FloodLAMP COVID-19 Biobank and Test Validation Protocol

Protocol Number: 20210401

REVISION HISTORY

ECR	Version Number	Date issued	Author(s) of changes	Details of changes made
N/A	01			Original release

KEY STUDY CONTACTS

Sponsor FloodLAMP Biotechnologies, PBC 930 Brittan Ave San Carlos, CA 94070
Primary Study Contact Randy True Chief Scientific Officer randy@floodlamp.bio xxx-xxx-xxxx

INVESTIGATOR SIGNATURE PAGE

Protocol Title: FloodLAMP COVID-19 Biobank and Test Validation Protocol

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The undersigned confirms that the following protocol has been agreed and accepted. I agree to conduct the trial in compliance with this protocol. I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I agree to conduct the clinical trial in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, 21 CRF 812.100 General responsibilities of investigators, and the current ICH GCP regulations (ICH E6 (R1) Section 4, the Sponsor's SOPs (if applicable), National Laws and Regulations, and other regulatory requirements as required.

I certify that I have not been terminated from an investigation due to compliance failure (debarment).

I agree to conduct the investigation(s) in accordance with the investigator agreement, investigational plan, current protocol, applicable regulatory requirements and regulations and conditions of approval imposed by the reviewing IRB.

I agree to personally conduct or supervise the described investigation.

I agree to ensure that all requirements of informed consent are met (if applicable).

I agree to submit sufficient accurate financial disclosure information and to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.

I agree not to use the device or permit it to be used for any purpose other than the investigational testing specified in the protocol.

I agree not to permit the device to be used before proper training has been given by myself, my study staff members, or sponsor.

I agree to maintain adequate and accurate records and to make those records available for inspection by the sponsor, its representatives, applicable regulatory authorities and the IRB.

I agree to comply with all other requirements regarding the obligations and responsibilities of investigators (21CFR 812.100 General responsibilities of investigators).

Investigator Printed Name	**Signature**	**Date**

PROTOCOL SYNOPSIS

Clinical Study Protocol Title	FloodLAMP COVID-19 Test Development Study
Protocol Number	20210401
Sponsor	FloodLAMP Biotechnologies, PBC
Investigational Products	FloodLAMP QuickColor™ Test, FloodLAMP QuickFluor™ Test, FloodLAMP EasyPCR™ Test, FloodLAMP Home Collection Kit
Instruments and Software	RT-PCR Instruments, FloodLAMP Mobile App
Controls	Not Provided but necessary: external positive control for the detection of SARS-CoV-2 and to monitor functioning of reagents along with a negative control, to monitor for contamination during sample processing.
Proposed Intended Use	The FloodLAMP COVID-19 Tests comprise several molecular assays that utilize a streamlined sample preparation protocol. The assays include polymerase chain reaction (PCR) and reverse transcriptase loop-mediated isothermal amplification (RT-LAMP). The tests are intended for the qualitative detection of RNA from SARS-CoV-2 in anterior nares (nasal) swab specimens from individuals suspected of COVID-19 by their healthcare provider and from individuals without symptoms or other epidemiological reasons to suspect COVID-19 infection. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests, or by similarly qualified non-U.S. laboratories. Sample pooling is at a baseline level of 4, with on-site and at-home modalities. Pooling of pools to levels greater than 20 will be investigated pending LoD determination and validation studies. Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in upper respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. 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 do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

	The assay is intended for use by qualified and trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and *in vitro* diagnostic procedures. The assay is only for use under the Food and Drug Administration's Emergency Use Authorization. Use of the FloodLAMP QuickColor™ Test in a general, asymptomatic screening population is intended to be used as part of an infection control plan that may include additional preventative measures, such as a predefined serial testing plan or directed testing of high-risk individuals. Negative results do not preclude current or future infection obtained through community transmission or other exposures. Negative results must be considered in the context of an individual's recent exposures, history, and presence of clinical signs and symptoms consistent with COVID-19.
Study Overview	The study will include up to 100,000 unique clinical specimens (will depend on prevalence in the intended population) from across at least 3 geographically diverse testing in the United States. Additional sample collection sites may be brought on to ensure sufficient enrollment for the study.
Clinical Specimen Categories	● Fresh Prospective ● Frozen Prospective
Inclusion/Exclusion Criteria	Inclusion: 1. The specimen is an anterior nasal swab and QR code labeled tube included with the FloodLAMP Home Collection Kit. 2. The swab specimen can be tested within 56 hours or less after collection. If frozen, specimens are to be stored at ≤-70℃ until tested. 3. Subjects with any of the following: o Suspected of COVID-19, whether or not symptomatic o Not experiencing symptoms and/or who have not notified a physician that they suspect they have COVID-19 o Had a positive COVID-19 test within the last 10 days 4. The specimen is from a consenting male or female subject of any age Exclusion: 1. The specimen was not properly collected, identified, transported, processed, or stored according to the instructions provided by the sponsor. 2. The specimen was not collected under informed consent.
Enrollment Dates	Approximately April 1, 2021 through April 1, 2022

Device Class	Class II, Nonsignificant Risk
Primary Objective	The objective of this study is to generate clinical performance and usability data for the FloodLAMP QuickColor™, QuickFluor™, and EasyPCR™ Tests and FloodLAMP Home Collection Kit.
Analysis Method	Upon completion of the clinical validation studies, Positive and Negative Percent Agreement for each target will be calculated and presented in 2x2 tables with the reference vs. subject device including 95% two-sided confidence intervals.

1. INTRODUCTION

1.1. BACKGROUND

The COVID-19 pandemic has revealed the value for new modalities of public health focused testing and screening. FloodLAMP's molecular tests and home collection kit combine streamlined extractionless, ultra-low cost, supply chain robust assay protocols with highly scalable at-home and on-site sample collection. Together these enable the new type of mass screening of interacting populations, such as schools and workplaces, to safely reopen society. Furthering this capability is needed (along with vaccines) to ultimately overcome the COVID-19 crisis, first in the U.S., then globally.

The populations most susceptible include the elderly over 65 years old and individuals who have preexisting comorbidities, including diabetes, obesity, and cardiovascular disease.

1.2. STUDY RATIONALE

The scope of the study is to validate the FloodLAMP COVID-19 Tests and Home Collection Kit with up to 100,000 unique clinical specimens from across three geographically diverse testing sites in the United States. Number of enrolled patients should be sufficient to ensure at least 20 positive samples are prospectively collected in the intended use populations. The results will be analyzed and compared against results from a CLIA lab that can run an EUA comparator test on dry swabs.

1.3. SAMPLE SIZE DETERMINATION

Will depend on the prevalence of SARS-CoV-2 in the intended use populations.

2. INVESTIGATIONAL DEVICE PROPOSED INTENDED USE STATEMENT

FloodLAMP QuickColor™ COVID-19 Test and FloodLAMP QuickFluor™ COVID-19 Test are reverse transcriptase loop-mediated isothermal amplification (RT-LAMP) assay. The FloodLAMP EasyPCR™ COVID-19 Test is a real-time reverse transcriptase polymerase chain reaction (RT-qPCR) assay. The tests are intended for the qualitative detection of RNA from SARS-CoV-2 in upper respiratory specimens including nasopharyngeal swabs, anterior nasal and mid-turbinate nasal swabs from individuals suspected of COVID-19 by their healthcare provider and from individuals without symptoms or other epidemiological reasons to suspect COVID-19 infection, when tested at a weekly interval with no more than 9 days between tests. Testing is limited to laboratories certified under the Clinical Laboratory

Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests, or by similarly qualified non-U.S. laboratories.

Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in upper respiratory specimens including nasopharyngeal swabs, anterior nasal and mid-turbinate nasal swabs during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. 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 test results to the appropriate public health authorities.

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

The FloodLAMP COVID-19 Tests are intended for use by qualified and trained clinical laboratory personnel specifically instructed and trained in the techniques of *in vitro* diagnostic procedures. The FloodLAMP COVID-19 Tests are only for use under the Food and Drug Administration's Emergency Use Authorization.

3. STUDY OBJECTIVE

The objective of this study is to generate clinical performance data for the FloodLAMP QuickColor™ COVID-19 Test, FloodLAMP QuickFluor™ COVID-19 Test, FloodLAMP EasyPCR™ COVID-19 Test, and the FloodLAMP Home Collection Kit.

4. STUDY DESIGN OVERVIEW

4.1. PROTOCOL SUMMARY

The purpose of this study is to determine the accuracy and usability of the FloodLAMP COVID-19 Tests and Home Collection Kit in the intended populations compared to a CLIA lab that can run an EUA comparator test on dry swabs. The primary outcome of the study will be to determine the sensitivity and specificity of the FloodLAMP COVID-19 Tests and usability of the Home Collection Kit.

Three modes of sample collection will be stratified:

Variation 1: The collection site is co-located with a current testing program for Persons Suspected of COVID that is utilizing a high sensitivity EUA PCR test, e.g., adjacent to Stanford or San Francisco city testing site. After completion of the EUA test specimen collection, the participant would be asked if they would like to participate in the FloodLAMP research study. If the participant accepts, a self-collection kit would be offered, and participants would collect according to printed instructions. Optionally, they may be asked if they would like to download the FloodLAMP app and follow collection instructions through the app. Participants would place the collected specimen tube in a biobag and deposit the biobag in a collection bin.

Variation 2: FloodLAMP would independently run a physical or mobile site (e.g., at tent outside the FloodLAMP lab in a parking lot), in the form of a drive thru. A self-collection kit would be picked up by participants or be handed through a car window. Specimens would be collected in the car according to instructions (printed or through app), specimen tubes placed in a biobag, and deposited into a collection bin.

Variation 3: Self-collection kits will be distributed, either at the sites described above, other physical locations or through delivery by mail or courier. These are termed "home" collection kits though they may be utilized in a workplace setting, in a car, or at other locations. The home kits will include variations for self-collection of both pooled specimens and individual collected samples. The home collection may include testing of the FloodLAMP app and involve user factors testing with surveys and other interactions with participants.

In all three variations, initial studies will comprise collection of two anterior nares swabs whereby the order of collection is randomized. In Variations 2 & 3, one swab would be sent to a CLIA lab to run an EUA approved Comparator test. The other swab would be used to run the FloodLAMP COVID-19 Tests. Subsequent studies may include collection of other specimen types, including saliva.

Recruitment would be performed online or through other standard means. Optionally, self-collection kits for multiple collections may be provided. Specimens may be pooled for validation studies.

Variations in the self-collection kits will include both supervised and unsupervised versions. Supervision may be provided in person at physical sites or remotely through video for collection in a participant's home or car.

4.2. PRIMARY MEASURE OF PERFORMANCE

The results of the FloodLAMP COVID-19 Tests will be compared against results from a reference test for the same set of patient specimens.

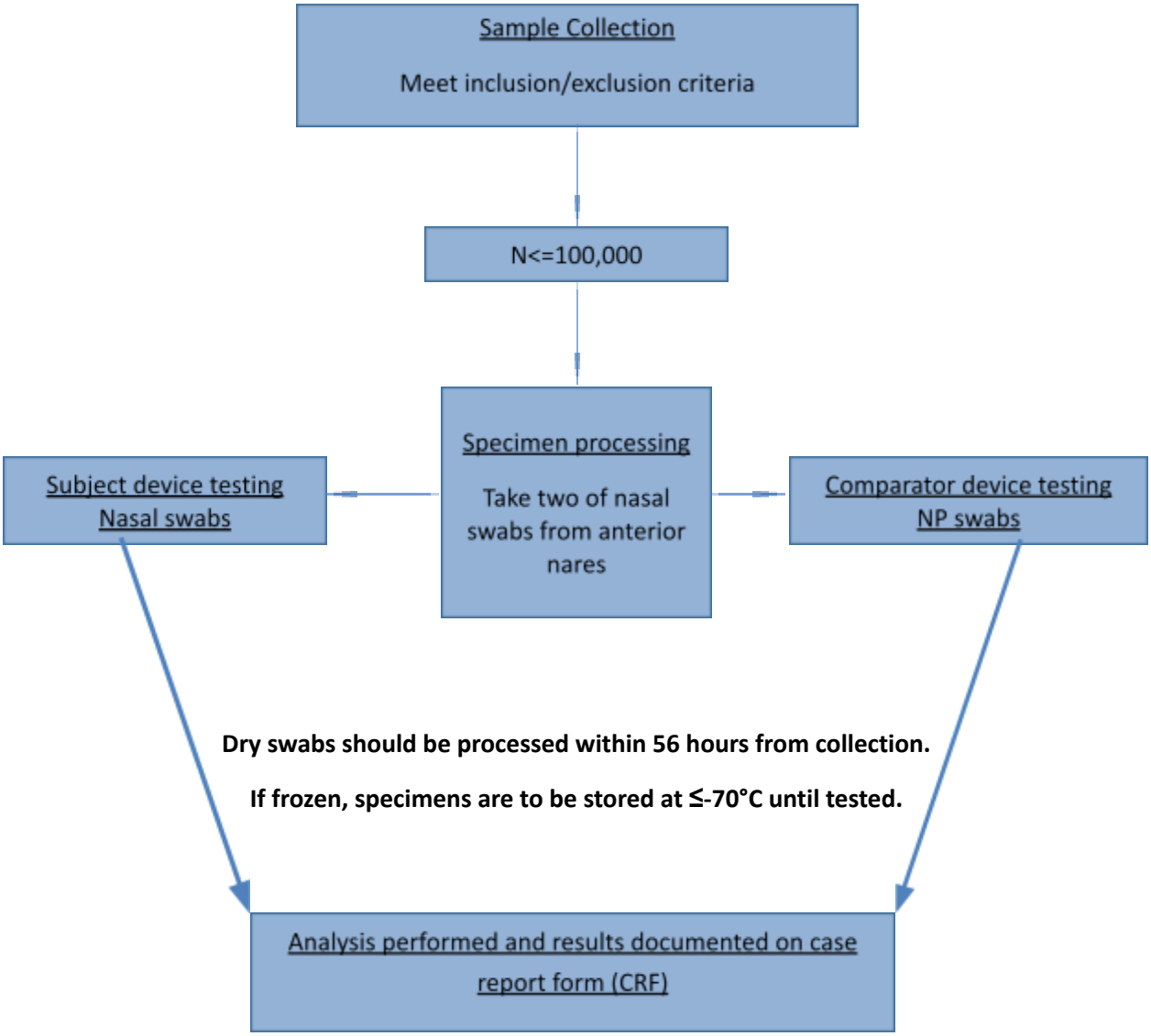
Examination and Interpretation of Patient Specimen Results:

Assessment of the FloodLAMP COVID-19 Tests of clinical specimen test results should be performed after the positive and negative controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted. Results will be interpreted according to the Instructions for Use.

4.3. ACCEPTANCE CRITERIA

Upon completion of the clinical validation studies, Positive and Negative Agreement for each target will be calculated and data stratified as previously described.

Figure 1: Study Workflow



5. DEVICE DESCRIPTION

See Instructions for Use: Principles of Procedure

5.1. INVESTIGATIONAL USE ONLY KIT CONFIGURATION

See Instructions for Use: Materials Provided but Not Required

5.2. REAGENTS, CONSUMABLES AND EQUIPMENT REQUIRED BUT NOT PROVIDED

See Instructions for Use: Standard Lab Equipment and Consumables

5.3. REAGENT HANDLING AND STORAGE

See Instructions for Use: Materials Provided but Not Required

5.4. CONTROLS

See Instructions for Use: Running Tests - Controls Preparation, Results Interpretation - Test Controls

5.5. INSTRUMENTS AND SOFTWARE

See Instructions for Use: Running Tests

6. STUDY SPECIMENS

6.1. SPECIMEN SELECTION

The enrollment period will span from the date of first specimen is enrolled to the date of last specimen is enrolled at a site as determined by the Sponsor. Valid specimens are those that meet the criteria outlined in sections 7.2 and 7.3. Patient informed consent (documented using forms provided by the site, provided online, or within the FloodLAMP Mobile App) will be required for this study. No results derived from the investigational device will be included as part of any subject patient management diagnostic algorithm.

6.2. INCLUSION CRITERIA

Specimens must meet all the below criteria to be considered for study enrollment.

1. The specimen is an anterior nasal swab using the swab and QR code labeled tubes included with the FloodLAMP Home Collection Kit.
2. The swab specimen can be tested within 56 hours of collection. If frozen, specimens are to be stored at <-70℃ until tested.
3. Subjects with any of the following:
    - Suspected of COVID, whether or not symptomatic
    - Not experiencing symptoms and/or who have not notified a physician that they suspect they have COVID-19
    - Had a positive COVID test within the last 10 days
4. The specimen is from a consenting male or female subject of any age.

6.3. EXCLUSION CRITERIA

Specimens that meet any of the below criteria may not be considered for study enrollment.

1. The specimen was not properly collected, identified, transported, processed, or stored according to the instructions provided by the sponsor.
2. The specimen was collected at a site which is not covered under the study IRB.

7. STUDY PROCEDURE

7.1. BLINDING OF THE STUDY AND PROCEDURES TO MINIMIZE BIAS

In order to preserve the confidentiality of subjects, the following procedures will be implemented:

1. Clinical data will be de-identified.
2. Available clinical information will be provided in such a way that it does not make the subject identifiable.
3. No personal identifiers or protected health information (PHI) will be collected or included as part of any study data so the confidentiality of each subject is protected.
4. Patient specimens will be assigned a unique study number by an individual with no direct involvement in the study (Honest Broker).
5. Testing personnel will not have access to any prior clinical data or reference method (comparator) results.

7.2. SAMPLE TYPES, SAMPLE COLLECTION, PROCESSING AND STORAGE

7.2.1. Specimen Types

Fresh Prospective

Best efforts will be made to enroll and test at least 20 fresh, prospectively (FDA guidance for asymptomatic testing) collected, confirmed SARS-CoV-2 positive subjects. A combination of fresh and frozen specimens may be tested to reach the 20 asymptomatic subjects required.

7.2.2. Specimen Collection and Processing

Refer to the Instructions for Use

FloodLAMP COVID-19 Test swab samples should preferably not be frozen or refrigerated prior to elution and should be tested within 56 hours from collection. If frozen, specimens are to be stored at <-70℃ until tested.

7.3. QUALITY CONTROL

Procedural Control:

Prior to testing patient specimens, QC for each test system should be run according to local, state and federal regulations and the Instructions for Use.

External Positive and Negative Controls:
One positive and one negative control will be included on every 96-well plate with up to 94 samples, or with every batch of strip tubes on each heater. All test controls should be examined prior to interpretation of patient specimen results. If the controls are not valid and the expected result, the specimen results cannot be interpreted. Refer to the Instructions for Use.

7.4. REFERENCE METHOD

Results from the subject device will be compared to a high sensitivity purified PCR EUA Authorized test. Reference testing may be performed at one or more of the clinical trial sites or a centralized testing

laboratory. If a site is also conducting testing of the subject device, different personnel will be assigned to oversee and perform reference testing.

8. RESULTS

8.1. RESULTS INTERPRETATION

Refer to the Instructions for Use.
Assessment of the results of FloodLAMP Tests should be performed after the positive and negative controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted.

8.2. DATA COLLECTION

Demographic Data

Age/age range, gender and ethnicity will be collected on each subject enrolled in the study.

Missing Data

If required data are missing for any subject, then the results of any testing may be excluded from the final data analysis set. An explanation will be provided in the EUA submission.

Determination of Sample Size

The total number of subjects that will be included in the study will depend on the prevalence of specimens that meet the inclusion criteria.

9. REGULATORY AND ADMINISTRATIVE REQUIREMENTS

9.1. PROTOCOL AMENDMENTS

Any modification to the protocol, which may impact on the conduct of the study, including changes of study objectives, study design, patient population, study procedures, and significant administrative aspects, will require a formal amendment to the protocol.

The approval letter, signed/approved by the IRB chairman, must refer specifically to the Investigator, the Sponsor protocol number, the protocol title, the protocol amendment number and the date of the protocol amendment.

Administrative changes to the protocol are minor corrections and/or clarifications that have no impact on the way the study is to be conducted and may not indicate an IRB formal review. These administrative changes will be agreed upon by the Sponsor and the Investigator. The IRB may be notified of administrative changes at the discretion of the Investigator.

9.2. DOCUMENTING AND HANDLING OF DEVIATIONS FROM THE PROTOCOL

Deviations to the protocol will be noted in the EUA Submission.

9.3. RECORD RETENTION

All records and documents pertaining to the conduct of the study, including but not limited to Electronic Data Record Form for a period of at least two years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in and ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period, however, if required by the regulatory requirements or by an agreement with the Sponsor (Good Clinical Practice: Consolidated Guidance (ICH-E6 section 4.9.5)).

9.4. CASE REPORT FORMS (CRF)

Individual subject's data will be recorded. No personal identifiers will be recorded on this form and at no point during the study (including the sample retention period) will the Investigator, study personnel, or the Sponsor, have access to patient identifiers.

9.5. MONITORING OF STUDY SITES

The clinical study shall be monitored by the trained clinical study personnel or designated representative via remote communications and/or on-site visits throughout the duration of the study. The study staff member or designated representative shall discuss any issues or problems concerning the conduct of the study with the Investigator and/or Sponsor.

9.6. QUALITY ASSURANCE AUDITS

During the study, representatives from the Sponsor may visit the site to carry out an audit of the study. Such an audit will require access to records that are relevant to the study. Sufficient prior notice will be provided to allow the investigator to prepare properly for the audit. Similar auditing procedures may also be conducted by agents of applicable regulatory agencies reviewing the results of the study. Participation in this study implies acceptance of potential inspections by the Sponsor or applicable regulatory authorities.

9.7. STUDY COMPLETION AND CLOSE OUT

Upon completion of the study, the Investigator shall notify the IRB of the conclusion of the study. The final report will be sent to the IRB.

10. STATISTICAL ANALYSES

Upon completion of the clinical validation studies, Positive and Negative Percent Agreement for each reportable target will be calculated and presented in 2x2 tables with the reference vs. subject device. Data will be combined across sites.

Initial call rates will be calculated. For specimens with invalid results, regardless of the reason, one repeat per specimen will be permitted. Final call rates will then be calculated using the results from the repeat analyses.

Exclusion of Specimens from Analysis

Any specimens that do not meet the Inclusion/Exclusion criteria will be removed from the final data set with a rationale provided in the EUA submission.

11. RISK ANALYSIS

11.1. CLINICAL STUDY SITES AND INFORMED CONSENT

This study has been determined by the Sponsor to be a Nonsignificant Risk. Each site will be responsible for submitting the Clinical Study Protocol and associated templates for institutional/third party IRB review and approval prior to study initiation. Subject recruitment will be performed, and informed consent will be required for this study. The testing personnel and sites will represent the environment for which the device is intended.

12. SAFETY

DEFINITIONS

Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including any abnormal medical finding) in subjects, users, or other persons whether or not related to the investigational medical device.

Serious Adverse Device Effect

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Unanticipated Serious Adverse Device Effect (USADE)

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

NOTE: Anticipated: an effect which by its nature, incidence, severity or outcome has been previously identified

13. ETHICS

Use of human subjects in this evaluation will be subject to approval by an Institutional Review Board (IRB). Written statements of the IRB approvals of this protocol will be documented in the study file. The current investigation is in accordance with 21 CFR Part 812 (c)(3) and the FDA Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors (January 2006).

14. ASSOCIATED DOCUMENTS

14.1. Instructions for Use FloodLAMP QuickColor™ COVID-19 Test v1.0

14.2. Instructions for Use FloodLAMP QuickFluor™ COVID-19 Test v1.0

14.3. Instructions for Use FloodLAMP EasyPCR™ COVID-19 Test v1.0

14.4. Instructions for Use FloodLAMP Home Collection Kit

14.5. Research Subject Information and Consent Form

14.6. Case Report Form