SPONSOR SIGNATURE PAGE

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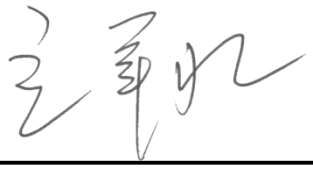

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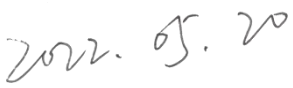

Date (DD-Mmm-YYYY)

Gao Xiang

Sponsor Printed Name

CEO

Title

INVESTIGATOR SIGNATURE PAGE

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SANCHEZ CALAVERA MARIA ANTONIA - DNI 73190563D

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Investigator Signature

Date (DD-Mmm-YYYY)

Investigator Printed Name

1 SUMMARY

Version Number	2.0
Version Date	20-May-2022
Sponsor	**CRDLIGHT** CRDLIGHT Optoelectronic Technology CO., Ltd. Floor 1-5 Building No. 7 & Floor 1-4 Building No, 5 No. 18 Xinyi Road, Jianghai District, Jiangmen City, Guangdong Province, China **EU Authorized Representative:** SUNGO Europe B.V. Olympisch Stadion 24, 1076DE Amsterdam, Netherlands
Investigational Device	SARS-CoV-2 RAT self-test diagnostic kit (SARS-CoV-2 Antigen Test Kit (Colloidal Gold)
Title of Study	Clinical Performance Study for the SARS-CoV-2 RAT self-test diagnostic kit diagnostic kit
Study Design	Non-interventional, non-randomized, open-label and single-center Clinical Performance Study.
Purpose of the clinical investigation	To determine the diagnostic accuracy (sensitivity and specificity) of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of SARS-CoV-2.
Target population	The SARS-CoV-2 Antigen Test Kit (Colloidal Gold) is intended for subjects who are suspected of SARS-CoV-2 infection
Investigator(s)	Dr. María Antonia Sánchez
Study site(s)	This clinical performance study will be conducted at 1 site in Spain.
Local CRO (Monitoring and Site Management)	AKRN Scientific Consulting
Data Management	AKRN Scientific Consulting
Key dates	Report cut-off date: 04-May-2022 Completion date: 09-May-2022 Date of database lock for report: 04-May-2022
First EC Approval	07-Apr-2022
First Site Activated	11-Apr-2022
First Patient In (FPI)	12-Apr-2022

End of enrollment	25-Apr-2022
Objectives	The main objective of this clinical performance study is to determine the diagnostic accuracy (sensitivity and specificity) of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of SARS-CoV-2 leftover specimens previously collected by standard-of-care procedures. The secondary objective is to determine the diagnostic accuracy (sensitivity and specificity) ofthe SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of SARS-CoV-2 in specimens from human anterior nasal swabs self-collected by lay users who are antigen-positive or unaware of their COVID-19 status.
Number of specimens/subjects required	100 SARS-CoV-2 specimens collected within 7 days since the onset of symptoms confirmed positive by RT-PCR, 100 SARS-CoV-2 specimens confirmed negative by RT-PCR collected from hospitalized patients and 300 SARS-CoV-2 specimens confirmed negative by RT-PCR, all obtained from leftovers. In addition, a minimum of 100 subjects will be recruited to perform a self-test.
Selection criteria	**Inclusion criteria:** 1. Leftover specimens collected with a human anterior nasal swab. 2. Leftover negative specimens from samples confirmed SARS-CoV-2 negative by RT-PCR, or leftover positive specimens from subjects within the first 7 days after symptom onset confirmed SARS-CoV-2 positive by RT-PCR. OR 1. Specimens from subjects over 18 years and capable to provide informed consent. 2. Specimens self-collected by the lay-person providing informed consent. 3. Specimens from subjects who are able to read and understand the device instructions. **Exclusion criteria:** 1. Leftover specimens stored at -70ºC that undergo more than 2 freeze/thaw cycles. 2. Contamination and/or deterioration of the specimen which, in the opinion of the investigator, may affect its handling and/or analysis. 3. The subject performing the self-test is deemed clinically unsuitable by the investigator.
Results and Conclusions	The results obtained from the performance analysis of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) for the detection of SARS-CoV-2 showed a diagnostic accuracy of 93.00% in specimens analyzed from lay-users and self-collected, while the diagnostic accuracy from leftovers was 96.8%. The reported sensitivity of the kit was 84.00% in specimens from leftovers, and 82.05% in specimens from lay-users and self collected, which is in-line with the requirements from the MDCG2021-21. In terms of specificity, the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) has been proved to be very effective, with a 100% probability of recognize the absence of target markers associated with SARS-CoV-2.

	In addition, the conclusions obtained from the interpretability of the kit showed that more than 90% of the subjects participating in the clinical performance study correctly identified the possible outcomes of the test, which provides further evidence on the comprehensibility of the test. Finally, the fact that no serious neither non-serious adverse events were reported, together with the absence of other complications associated with the device, confirmed the safety profile of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold).

2 INTRODUCTION AND BACKGROUND

In late December 2019, an outbreak of an unusual viral pneumonia began in Wuhan, China. The pathogen of the outbreak was later identified as a novel beta-coronavirus designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1].

Identification of people infected with SARS_CoV_2 has been essential for controlling its spreading and public health management. Owing to the development of molecular biology technologies, molecular diagnostic methods have developed rapidly. Among these, polymerase chain reaction (PCR) based assays are regarded as the gold standard for virus detection because of their high sensitivity and specificity [2]. However, PCR-based detection has many limitations such as the requirement of high purity sample, expensive laboratory equipment, training of specialists, and long reaction time [3].

The scientific community has achieved extraordinary progress in response to the limitations of PCR-based assays, resulting in the development of rapid diagnostic tools for improving SARS-CoV-2 surveillance. Rapid antigen tests (RATs) offer results more rapidly (approximately 15–30 min), are easy to perform and do not require highly trained staff and specialized laboratory equipment[4]. The RAT are based on the immunochromatographic principle, and the mechanism of action is based on detecting the SARS-CoV-2 nucleocapsid protein (N) at or near the place where a specimen is collected, providing results within few minutes[5].

Each test strip consists of a plastic backing card, sample pad, conjugate pad with mouse anti-N-protein antibody conjugated to gold particles, nitrocellulose detection membrane with immobilized antibodies, and wicking pad[6]. If the patient sample contains SARS-CoV-2 antigen, it will bind to the antibodies of the conjugate pad forming an immunocomplex. These will migrate along the strip and will be captured by a second anti-SARS-CoV-2 antibody immobilized on the test line. Accumulation of immunocomplexes in this area gives rise to coloured band, only if the sample is positive. The coloured control line (C) must be present for a test to be valid[7].

Considering the ease-of-use of the RAT tests, self-testing has been increasingly employed[8]. From a public health perspective, self-tests can complement point-of-care tests by allowing more globally scaled testing. Self-testing provides a quick result and does not require attendance to a healthcare center, thereby supporting the early detection and isolation of COVID-19 cases[9].

The SARS-CoV-2 Antigen Test Kit (Colloidal Gold) is a rapid lateral flow immuno-chromatographic sandwich assay intended to directly detect nucleocapsid protein of SARS-CoV-2 in nasopharyngeal swab, nasal swab and saliva specimens for the diagnosis of SARS-CoV-2 infection. This test is for non-prescription home use with self-collected anterior nasal swab specimens directly from individuals.

The Clinical Performance Study has been carried out as described in the corresponding clinical performance study plan (CPSP) developed according with ISO 20916:2019 and the regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices (IVDR). Is a non-interventional, non-randomized, open-label and single-center Clinical Performance Study. A total amount of 500 specimens from leftovers (100 SARS-CoV-2 positive specimens and 400 SARS-CoV-2 negative specimens) and at least 100 self-collected specimens from lay users will be included.

The primary objective was to determine the diagnostic accuracy (sensitivity and specificity) of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of SARS-CoV-2 leftover specimens previously collected by standard-of-care procedures. As a secondary objective, the diagnostic accuracy (sensitivity and specificity) of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of SARS-CoV-2 specimens from human anterior nasal swabs self-collected by lay users who are antigen-positive or unaware of their COVID-19 status was assessed.

This document is a Clinical Performance Study Report to present the main results and conclusions obtained from the clinical performance study conducted to evaluate the diagnostic specificity and sensitivity of SARS-

CoV-2 Antigen Test Kit (Colloidal Gold). This clinical investigation was conducted at 1 site located in Spain. The study concludes that the diagnostic accuracy IVD medical device achieve the minimum expectation in terms of specificity and sensibility rates according to the current guidelines.

3 STUDY PROGRESS

The first EC approval was received on 07-Apr-2022 in L'Hospitalet de Llobregat, Spain for the "Clinical Performance Study for the SARS-CoV-2 Antigen Test Kit (Colloidal Gold)" study. The single participating site was activated on 11-Apr-2022 in Zaragoza, Spain. A total of 100 subjects were enrolled between 12-Apr-2022 and 25-Apr-2022 at this site. Enrolment in the study was closed on 27-Apr-2022. The report cut-off date and database lock were performed on 04-May-2022.

4 MATERIALS AND METHODS

4.1 Intended use

The SARS-CoV-2 Antigen Test Kit (Colloidal Gold) is intended for qualitative detection of the nucleocapsid protein antigen of SARS-CoV-2 in anterior nasal specimens from individuals within 7 days of symptom onset or without symptoms or other epidemiological reasons to suspect of COVID-19 infection.

4.1.1 Intended user

The SARS-CoV-2 Antigen Test Kit is intended for subjects who are suspected of COVID-19 by their healthcare provider, with or without signs and symptoms of COVID-19. This test is for non-prescription home use with self-collected anterior nasal swab specimens directly from individuals aged 18 years and older or with adult-collected anterior nasal samples directly from individuals aged 2 years or older.

4.1.2 Manufacturing process

Each SARS-CoV-2 Antigen Test kit contains a test cassette, a sample tube pre-filled with the antigen extraction buffer, single packaged nasal swab, waste bag tube holder and IFU. All kit components should be stored at 2 ~ 30 °C in the closed original condition with a humidity <70%.

4.1.3 Duration of device usage

SARS-CoV-2 Antigen Test Kit components are stable until the expiration date printed on the label, and past this date the cassette cannot be used. In these conditions the test kit is provisionally valid within 18 months. The opened test reagent card should be used within 30 minutes. Immediate use is recommended.

4.1.4 Device sterility

There are no specific requirements regarding SARS-CoV-2 Antigen Test Kit (Colloidal Gold) sterility process, therefore this section is not applicable.

4.1.5 Principles of operation

The SARS-CoV-2 Antigen Test Kit (Colloidal Gold) is a rapid immuno-chromatographic assay used for the qualitative in vitro determination of the SARS-CoV-2 antigen. Inside the test cassette there is a strip with gold particle-modified monoclonal antibodies for capturing SARS-CoV-2 antigen (immunocomplex). When specimens are processed and added to the test cassette, the sample migrates by capillary action:

- If the sample contains SARS-CoV-2 antigen, it binds to the gold particle-modified monoclonal antibodies forming the immunocomplex. As the sample flows past to the test zone (T), the gold particle-modified monoclonal antibodies are captured by the second anti-SARS-CoV-2 antibody immobilized on the test line. Accumulation of immunocomplexes in this area gives rise to a first band, only if the sample is positive.
- If the sample does not contain SARS-CoV-2 antigen, the gold particle-modified monoclonal antibodies will not bind to the test line.

As an internal control, the kit contains a control zone (C), upstream of the test zone, with bound antibodies. These do not recognize the SARS-CoV-2 antigen, but the modified antibodies.

When the sample reaches this zone, whether or not it contains SARS-CoV-2, the modified antibodies will be recognized and will always give rise to a band, indicating that the test is working and that the required volume of sample has been added.

4.1.6 Device usage in conjunction with other medical devices or medical technologies

No interactions between the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) and other medical devices and/or therapies have been reported.

4.1.7 Cautions, warnings and precautions

The following cautions and precautions need to be taken into consideration for the proper handling of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold):

1. For in vitro diagnostic use only.
2. Children under 18 years of age should be assisted by an adult.
3. Read the Instructions for Use (this leaflet) carefully before use.
4. Keep the test kit and kit components out of the reach of children and pets before and after use.
5. Do not open the sealed foil pouch until ready for immediate use.
6. Do not use the test kit if any of the kit components are missing, broken, or unsealed.
7. Do not use components from different batch lots.
8. Do not re-use the test kit.
9. Use the nasal swab provided in the test kit to ensure optimal performance of the test.
10. The specimens should be tested immediately after collection.
11. Handle all specimens, used material and test cassettes as potentially infectious.
12. Inadequate or inappropriate sample collection, storage, and transport can result in incorrect results.
13. Correct specimen collection is a quite important step during the testing procedures. Make sure to collect enough specimens with the nasal swab.
14. Use of Nitrile, Latex (or equivalent) gloves is recommended when conducting test.
15. Avoid using visually bloody or overly viscous samples for testing.
16. Sample handling and waste disposal must comply with relevant regulations. Wash hands thoroughly after handling.
17. Store the test kit at 2-30℃Do not freeze.
18. The test should be used at room temperature (8-30℃). If the test has been stored in a cool area (less than 8℃), leave it at normal room temperature for 30 minutes before using.
19. Apply the drops of test specimen only to the sample well (S) on the test cassette.
20. Too many or too few drops of processed solution may result in invalid or incorrect test result.
21. The specimen collection procedures may be uncomfortable. Do not insert the swab too much deeper, please stop it if you feel strong resistance or pain.
22. Wear safety mask or other face covering when collecting swab specimen from child or another individual.
23. The sample tube contains a salt solution. If the solution contacts the skin or eye, flush with copious amounts of water.

For additional information, please refer to the Instructions For Use (IFU).

4.1.8 Potential adverse events/side effects

Discomfort was observed during specimen self-collection, as usually associated with the collection procedure. However, there were no potential adverse events or side effects, neither related to the device nor to its use.

4.2 Clinical study protocol overview

Study timing:

This study had an enrollment period of 14 days and no follow-up was required. As the clinical performance study only analyzed the diagnostic accuracy of the test, the treatment period per each subject was one day.

Study location:

This clinical investigation was conducted in one site in Zaragoza, Spain.

4.2.1 Study Objectives

This clinical performance study has been designed in order to determine the diagnostic accuracy, in terms of sensitivity and specificity, of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of SARS-CoV-2 leftover specimens previously collected by standard-of-care procedures.

4.2.2 Selection of study population

A total of 100 patients were enrolled for the participation in the clinical investigation. The enrolment period started on 12-Apr-2022, and continued until 27-Apr-2022. This clinical performance study has no timepoints of follow-up.

Patients must meet all eligibility criteria and provide written informed consent prior to conducting any investigation-specific procedures not considered standard of care. Assessment for general eligibility criteria is based on medical records of the site and interview with a patient candidate. The criteria considered for the selection of individuals are presented in the following sections.

4.2.2.1 Inclusion criteria

1. Leftover specimens collected with a human anterior nasal swab.
2. Leftover negative specimens from samples confirmed SARS-CoV-2 negative by RT-PCR, or leftover positive specimens from subjects within the first 7 days after symptom onset confirmed SARS-CoV-2 positive by RT-PCR.

OR

1. Specimens from subjects over 18 years and capable to provide informed consent.

4.2.2.2 Exclusion criteria

1. Leftover specimens stored at -70ºC that undergo more than 2 freeze/thaw cycles.
2. Contamination and/or deterioration of the specimen which, in the opinion of the investigator, may affect its handling and/or analysis.

4.2.2.3 Withdrawal of patients from the therapy or assessment

Patients were free to withdraw from the study at any time without giving a reason. Patients were advised that if they requested to withdraw from the study, at any time during the trial, then this would have no negative consequences.

4.2.3 Clinical study endpoints

4.2.3.1 Primary endpoint

The primary endpoints of this clinical investigation include the evaluation of the following:

1. The diagnostic accuracy of SARS-CoV-2 Antigen Test Kit (Colloidal Gold), defined in terms of the sensitivity and specificity as the positive SARS-CoV-2 detection rate of the RT-PCR confirmed positive samples, and the negative detection rate of the RT-PCR confirmed negative samples both from leftover specimens.

4.2.4 Treatments

4.2.4.1 Sample collection procedure

In order to collect the anterior nasal swab sample, the subject must insert the swab into the nasal meatus, stay for a while, and then slowly rotate to exit. Consequently, the subject must use the same swab to collect the other nostril in the same way to ensure that adequate samples are collected from both nasal passages.

For further information regarding the treatment, please refer to the Instructions for Use (IFU).

4.2.4.2 Concomitant medication

Participants exclusively receive SARS-CoV-2 Antigen Test Kit (Colloidal Gold) during this clinical performance study. There was no concomitant medication during the study.

4.2.5 Post-study care

No specific post-study care was required for the subjects participating in this clinical performance study.

4.3 Study conduct

4.3.1 Protocol revision history/amendments

Two different versions of the CPSP were released during the conduct of the study; all of them were approved by the appropriate EC of the respective clinical site, as specified by local regulations and requirements before implementation in the participating sites. Two additional minor modifications, which include the correction of typos, were notified to the EC. CPSP modifications did not affect study design nor study objectives. The last version of the CPSP is version 2.1, released on 19-Apr-2022.

The different versions of the CPSP are listed in **Table 4-1**.

Table 4-1: Protocol versions released

Previous Version	Creation Date	Approval Date	Major Changes
CPSP Version 1.0	11-Mar-2022	15-Mar-2022	N/A
CPSP Version 2.0	01-Apr-2022	01-Apr-2022	- Clarifications on collection of prospective samples from lay users. - Further rationale on processing of personal data.
CPSP Version 2.1	19-Apr-2022	19-Apr-2022	Clarification on the minimum of 60 specimens for SARS-CoV-2 self-collected by lay persons who are unaware of their status.

4.3.2 Ethical considerations

4.3.2.1 Compliance to the laws and guidelines

The investigator agrees that the study was conducted according to the CPSP, the Declaration of Helsinki, law 14/2007 of 3 July 2007 on Biomedical Research, ISO 20916:2019, Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices (IVDR) and EU General Data Protection Regulation. The investigator conducted all aspects of this study in accordance with all national

and local laws or regulations.

Prior to starting the study at the sites, the regulatory documentation and amendments were submitted for review to Comité de Ética de Investigación con Medicamentos (CEIm) del Hospital Universitario de Bellvitge as central EC for the study and written documentation of the regulatory approvals of both the protocol and the informed consent form.

4.3.3 Data management and quality assurance

4.3.5.1 Common protocol and training

All research procedures performed in this study were in accordance with the approved protocol. Each investigational site was provided with a deep review of the protocol and procedures and investigators completed a protocol training. Site training emphasized the protocol and study compliance, compliance with applicable regulations, subject selection, functioning of SARS-CoV-2 Antigen Test Kit (Colloidal Gold) and its usage/application, and the essential ancillary equipment necessary to perform the procedure with the device.

4.3.5.2 Data management

IVDR 2017/746, ISO 20916:2019, and Good Clinical Practice (GCP) standard 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 have been 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).
- AEs reported and their resolution, including supporting applicable documents, such as discharge summaries, catheterization laboratory reports, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- Notes regarding CPSP-required and prescription medications taken during the clinical investigation (including start and stop dates).
- Subject's condition upon completion of or withdrawal from the clinical investigation.
- 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.

For leftover specimens, a risk-based monitoring of selected data points has been performed. Source Data Verification (SDV) was carried out on 50% of the specimens from the participating sites. The 100% SDV was required on study endpoints, including:

- Inclusion and exclusion criteria
- All endpoint related data
- Device deficiencies.

On the other hand, targeted monitoring has been conducted for those samples self-collected from lay-users. In this case, SDV was focused on study endpoints and patient safety data, including:

- Informed consent forms
- Inclusion and exclusion criteria
- All endpoint-related data
- Device deficiencies

Regarding CRF completion, primary data collection based on source-documented hospital and/or clinic chart reviews was performed clearly and accurately by site personnel trained on the CPSP and CRF completion.

The investigator ensured accuracy, completeness, legibility and timeliness of the data reported to the sponsor on the CRFs and in all required reports.

Data on CRFs was collected for all patients that were enrolled into the clinical investigation. Only authorized site personnel were permitted to enter the CRF data through the electronic data capture (EDC) system deployed by the Sponsor. An electronic audit trail was used to track any subsequent changes of the entered data.

4.3.5.3 Maintaining records

All study related documentation, including CRFs, informed consents, regulatory documents, study manuals, training materials, device accountability records, and source documents were maintained until the end of the study, where data can be archived according to local procedures.

4.3.4 Notification to the EC or Competent Authority

According to IVDR 2017/746 and ISO 20916:2019 and current national and local regulations, the Comité de Ética de Investigación (CEI) con Medicamentos (CEIm) del Hospital Universitario de Bellvitge was informed about any major protocol deviations produced in the conduct of this clinical performance study.

5 DATA ANALYSIS

The information to complete this section is explained in detailed in the Statistical Analysis Plan (SAP) and the statistical section of the CPSP.

5.1 Statistical methodology

A Statistical Analysis Plan (SAP) was written to provide a more technical and detailed elaboration of the principal features of the analysis described in the protocol Clinical Performance Study for the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) Ver 2.1 and to include detailed procedures for executing the statistical analysis of the primary and secondary endpoints and other data.

5.1.1 Sample size justification

The sample size calculation was based on the objective to demonstrate an 80% sensitivity and a 98% specificity of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold), defined as the minimum requirements in the MDCG2021-21. Considering that this IVD is designed to be used by lay persons for self-testing, a total number of 600 specimens are needed for the following parameters:

- 100 positive specimens of SARS-CoV-2 to test sensitivity.
- 400 negative specimens of SARS-CoV-2 to test specificity.
- A minimum of 30 known antigen positive specimens of SARS-CoV-2 self-collected by lay persons to test sensitivity.
- A minimum of 60 specimens for SARS-CoV-2 self-collected by lay persons who are unaware of their status, to test specificity.

5.1.2 Hypotheses testing

No formal hypothesis testing has been performed for the primary or secondary endpoints:

- Evaluation of the diagnostic accuracy of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold), defined in terms of sensitivity and specificity.
- Collection of data regarding the interpretability of the possible results obtained from the self-assessment of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold).

5.2 Patient population

5.2.1 Patient data

All data related to various study endpoints have been displayed in data listings sorted by subject population. Summary data have been presented in a tabular format. Categorical data have been summarized by the number and percentage of patients in each category. Continuous variables have been summarized by descriptive statistics including N, mean, standard deviation, median, and range, if applicable.

5.2.2 Justification of pooling

There was not pooling analysis in this study.

5.2.3 Population(s) for analysis

During this clinical performance study, the following population was considered for analysis:

- Per-Protocol population (PP). This population includes all leftover specimens meeting the I/E criteria and all self-collected specimens from subjects who have completed the Informed Consent Process and performed a valid rapid antigen test.

5.3 Device performance analysis

This clinical performance study has been focused on the evaluation of the diagnosis accuracy of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of COVID-19 in both leftover specimens and specimens self-collected by lay-persons. This diagnosis accuracy has been assessed in terms of sensitivity and specificity:

- The sensitivity is defined as the ability to detect a target marker, which in this case is a viral protein, that is associated with the SARS-CoV-2 virus. Therefore, the sensitivity is related with the capacity to detect positive samples of COVID-19. Considering this definition, the sensitivity of SARS-CoV-2 Antigen Test Kit (Colloidal Gold) has been obtained as the ratio of the True Positive measurements (TP) to total known positive measurements (True Positive + False Negative).

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

- On the other hand, the specificity is defined as the ability to recognize the absence of a viral protein associated with the SARS-CoV-2 virus, which in this case is considered the target marker. Therefore, the specificity means the capacity of the test 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).

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

5.4 Device results interpretability analysis

Additionally, this clinical performance study aimed to evaluate the interpretation of the results performed by lay users of the contrived test results, determining the concordance of the readings between lay-persons and professional readers. Within this context, the participants of the study were asked to complete a questionnaire in which the four possible outcomes of the test were presented, analyzing the percentage of options properly identified by the subjects.

Finally, the participants have been also asked to interpret the results obtained from their own rapid antigen test, which was also assessed by the healthcare professional present during the test, evaluating the clinical equivalence observed between both assessments.

6 RESULTS

6.1 Primary endpoint results

6.1.1 Analysis of the primary endpoint in specimens collected by lay-users

The primary endpoint of this clinical performance study has been focused on the evaluation of the diagnostic accuracy of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of COVID-19 in both leftover specimens and specimens self-collected by lay-persons. Generally, the diagnostic accuracy is defined by the sensitivity (ability to detect true positive specimens) and specificity (ability to recognize the absence of a specific target marker). The formulas used to calculate the sensitivity and specificity are the followings:

$$Sensitivity = \frac{(TP)}{(TP + FN)} \qquad Specificity = \frac{(TN)}{(TN + FP)}$$

The analysis to determine the diagnostic accuracy of the kit has been performed using samples from lay-users and leftovers separately. Regarding the results from lay-users, the data obtained is presented in the **Table 6-6**.

Table 6-6. COVID-19 diagnostic accuracy from self-collected specimens

Parameter	(%)	[95% CI]
Sensitivity	82.05%	[66.46%, 92.46%]
Specificity	100%	[94.13%, 100%]

According to the results, the overall diagnostic accuracy of the kit when used by lay persons was 93 .00% [86.11%, 97.14%, 95% CI]. Therefore, considering the outcomes from the measurements performed, the results in the case of lay-users showed a sensitivity and specificity of 82.05% [66.46%, 92.46%] and 100% [94.13%, 100%], with a 95% CI.

6.1.2 Analysis of the primary endpoint in specimens collected from leftovers

On the other hand, the results obtained from the leftover specimens collected from the biobank showed better results in term of sensitivity, with a value of 84.00% [75.32%, 90.57%], with a 95% CI (**Table 6-7**). Again, the specificity obtained was 100% [99.08%, 100%] and 95% CI, which determined an overall diagnostic accuracy of 96.8% [94.86%, 98.16%], with a 95% CI.

Table 6-7. COVID-19 diagnostic accuracy from leftover specimens

Parameter	(%)	[95% CI]
Sensitivity	84.00%	[75.32%, 90.57%]
Specificity	100%	[99.08%, 100%]

6.2 Secondary endpoint results

The secondary endpoints of this clinical performance study aimed to assess the interpretation, by lay users, of the contrived test results by the determination of concordance of lay reading of the same tests by professional readers. To do so, a representative image of one of the 4 possible outcomes of the test (strong positive, limited positive, negative or invalid) has been presented to the subject. According to the current guidelines, images presenting limited positive results should be presented in a higher frequency due to a more difficulty to properly interpret this result. A summary of the findings obtained from this assessment is presented in the table below:

Table 6-8. Correct outcome interpretation result

Option	n/N (%)	[95% CI]
Strong Positive	17/19 (89.47%)	[66.86%, 98.70%]
Limited Positive	27/32 (84.38%)	[67.21%, 94.72%]
Negative	20/20 (100%)	[83.16%, 98.77%]
Invalid	24/29 (82.76%)	[64.22%, 94.15%]

The results obtained from this analysis revealed that 88% of the subjects correctly identified the outcome of the test. Additionally, this assessment was performed per type of outcome, showing that the strong positive image was identified by 89.47% of the subjects asked, while the rate of correct answers for the negative and invalid results was 100% and 82.76%, respectively. Finally, 84.38% of the participants responded correctly when asked about the limited positive outcome.

On the other hand, the subjects performing the self-testing using the device under investigation were asked to assess the results obtained from their own test to confirm the interpretability of the kit. The results obtained from this questionnaire are shown.

Table 6-9. Interpretation equivalence between lay-users and healthcare professionals

Parameter	n/N (%)	[95% CI]
Positive result	32/33 (96.97%)	[84.24%, 99.92%]
Negative result	67/67 (100%)	[94.64%, 100%]

As shown in **Table 6-9**, 99.00% of the subjects correctly assessed the results obtained from their own rapid antigen test. When analyzed separately according to the diagnostic outcome, 96.97% of the subjects identified the positive result, while the negative COVID-19 diagnostic was detected in 100% of the cases.

7 DISCUSSION

During the conduct of this clinical performance study, performance analyses have been performed to determine the diagnostic accuracy (sensitivity and specificity) of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) in the diagnosis of SARS-CoV-2. In addition, the interpretability of the possible outcomes of the test by lay-user has been also analyzed, as well as the incidence of (S)AEs related to both the device or the procedure to confirm the safety profile of the investigational device.

First, the safety analysis performed proved that, during the conduct of the clinical performance study, no (S)AEs, discomfort or any other more severe complications (including deaths) have been reported. Therefore, the data obtained from this assessment provide enough evidence to confirm that the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) is safe to be used by lay-users.

Regarding the primary endpoint, this study was focused on determining the diagnostic efficacy, in terms of sensitivity and specificity, of the investigational device. As this kit is designed to be used by lay-persons, the diagnostic accuracy has been determined separately for both samples obtained from self-testing and specimens from leftovers, which were isolated and analyzed by healthcare professionals. The results obtained from this analysis show a diagnostic accuracy of 93% and 96% for lay-users and leftovers, respectively.

In terms of sensitivity, this study demonstrated a sensitivity value of 84% (95% confidence interval 75% to 91%). This value is in line with the minimum sensitivity acceptance criteria (80%) required by the MDCG2021-21 guidance document. With a statistic calculated for the sample of observations (a mean value of 84%), and a confidence interval with a range of values from 75% to 91% around that statistic, there is a 95% probability that the true value of that statistic (i.e., the population value) is included. Taken together, the results from this study demonstrate that the device meets the required minimum sensitivity acceptance criteria.

In terms of specificity, the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) is demonstrated to be very effective, showing a 100% capacity of discriminating subjects with absence of target markers associated with SAR-CoV-2.

Additionally, this clinical performance study aimed to evaluate the interpretability of the possible outcomes obtained from the investigational device. This analysis showed a high understanding (above 90%) of the different test results in both the images presented to the subjects and in the tests performed by the lay-users. Therefore, we may conclude that the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) can be considered a diagnostic method that is easy to understand for lay users and can contribute to the control of the pandemic.

Finally, the safety analysis performed demonstratedthat, during the conduct of the clinical performance study, no (S)AEs, discomfort or any other more severe complications (including deaths) have been reported. Therefore, the data obtained from this assessment provide enough evidence to confirm that the HUIAN SARS-CoV-2 Antigen Test Kit (Colloidal Gold)is safe to be used by lay-users.

8 CONCLUSIONS

The clinical data generated from this clinical performance study demonstrate that:

- The investigational device is a safe IVD medical device for COVID-19 self-testing.
- The sensitivity capacity of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) has been proved to be in line the minimum acceptance criteria required by the MDCG2021-21.
- The ability of the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) to recognize the absence of target markers associated with COVID-19 has been showed to be very effective, with a sensitivity of 100%.
- The conclusions obtained from the interpretability analysis of the outcomes of the test provide sufficient evidence to confirm that the device is easy to use, with a high understanding of the different results.

The data presented here demonstrated that the SARS-CoV-2 Antigen Test Kit (Colloidal Gold) fulfils the safety and performance requirements and is eligible for CE mark certification under the Directive 98/79/EC (IVDD).