CLINICAL PERFORMANCE STUDY PLAN

EuGeni SARS-CoV-2 Antigen Rapid Diagnostic Test

AnteoTech LTD.

Document reference number: CT013, Version 3.0

Date: 19-Sep-2022

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CLINICAL PERFORMANCE STUDY PLAN (CPSP) SUMMARY

Version Number	3.0
Date	19-Sep-2022
Sponsor	**AnteoTech Ltd** Unit 4, 26 Brandl Street Brisbane Technology Park Eight Mile Plains QLD 4113 Australia Phone: +61 7 3219 0085 **EU authorized representative:** MT Promedt Consulting GmbH Altenhofstrasse 80 66386 St. Ingbert Germany Phone | + 49 6894 581020 Fax |+ 49 6894 581021
Clinical Performance Study Name	EuGeni SARS-CoV-2 Antigen Rapid Diagnostic Test Clinical Performance Study
Clinical Performance Study Code	CT013
Objectives	To determine the diagnostic accuracy in terms of specificity and sensitivity of the EuGeni SARS-CoV-2 Antigen Rapid Diagnostic Test in the diagnosis of SARS-CoV-2 in specimens prospectively collected by healthcare professionals from subjects suspected of COVID-19 disease or with unknown COVID-19 status.
Device Under Investigation	EuGeni SARS-CoV-2 Ag RDT assay and EuGeni Reader
Number of Required Specimens	A minimum estimated of 1850 prospective specimens divided as follows: Nasopharyngeal specimen collection: ○ 300 positive specimens from symptomatic subjects ○ 120 negative specimens from hospitalized patients ○ 505 negative specimens from subjects with respiratory symptoms Combined nasal mid-turbinate and throat specimen collection: ○ 300 positive specimens from symptomatic subjects ○ 120 negative specimens from hospitalized patients ○ 505 negative specimens from subjects with respiratory symptoms
Planned Number of Sites	Up to 10 sites in Europe
Study Design	This is a non-interventional, two-arm, prospective, non-randomized, open-label and multi-center Clinical Performance Study

Primary Endpoints	To assess the EuGeni SARS-CoV-2 Ag RDT diagnostic accuracy in terms of sensitivity and specificity measured as the following: • The diagnostic sensitivity will be assessed as the ability to identify the presence of a target marker associated with SARS-CoV-2, of nasopharyngeal specimens and combined nasal mid-turbinate and throat specimens, respectively, compared with gold-standard SARS-CoV-2 RT-PCR. • The diagnostic specificity will be assessed as the ability to recognise the absence of a target marker associated with SARS CoV-2, of nasopharyngeal specimens and combined nasal mid-turbinate and throat specimens, respectively, compared with gold-standard SARS-CoV-2 RT-PCR.
Secondary Endpoint	To compare the specificity and sensitivity rates of EuGeni SARS-CoV-2 Ag RDT between the two specimen collection methods.
Inclusion Criteria	1. Specimens from subjects over 12 years old agreeing to participate in the study and with a legal representative able to provide informed consent, OR; 2. Specimens from subjects over 18 years old able to provide informed consent. 3. Specimens collected with nasopharyngeal swabs, OR; 4. Combined nasal mid-turbinate and throat specimen collection.
Exclusion Criteria	1. Specimens and testing methods that are not deemed to be in line with gold-standard RT-PCR standards. 2. Specimens stored for over 2 hours at 2-8 ºC temperature between collection and testing with EuGeni SARS-CoV-2 Ag RDT 3. Specimens stored for over 5 days at -20ºC between collection and testing with RT-PCR. 4. Specimens stored for over 24h at 4ºC between collection and testing with RT-PCR. 5. Contamination and/or deterioration of the specimen which, in the opinion of the investigator, may affect its handling and/or analysis. 6. The subject is deemed unsuitable to participate in the study by the investigator.
Coordinating Investigator	To be determined
Electronic Data Capture (EDC)	Castor EDC (Amsterdam, The Netherlands)
Data Management & Biostatistics	AKRN Scientific Consulting S.L. (Madrid, Spain)
Contract Research Organization (CRO)	AKRN Scientific Consulting S.L. (Madrid, Spain)
Expected Duration of the Study	Expected start date in June 2022 with the duration of 5 months

INVESTIGATOR PROTOCOL SIGNATURE PAGE

I have read the Clinical Performance Study Plan (CPSP) and I agree to conduct this clinical performance study as outlined and in accordance with all applicable laws and regulations, including Good Clinical Practice (GCP) guidelines. In addition, I agree to provide all the information requested in the case report forms presented to me by the Sponsor in a manner to assure completeness, legibility and accuracy.

Investigator Signature	Date (DD-Mmm-YYYY)
Investigator Printed Name	Study Role
Investigational Site Name	

COORDINATING INVESTIGATOR PROTOCOL SIGNATURE PAGE

I have read and agree to adhere to the Clinical Performance Study Plan (CPSP) and all regulatory requirements applicable in conducting this clinical investigation.

Investigator Signature	Date (DD-Mmm-YYYY)
Investigator Printed Name	
Investigational Site Name	

SPONSOR SIGNATURE PAGE

The sponsor will conduct the clinical study in compliance with GCP, ISO20916, with the appropriate regulatory requirements and with the Clinical Performance Study Plan (CPSP) agreed to by the sponsor and given approval/favorable opinion by the IRB/IEC. The sponsor will comply with the procedures for data recording/reporting, and to permit monitoring, auditing and inspection. The sponsor is to retain the essential documents that should be in the investigator files. The sponsor should obtain a signed Clinical Trial Agreement of the institution.

Sponsor Signature	Date (DD-Mmm-YYYY)
Sponsor Representative Printed Name	Sponsor Representative Role

COMPLIANCE STATEMENT:

This clinical performance study will be conducted in accordance with this Clinical Performance Study Plan, the Declaration of Helsinki, law 14/2007 of 3 July 2007 on Biomedical Research, applicable Good Clinical Practices, ISO 20916:2019 standards and regulations: EU 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices (IVDR), repealing Directive 98/79/EC and Commission Decision 2010/227/EU, EU General Data Protection Regulation and WHO International health regulations.

The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical performance study will be approved by the appropriate Institutional Review Board (IRB)/Ethics Committee (EC) of the respective investigational site and by the applicable regulatory authorities.

CONFIDENTIALITY STATEMENT

This document is confidential and is to be distributed for review only to investigators, potential investigators, consultants, study staff, and applicable independent Ethics Committees or Competent Authorities. The contents of this document shall not be disclosed to others without written authorization from the Sponsor unless it is necessary to obtain informed consent from potential study participants.

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1. INTRODUCTION

Rapid antigen detection (RAD) tests are used to perform rapid diagnosis of SARS-CoV-2 infection based on a qualitative approach. RAD tests detect the viral antigen by the immobilized coated SARS-CoV-2 antibody placed on the device. The results of these tests are available in a short time, reducing the workload in diagnostic hospitals and laboratories and improving the turn-around time.

EuGeni SARS-CoV-2 Antigen Rapid Diagnostic Test is an *in vitro* Diagnostic (IVD) medical device intended to be used for the qualitative detection of SARS-CoV-2 nucleocapsid antigen. The result from this IVD test identifies the presence or absence of the SARS-CoV-2 antigen as an aid for the diagnosis of COVID-19 infection.

1.1 Background and rationale

In 2019 a novel corona virus, designated as SARS-CoV-2 and associated with unusual viral pneumonia named Corona virus Disease 19 (COVID-19), sprouted in the city of Wuhan, China, and rapidly spread to create a global pandemic. Identification of people infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is essential for controlling its spreading and public health management.

Since the beginning of the COVID-19 outbreak, tests that can enable both mass screening and reliable detection of infected people are needed[1]. The reliance on testing underscores the importance of analytical sensitivity of virus assays, being the real-time quantitative polymerase chain reaction (RT-qPCR) from nasopharynx swab the gold-standard [2]. However, RT-PCR is expensive, time-consuming, and requires specialized laboratory personnel and instrumentation compared to rapid tests [3].

New developments in SARS-CoV-2 diagnostics have the potential to reduce cost and turnaround time [4–6]. Several diagnostic strategies are available for identifying or ruling out current infection, identifying people in need of care escalation, or testing for past infection and immune response. Point-of-care (POC) antigen and molecular tests for the detection of current SARS-CoV-2 infections are rapid antigen detection (RAD) tests, which allow earlier detection and isolation of confirmed cases compared to laboratory-based diagnostic methods.

Coronavirus RAD tests, have demonstrated good sensitivity and specificity in comparison to RT-qPCR [7–9]. Moreover, previous studies have shown that RADs can exhibit high sensitivity in detecting samples containing infectious virus, indicating a high sensitivity to detect contagious individuals [10,11]

The RAD tests, based on the immunochromatographic principle, detect SARS-CoV-2 nucleocapsid protein (N) at or near the place where a specimen is collected, providing results within few minutes[3]. In general, RAD tests consist of fixing match-paired antibodies to the surface of the cassette and coupling an anti-antigen match-paired antibodies to the detection nanoparticles. This match-paired antibody could be coupling with colloidal gold particles or europium (III) chelate microparticle[12] depending on its construction. If the patient sample contains anti-SARS-CoV-2 antigens, these will be captured by the antibody-particle conjugate present in the conjugation pad of the cassette and the complex formed will migrate to the membrane-bound anti-N antibody, then a coloured or fluorescent band will then appear on the test line. To be validated, the tests have to present a positive line for control[13].

EuGeni SARS-CoV-2 Ag RDT is a fluorescent immunochromatographic RAD test for COVID-19 rapid detection using the EuGeni AX-2X-S Reader for results interpretation. The EuGeni AX-2X-S Reader is expected to provide positive, negative, or invalid result for the presence of SARS-CoV-2 antigen. The EuGeni device is intended to be used by healthcare professionals only.

2. IN-VITRO DIAGNOSTIC MEDICAL DEVICE OVERVIEW

2.1 IVD Medical Device under investigation

The EuGeni SARS-CoV-2 Ag RDT is a test strip based on lateral flow technology which utilizes nanoparticles, doped with europium, as the fluorescence reporter system. The test strip (Figure 2-1A) is housed in a cassette which is read by the EuGeni AX-2X-S Reader (Figure 2-1B), a portable instrument that reads EuGeni fluorescent lateral flow tests.

Figure 2-1: EuGeni SARS-CoV-2 Ag RDT kit (A) and EuGeni AX-2X-S Reader (B)

The kit includes individually packaged test cassettes, lysis buffer filled in dropper bottles, sterile disposable swabs and the Instructions for Use (IFU). All kit components should be stored in the original packaging at 4-30°C avoiding freezing. Further information about the device and its components can be found in Table 2-1 and the IFU.

Table 2-1: Reagents and materials of Eugeni SARS-CoV-2 Ag RDT kit

Component	Specification/Qty.
Test Cassette individually packaged	25
Lysis buffer pre-filled tubes	25
Sterile disposable swabs	25
Instructions for Use	1

2.2 Intended Purpose

The EuGeni SARS-CoV-2 Ag RDT is a single use, disposable immunochromatographic rapid diagnostic test intended to be used by healthcare professionals for the qualitative detection of SARS-CoV-2 nucleocapsid antigen in nasopharyngeal, or combined nasal mid-turbinate and throat specimens from individuals who are suspected of COVID-19 infection.

The result from this *in vitro* diagnostic test identifies the presence or absence of the SARS-CoV-2 antigen as an aid for the diagnosis of COVID-19 infection. A Positive result indicates that the patient may have a COVID-19 infection. A Negative result does not rule out COVID-19 infection and should not be used as the sole basis for treatment or patient management decisions. If deemed necessary, results may be confirmed with a molecular (RT-PCR) assay.

2.3 Intended User

The EuGeni SARS-CoV-2 Ag RDT is intended to be used by healthcare professionals which must be qualified and trained. This test is intended for use at the Point of Care (POC) and laboratory settings.

2.4 Mechanism of action of the Device Under Investigation

The EuGeni SARS-CoV-2 Ag RDT is a test strip based on lateral flow technology and utilizes nanoparticles, doped with europium, as the fluorescence reporter system. It includes europium nanoparticles labelled with a monoclonal mouse antibody for detection but not differentiation of SARS-CoV and SARS-CoV-2 antigen, and for internal assay control. The test strip is housed in a cassette which is read by the EuGeni AX-2X-S Reader, a portable instrument that reads EuGeni fluorescent lateral flow tests.

The test line contains an immobilized monoclonal mouse antibody to capture SARS-CoV-2 antigen and the control line contains an immobilized control anti-mouse antibody.

The test sample is added to the sample well of the test cassette and then reconstitutes the dried europium nanoparticle antibody conjugate from the conjugate pad. The sample flows along the test strip by capillary action.

- If the sample contains SARS-CoV-2 antigen, it binds to the antibody-labelled europium nanoparticle. When the sample flows past the test line, the europium bound antigen is captured by the second anti-SARS-CoV-2 antibody immobilized on the test line. A fluorescent signal detected by the EuGeni AX-2X-S Reader at this test line indicates that the specimen is SARS-CoV-2 antigen Positive.
- If the sample does not contain SARS-CoV-2 antigen, the europium-labelled anti-antigen antibody will not bind to the test line. This indicates that the specimen is SARS-CoV-2 antigen Negative.

The sample continues to flow along the strip and when it passes over the control line, antibody-labelled europium nanoparticles are captured by the immobilized anti-mouse antibody. The control line must be detected by the EuGeni AX-2X-S Reader for the test to be valid. If the control line is not detected, the test is considered invalid and must be repeated using another test cassette.

For more precise information on the device description and the reader, please refer to the IFU.

2.5 Device Handling

All investigational products shall be stored according to the labeling and Instructions for Use (IFU) in a secure area to prevent unauthorized access or use.

The original packaging should be stored at 4-30°C, avoiding freezing or storage in any area above 30ºC. The devices shall be shipped together with temperature loggers to track the temperature they have been subjected to during their transportation. The test cassette is stable until the expiration date printed on the sealed foil pouch and must remain on it until use. Once opened, the test should be used immediately. Kit components are stable until the expiration date printed on the label, and past this date the cassette cannot be used.

The EuGeni AX-2X-S Reader should be handled with caution and should not be returned to the Sponsor until the decontamination process has been followed.

For further device handling warnings and precautions, please see the details in the IFU.

3. CLINICAL PERFORMANCE STUDY OVERVIEW

3.1 Clinical Performance study Objective

The objective of this clinical performance study (CPS) is to determine the diagnostic accuracy (sensitivity and specificity) of the EuGeni SARS-CoV-2 Antigen Rapid Diagnostic Test in the diagnosis of SARS-CoV-2 in specimens from subjects suspected of COVID-19 disease or with unknown COVID-19 status.

4. CLINICAL PERFORMANCE STUDY DESIGN AND PROCEDURES

4.1 Clinical performance study design

This clinical performance study (CPS) is designed as a non-interventional, two-arm, prospective, non-randomized, open-label and multi-center study. The two study arms as defined depending on the specimen collection method:

1. Nasopharyngeal specimen collection for comparison with gold-standard RT-PCR
2. Combined nasal mid-turbinate and throat specimen collection for comparison with gold-standard RT-PCR

The expected minimum number of specimens for this CPS is 1850, divided as follows:

Nasopharyngeal specimen collection:

- 300 positive specimens collected from subjects at different timepoints post onset of symptoms: days 0-3 (40%), days 4-7 (40%) and more than 7 days (20%).
- 120 negative specimens from hospitalized patients
- 505 negative specimens from subjects with respiratory symptoms

Combined nasal mid-turbinate and throat specimen collection:

- 300 positive specimens collected from subjects at different timepoints post onset of symptoms: days 0-3 (40%), days 4-7 (40%) and more than 7 days (20%).
- 120 negative specimens from hospitalized patients
- 505 negative specimens from subjects with respiratory symptoms.

Consideration will be given to at least 20% of positive samples for both nasopharyngeal and nasal mid-turbinate and throat specimens, which will have Ct result by PCR greater than 30. The estimated numbers for each specimen type are approximate and may vary depending on the natural recruitment at the investigational sites to ensure the correct distribution of sample size requirements.

The study has been designed to involve as little pain, discomfort, fear and any other foreseeable risk as possible for the subjects, and both the risk threshold and the degree of distress are specifically defined in the clinical performance study plan (CPSP) and constantly monitored.

The CPS will be conducted in up to 10 sites in Europe. The primary and secondary endpoints will be evaluated when all specimens have been collected and analyzed. Positive and negative specimens of those subjects who give their consent, will be frozen and stored for further validation and genotyping as required by applicable guidelines with the purpose of confirming the type of variant, as well as for their potential use in similar future investigations. The specimens will be stored according to the patient´s consent, and all other specimens will be discarded after all analyses are concluded

4.2 Clinical Performance Study Procedures

The Clinical Performance Study will occur in a single subject visit, and no clinical follow up will be required.

4.2.1 Informed Consent and Specimen collection

Before starting any study-related activity, the subject must have provided the signed informed consent form following the requirements in [Section 6.1.2]. Next, the specimen collection will be performed by professionally trained and qualified healthcare personnel.

One bilateral swab will be taken to be analyzed with the device under investigation and another bilateral swab will be taken to be analyzed with the gold-standard RT-PCR. The specimen collection method for EuGeni analysis will be performed using either a combined nasal mid-turbinate and throat swab, or a nasopharyngeal swab, which will determine the inclusion into one of the two study arms. Enrolment into the combined nasal mid-turbinate and throat arm or nasopharyngeal will not be randomized, however consecutive and parallel enrollment in both arms will take place. Regardless of the study arm, the RT-PCR specimen collection will always occur to allow result comparison between the investigational device and RT-PCR.

For further information on specimen collection, please refer to IFU and the Appendix III in this CPSP.

4.2.2 Specimen analysis procedure

The specimen analysis shall be performed by professional healthcare personnel. Specimens to be analyzed by the gold-standard RT-PCR shall follow the procedures established by the standard of care. To comply with MDCG 2021-21, the viral loads and their distribution shall also be shown and characterized by Ct-values of RT-PCR.

Those specimens analyzed by the EuGeni SARS-CoV-2 Antigen Rapid Diagnostic Test shall follow the procedures laid down in the IFU and protocol. Once the sample is processed and put into the cassette according to the IFU, the cassette shall be incubated for 15 minutes before it is placed in the EuGeni AS-2X-S for the obtention of the result. The EuGeni AX-2X-S Reader will read the test cassette and display the results on screen in less than one minute. If a printer has been connected to the EuGeni Reader, a printout (Figure 4-1) can be automatically generated. This should be kept as CPS documentation.

a) Positive results indicate the presence of SARS-CoV-2-antigen and is indicative of primary SARS-CoV-2 infection. These results do not rule out bacterial infection or co-infection with other viruses. If the specimen contains SARS-CoV-2 antigen, a fluorescent control and test line will be displayed in the EuGeni AX-2X-S reader indicating that the specimen is SARS-CoV-2 antigen Positive.

b) Negative results indicate the specimen does not contain SARS-CoV-2 antigen. In this case, only the fluorescent control line will be displayed. Negative results should be treated as presumptive and should not be used as the sole basis for clinical diagnosis and treatment. Results shall be confirmed with a molecular (RT-PCR) assay, within nationally accredited laboratory for COVID testing.

c) If a test is Invalid, a new test should be performed with a new subject specimen and a new cassette. Internal procedural controls are included in the test to confirm sufficient specimen volume and correct procedural technique.

For more information on the interpretation of results, please refer to the EuGeni SARS-CoV-2 Antigen Rapid Diagnostic Test IFU.

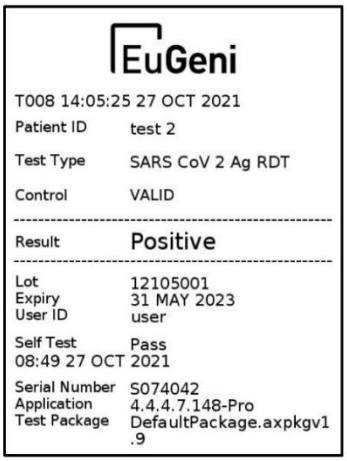


Figure 4-1: Results printout

All results obtained from the investigational device should only be noted in the Case Report Form. These results will not impact or drive patient management decisions. The gold-standard RT-PCR results will provide this information to the healthcare professionals and the enrolled subjects.

4.2.2.1 Specimen handling and storage

Study site personnel shall ensure proper storage of specimens in accordance with the IFU. Those specimens to be tested with the device under investigation must be stored at 2-8ºC for up to 2 hours between collection and testing. Specimens to be analyzed with RT-PCR shall be stored at -20ºC up to 5 days or at 4ºC for a maximum of 24h between collection and testing.

The study will use fresh human specimens, potentially containing active virus and infectious materials. The handling of samples will be conducted in accordance with standard laboratory containment procedures and following local government guidance for handling SARS-CoV-2 and SARS-CoV-2 containing material.

To inactivate the virus, the EuGeni SARS-CoV-2 Ag RDT test kit includes a lysis buffer to pre-treat the samples. This buffer disrupts the viral membrane and the nucleocapsid antigens are exposed, facilitating detection. Despite this viral inactivation step, all materials used during the testing process must be treated as potentially infectious material and discarded as per standard laboratory procedures for medical waste handling (Articles 17, 23, 24 and 25 of Directive 2008/98/EC on waste, concerning hazardous waste and permit requirements).

Any instrumentation must also be decontaminated after use, following the standard procedures in place.

Equipment such as the EuGeni AX-2X-S Reader, where internal surfaces cannot easily be accessed, should be handled with caution and should not be returned to the Sponsor until the SARS-CoV-2 virus inactivation is ensured.

4.2.2.2 Final disposition of the specimens

Positive and negative specimens of those subjects who give their consent, will be frozen and stored for further validation and genotyping as required by applicable guidelines with the purpose of confirming the type of variant, as well as for their potential use in similar future investigations. The specimens will be stored according to the patient´s consent, and all other specimens will be discarded after all analyses are concluded.

4.3 Measures Taken to Avoid and Minimize Bias

This clinical performance study has been designed to be multicenter in order to minimize bias related to site specific standard of care patient and specimen collection method.

All participants who meet the inclusion and exclusion criteria will be eligible to join the study. Inclusion into the two study arms will not be randomized, however sites will be instructed to consecutively enroll subjects into both arms. Recruitment at each investigational site will be limited to 50% of the total sample size.

To avoid bias related to the collection method, all study subjects will have a bilateral swab specimen collection for investigational device analysis and for RT-PCR analysis, for direct comparison within the same subjects.

5. ENDPOINTS

5.1 Primary Endpoints

The primary endpoint of this clinical performance study is to assess the EuGeni SARS-CoV-2 Ag RDT diagnostic accuracy in terms of sensitivity and specificity measured as the following:

- The diagnostic sensitivity of EuGeni SARS-CoV-2 Ag RDT, defined as the ability to identify the presence of a target marker associated with SARS-CoV-2, of nasopharyngeal specimens and combined nasal mid-turbinate and throat specimens, respectively, compared with gold-standard SARS-CoV-2 RT-PCR.
- The diagnostic specificity of EuGeni SARS-CoV-2 Ag RDT, defined as the ability to recognise the absence of a target marker associated with SARS CoV-2, of nasopharyngeal specimens and combined nasal mid-turbinate and throat specimens, respectively, compared with gold-standard SARS-CoV-2 RT-PCR.

5.2 Secondary Endpoint

The secondary endpoint of this clinical performance study is to compare the EuGeni SARS-CoV-2 Ag RDT diagnostic accuracy (specificity and sensitivity) between the two specimen collection methods (nasopharyngeal and combined nasal mid-turbinate and throat) to assess any potential impact on diagnostic accuracy.

6. SELECTION OF SPECIMENS

6.1 Specimens and subjects providing specimens

The specimens used in this clinical performance study will be selected from any gender of subjects of the general population suspected to be infected with SARS-CoV-2 or with unknown COVID-19 status.

The Principal Investigator or designee, previously trained in this CPSP, will revise subject and specimen eligibility according to the inclusion/exclusion criteria. Those who meet all the inclusion criteria and no exclusion criteria shall be suitable to participate in the study.

6.1.1 Subject Screening

Enrolled subjects will be fully informed about the clinical performance study, following the established Informed Consent process (described in the next section). Once a duly dated and signed Informed Consent form is obtained, the clinical performance procedures may begin. Subjects under 18 years of age must be accompanied by a parent or legal representative who must also give consent for the under-age's participation in the study.

The following assessments are performed as part of the screening process:

- Evaluation of the subject's inclusion and exclusion criteria.
- Evaluation of the subject's SARS-CoV-2 infection status, if known.

Subjects must be screened for clinical performance study eligibility by a member of the site's clinical performance study team previously trained to the CPSP.

In case the subject does not meet all inclusion criteria or meets any of the exclusion criteria, the subject is considered a screening failure. The Principal Investigator or the delegated clinical performance study personnel will record the screening failure in the hospital records and on the screening log as required.

Subjects meeting general inclusion criteria and no exclusion criteria will be asked to sign an Informed Consent form if they wish to participate in the clinical performance study. These patients will also be entered into the screening log.

Subject data will be collected following enrollment into the clinical performance study.

6.1.2 Informed Consent

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's EC. This process will include a verbal discussion with the subject on all aspects of the clinical performance study that are relevant to the subject's decision to participate, such as details of clinical performance study procedures, anticipated benefits, and potential risks of clinical performance study participation. Subjects must be informed about their right to withdraw from the clinical performance study at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical performance study will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. Financial incentives will not be given to the subject. Subjects may be compensated for time and travel directly related to the participation in the clinical performance study. The subject shall be provided with the Informed Consent form written in a language that is understandable to the subject and has been approved by the center's EC. The subject shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts

to ensure that the subject understands the information provided. If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any clinical performance study-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

Failure to obtain informed consent from a subject prior to clinical performance study enrollment should be reported to Sponsor within 3 working days and to the reviewing center's EC according to the EC's reporting requirements.

If, during the clinical performance study, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee (if applicable) will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing informed consent in writing.

6.1.2.1 Special Circumstances for Informed Consent

Individuals under age of 18 or under age of legal consent:

Individuals who are minors (under the age of 18 or age of legal consent, but over 12 years old) may be enrolled in this clinical performance study. Informed consent must be obtained using the IRB/EC approved informed consent in accordance with IRB/EC requirements.

In this special circumstance, the legally acceptable representative will represent the individual during the Informed Consent process, which will be performed according to the requirements in [Section 6.1.2]. The minor will also be informed about the CPS within his/her ability to understand. The explicit wish of the minor who can form an opinion and assess information to decline participation or withdraw from the study at any time will be respected.

6.2 Eligibility Criteria

6.2.1 Inclusion Criteria

1. Specimens from subjects over 12 years old agreeing to participate in the study and with a legal representative able to provide informed consent, OR;
2. Specimens from subjects over 18 years old able to provide informed consent.
3. Specimens collected with nasopharyngeal swabs, OR;
4. Combined nasal mid-turbinate and throat specimens' collection.

6.2.2 Exclusion Criteria

1. Specimens and testing methods that are deemed not compatible with gold-standard RT-PCR standards.
2. Specimens stored for over 2 hours at 2-8 ºC in between collection and testing with EuGeni SARS-CoV-2 Ag RDT
3. Specimens stored for over 5 days at -20ºC between collection and testing with RT-PCR.
4. Specimens stored for over 24h at 4ºC between collection and testing with RT-PCR.
5. Contamination and/or deterioration of the specimen which, in the opinion of the investigator, may affect its handling and/or analysis.
6. The subject is deemed unsuitable to participate in the study by the investigator.

6.3 Subject Enrolment

A subject is considered enrolled in the CPS from the moment the subject provides written informed consent and has been confirmed to meet all inclusion criteria and none of the exclusion criteria.

6.4 Expected Duration of the Participants in the Clinical Performance Study

The expected duration of enrollment is 12-16 weeks. The expected duration of each subject's participation is one day, including screening and specimen collection. Subjects will be exited from the study after the collection of both swabs. Therefore, the total duration of the clinical performance study is expected to be 3 months, consisting of approximately 12-16 weeks of specimen collection and 3 weeks of results analysis. No clinical follow-up is needed in this clinical performance study. The end of the clinical performance study will occur when all samples are analyzed.

6.4.1 Suspension or Early Termination of the Clinical Performance Study

While no formal statistical rule for early termination of the clinical performance study for insufficient accuracy of the device under investigation is defined, the Sponsor reserves the right to discontinue the clinical performance study at any stage with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- Unanticipated adverse device effect (e.g., UADE) occurs and it presents an unreasonable risk to the participating subjects.
- Further product development is cancelled.

Should the clinical performance study be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements. The investigator shall return all clinical performance study materials (including devices) to the Sponsor and provide a written statement to the IRB/EC (if applicable). All applicable clinical performance study documents shall be subject to the same retention policy as detailed in Section 10.5 of the CPSP.

A Principal Investigator, IRB/EC or regulatory authority may suspend or prematurely terminate participation in the clinical performance study at the investigational site(s) for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

If the Sponsor suspends or prematurely terminates the clinical performance study at an individual site in the interest of safety, the Sponsor will inform all other Principal Investigators.

If suspension or premature termination occurs, the Sponsor will remain responsible for providing resources to fulfill the obligations from the CPSP and existing agreements for following the subjects enrolled in the clinical performance study, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate.

If suspension or premature termination occurs, the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate, and return patients to their standard medical treatment.

7. ADVERSE EVENTS

The study has been designed to involve as little pain, discomfort, fear, and any other foreseeable risk as possible for subjects. Adverse Events (AEs) can only occur during specimen collection. Thus, the definitions and requirements set out in this section are only applicable to this study phase. To comply with the applicable standards and guidelines on clinical performance study adverse event reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

7.1 Definition

7.1.1 Adverse Event

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

Note 1: This definition includes events related to the medical device under investigation or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to medical devices under investigation.

7.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE).

a) Led to a death,

b) Led to a serious deterioration in health of the subject, that either resulted in

   1. a life-threatening illness or injury, or
   2. a permanent impairment of a body structure or a body function, or
   3. in-patient hospitalization or prolongation of existing hospitalization, or
   4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
   5. chronic disease

c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

Note: A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be an SAE.

7.1.3 Device Deficiency/Device Malfunction

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CPSP.

7.2 Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device under investigation caused or contributed to an AE is to be performed by the Investigator and recorded on the appropriate CRF form. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

7.2.1 Unanticipated (Serious Adverse) Device Effect [U(S)ADE]

Unanticipated serious adverse device effect (USADE) refers to any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

7.3 Adverse Event and Device Deficiency/Device Malfunction Reporting

7.3.1 Adverse Event Reporting

General AE Reporting

Safety surveillance and reporting starts as soon as the patient is enrolled in the clinical performance study. Safety surveillance and reporting will continue until the last study activity has been performed, the subject is deceased, the subject concludes participation in the clinical performance study or the subject withdraws from the clinical performance study. All adverse event data, including deaths and device deficiency data (if applicable), will be collected throughout the time period defined above and will be reported to the Sponsor on a CRF. Additional information with regard to an adverse event should be updated within the appropriate CRF.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

Given that this study will be utilizing and EDC system, an offline form will be made available to allow the investigator to report SAEs in the event the entry cannot be made in the EDC. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

All adverse events will be collected on each subject through the study duration

SAE Reporting

The investigator should report all SAEs to the Sponsor as soon as possible but no later than outlined below.

Clinical Site	Reporting timelines
All Sites	SAEs must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

The date the site staff became aware the event met the criteria of an SAE must be recorded in the source document. The Investigator may need to further report the SAE that could have led to a serious adverse device effect to the local IRB/EC, if required by the IRB/EC.

Please take into consideration the following table (MDCG2020-10).

Translation period	
From May 26th, 2021 and until Eudamed is available	The Tabular format of MDCG2020-10 (Appendix-Summary Reporting Form) should be used.
When Eudamed is available but not yet mandatory and until the timepoint when Eudamed becomes mandatory	Either the Tabular format of this guidance (Appendix- Summary Reporting Form) or the Eudamed web form can be used. Note: Once the shift to Eudamed reporting has been made for a specific clinical investigation, Eudamed should continue to be used for reporting all new events and updates to those events throughout to remainder of the clinical investigation.

7.3.2 Unanticipated Serious Adverse Device Effect Reporting to Sponsor and EC

The Sponsor requires the Investigator to report any USADE to the Sponsor within 3 calendar days of the investigator's knowledge of the event, unless local requirements are more stringent, and to the IRB/EC per IRB/EC requirements.

7.3.3 Device Deficiency/Malfunction Reporting

All device deficiencies/malfunctions should be reported on the appropriate CRF form.

The investigator should report all device deficiencies/malfunctions to the Sponsor as soon as possible but no later than outlined below.

Clinical Sites	**Reporting timelines**
All Sites	Device deficiencies/malfunctions must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

The device, if not implanted or not remaining in the subject, should be returned to the Sponsor.

The Investigator may need to further report the SAE that could have led to a serious adverse device effect to the local IRB/EC, if required by the IRB/EC.

An offline form will be made available to allow the investigator to report device deficiencies/malfunctions in the event that the entry cannot be made in the EDC system. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

In case a device deficiency/malfunction occurred before the patient ID has been assigned, the device deficiency should be reported to the Sponsor via the offline reporting form.

8. STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical performance study. Additional details on statistical analyses, including justification of study design, sensitivity analyses, poolability analyses, subgroup analyses and analysis of descriptive endpoints, may be maintained in a separate Statistical Analysis Plan (SAP).

8.1 Analysis Populations

8.1.1 Per-protocol population

The analysis population is defined as per-protocol population (PP), including all specimens that meet the study eligibility and informed consent requirements. This population will be divided in two arms, according to the specimen collection method:

- Arm 1, including specimens collected with nasopharyngeal swabs
- Arm 2, including specimens collected with combined nasal mid-turbinate and throat swabs

8.2 Statistical Analyses

8.2.1 Primary Diagnostic Accuracy Endpoint(s) Analyses

The evaluation of the accuracy of the EuGeni SARS-CoV-2 Ag RDT in the diagnosis of COVID-19 will be analyzed by means of the sensitivity and specificity capacity of this test.

- The sensitivity is the ability to detect a target marker (viral proteins) associated with SARS-CoV-2. The sensitivity means the capacity to detect positive samples of COVID-19. Therefore, sensitivity will be calculated as the result of the ratio of the True Positive measurements (TP) to total known positive measurements (True Positive + False Negative). At least 20% of these specimens shall have Ct values > 30 on the comparator PCR assay.

$$Sensitivity = \frac{True\ Positive}{(True\ Positive + False\ Negative)}$$

- The specificity is the ability to recognise the absence of a target marker (viral proteins), associated with SARS-CoV-2, which means the capacity to detect true negative samples of COVID-19. Consequently, specificity will be determined as the ratio of the True Negative measurements (TN) to total known negative measurements (True Negative + False Positive).

$$Specificity = \frac{True\ Negative}{(True\ Negative + False\ Positive)}$$

The primary endpoint will be analyzed in the PP population.

8.2.2 Secondary Endpoint Analysis

The secondary endpoint assesses any potential impact of the specimen collection method (arms 1 and 2) on EuGeni SARS-CoV-2 Ag RDT diagnostic accuracy (specificity and sensitivity rates). Considering that this is an exploratory endpoint, no formal hypothesis is defined, and the analysis will be focused on potential differences.

The secondary endpoint will be analyzed in the PP population.

8.3 Sample Size Calculation and Assumptions

The sample size calculation is based on the objective to demonstrate an 80% sensitivity and a 98% specificity of the EuGeni SARS-CoV-2 Ag RDT for COVID-19 testing, defined as the minimum requirements in the MDCG2021-21, World Health Organization (WHO) and EU Common list of COVID-19 rapid antigen tests guidelines. Considering that this IVD is intended to be used by healthcare professionals, approximately 925 specimens are needed per study arm, distributed as follows:

- 300 positive specimens collected from subjects at different timepoints post onset of symptoms.
- 120 negative specimens from hospitalized patients
- 505 negative specimens from subjects with respiratory symptoms

Since this clinical performance study is a two-arm investigation, the total number of participants will be minimum of 1850.

8.4 Timing of Analysis

The study endpoints will be analyzed when all specimens are processed and analyzed, and the corresponding dataset is complete and locked.

8.5 Subgroup Analysis

Subgroup analyses may be conducted to assess the impact of different variables to the investigational device performance.

If conducted, the methods and plan for these subgroup analyses will be detailed in the corresponding Statistical Analysis Plan (SAP).

8.6 Multiplicity

There is no simultaneous multiple hypothesis in this clinical performance study. Therefore, no multiplicity control is required.

8.7 Pooling Strategy

Upon Sponsor´s request a pooling strategy may be carried out and would be further described (if any) in the SAP.

8.8 Procedures for Accounting for Missing Data

All variables and endpoints will be assessed as recorded in the database. Therefore, there will not be any imputation of missing data, unless otherwise specified.

8.9 Planned Interim Analysis

Upon Sponsor´s request, an interim analysis may be carried out and would be further described (if any) in the SAP.

8.10 Statistical Criteria for Termination

There are no statistical criteria for termination of this clinical performance study.

8.11 Success Criteria

This clinical performance study will be considered successful when the primary endpoint is met.

8.12 Deviations from Statistical Plan

Any major changes to the statistical plan will be documented in an amendment to the statistical plan. Less significant changes to the planned analyses will be documented in the final report.

9. QUALITY CONTROL AND QUALITY ASSURANCE

9.1 Selection of Clinical Sites and Investigators

The Sponsor or designee will select investigators qualified by education, training and experience to participate in the clinical performance study. Sites will be selected based upon review of a recent site assessment and the qualifications of the investigators who will participate in the clinical performance study.

9.2 Finances and Agreements

The clinical performance study will be financed by AnteoTech., Ltd. Investigational sites will be compensated by AnteoTech., Ltd for participation in the clinical performance study per the conditions set out in the Clinical Trial Agreement (CTA) between the Sponsor and the Investigational site.

9.3 CPSP Amendments

Approved CPSP amendments will be provided to the Investigators by the Sponsor prior to implementing the amendment.

Acknowledgement/approval by the IRB/EC of the CPSP amendment must be documented in writing prior to implementation of the CPSP amendment. Copies of this documentation must also be provided to the Sponsor.

9.4 Training

9.4.1 Site Training

All Investigators and clinical performance study personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Video call or self-training may take place as required. Training of Investigators and clinical performance study personnel will include, but is not limited to, the CPSP requirements, investigational device usage, electronic case report form completion and clinical performance study personnel responsibilities. All Investigators and clinical performance study personnel that are trained will receive a EuGeni user training certificate and they must also sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigators and clinical performance study personnel must not perform any CPSP-related activities that are not considered standard of care at the site.

9.5 Monitoring

Sponsor and/or designee will monitor the clinical performance study over its duration according to the CPSP-specific monitoring plan which will include the planned extent of source data verification. This monitoring plan will be a separate document that can be updated during the course of the study.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

The investigator understands and accepts the obligation to conduct the clinical performance study according to the CPSP and applicable regulations, and has signed the Clinical Trial Agreement.

The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical performance study and should have access to an adequate number of appropriate subjects to conduct the clinical performance study.

Source documentation (including original medical records) must be available to substantiate proper informed consent procedures, adherence to CPSP procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.

A monitoring visit sign-in log will be maintained at the site. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of clinical performance study-related documents.

9.6 Deviations from CPSP

The Investigator should not deviate from the CPSP for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety and well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify Sponsor immediately by phone or in writing.

No waivers for CPSP deviations will be granted by the Sponsor. All deviations must be reported to the Sponsor using the Deviation CRF. The occurrence of CPSP deviations will be monitored by the Sponsor for evaluation of investigator compliance to the CPSP and regulatory requirements and dealt with according to written procedures. Investigators will inform their IRB/EC or equivalent committee of all CPSP deviations in accordance with their specific IRB/EC or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the CPSP or any other conditions of the clinical performance study may result in further escalation in accordance with the Sponsor's written procedures, including securing compliance or, at its sole discretion, Sponsor may terminate the investigator's participation in the clinical performance study.

9.7 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical performance study records, including source documentation, for inspection during a Quality Assurance audit.

In the event that an investigator is contacted by a Regulatory Agency in relation to this clinical performance study, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide Sponsor with copies of all correspondence that may affect the review of the current clinical performance study (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). Sponsor may provide any needed assistance in responding to regulatory audits.

9.8 Sponsor Auditing

Sponsor audits are mandatory if data will be used for pre-CE mark and PMCF studies. Sponsor audits may be performed for other clinical performance studies as required by the design and/or regulatory impact of the investigation.

1. The Sponsor shall prepare an audit plan as well as the operating procedures for the related duties, and conduct audits in accordance with the audit plan and the operating procedures.
2. Individual engaged in auditing (hereinafter referred to as "auditor") shall be different than those in charge of medical device development or monitoring.
3. The auditor shall prepare an audit report documenting the matters confirmed in the audit to certify and verify that the audit has been conducted, and submit them to the Sponsor

10. DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the CPS.

CRF data collection will be performed through a secure web portal and only authorized personnel will access the Electronic Data Capture (EDC) system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor.

At the conclusion of the CPS, completed CRFs with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be provided to the investigational sites.

For the duration of the study, the Investigator will maintain complete and accurate documentation including, but not limited to study progress records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with the IRB/EC and study monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the CPS.

10.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical performance study.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a ‘need to know’ basis, including periodic review of access rights, and revocation of access when an individual’s employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to transfer into Sponsor’s data management systems only pseudonymous Personal Information (key-coded) necessary to conduct the clinical performance study, such as the patient’s medical condition, treatment, dates of treatment, etc. The Sponsor discloses as part of the clinical performance study informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. Confidentiality of Personal Information will be observed by all parties involved at all times throughout the clinical performance study. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical performance study data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

10.2 Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data entry and collection. Data review and data cleaning, and issuing, resolving data discrepancies and methods for data base lock. The DMP will include

procedures for the verification, validation and securing of electronic clinical system, if applicable. As well as procedures for maintaining and protecting subjects' privacy.

If appropriate, the DMP may be updated throughout the duration of the clinical performance study. All revisions will be tracked and document controlled.

10.3 Source Documentation

The investigator/institution will permit direct access to source data/documents for the purpose of performing clinical performance study-related monitoring, audits, IRB/EC review and regulatory inspections.

Subjects providing informed consent are agreeing to allow clinical performance study monitors or regulatory authorities including foreign countries to review, in confidence, any records identifying the subjects in this clinical performance study. This information may be shared with regulatory agencies; however, Sponsor undertakes not to otherwise release the subject's personal and private information.

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. In order to comply with these regulatory requirements/GCP, the following information should be included in the subject record at a minimum and if applicable to the clinical performance study:

- Medical history/physical condition of the subject before involvement in the clinical performance study sufficient to verify CPSP entry criteria
- Dated and signed notes on the day of entry into the clinical performance study referencing the Sponsor, CPSP number, subject ID number and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- Subject's condition upon completion of or withdrawal from the clinical performance study
- Any other data required to substantiate data entered into the CRF
- Patient reported outcome measures may be completed using CRF worksheets. These serve as the source documentation.

10.4 Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CPSP and CRF completion. The investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

Data on CRFs will be collected for all subjects that are enrolled into the CPS. Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. An electronic audit trail will be used to track any subsequent changes of the entered data.

10.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the CPS as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any CPS records.

The device and kit serial numbers, shipping details and device training and set up will be documented and tracked by both the Sponsor and trial site. All tests performed on the device will be recorded on source and in the Case Report Form (CRF) and Electronic Data Capture system (EDC). The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any CPS records or before moving the device from the primary testing site it was shipped to.

10.6 Investigational Devices Accountability

The Sponsor will ship investigational devices only to the Principal Investigator (the responsible leader of the investigational site) or his/her legal designee of each site, after sites receive documentation of site activation and shipping authorization is complete. The Investigator or an authorized designee must maintain adequate records of the receipt and disposition of each investigational device, including part number, batch number, and serial number (if applicable), date used, subject identification, and treating physician.

Storage locations for the devices at investigational sites must be locked with access restricted only to investigators and authorized personnel. Inventory Accountability Log supplied by the Sponsor will be used. The Inventory Accountability Log must document the disposition of all investigational devices including those that have been returned to Sponsor.

All investigational devices that are associated with a device failure or device deficiency must be returned immediately to the Sponsor.

11. RISK ANALYSIS

Recruited subjects for specimen collection may have anticipated risks associated with the specimen collection procedure. A risk analysis is conducted and identified risks are similar to those well-known for standard of care collection procedures (e.g., swab collection for gold-standard RT-PCR) and are described in the IFU.

11.1 Anticipated Clinical Benefits

The clinical benefit of this clinical performance study is a public health improvement due to the increase in alternatives and availability for rapid SARS-CoV-2 testing. This reduces the collapse of primary care centers and avoids the spread of the disease. There is no direct benefit to enrolled subjects.

11.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Risks associated with the specified device and procedure, together with their likely incidence, are described in IFU. These risks are related to pain and discomfort during the specimen collection procedure. No risks are anticipated during specimen processing and analysis, other than standard biosafety risks associated with highly infectious diseases. There may be risks related to the device under investigation that are unknown at present. Likewise, the exact frequency of the risk may be unknown.

11.3 Residual Risks Associated with the Device Under Investigation

The IVD medical device under investigation is indicated for qualitative detection of the nucleocapsid protein antigen of SARS-CoV-2 in specimens of combined mid-turbinate nasal with throat or nasopharyngeal swabs from individuals suspected of SARS-CoV-2 infection. The SARS-CoV-2 Rapid Antigen Test is not intended for use except as indicated.

According to the risk analysis, all risks has been identified and those which are non-accepted have been controlled by measures taken by the manufacturer. The device is analyzed according to ISO14971:2019. The analysis is objective and the conclusion is valid. Through security risk control, the risk level of the product is reduced, and all items are within acceptable ranges.

In summary, all risks of the product have been reduced to acceptable levels through risk control measures, and no additional risks have been generated during the period. Through prior security risk analysis and preventive measures, we have reduced hazards to acceptable levels throughout the development phase. After the product reaches the user, precautionary measures such as the user's qualification will be notified with warning statements in the instruction manual to minimize harm. The product will be continuously improved from user feedback in future use to minimize risks.

11.4 Risks Associated with Participation in this Clinical Performance Study

There are no additional risks associated with participation in this study.

11.5 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions and instructions regarding device handling and to the device's operation are included in the IFU and Quick Start Guide.

Risks associated with the use of the device under investigation are minimized through device design, investigator selection and training, pre-specified patient eligibility requirements and study monitoring to ensure

adherence to the protocol. All adverse events and device deficiencies will be reported to the Sponsor and will be monitored internally for safety surveillance purposes.

11.6 Benefit to Risk Rationale

Based on the previous sections, it can be concluded that the benefits of the device under investigation outweigh the risks. While there are no additional risks associated with study participation, the public health may be benefitted.

12. ETHICAL CONSIDERATION

12.1 Institutional Review Board/Ethics Committee Review and Approval

Institutional Review Board (IRB)/Ethics Committee (EC) approval for the CPSP and ICF/other written information provided to the patient will be obtained at each investigational site prior to consenting and enrolling patients in this clinical performance study. The approval letter must be received prior to the start of this clinical performance study and a copy must be provided to the Sponsor.

Any amendments to the CPSP as well as associated ICF changes will be submitted to the IRB/EC and written approval obtained prior to implementation, according to each institution's IRB/EC requirements.

No changes will be made to the CPSP or ICF or other written information provided to the patient without appropriate approvals, including IRB/EC, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical performance study is completed, the Investigator will advise his/her IRB/EC of the progress of this clinical performance study, per IRB/EC requirements. Written approval must be obtained from the IRB/EC yearly to continue the clinical performance study, or according to each institution's IRB/EC requirements.

No investigative procedures other than those defined in this CPSP will be undertaken on the enrolled subjects without the written agreement of the IRB/EC and the Sponsor.

13. CLINICAL PERFORMANCE STUDY CONCLUSION

The clinical performance study will be concluded when:

- The investigational site is closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical performance study closure.

The Sponsor shall submit the clinical performance study report (CPSR) within one year of the end of the investigation as applicable per the study.

14. PUBLICATION POLICY

The data and results from the clinical performance study are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical performance study. The Investigators will not use this clinical performance study-related data without the written consent of the Sponsor for any purpose other than for clinical performance study completion or for generation of publication materials, as referenced in the Clinical Trial Agreement. Single-center results are not allowed to be published or presented before the multi-center results. Any proposals for publications or presentations by the investigators must be reviewed and approved by the Sponsor in a timely manner to enable Sponsor review in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

The Sponsor will be responsible for registering the clinical performance study in a publicly accessible database, such as www.clinicaltrials.gov, in accordance with the International Committee of Medical Journal Editors guidelines, ISO20916:2019, and any other applicable international guideline. The Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. The Institution and/or Principal Investigator(s) shall not take any action to register the clinical performance study in public databases.

APPENDIX I: ABBREVIATIONS AND ACRONYMS

Abbreviation/Acronym	Words
AE	Adverse Event
ADE	Adverse Device Effect
CPS	Clinical Performance Study
CPSP	Clinical Performance Study Plan
CPSR	Clinical Performance Study Report
CRF	Case Report Form
CTA	Clinical Trial Agreement
DMP	Data Management Plan
EC	Ethics Committee
EDC	Electronic Data Capture
ICF	Informed Consent Form
IFU	Instructions For Use
IVD	*In vitro* Diagnostic
RT-PCR	Real-Time Polymerase Chain Reaction
PI	Principal Investigator
RAD	Rapid Antigen Detection
RDT	Rapid Diagnostic Test
SAP	Statistical Analysis Plan
SAE	Serious Adverse event

APPENDIX II: DEFINITIONS

Specimen:

Discrete portion of a body fluid or tissue taken for examination, study, or analysis of one or more quantities or characteristics to determine the character of the whole.

Sample:

One or more representative parts taken from a specimen which are intended to provide information.

Recruitment

The period prior to consent (the point of enrollment per ISO14155) where sites identify patients likely to satisfy all clinical investigation eligibility criteria. Sites may not perform any CPSP-specific screening measures requiring consent during this period; however, sites will review existing knowledge of the patient's medical history and assess against the general clinical investigation eligibility criteria to allow informed consent of appropriate patients.

Recruitment Failure

Patients who do not satisfy the general clinical investigation eligibility criteria prior to informed consent.

Enrollment

The time at which a patient signs and dates the Informed Consent Form (ICF).

Screening

The period after consent/enrollment where any non-standard of care and/or invasive screening measures occur to identify subjects who satisfy any additional clinical investigation eligibility criteria not considered during the recruitment period. Subjects who do not ultimately satisfy these additional clinical investigation eligibility criteria are considered screen failures*.

*Recruitment and screening occur simultaneously prior to obtaining informed consent for those clinical investigations without invasive and/or non-standard of care screening requirements following informed consent.

Screen Failure

Subjects who do not satisfy all invasive and/or non-standard of care clinical investigation eligibility criteria following informed consent, when required. Screen failure subjects should be withdrawn from the clinical investigation.

For those clinical investigations where recruitment and screening occur simultaneously prior to consent (no invasive or non-standard of care screening required following consent), patients who do not satisfy the recruitment/screening criteria are considered recruitment failures as described above.

Withdrawal

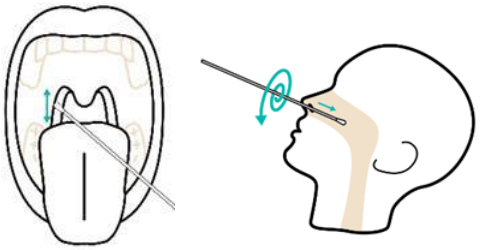
Enrolled subjects who are subsequently removed from the clinical investigation before the end of the study.

APPENDIX III: SPECIMEN COLLECTION PROTOCOL

Combined nasal mid-turbinate and oropharyngeal (throat) specimen collection

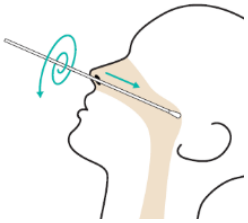
Use the swab provided in the kit to collect a throat and mid-turbinate specimen, in accordance with national guidelines. Insert swab into the posterior pharynx and tonsillar areas. Rub swab over both tonsillar pillars and posterior oropharynx and avoid touching the tongue, teeth, and gums.

Then with the same swab, aim to collect nasal epithelial cells and avoid nasal secretions. While gently rotating the swab, insert it less than one inch (about 2 cm) into nostril parallel to the palate until resistance is met at turbinates. Rotate the swab several times against nasal wall. Remove swab, insert it into the other nostril and repeat the process.



Nasopharyngeal specimen collection

Use the swab provided in the kit to collect a nasopharyngeal specimen. The swab must go all the way to the septum floor of the nose while gently pushing the swab into the posterior nasopharynx as illustrated. The swab must be rotated several times before removal.



APPENDIX IV: BIBLIOGRAPHY

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APPENDIX V: SUMMARY OF CHANGES

Revision	Summary of Changes
1.0	Document release
2.0	• Rephrase inclusion and exclusion criteria • Rephrase primary endpoints • Inclusion of Appendix III “Specimen Collection Protocol” • Inclusion of additional information related to “How to minimize bias” under section 4.3
3.0	Update sample size requirements

APPENDIX VI: REVISION HISTORY

This CPSP may be amended as appropriate by the Sponsor. Rationale will be included with each amended version in the revision history table below. The version number and date of amendments will be documented.

IRB/EC and relevant Regulatory Authorities, if applicable, will be notified of amendments to the CPSP.

Author	Amendment Number	Version	Date	Details	Rationale
AKRN Scientific Consulting	Not Applicable	1.0	05May2022	First release of the CPSP	NA
AKRN Scientific Consulting	Not Applicable	2.0	31May2022	CPSP updated before first Ethics Committee submission. See summary of changes.	NA
AKRN Scientific Consulting	1	3.0	19Sep2022	Update sample size requirements	Increased sample size to allow for subgroup analysis