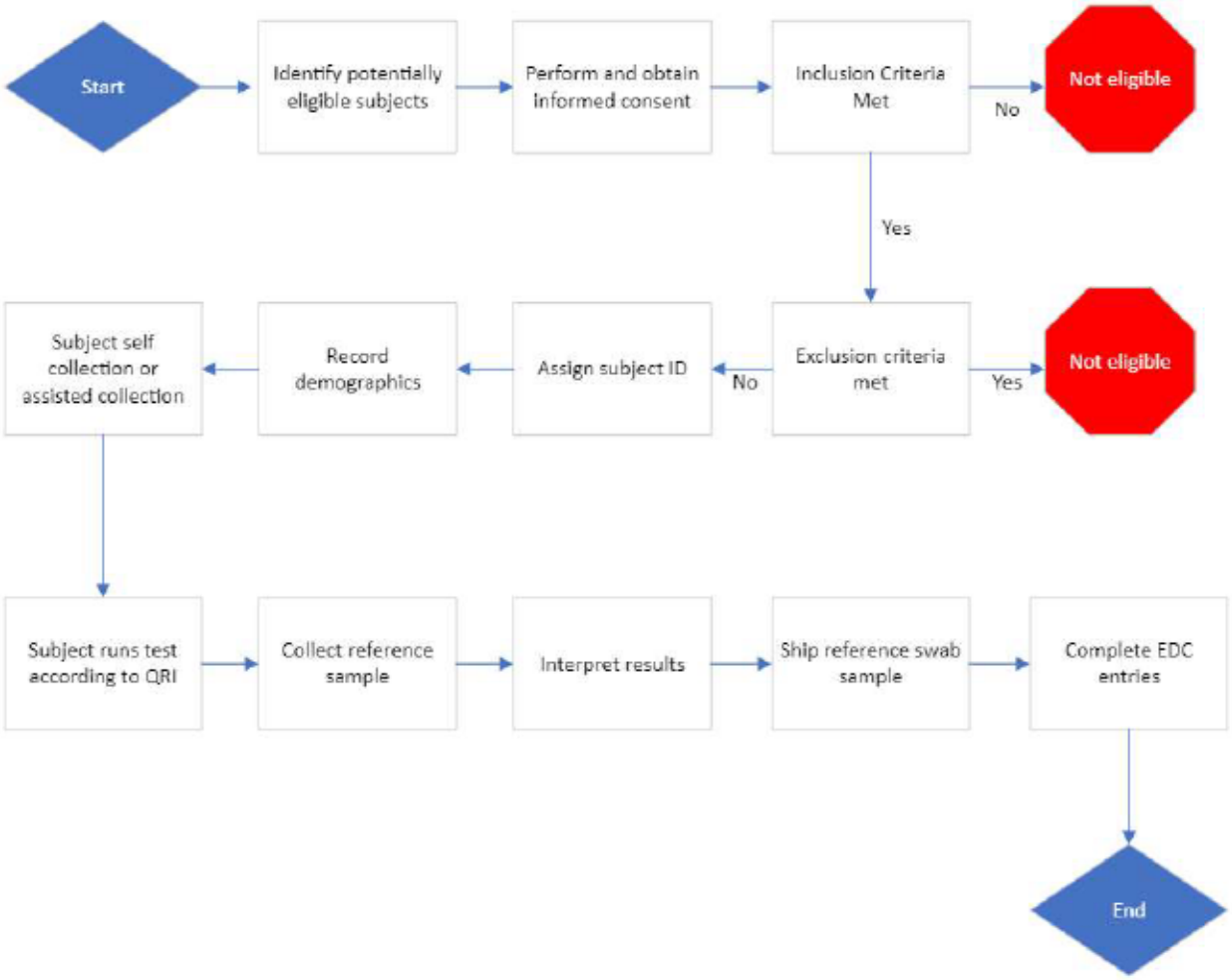
Abbreviation/Term	Description
Subject	A research participant, also called a human subject or an experiment, trial, or study participant or subject, is a person who participates in human subject research by being the target of observation by researchers

1.1 SYNOPSIS

Protocol Title	Performance Evaluation of the Lucira COVID-19 & Flu Test as Compared to FDA cleared/authorized SARS-CoV-2 and Influenza A&B Assays
Protocol Number	09A-CLI-001
Objective(s)	The primary objective is to evaluate the performance of the Lucira COVID-19 & Flu Test as compared to FDA cleared or authorized SARS-CoV-2 and Influenza A&B Assays.
Number of Subjects	Minimum of 1000 Symptomatic subjects
Number of Sites	Minimum of 3 sites from at least 2 geographically diverse locations
Study Duration	At least 12 weeks

Study Design	This study is a prospective, multi-center study to evaluate the performance of the Lucira COVID-19 & Flu Test, a real-time RT-LAMP test intended for the qualitative detection and differentiation of RNA from SARS-CoV-2, Influenza A and Influenza B in self-collected nasal swab samples designed to report rapid test results. The Lucira COVID-19 & Flu Test will be compared with a composite reference method for the detection and differentiation of COVID-19, influenza A and influenza B virus in nasal swabs from patients with signs and symptoms of COVID-19 and/or flu-like illnesses. After determining subject eligibility and following the completion of the informed consent process, each subject will receive a unique study identification number. A subject's participation in this study will consist of one study visit. The subject self-collects a nasal swab sample according to Lucira COVID-19 & Flu Test instructions and runs test according to Quick Reference Instruction (QRI). Following the Lucira COVID-19 & Flu Test self-collection will be an additional swab collection for reference method testing. One (1) additional NS specimen will be collected by the health care professional, prepared in Transport Medium, and sent to the reference laboratory as directed by the Study Operations Manual. Each collection component (investigational product and reference method) may have a maximum of two swabs, including retests, for a maximum of four swabs per visit.
Study Population	Subject demographics including gender, age, education level, employment status, and household income shall be collected.

1.2 SCHEMA



1.3 SCHEDULE OF ACTIVITIES

Procedure	Subject Identification	Enrollment	Swab Collection	Reference Testing
Identify Potential Subjects	X			
Obtain Written Informed Consent	X			
Review Inclusion/Exclusion Criteria	X			
Assign Subject Number to Eligible Subjects		X		
Record Demographics and Baseline Characteristics		X		
Subject self-collects Nasal Swab Sample and starts test running*			X	
Collect Reference Sample			X	
Ship Reference Samples				X
Complete EDC Entries	X			
Adverse Event/Serious Adverse Event Recording		X		

* Subjects 2-13 years old shall have the collection performed by a parent/guardian/adult with their assent

2 INTRODUCTION

The Lucira COVID-19 & Flu Test is a real-time RT-LAMP test intended for the qualitative detection and differentiation of RNA from SARS-CoV-2, Influenza A and Influenza B in self-collected nasal swab samples.

The test consists of a nasal swab, a sample vial the nasal swab sample is placed in to prepare the sample for testing, and a test unit which detects whether SARS-CoV-2, Influenza A, and Influenza B virus is present within the specimen. The Lucira test uses a proprietary, molecular based detection process to detect whether a person is actively shedding the genomic RNA from the SARS-CoV-2, Influenza A, or Influenza B virus.

The purpose of this study is to investigate the Lucira COVID-19 & Flu Test for the in vitro qualitative detection and differentiation of RNA from SARS-CoV-2, Influenza A, and Influenza B in nasal swab specimens from patients suspected of COVID-19 or Influenza A or Influenza B. The primary objective is to test at least 1000 self-collected nasal swab samples for SARS-CoV-2 and Influenza A&B as compared to FDA cleared/authorized SARS-CoV-2 and Influenza A&B Assays.

Data generated collected in this study shall support an FDA and/or other notified body submission(s).

Known Potential Risks

For this study, the risks to human subjects are minimal. Furthermore, the protocol is exempt from IDE according to §812.2(c) of the IDE regulations because it:

- is non-invasive
- does not require an invasive sampling procedure that presents significant risk
- does not by design or intention introduce energy into a subject; and
- is not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure.

The procedures outlined in this protocol do not involve significant risk to subject safety. Subjects will be provided the Investigator's contact information and will be instructed to notify them of any Adverse Events (AE) they experience during or secondary to specimen collection procedures. For all forms of swab collection, there is a minimal risk for visibly bloody swabs.

Known Potential Benefits
There is no direct benefit for a subject's participation.

3 INVESTIGATIONAL DEVICE

3.1 NAME AND DESCRIPTION OF INVESTIGATIONAL PRODUCT

The Lucira COVID-19 & Flu Test is a rapid, single-use, molecular test for the qualitative detection and discrimination of SARS-CoV-2 viral RNA in nasal swab samples.

3.2 INTENDED USE

The Lucira COVID-19 & Flu Test is a single use real-time RT-LAMP test kit intended for simultaneous rapid qualitative detection and differentiation of RNA from SARS-CoV-2, Influenza A, and Influenza B virus from self-collected anterior nasal (nasal) Swab specimens, in individuals aged 14 years and older (self-collected), or individuals ≥ 2 years (collected by an adult) suspected of respiratory viral infection consistent with COVID-19, Influenza A, and/or Influenza B. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2 and influenza can be similar. The Lucira COVID-19 & Flu Test is intended for use as an aid in the differential diagnosis of SARS-CoV-2, Influenza A, and Influenza B, in humans, and is not intended to detect Influenza C.

The SARS-CoV-2, Influenza A, or Influenza B RNA is generally detectable in nasal Swab samples during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2, Influenza A, or Influenza B RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient 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.

Persons who test positive with the Lucira COVID-19 & Flu Test should seek follow up care with their physician, or healthcare provider, as additional testing and public health reporting may be necessary.

Negative results do not preclude infection from SARS-CoV-2, Influenza A, and/or Influenza B and should not be used as the sole basis for treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

This Lucira COVID-19 & Flu Test is intended for self-testing in a non-laboratory setting, or for home use.

Note: This clinical study and study protocol was initiated with the objectives noted in this protocol, namely, to "[…] confirm the Lucira COVID-19 & Flu Test provides similar performance to a high complexity lab molecular diagnostic RT-PR assay(s) with known high sensitivity." While this objective was initially driven by a request by the US FDA, and as such the Intended Use of US product is included here in the protocol, the intent of this study and the potential results of this study are agnostic of any specific market. Any (slight) variability and differences noted in the this Intended Use versus that of the Intended Use(s) approved or authorized any other market is very minor and does not alter the principle mode of action of the device, the intended patient population, or the fundamental Intended Use of the device.

3.3 PRODUCT LABELING

Product will be labeled according to internal procedures and 21 CFR Part 809.10. Investigational material will be labeled minimally Lucira Health's name, expiration date, lot number, storage conditions and the

federal caution statement "For Investigational Use Only. The performance characteristics of the product have not been established."

3.4 STORAGE AND HANDLING

All study supplies should be stored in a controlled location with limited access. the Lucira COVID-19 & Flu Test should not be opened until ready to use. Sample vials and test cartridges should be stored in their foil pouches until testing is performed. Sample vials and test cartridges are for a single use only and should not be reused. Test cartridges that have been out of the desiccated pouch for more than 20 minutes should be discarded. None of the test components should be frozen. All study supplies should be stored at room temperature.

4 OBJECTIVES

The primary objective is to confirm the Lucira COVID-19 & Flu Test provides similar performance to a high complexity lab molecular diagnostic RT-PCR assay(s) with known high sensitivity. The sensitivity and specificity endpoint are PPA ≥80%/NPA ≥98% for COVID-19 and PPA ≥90%/NPA ≥95% for Flu A&B.

5 STUDY DESIGN

5.1 STUDY DESIGN

The study is a prospective with a minimum of three (3) sites in the U.S. will participate in the study. The Investigational device shall be tested on-site, and the reference samples shall be sent a reference laboratory in the U.S. Testing in the reference laboratory will be performed by trained laboratory personnel. This investigational device testing is to be performed in a simulated-home environment with medical staff on site and shall include nasal swabs self-collected by study subjects per the QRI.

A qualified research person will be designated as the Investigator at each site, with the responsibility for oversight of the study in accordance with Good Clinical Practice (GCP) and regulatory requirements. The protocol and subject informed consent will be reviewed by an Institutional Review Board (IRB) and written IRB approval will be issued prior to enrollment of subjects into the study at that site.

A subject's participation in this study will consist of a single visit. Following completion of the informed consent process and a review of Inclusion/Exclusion criteria to determine eligibility, each subject will receive a unique study identification number.

Subjects will then be asked relevant medical history questions, including inquiries regarding the presence or absence of COVID-19 and influenza signs and symptoms, vaccine status and current medications taken. Subject demographics including age, sex, race, and ethnicity should also be collected at this time.

Two (2) swabs should be collected for this study: One (1) nasal swab for the Lucira COVID-19 & Flu Test and one (1) nasal swab for composite reference testing. The Lucira COVID-19 & Flu Test study swabs will be collected as directed in the Lucira COVID-19 & Flu Test Quick Reference Instruction (QRI). The reference method swab collection shall be collected by the HCP and prepared in Transport Medium. Each collection may have a maximum of two swabs, including retests, for a maximum of four swabs per visit. Swab specimens required for standard of care testing should be collected prior to the specimens collected for this investigation.

Subject shall be observed during the swabbing collection by the HCP and HCP shall document collection details and any collection issues. Nasal swabs obtained from self-collection will be discarded after having been used for testing per QRI. HCP to interpret and document results.

Reference lab shall receive study samples and run samples against FDA cleared/authorized approved SARS-CoV-2 and Influenza A&B Assays. Discrepant analysis samples may be run on a separate FDA cleared/authorized SARS-CoV-2 or Influenza A&B Assays.

Reference testing shall characterize specimens as negative or positive for SARS-CoV-2 and Influenza A&B. Therefore, sensitivity and specificity of the Lucira COVID-19 & Flu Test will be calculated by comparison with the reference methods.

Upon study completion, remnants should be returned to the Sponsor.

5.2 SUBJECT DE-IDENTIFICATION

Each subject will be identified with a unique number. All forms and documents related to each subject will be labeled with this unique number. At no time shall study paperwork or specimens be marked with a subject's name, any traceable identifier, or Protected Health Information (PHI) except for the ICF, which is signed by the subject and/or parent/guardian. The ICF will be kept separate from the other forms and documents.

5.3 SUBJECT DURATION

The study consists of a single visit. The visit will take approximately 30-45 minutes to compete, and subject participation is complete at the end. Subjects will be provided with the Investigator's contact information and instructed to notify the Investigator if they experience any complications from specimen collection procedures.

Subjects are free to withdraw consent and discontinue participation in the study at any time. A subject's participation in the study may be discontinued at any time at the discretion of the study staff. The following may be justifiable reasons for the study staff to remove a subject from the study:

1. The subject was erroneously included in the study or was found to have an exclusion criterion.
2. The subject is uncooperative or unable to complete the required study tasks
3. The subject experiences an Adverse Event (AE)/Serious Adverse Event (SAE) during the specimen collection procedure that is considered intolerable by subject or Investigator.

To the extent possible, safety data will be collected on subjects who discontinue participation in the study due to safety reasons.

6 STUDY POPULATION

6.1 INCLUSION CRITERIA

1. Individuals aged 14 years and older (self-collected) or individuals less than 14 years old but ≥ 2 years old (collected by an adult)
2. Human subjects suspected of respiratory viral infection consistent with COVID- 19 or Influenza by their healthcare provider within 4 days of symptom onset
3. Must be willing to try Lucira COVID-19 & Flu test with an anterior nasal (nasal) swab specimen collected from both nostrils
4. Subject information shall include: gender, age, collection date, collection time, race, ethnicity, temperature, signs/symptoms, date of symptom onset, symptom severity, vaccination status, household income, education status, employment status, routine test data (results, methodology, date of collection, if available)

6.2 EXCLUSION CRITERIA

1. Currently suffering from nasal trauma such as a nosebleed
2. Received a nasal rinse/wash/aspirates for standard of care testing
3. The subject is undergoing treatment for COVID-19 or Flu currently and/or within the past 14 days of the study visit, including but not limited to: inhaled influenza vaccine (FluMist®) or flu antiviral medication, which may include but is not limited to Amantadine (Symmetrel®), Rimantadine (Flumadine®), Zanamivir (Relenza®), Oseltamivir (Tamiflu®), or Baloxavir marboxil (Xofluza®).
4. The subject is currently receiving or has received within the past 30 days of the study visit an experimental biologic, drug, or device including either treatment or therapy.
5. The subject has previously participated in this research study
6. Incorrect comparator swab type or transport media
7. Incorrect specimen handling
8. Subjects not consented

6.3 SUBJECT COMPLETION, DISCONTINUATION AND WITHDRAWAL

6.3.1 SUBJECT COMPLETION

Subject's participation is complete after sampling procedures. Subjects will be provided with the Investigator's contact information and will be instructed to notify the Investigator if they experience any complications from the specimen collection procedures.

6.3.2 SUBJECT DISCONTINUATION AND WITHDRAWAL

Subjects are free to withdraw consent and discontinue participation in the study at any time. A subject's participation in the study may also be discontinued at any time at the discretion of the Principal Investigator. The following may be justifiable reasons for the Investigator to remove a subject from the study:

- The subject was erroneously included in the study or was found to have an exclusion criterion.
- The subject is uncooperative (i.e., not providing swabs specimens for this research).
- The subject experiences an Adverse Event (AE)/Serious Adverse Event (SAE) during the specimen collection procedure that is considered intolerable by subject or Investigator.

If a subject decides to discontinue participation in the study, information about the reason(s) for discontinuation and recording of any potential AEs should be documented. The Investigator will provide information describing the reason for discontinuation. The Investigator will attempt to follow all AEs until resolution.

7 STUDY ASSESSMENTS AND PROCEDURES

7.1 MATERIALS

7.1.1 MATERIALS PROVIDED BY SPONSOR

- Lucira COVID-19 & Flu Test which includes: 2 AA batteries, Test Unit, Sample Vial, Nasal Swab, and Quick Reference Instruction (QRI)
- Reference Swab Collection Kit including: Nasal swab, 3ml VTM, and biohazard collection bag with absorbent sheet
- Refrigerated shipping containers and shipping supplies
- Case Report Forms (CRF)

Test kits will be provided by the Sponsor and a Test Kit provided to each subject by the Investigator. The Investigator or designee is responsible for maintaining accountability records for all inventory transactions (i.e., receipt, utilization, and return). The investigational product may only be used in accordance with this approved protocol and must not be used for any other purpose. Investigational product may only be used for subjects who have provided written informed consent to participate in this study and meet all inclusion/exclusion criteria.

An Investigational Product Accountability Log details the quantity of the device, the shipment of investigational material, and clinical supplies from the Sponsor or its representative to the Investigator. The Investigator must ensure that the investigational product is maintained at the prescribed environmental conditions in a controlled location with limited access, as directed in the Study Operations Manual.

The Investigator or designee must complete an Accountability Log upon completion or termination of the study. All unused study materials, after device accountability, together with a copy of the Accountability Form, will be returned to the Sponsor or its representative. A copy of all Accountability forms should be retained in the site files.

7.2 SCREENING AND ENROLLMENT

7.2.1 IDENTIFY POTENTIAL SUBJECTS

The potential subject will be asked to provide relevant medical history information regarding COVID-19 and Influenza, which will be evaluated against all inclusion and exclusion criteria. At the time of the study visit, the subject must be suspected of respiratory viral infection consistent with COVID-19 or Influenza by a healthcare provider. To be eligible for this study, subject must also be willing to try the Lucira COVID-19 & Flu test with an anterior nasal (nasal) swab specimen collected from both nostrils. Preliminary assessment of the subject by the Investigator/designee should be suggestive of COVID-19 or Influenza based upon his/her medical judgment.

7.2.2 OBTAIN WRITTEN INFORMED CONSENT

All potential study participants must be given time to review the consent form, have their questions answered to their satisfaction, and complete the IRB-approved informed consent prior to performing any study procedures. The informed consent process will be recorded on the source document to confirm that no study procedures were performed prior to obtaining the subject's consent/assent. Subjects will be given a copy of the informed consent form.

7.2.3 REVIEW INCLUSION/EXCLUSION CRITERIA

The Investigator and/or designee should review all criteria to determine if the subject is eligible for enrollment. Eligibility will be documented in the source document and CRF.

7.2.4 PRIOR AND CONCOMITANT MEDICATIONS AND THERAPIES

No subject should be denied necessary treatment because of being a participant in this study.

7.2.5 RECORD DEMOGRAPHICS, BASELINE CHARACTERISTICS, AND MEDICAL HISTORY

Data shall be documented and recorded during initial study visit.

7.3 PROCEDURE

The Lucira COVID-19 & Flu Test shall be performed before reference test specimen collection at the clinical site. A study staff member will provide each subject with a Lucira COVID-19 & Flu Test Unit. Participants performing the self-collection or assisted collection will be asked to read the Quick Reference Instructions (QRI) .

Participants shall be instructed to begin the Lucira test on their own according to the QRI. This will involve a nasal self-collection and running the test. The study staff shall document all observations during the subject collection. The study staff shall interpret the test result and document the results on the source documentation.

While the Lucira COVID-19 Test is running, the reference nasal swab shall be collected by the study staff. The study staff shall document collection details and ship samples to reference laboratory.

7.3.1 QUALITY CONTROL PROCEDURES

The Lucira COVID-19 & Flu Test does not require an external control be performed.

7.3.2 TESTING PROCEDURE

- Sample Collection and Specimen Testing
  The Lucira nasal swab shall be obtained before the reference test sample is collected. Subjects will be provided with the Lucira COVID-19 & Flu Test and collect one (1) nasal swab according to the QRI. The participant shall test the sample on the Lucira COVID-19 & Flu Test. HCP shall observe the participant during this process and document any observations or deviations from the QRI.
  If a swab is contaminated or the test is invalid, participants will be asked to collect a new sample and test the sample on a new device. The date and time of collection shall be documented. Contaminated swabs (e.g., dropped) should be discarded. One additional attempt shall be made to collect a clean swab.

- Reference Nasal Swab (NS) Collection
  One NS for reference testing shall be obtained from each subject who completes the collection step specified in the QRI and runs the Lucira COVID-19 & Flu Test regardless of result. The reference collection is collected by the study staff.
  If a swab is contaminated or the test is invalid, subjects will be asked to collect a new sample and test the sample on a new device. The date and time of collection will be documented. Contaminated swabs (e.g., dropped) should be discarded. One additional attempt may be made to collect a clean swab.

7.3.3 COMPENSATION

Subjects will be compensated for their visit time and inconvenience. Subjects who are disqualified during the study or are unable to complete the research through no fault of their own may still receive compensation. Compensation may be provided in the form of a Gift card. Proper handling of compensation shall require sites to document individual subject compensation in the associated source documents, followed by tracking in the site Compensation log.

7.3.4 DISPOSAL OF USED TEST UNITS

At the discretion of the Sponsor, all used Test Units may be collected and returned to sponsor for download of internal data and proper destruction of unit.

7.3.5 REFERENCE METHOD AND ADDITIONAL TESTING METHODS

Nasal swab samples are important as they provide a natural nasal matrix to conduct analytical reference testing and research. It is imperative that specimens obtained for reference testing are prepared and shipped to the reference laboratory.

Specimens should be stored refrigerated and shipped daily (within 24 hours of collection). Site staff will receive training from the Sponsor or its representative on procedures required to process specimens for shipment to the reference laboratory. Specimens should be shipped with cold packs to maintain the required temperature (2-8°C). Specimen manifest shall accompany the specimens. Inadequate documentation could result in a delay in testing and possible specimen rejection.

Upon receipt, the reference laboratory shall verify the contents of each shipment and communicate any missing or damaged contents to the Sponsor. Aliquots shall be stored for future testing to be performed both during or after the study. All results shall be communicated to the Sponsor or its representative.

Additional testing for discrepant results may be performed to investigate the discrepancy. The discrepant sample, along with some or all non-discrepant samples, may undergo additional testing.

At the end of the study, at Sponsor's discretion, all residual remnant aliquots remaining at the reference laboratory or additional testing laboratories will be sent to the Sponsor or its representative or destroyed.

7.4 RISKS AND ADVERSE EVENTS

No side effects or adverse effects are anticipated in this study. However, events that may be related to the specimen collection procedure, but result only in local, mild, and transient discomforts include (a) local, mild discomfort or "tickling sensation" in the nose, (b) sneezing, (c) slight gagging or mild irritation in the nose, (d) eye tearing or (e) minor/temporary nosebleed. These risks will not be considered AEs for this study but will be recorded in source documentation.

AEs experienced by the study staff conducting the study shall include any unintended direct contact or bodily exposure to biological fluids or specimens while performing protocol related testing. Personnel performing the test will also be instructed to report any AEs that happen during testing.

The investigator and designated study personnel shall monitor each subject for AEs during the study. AEs reported between consent and completion will be recorded in the Adverse Event Reporting Form. All AEs reported will be tabulated and reviewed during the study in accordance with the procedure for reporting AEs and SAEs.

Follow-up of AEs will occur in accordance with each individual case. Subjects shall be reimbursed for any further medical costs from any treatments or tests that arise because of an adverse event directly related to this study. All AEs reported will be tabulated and reviewed during the study in accordance with Sponsor's or its representative's internal procedures and 21 CFR 812.150 and 21 CFR 812.46.

The study consists of a single visit and there will be no follow-up. The onset for an AE or SAE experienced by a subject will be recorded from the time of signing the informed consent form and assent form, if applicable, until study completion or termination (if self-reported by the subject). The Investigator and/or designee will continue to monitor the subject with additional assessments until the event is considered resolved, stabilized, or is lost to follow-up. The date of resolution will also be recorded on the source document.

The full description of any AE or SAE, including the nature, date and time of onset and resolution, determination of seriousness, frequency, severity, treatment, outcome, and relationship to the study will be recorded on the Adverse Event & Serious Adverse Event Report Form.

SAEs must be reported to Lucira Health or its representative within 24 hours of the Investigator's first knowledge of the event. A completed SAE report and supporting documentation, using the form entitled "Unanticipated Event" form, shall be completed and transcribed into the EDC system within 24 hours of Investigator's first knowledge. Within this same timeframe, an email documenting knowledge of a potential SAE must be sent to Lucira Health Clinical Affairs.

A serious adverse event (SAE) is defined as any adverse event that results in any of the following outcomes:

- Death
- Life-threatening experience
- Required or prolonged inpatient hospitalization
- Persistent or significant disability/incapacity
- Congenital anomaly
- Important medical events that may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed above

Regulatory Reporting Requirements for Adverse Events

The Sponsor is responsible for submitting reports of SAE/UADE events to the FDA within 10 working days of the Sponsor first becoming aware of the event, and follow-ups as requested by the FDA.

IRB Reporting Requirements for Adverse Events

If a subject experiences an Unanticipated Adverse Device Event (UADE) because of this study, the Investigator must submit an Unanticipated Event Form, as per the instructions on the form, to the Sponsor within 24 hours, and the IRB within the time specified by the IRB. Incidents and deviations relating to subject safety and informed consent shall be reported to the Monitor and the IRB. All other AE must be communicated to the Monitor within 24 hours, and the Monitor will then notify the Sponsor. The Monitor shall submit to the IRB per the IRB guidelines.

8 DATA ANALYSIS AND STATISTICAL CONSIDERATIONS

8.1 SAMPLE SIZE

Clinical agreement specimen enrollment shall target 50 positive Flu A, 30 positive Flu B, and 120 positive COVID-19 until at least 1000 negative subjects are recruited to satisfy specificity requirements of ≤98% for COVID-19 and ≤95% for Flu A&B.

8.2 SUBJECT CHARACTERISTICS

The number of patients enrolled in the study, number withdrawn, and reasons for withdrawal shall be summarized.

- Demographics: Subject demographic data will be summarized for the entire study population. Demographic variables will include:
  - Sex
  - Age (years) as a continuous measure and categorized (N, %) by the following age groups:
    - 2 – 5 years
    - 6 – 21 years
    - 22 – 59 years
    - ≥ 60 years

- Unknown
- Race categorized as: American Indian/Alaska Native, Asian, African American/Black, Caucasian/White, Native Hawaiian/Pacific Islander, Other, Unknown, or Refused.
- Ethnicity categorized as: Hispanic or Latino, Not Hispanic or Latino, Other, Unknown, or Not provided.
- Education Level
- Employment status
- Household Income

8.3 DATA ANALYSIS

All summaries and analyses should be presented in tabular or graphical form.

- Analysis Sets

  There will only be one analysis set consisting of samples with valid Lucira COVID-19 & Flu Test results and valid reference results. Valid Lucira COVID-19 Test results may be positive or negative for COVID-19. The percentage of the expected result shall be computed individually along with the associated 95% Wilson Score Confidence Interval for each set.

  For all invalid Lucira COVID-19 & Flu Test results, one additional specimen collection should be attempted, and the Lucira COVID-19 & Flu Test should be re-run with a new Test Kit. If specimen recollection leads to a valid Lucira COVID-19 & Flu Test result, that valid retest result should be reported. If the Lucira COVID-19 & Flu Test result is "Invalid", then this test result shall be considered completely invalid and therefore non-evaluable.

- Prevalence Rate / Expected Values

  Study prevalence of SARS-CoV-2 and Influenza A&B should be summarized by counts and percentages

- Collection Performance/ Incidence Rate

  Relevant study observations should be summarized by counts and percentages:
  - Self-Collection
  - Assisted Collection

- Missing Values

  Missing values should not be imputed for any of the study assessments.

- Data Exclusions

  The following shall result in subjects being removed from final data analysis:
  - Subject withdrawals
  - Subject does not meet inclusion/exclusion criteria
  - Swab specimens were not processed according to protocol
  - Missing results
  - Excluded by an Event

  This analysis should be presented across all study sites and by individual study site.

- Efficacy Analysis

  Sensitivity and specificity along with their associated 2-sided Wilson Score 95% Confidence Intervals will be estimated for SARS-CoV-2 and Influenza A&B on the Lucira COVID-19 All-In-One Test in comparison to the reference test using the formulas below and a 2 x 2 contingency table (Table 13.1).

Positive Percent Agreement: a/(a+c) x 100

Negative Percent Agreement: d/(b+d) x 100

Table 13.1: 2 x 2 table for calculation of positive percent agreement and negative percent agreement:

	Reference Positive	Reference Negative	Row Totals
Lucira Positive	a	b	a+b
Lucira Negative	c	d	c+d
Column Totals	a+c	b+d	a+b+c+d

- Invalid Rate
  The initial invalid rates and unresolved invalid rates should be estimated for the Lucira COVID-19 & Flu Test.

9 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

9.1 REGULATORY, ETHICAL AND STUDY OVERSIGHT CONSIDERATIONS

9.1.1 INFORMED CONSENT PROCESS

Upon receiving IRB approval, the Investigator must receive IRB-approved informed consent and the letter from the IRB granting approval. The letter(s) must clearly state the version of the protocol and the informed consent that they have approved as well as any other documents, such as advertisements or other materials, they may have been reviewed and approved.

Before recruitment and enrollment into the study, each prospective candidate shall be given a full explanation of the nature and purposes of the study and a copy of the IRB-approved informed consent form to review. Once the essential study information has been provided and the Investigator is assured that each individual volunteer understands the implications of participating in the study, the subject will be asked to give consent to participate in the study by signing the informed consent form. The consent forms shall be signed and dated by the appropriate parties. The subject will be given a copy of the signed informed consent form.

9.1.2 STUDY DISCONTINUATION AND CLOSURE

If Lucira Health or its representative, the Investigator, or any national regulatory officials discover conditions during the study that indicate that the study, site or intended use operator should be terminated, this action may be taken after appropriate consultation between Lucira Health, its representative, and the Investigator. The study may be terminated prematurely by the Principal Investigator or his/her designee and Lucira Health if:

- The number and/or severity of AE justifies termination of the study
- The discovery of an unexpected, serious, or unacceptable risk to enrolled subjects
- New data becomes available which raise concern about the safety of the study device, such that continuation might cause unacceptable risk to subjects

- The study may be terminated at an individual site and another site sought if there is a failure to recruit enough subjects for the study
- The decision on the part of Lucira Health to suspend or discontinue testing, evaluation, or development of the study device
- Failure of the Investigator to comply with pertinent regulations
- Submission of knowingly false information from the research facility to Lucira Health, Monitor or any regulatory officials
- Insufficient adherence to protocol requirements

In addition, the Sponsor reserves the right to discontinue the study, but intend only to exercise this right for valid scientific or administrative reasons.

After such a decision, written notification must be sent to the IRB along with any IRB-required filings. Study termination and follow-up will be performed in compliance with the conditions set forth in GCP requirements.

9.1.3 CONFIDENTIALITY AND PRIVACY

Confidentiality

During the enrollment process, each subject will be given a unique identifier to ensure anonymity. All study-related materials, specimens, documents, and data held by the Sponsor will refer to the subject's unique subject ID. Any data that may be published in internal reports, abstracts, scientific journals, or presented at medical meetings will reference a unique subject code and will not reveal the subject's identity. At no time should any data forms or specimens be marked with the subject's name or any other traceable identifier. The informed consent form (ICF), which contains the subject's name, will be kept separately at the patient enrollment sites in a secure locked location. At no time will the original or a copy of the ICF revealing the subject's name be distributed outside of the patient enrollment site research team.

Disclosure of Data

All information obtained during the conduct of this study will be regarded as confidential and written permission from Lucira Health is required prior to disclosing any information relative to this study.

Data Access

The Investigator and the Investigators' designated staff personnel will have access to the following subject data: Name or Initial, and previous research record.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator.

9.1.4 KEY ROLES AND STUDY GOVERNANCE

9.1.4.1 CANDIDATE DEVICE TESTING SITES

- Provide a simulated Home Use Environment (e.g., table free of clutter, sink, clock, lamp, etc.)
- Identify suitable subjects for enrollment
- Assign study subject identification numbers

- De-identify Protected Health Information (PHI) from potential respiratory research participants specimens
- Sites shall provide de-identified source documentation that provides subject demographics and test results
- Collect comparator nasal swabs by a qualified health care professional
- Specimen handling - Prospective fresh reference method specimen shall be stored and transferred at 2-8°C
- Comparator specimens shall be shipped daily to the designated lab
- Study data EDC entries shall be completed daily

9.1.4.2 REFERENCE METHOD TESTING SITE

- Document the receipt of clinical specimens
- Designate operators to perform reference method testing
- Perform reference method testing on enrolled samples to obtain qualitative results
- Study data results shall be provided daily

9.1.4.3 STUDY SPONSOR

- Provide investigational product and materials to the investigative sites for Lucira investigational testing
- Ensure that the site staff receive appropriate training to conduct the study
- Monitor the study activities through on-site visits, remote visits, or other means (e.g., phone calls, emails)
- Review and compile study data received from the candidate device and reference method testing sites

9.1.5 CLINICAL MONITORING

The task of the study monitor is to ensure the acceptable conduct of the study through frequent contacts by phone, email, and in person with the responsible Investigator/designee, in accordance with the Sponsor's or its representative's internal procedures.

Lucira Health will monitor study progress in accordance with the protocol and applicable regulations. To ensure equal distribution of enrolled subjects based on FDA EUA guidance and satisfy specificity requirements, enrollment will be closely monitored. Lucira Health personnel or designee may perform an audit at any time during or after completion of the study, and all data pertaining to a subject's participation and all study-related documentation in this investigation must be made available. In addition, a representative from a regulatory authority may choose to inspect a study site at any time prior to, or after completion of the clinical study. All pertinent study data shall be made available to the regulatory authority for verification, audit, or inspection purposes.

When the enrollment goal is reached, Lucira Health or its representative will notify the sites the study is complete.

The duration of the study is expected to be at least *12 weeks*. When the study is ready to be terminated, a Site Closeout Visit shall be conducted. Sites will be instructed on the disposition of unused investigational materials by Lucira Health or its representative at that time. Study documents will be checked for completeness and filed. The Investigator will allow Lucira Health and/or its representative and/or any regulatory authority to inspect all CRFs and study-related documents to verify the study was performed according to protocol. Monitors will review informed consent forms for completeness as well as verify source documentation.

To ensure the accuracy of data, direct access to source data by the Sponsor, its representative, and regulatory authorities is mandatory. Direct access to source data may be required to perform de-identified analysis both during and after the study. The Sponsor reserves the right to terminate the study for refusal of the Investigator/Institution to supply source documentation of work performed in the study.

9.1.6 QUALITY ASSURANCE AND QUALITY CONTROL

Lucira Health is responsible for the training, organization, monitoring supply of study materials, and quality assurance for the clinical study. Prior to the start of this study all study staff shall be trained on the protocol, roles and responsibilities, data management and regulatory requirements.

9.1.7 DATA HANDLING AND RECORD KEEPING

9.1.7.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data gathered during the study visit will be recorded on the source document and CRFs provided by Lucira Health. Data collection is the responsibility of the clinical trial staff at the site under the supervision of the investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. All entries must be in permanent, black or blue ink. Error corrections must remain legible with a single line drawn through it with the correct data, recorder's initials, and date of correction entered beside it. Erasing or obliterating errors, including the use of correction fluid (e.g., "white out") is prohibited unless it involves protected health information of a subject.

9.1.7.2 STUDY RECORDS RETENTION

Essential documents are those documents, which individually and collectively, permit evaluation of the conduct of a study and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, Lucira Health and its representative with the standards of GCP and with all applicable regulatory requirements. The Investigator is responsible for compliance with GCPs and completion/updating of all required regulatory documentation (e.g., Investigator agreement, Financial Disclosure, CVs from personnel listed on Investigator Agreement, etc.). In particular, the Investigator will ensure Lucira Health, or its representative is provided with financial disclosure information, including staffing changes and changes to financial arrangements, which will be updated during the course of the study, at site closure/database lock and for 1 year following completion of the study. The Investigator or designee will also maintain and provide an Authorized Study Personnel Log and protocol deviation forms to Lucira Health or its representative and to the IRB.

US Federal law codified in 21 CFR section 812, requires a copy of all records (source documents, data forms, test article disbursement records, etc.) that support this study must be retained in the files of the responsible Investigator for a minimum of *two years* following US regulatory clearance or approval for the claim investigated. The Sponsor will retain records for a minimum of *5 years* after the termination of the study. If no FDA application is filed, the Sponsor will retain records for a minimum of *7 years* (25 years in Canada) after the product is no longer sold or as agreed upon with the Sponsor or its representative.

9.1.8 PROTOCOL DEVIATIONS

No changes in protocol execution, except to eliminate an immediate hazard, shall be affected without the mutual agreement of the Investigator and Lucira Health. It is the responsibility of the site investigator to

use continuous vigilance to identify and report deviations within 2 working days of identification of the protocol deviation, or within 2 working days of the scheduled protocol-required activity.

Clinical study events shall be reported using an Unanticipated Event Form and follow-up will take place accordingly. Deviations that affect subject safety will be reported to the IRB. Deviations and any incidents or queries that result in data exclusion will be reported in the final report.

9.1.9 PUBLICATION POLICY

The publication policy is detailed in the Clinical Trial Agreement for this study. All information obtained during the conduct of this study will be regarded as confidential, and written permission from Lucira Health is required prior to disclosing any information relative to this study. Only summary manuscripts prepared for publication by Lucira Health in accordance with the policy established and previously presented to the Investigator by Lucira Health shall be permitted. This requirement should not be construed as a means of restricting publication; it is intended to assure concurrence regarding data, evaluations, and conclusions, and to provide an opportunity to share with the Investigator any new and/or unpublished information of which the investigator may be unaware.

9.1.10 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial shall be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial.

9.2 PROTOCOL AMENDMENTS

The protocol may be amended during the study. Changes that affect the study population or conduct of the study will be described in detail in the Clinical Study Report.

Neither the Investigator nor the Sponsor will amend the Protocol without first obtaining the approval of the amendment in writing by the IRB. No changes in protocol execution, except to eliminate an immediate hazard, shall be affected without the agreement of the Investigator and Lucira Health. All changes must be documented by signed protocol amendments and submitted to the IRB.

Protocol amendments will be approved by the IRB, including changes to the Informed Consent Form. It should be noted that where an amendment to the Protocol substantially alters the study design or the potential risks to subjects, each subject's consent to continue participation should be obtained.

Once the final protocol has been issued and signed by the Investigator and the Sponsor, it shall not be formally altered. Protocol amendments are alterations to a legal document and have the same legal status. Therefore, they must pass through appropriate steps before being implemented. In general, any important change that theoretically increases risk to subjects constitutes an amendment.

The original signed copy and amendments will be kept in the Sponsor Regulatory Binder unless requested by the Investigator or the IRB.

Version	Date	Description of Change	Brief Rationale
A	12/30/2021	Initial document	Initial document
B	7/27/2022	Revision for the post authorization protocol	• Reduced repetition to lessen redundancy and increase clarity

Version	Date	Description of Change	Brief Rationale
		continuation	• Updates to align with the notified body goals

END DOCUMENT