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REAGEN

Medical & Drug ● IVD & POCT ● Food & Safety

SARS-CoV-2 Antigen IVD Kit NASAL

Clinical Evaluation Report

Product name:SARS-CoV-2 Antigen IVD Kit NASAL

Packing specification：25 Tests/ Kit

Clinical evaluation category: Comparison with clinical PCR results

Clinical evaluation place: R7777,Hangcheng Wisdom Science Park, Hangcheng street,Bao'an District Shenzhen 518128,China

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1. Overview

1.1 Abstract

Objective:

To evaluate the detection capability of SARS-CoV-2 Antigen IVD Kit NASAL (Colloidal Gold) produced by Shenzhen Reagent Technology Co.,Ltd. is equivalent to the clinical diagnostic criteria when used for qualitative detection of SARS-CoV-2 antigen in human nasal samples in vitro.

Methods:

Synchronous blind test and methodological comparison design.

1.2 Abbreviation

Severe Acute Respiratory Syndrome Coronavirus 2：SARS-CoV-2

2. Main Content

2.1 Basic Content

2.1.1 Introduction

The novel coronavirus (SARS-CoV-2) belongs to beta coronavirus, has an envelope, and the particles are round or elliptic, often polymorphic, with a diameter of 60-140nm. Its genetic characteristics are significantly different from SARAr-CoV and MERSr-CoV. When isolated and cultured in vitro, SARS-CoV-2 can be found in human respiratory epithelial cells in about 96 hours, while it takes 6 days to isolate and culture in Vero E6 and Huh-7 cell lines. It can be transmitted through respiratory droplets and contact, and the population is generally susceptible. The incubation period is 1-14 days, mostly 3-7 days. Main symptoms are fever, fatigue, and dry cough. A few patients have symptoms such as nasal congestion, runny nose, sore throat, and diarrhea. Severe patients often have dyspnea, septic shock, difficult to correct metabolic acidosis, and coagulation dysfunction after one week of onset. The elderly and those with chronic underlying disease have a poor prognosis, and children are relatively mild. The recovery period of IgG antibody titers increased by 4 times or more compared with the acute phase. Two consecutive negative nucleic acid tests for SARS-CoV-2 in suspected cases (Sampling time shall be at least 24 hours apart) and still negative IgG and IgM of SARS-CoV-2 specific antibodies 7 days after onset can rule out the diagnosis of suspected cases.

The SARS-CoV-2 Antigen IVD Kit NASAL (Colloidal Gold) produced by Shenzhen Reagent Technology Co.,Ltd. is used to qualitatively detect the SARS-CoV-2 antigen in human nasal samples.

2.1.2 Research purpose

To evaluate the detection capability of SARS-CoV-2 Antigen IVD Kit NASAL (Colloidal Gold) produced by Shenzhen Reagent Technology Co.,Ltd. is equivalent to that of similar products on themarket when used for qualitative detection of antigen in nasal samples in vitro.

2.1.3Testing management

This clinical trial was conducted by Shenzhen Reagent Technology Co.,Ltd. in accordance with “Technical Guidelines for Clinical Trials of Diagnostic Reagents in Vitro” and “Technical Review Points for Registration of SARS-CoV-2 Antigen Detection Reagents (Trial)” and supervised the implementation of the entire clinical evaluation trial.

During the trial, the main investigator is responsible for the coordination and management of the entire clinical trial, and the main participants are responsible for the main trial work. During the clinical trial, the main researcher supervises the quality control of the testing laboratory. Any problems found in the test must be contacted with the main researcher in time and appropriate measures should be taken. The final test results are statistically analyzed by the person in charge of statistics (SPSS statistical software was used, etc), and the main investigator confirmed andwrote the report. Finally, Shenzhen Reagent Technology Co.,Ltd. issued a clinical trial report inaccordance with the requirements of exempting clinical trials.

2.1.4 Research design

2.1.4.1General design

This test uses synchronous blind test and methodological comparison design.

In order to eliminate the possible impact of the subjective biases and personal preferences of researchers on the test results during the clinical trial process, this test uses a blind test. That is, the test personnel in this test do not know the specific information of the sample, and the clinical information of the sample may not be released until the end of the test. After the samples were enrolled, the samples were coded by the blind editor authorized by the clinical trial, in which the blind editor authorized by the clinical trial was not involved in the test operation of the clinical trial. Testing personnel shall test the coded sample according to the reagent test specification. In the process of test operation, clinical test researchers should strictly follow the requirements of the product specification for test operation and interpretation check, and the results obtained in the test process should be truthfully recorded in the data collection table.

2.1.4.2 Measures to reduce and avoid bias

1) Subjects were screened strictly according to the inclusion and exclusion criteria of the

clinical trial protocol to reduce the selection bias.

2) Prior to the start of the trial, the sponsor shall train the participants in the clinical trial protocol and the use of the research reagent, ensure the consistency of the clinical trial protocol and the operation of the research reagent, and promote communication among the clinical trial investigators during the clinical trial.

3) Prior to the start of the trial, the clinical trial personnel shall maintain and calibrate or quality control all the equipment to be used. The applicant shall conduct the pre-test of the clinical trial with the clinical trial researcher, so as to make the applicant familiar with and master the operation method, technical performance, etc. of the product, and control the trial operation error to the maximum extent.

4) In the process of the test, the clinical test researcher must do the quality control work according to the requirements of the reagent specification and operate in strict accordance with the test plan. The clinical trial supervisor shall supervise the work to ensure that the clinical trial researchers operate and implement the test plan strictly.

5) When the clinical trial is completed, the data shall be kept and sorted out. When problems are found in the data, the researcher shall check and confirm the data to avoid recording errors.

2.1.4.3 Clinical sample selection

2.1.4.3.1 Inclusion criteria

As this kit is an in vitro qualitative test kit, it can only be used for the auxiliary diagnosis of pneumonia caused by SARS-CoV-2 in clinic, and it cannot identify the clinical disease. Therefore, the positive and negative samples are mainly differentiated in clinical practice, and the samples included are from suspected cases of pneumonia caused by SARS-CoV-2.

Using the results of reference group as the classification basis, the subjects of this clinical study were divided into positive group and negative group. In the consistency comparison of experimental reagent and reference group, the result of PCR was used as the classification basis.

1) Sample inclusion criteria: the sample should be a sample with sufficient margin and clearly recorded source, including different age, gender and other factors. The collection and treatment of samples are in accordance with the reagent specification or relevant regulations. Sample information should be complete, including age, sex, sample collection date, clinical diagnosis such

as confirmation or exclusion of SARS-CoV-2 infection.

2) Inclusion criteria for the positive group: clinically confirmed cases were collected, and the samples met the requirements of 1).

3) Inclusion criteria for the negative group: clinical excluded cases were collected, and the samples met the requirements of 1).

2.1.4.3.2 Exclusion criteria

1) The time of sample collection or case information is not clear.

2) The sample size is not enough to complete the test.

3) Before the test operation, it was found that the sample preservation process was polluted, resulting in turbidity.

4) The researchers believe that the sample does not meet the test requirements.

2.1.4.3.3 Rejection criteria

1) Samples that are unable to complete the test process due to instrument or human factors (sample contamination during operation).

2) The sample test results are from the samples that are not stored and tested according to the instructions of the experimental reagent.

2.1.4.4 Samples distribution

Specific requirements for clinical sample size are as follows:

1) The number of confirmed cases should be no less than 100.

2) The excluded cases are recommended to be no less than 100.

2.1.4.5 Sample collection, transportation methods

Collection of nasal samples:

1.While gently rotating the swab, insert swab about 2.5 cm(1 inch) into nostril until resistance is met at turbinates.

2.Rotate the swab several times against nasal wall and repeat in other nostril using the same swab.

If transport of samples with universal transport medium (UTM-RT System, Copan Diagnostics, Murrieta, CA, USA) is required, minimal dilution of the sample is recommended, as dilution may result in decreased test sensitivity. Whenever possible, 1 mL or less is best to avoid excessive dilution of the patient sample.

2.1.4.6 Reagents and instruments for clinical research

1) The assessment reagent information is shown in Table 1:

Table 1 Assessment Reagent Information

Reagent Name	SARS-CoV-2 Antigen IVD Kit NASAL
Specification	25 Tests/ Kit
Company	Shenzhen Reagent Technology Co.,Ltd.
Lot Number	20210501
Preservation Condition	4℃~30℃

2) The reference reagent information is shown in Table 2:

Table 2 Reference Reagent Information

Reagent Name	Novel Coronavirus(2019-nCoV) Nucleic Acid Diagnostic Kit(PCR-Fluorescence Probing)
Specification	48 Tests/ Kit
Company	Sansure Biotech Inc.
Lot Number	20210121
Preservation Condition	Store at -20±5℃ and protected from light

2.1.4.7 Quality control

1）Definition

Quality control is defined as the operation of techniques and activities, such as monitoring,

under the quality assurance system to verify that the research quality meets the requirements. Quality control must be applied at every stage of data processing to ensure that all data is trusted and properly located.

2） Study monitoring

During the outbreak, authorized and qualified inspectors will conduct regular remote primary data checks according to the monitoring plan to verify compliance with protocols and regulations and assist investigators.

3） Laboratory quality control

The laboratory of the testing shall establish a unified test index, standard operating procedures and quality control procedures.

4） Quality control of reagent testing process

In each test, the quality control line shall have red strip (qualified quality control). If the quality control line does not have red strip (unqualified quality control), the cause shall be found out and retested until the quality control result is qualified, so as to ensure the reliability and stability of the system.

5） Qualification of researchers

The researchers participating in the clinical trial must have the specialty, qualification and ability of the clinical trial, and pass the qualification examination. The personnel requirements should be relatively fixed.

6） Training for researchers before the experiment

Shenzhen Reagent Technology Co.,Ltd. is responsible for the training of researchers before the start of the trial to help clinical researchers fully understand the overall situation, scheme, CRF, etc. of the trial.

2.1.4.8 Statistical analysis method of clinical trial data

Use statistical software or the following formula for statistical analysis.

Table 3 Consistency data analysis

Experimental Group	Reference Group		Sum
	Positive	Negative	
Positive	a	b	a+b
Negative	c	d	c+d
Sum	a+c	b+d	a+b+c+d
Sensitivity		a/(a+c)	
Specificity		d/(b+d)	

2.2 Clinical Trial Results and Analysis

2.2.1 Overall distribution of samples

In this test, a total of 260 samples were enrolled for the consistency comparison of the detection results of nasal samples by experimental reagent and PCR result, and 0 duplicate samples were excluded, and therefore, a total of 260 samples were included in the statistical analysis. Among them, 105 cases were positive samples and 155 cases were negative samples of PCR result.

Table 4 Proportion and concentration distribution of clinical trials

Sample type	Number of total cases	Positive samples		Negative samples	
		Number of cases	Ratio	Number of cases	Ratio
NASAL	260	105	23.08%	155	76.92%

2.2.2 Consistency analysis of test result

2.2.2.1 Consistency comparison of the detection results of nasal samples by experimental reagent and the clinical diagnostic criteria

In this test, a total of 105 samples were enrolled for the consistency comparison of the detection results of nasal samples by experimental reagent and PCR result. There were 32cases of symptomatic patients with CT value less than 30, of which 31 cases were positive, the positive agreement was 96.88%; 105 cases of symptomatic patients with CT value less than 36, 101 cases were positive, the positive agreement was 96.19%.

There were 155 samples with negative test results of experimental reagent and PCR result, and 2 samples in which the experimental reagent was positive and the PCR result was negative. Hence, the specificity was 98.71%

Table 5 Statistical analysis of PCR results

CT values	Number of samples	2019 nCoV RT-PCR Results	SARS-CoV-2 Antigen test result as compared to RT-PCR
≤30	32	Positive	31/32=96.88% （95%CI:86.47%~98.80%）
≤36	105	Positive	101/105=96.19% （95%CI:85.64%-98.26%）
>40	155	Negative	151/155=98.71% （95%CI:86.13%-99.10%）

2.3 Test Reliability

1)The collection and preservation methods of all test samples are reliable.

2) The operators have received special training throughout the test process to ensure the reliability of the test results.

3) When conducting clinical trials, the tests shall be conducted in strict accordance with the requirements of laboratory quality control and clinical trial program in clinical hospitals. The results were analyzed by experienced researchers to ensure the reliability of clinical trials.

2.4 Conclusion

This clinical trial has performed a full analysis of the experimental reagents through methodological comparisons, and the results all meet the criteria for clinical evaluation. It has been verified that there is no difference between the experimental reagent's nasal samples detection ability and PCR result. All the results are accurate, stable and reliable which meet the needs of clinical testing.