Novel Coronavirus 2019-nCoV Antigen Test

(Colloidal Gold)

Report of Risk Management

1 Product specifications

1T/kit, 5T/kit, 20T/kit, 25T/kit, 40T/kit, 50T/kit.

2 Product Overview

2.1 Principle

This kit is based on the colloidal gold immunochromatographic technology, and uses double antibody sandwich method to detect of SARS-CoV-2 antigen in human anterior nasal swab samples. The detection line (T line) of the novel coronavirus antigen test cassette was coated with novel coronavirus antibody, and the quality control line (C line) was coated with sheep anti-mouse. During the test, the sample is dropped into the test cassette and the liquid is chromatographed upward under the capillary effect. The novel coronavirus antigen in the sample first binds to the colloidal gold-labelled novel coronavirus antibody to form a solid phase novel coronavirus antibody-novel coronavirus antigen-labelled novel coronavirus antibody-colloidal gold complex at the T line position, and form a solid phase sheep anti-mouse-labelled novel coronavirus antibody- colloidal gold complex was formed at the C line position. After the test is completed, observe the colloidal gold color reaction of T line and C line to determine results of novel coronavirus antigen in human anterior nasal swab samples.

2.2 Use range

This kit is used for in vitro qualitative determination of novel coronavirus antigen in human anterior nasal swab samples.

2.3 Manufacturer Address

Beijing Hotgen Biotech Co., Ltd.

Address: 9th Building, No. 9 Tianfu Street, Biomedical Base, Daxing District,

Beijing, 102600, P.R. China.

2.4 Brief Introduction of the Implementation of Risk Management

We carries out the planning for the risk management activity and make the plan of risk management when Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold) is planned and proposed. The risk acceptable criterion of Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold) is decided in the risk management plan of the product, which also arranges the risk management activity in the design and development (including the trial production) and the assessment requirement on the method for obtaining information in and after production.

The company establishes a risk management team and confirms the risk management responsible person of the project so as to ensure the risk management activity of the project be effectively implemented according to the risk management plan.

2.5 Purpose of Assessing Risk Management

The purpose of the assessment of risk management is to ensure the risk management plan be successfully completed, by overall assessing the the risk management activity of Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold) in all stages before being released into the market, and verify the product risk has been managed and controlled in the acceptable range through the risk analysis, risk assessment and risk control of the product as well as the acceptability assessment of the comprehensive residual risk.

3 Date of Assessment

April 02, 2020 - February 3, 2021

4 Reviewers and Responsibilities

Name	Position	Responsibilities
Lin Changqing	General Manager	Guarantee the manpower and material for risk management
Sun Haifeng	Management Representative	Risk control of the system
Zhang Hongrui	Head of R & D Department	Estimate the probability of malfunction from a technical perspective
Li Jing	Head of Quality Department	Estimate damage severity from an application perspective

Yu Shaohua	Head of Marketing Department	Provide customer feedback
Wu Liping	Project manager	Person in charge of risk management

5 Relevant Regulations and Standards

GB/T 1.1-2009 Guidelines for Standardization Work Part 1: Structure and Compilation of Standards

YY/T 0287-2017 Medical device quality management system Requirements for regulations

YY/T 0316-2016 Medical devices Application of risk management to medical devices

Regulations on the Supervision and Administration of Medical Devices (State Council Order No. 650)

Administrative Measures for the Registration of Medical Devices (Administrative Decree No. 4)

Administrative Measures for the Registration of In vitro Diagnostic Reagents (Administrative Decree No. 5)

Regulations on Management of Medical Device Instructions and Labels (Administrative Decree No. 6)

6 Assessment Input Data

6.1 Risk Management Plan

6.2 Risk Acceptance Criterion

6.2.1 Severity Level of Risk

Level name	No.	Definition of system risk
Negligible	1	Inconvenience or temporary discomfort
Minor	2	Causes temporary injury or damage that does not require professional medical intervention
Severe	3	Cause damage or injuries that require professional medical intervention
Critical	4	Cause permanent damage or life-threatening injury
Disastrous	5	Cause patient death

Possible level	No.	Frequency (per year)
Rare	1	$<10^{-6}$
Few	2	$<10^{-5}$ and $\geq 10^{-6}$
Seldom	3	$<10^{-4}$ and $\geq 10^{-5}$
Sometimes	4	$<10^{-3}$ and $\geq 10^{-4}$
Often	5	$\geq 10^{-3}$

6.2.2 Probability level of risk

6.2.3 Risk Acceptance Criterion

Risk = severity level × probability level

RL (Risk level)	Acceptability (abbreviated code)
1-4	Widely Acceptable Area
5-12	Reasonable and feasible reduction zone
13-25	Inadmissible zone

6.2.4 Product Risk Evaluation Form

Probability		Severity				
		1	2	3	4	5
		Negligible	Minor	Severe	Critical	Disastrous
Often	5	R	R	U	U	U
Sometimes	4	A	R	R	U	U
Seldom	3	A	R	R	R	U
Few	2	A	A	R	R	R
Rare	1	A	A	A	A	R

Note: A Acceptable risk;

R Reasonable and feasible reduced risk

U The unacceptable risk judged without risk/revenue analysis.

6.3 Judgment Records of Application and Feature

Appendix 1

List of safety feature questions of Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold). The list is based on the questions in Appendix C and Appendix H of YY/T 0316-2016 standard, and based on the results of the question, the list of initially recognized and foreseeable hazards (sources) is listed according to Appendix E and give Countermeasures adopted in design and development.

Questions	Feature judgment	Danger (source) identification
C.2.1 What is the intended use of the medical device and how to use?	Intended use: This kit is used for in-vitro qualitative determination of novel coronavirus antigen in human anterior nasal swab samples; This kit is for home use by laymen in a non-laboratory setting (such as person's home or certain non-traditional sites	E2 E3

	such as offices, sporting events, airports, schools etc.). Refer to the instruction for details of use.	
C.2.2 Is the medical device anticipatively implanted?	/	/
C.2.3 Does the medical device anticipatively contacts with the patient or other personnel?	Contacts with detection personnel	E1 E10
C.2.4 What material or component is used in the medical device or use together or contact with the medical device?	1. SARS-CoV-2 Antigen Test Cassette 2. Sample extraction buffer 3. Disposable virus sampling swab 4. Biohazard specimen bag	E1 E4
C.2.5 Is there any energy given to or obtained from the patient ?	/	/
C.2.6 Is there any substance given to or obtained from the patient?	/	/
C.2.7 Does the medical device process biological material for the subsequent reuse, infuse dried powder/blood or transplant?	/	/
C.2.8 Is the medical device provided in a sterile type or anticipated to be sterilized by the user or other microbiological process?	/	/
C.2.9 Is the medical device anticipated to be regularly cleaned and sterilized by the user?	Yes	/
C.2.10 Is the medical device anticipated to improve the patient environment?	/	/
C.2.11 Is detection carried out?	In-vitro qualitative determination of novel coronavirus antigen in human anterior nasal swab samples.	E11
C.2.12 Is the medical device analyzed and processed?	/	/
C.2.13 Is the medical device anticipated to be used together with other medical device, medicine or other medical technology?	No testing equipment required	/
C.2.14 Is there any unexpected energy or substance outputted?	/	/

C.2.15 Is the medical device sensitive to the environment influence?	Keep the temperature between 4°C to 30°C in transportation.	E4
C.2.16 Does the medical device influence the environment?	The waste generated after use, if not discarded in special containers, will pollute the environment.	E9
C.2.17 Is there any basic consumables or accessory of the medical device?	1. SARS-CoV-2 Antigen Test Cassette 2. Sample extraction buffer 3. Disposable virus sampling swab 4. Biohazard specimen bag	/
C.2.18 Does the medical device need to be maintained and calibrated?	/	/
C.2.19 Is there any software in the medical device?	/	/
C.2.20 Does the medical device have storage shelf life?	Self life: 18 months	E4 E6
C.2.21 Is there any delayed or long-time use effect?	/	/
C.2.22 What kind of mechanical force is born by the medical device?	/	/
C.2.23 What decides the shelf life of the medical device?	Storage environment and product stability	E4 E8
C.2.24 Is the medical device anticipated for one-time use?	One-time use	E7
C.2.25 Does the medical device need to safely exit running or be processed?	/	/
C.2.26 Is professional training or skill required for mounting or using the medical device?	This kit is for home use by laymen in a non-laboratory setting.	E10
C.2.27 How to provide the information of safe use?	Instructions for use	E11
C.2.28 Does a new manufacturing process need to be established or introduced?	/	/
C.2.29 Is the human factor such as the user interface crucial to successful use of the medical device?	/	/
C.2.30 Is the alarming system used for the medical device?	/	/

C.2.31 In which way the medical device may be intentionally misused.	1. Testing of other sample types except anterior nasal swab samples. 2. Improper sampling 3. Wrong test execution 4. Waiver of protective measures 5. Not reading the instructions for use 6. Used for early detection. 7. Incorrect labeling of packaging and instructions for use 8. Wrong temperature during implementation 9. Wrong interpretation of the intended purpose	E3
C.2.32 Is there key data of the medical device for patient care?	/	/
C.2.33 Is the medical device anticipated to be movable or portable?	Yes	/
C.2.34 Does the medical device depend on basic performance for use?	/	/

Appendix H:

Question	Feature judgment	Danger (source) identification
H.2.1 Identification of the intended use	It is used for in vitro qualitative determination of novel coronavirus antigens in human anterior nasal swab samples. This kit is for home use by laymen in a non-laboratory setting (such as person's home or certain non-traditional sites such as offices, sporting events, airports, schools etc.).	E10
H.2.2 Identify possible use mistakes The user's possible use mistake: -Improper calibration substance, reagent, device or sample substrate is used in the IVD medical device.	Cause the mistake of the test result.	E8 E10
- Simplify the test procedure (adopt the shortcut);	Cause deviation of the test result.	E10
-Neglect the device maintenance;	/	/
-the safety device doesn't work;	/	/
-operate under an adverse environment;	Cause deviation of the test result.	E4 E6
-Use IVD test results to screen for a disease in the	Reagent performance	E7

Question	Feature judgment	Danger (source) identification
population when the test procedure is intended to assist in the diagnosis of the disease;	characteristics are not suitable for screening of populations	
-Insufficient sample volume;	Cause deviation of the test result.	E10
H.2.3 Identification of Safety-related features	/	/
H.2.3.1 Performance characteristics of quantitative inspection programs The quantitative test procedure is anticipated to be used for determining the content or concentration of the substance to be analyzed. The results are reported in an interval scale way. The main analysis performance features of the quantitative detection program are precision (imprecision), accuracy (deviation), analysis specificity and quantitative range. The performance requirements depend on the medical application.	/	/
H.2.3.2 Dependence features When the physician make the emergency medical decision depending on the IVD test results, if intensive care is arranged, the timely result is as important as the accurate one.	The results which are in time and accurate are helpful for doctor giving the accurate judgment.	E8
H.2.3.3 Supported patient information Sometimes the test results may require demographic information about the patient, as well as information about the sample or its test in order to make an appropriate interpretation. Examples of the above information may include patient identification, sample identification, sample type, sample description, measurement unit, reference range, age, gender, and genetic factors, which may be manually entered by a laboratory analyst or automatically entered by a laboratory computer system.	/	/
H.2.4 Identify the known and foreseeable hazards (source)	/	/

Question	Feature judgment	Danger (source) identification
H.2.4.1 Hazards (source) to the patient From the patient's standpoint, an IVD test result is a Hazard (source) if it may lead to: (1) inappropriate medical measures that may cause injury or death; (2) failure to take appropriate medical measures that may prevent injury or death. An incorrect or delayed IVD inspection result may result from a malfunction of the IVD medical device, which is the initial hazard (source) in the sequence of foreseeable events leading to a hazard (source) situation. The identification of hazards (sources) and sequences of events is expected to assist manufacturers in compiling a comprehensive list of hazardous situations. The manufacturer determines what is considered as harzard (source) during the risk analysis. A hazardous situation can occur if a health care provider receives an incorrect result and takes action based on it. Hazardous situations can also occur if inspection results are not available when needed. For quantitative inspection procedures, if the deviation of the inspection result from the correct value exceeds the limit based on clinical application, the result can be considered to be incorrect. The clinical significance of incorrect results can depend on the difference between the measured and correct values and the patient's physical condition (such as hypoglycemia or hyperglycemia).	Wrong test results can lead to inaccurate judgments for patients.	E11
H.2.4.2 Relation to the performance feature Failure to meet specifications for any performance characteristics related to safety should be evaluated to determine if a hazardous situation has occurred.	/	/

Question	Feature judgment	Danger (source) identification
H.2.4.3 Identify hazards (source) under fault conditions When identifying the hazard (source) of IVD under fault conditions, should consider failure modes that may cause performance characteristics (eg, correctness, accuracy, specificity, etc.) which can't meet the medical device application, such as: --- non-uniformity within the same batch; --- Inconsistencies between different batches; --- the value of the non-traceable calibrator; --- irreplaceable calibrator; ---Non-specificity (for example, interference factors) --- residual transfer effect of sample or reagent; ---Imprecise measurement (related to the instrument) --- Stability failure (storage, transportation, use)	Overdue products can cause inaccurate test results	E11
When identifying the hazard (source) of IVD under fault conditions, should consider failure modes that may lead to delayed results in emergency care situations, such as: --- incorrect patient name or identification number; --- incorrect birth date or age; --- incorrect gender;	/	/
H.2.4.4 Identify hazards (source) during normal use Even if the IVD medical device meets the performance characteristics declared by the manufacturer, incorrect results may occur during normal use. This may be due to the uncertainty of the test results, the biological changes of the patient sample, the choice of judgment value or other factors. Incorrect results under correct use conditions can cause hazardous situations for patients, such as: ---Incomplete distinction between positive and negative samples: Qualitative testing procedures often exhibit inherent false positives and false negatives,which is caused partially by deciding the uncertainty of the proper judgment value. ---Uncertainty of measurement: The current level of	The interference factors in the sample and the experimental process will be described in the instructions	E10

Question	Feature judgment	Danger (source) identification
technological development may limit the accuracy of quantitative IVD medical devices. ---Unexpected effects of other components (interfering factors) in the sample matrix: new drugs, biochemical metabolites, heterophilic antibodies and sample preparation materials may affect the performance characteristics of IVD testing procedures. ---Natural heterogeneity of analytes: Antibodies and other proteins in blood samples are a mixture of different subtypes. The performance characteristics of published IVD testing procedures may not apply to all components of the mixture.		
H.2.4.5 Identify hazard situations Examples of hazardous situations caused by IVD medical devices include: ---When screening blood for transfusion, the blood bank obtained false negative HIV or false negative HBsAg (Hepatitis B surface antigen) results. ---Doctors make liver disease diagnosis based on liver function test results affected by bilirubin interference; ---Hypoglycemic diabetes patient obtained inaccurate blood glucose concentration from self-monitoring devices.	Wrong test results.	E3
H.2.5.1 Estimating patient risk The risk estimation is based on the severity and probability of injury caused by the hazardous situation of each IVD medical device judged under normal and fault conditions. In the case of incorrect IVD test results, the main determining factors are: a) the probability that the result is incorrect; b) the possibility that the results may cause adverse medical practices.	/	/
For results that falsely indicate "no medical intervention is required" (eg, false negative results or false "normal" results), the risk assessment should include: (1) Prognosis for this condition without treatment (2) Possibility of diagnosing this condition by other	Confirmation with other diagnostic methods	/

Question	Feature judgment	Danger (source) identification
methods (3) Implicate people other than patients (such as the spread of infectious agents or genetic diseases, and exposure of fetuses to hazard situations).		
For results that falsely indicate that "medical intervention is required" (eg, false positive results or false "abnormal" results), the risk assessment need include (1) Possible injury due to inappropriate treatment; (2) Exclude the possibility of this situation through other methods (3)Inferences from others (for example, examinations or treatments of exposure to infectious agents, discussions or treatments of genetic diseases)	Confirmation with other diagnostic methods	E10
H.2.5.2 Estimate the severity of the injury		
The medical application of IVD test results determines the possible harm to patients caused by incorrect results.	Cause inaccurate test results	E11
The severity of the injury requires an understanding of the medical uses of the IVD test results, the analytical performance requirements for each application, and the extent of medical decisions made based on the IVD test results. For this reason, desirable medical input to the risk estimation process is required.	/	/
H.2.5.3 Evaluate the probability of occurrence The probability that an IVD medical device may cause injury depends on the cumulative probability of a series of events. For IVD medical devices used in the laboratory, these probabilities include: ---The probability that the IVD medical device will give an incorrect result; ---The probability that the laboratory will fail to detect incorrect results and report incorrect results; ---The probability that the doctor did not identify the wrong result and took (or did not take) action; ---The probability of harm to the patient caused by the doctor doesn't take or take the measures. Reasons that laboratories recognize incorrect results	Cause inaccurate test results	E11

Question	Feature judgment	Danger (source) identification
include: ---The quality control system determines that the progress of the testing procedures has changed; ---The values of the measured characteristics are inconsistent with the survival status; ---The result exceeds the limit that the test result needs to be confirmed; ---The deviation exceeds the expected or acceptable value compared with the patient's previous results; When estimating the probability of occurrence, you should consider that not all laboratories have effective detection systems to prevent them reporting false results. The doctor may recognize the reasons why the results are wrong: ---The result is physiologically impossible; ---The results are inconsistent with the patient's clinical condition; ---The results contradict other data; When IVD medical devices are used outside the laboratory, normally there is no adequate or effective detection system. A lay user may not know that some results are inaccurate. For these IVD medical devices are used outside the laboratory, the examples in the clause should be modified by deleting events and probabilities that are not applicable.		
H.2.5.4 Points to consider when estimating patients		
H.2.5.4.1 What is the probability that the IVD medical device generates incorrect results: --In the possible failure mode? --In the normal use condition? --In the reasonable and foreseeable condition of false use?	In the possible failure modes: There is no line in the position of the quality control line (C line) in the observation window, which indicates that the test is invalid, should re-sample and run a new test. Under normal use conditions: 1. Two color bands appear in the observation window, that is, a red or magenta line appears at both of the quality control line (C line) and	E3 E10

Question	Feature judgment	Danger (source) identification
	detection line (T line); 2. A red or magenta line appears at the quality control line (C line) in the observation window, and no line appears at the detection line (T line).	
H.2.5.4.2 What is the probability that the incorrect IVD test results are found by the user/laboratory? ---Is the quality control provided with the IVD medical device? ---Is the control unit integrated into the device to detect a fault condition? ---How effective is the control device in detecting a fault condition? ---Are there other quality assurance measures to detect incorrect results (e.g. cutoff value system, authenticity check)? ---can the false information remind the user to correct the mistake or recheck to confirm the test results? For example, the "insufficient blood sample" message on the self-testing instrument is intended to prompt the user to retest. ---If the device is intended for use in a laboratory, does the laboratory have an effective system for detecting such incorrect results?	Users can compare the results with other detection methods.	E10
H.2.5.4.3 What is the possibility that the incorrect IVD test results are found by the doctor? --Does the current standard of medical practice require a definitive test for the analyte? --Does the laboratory automatically complete a definitive test after the results of a positive screening test? ---Can this type of incorrect result be recognized by other results, conditions, symptoms, and the patient's medical history? ---Does the doctor routinely verify the results of such analyses by other methods and question those that do not match the clinical symptoms? ---Are there other authenticity checks for this analysis to warn doctors to pay attention to mistake?	Analytical test results can be confirmed by other methods.	E10

Question	Feature judgment	Danger (source) identification
---Are test results the sole basis for important medical decisions? What's the extent that the diagnosis depends on the test results (that is, how the test results affect medical decisions) ---Does the urgency of the environment require an immediate decision without the opportunity to validate the data or confirm the information? Does the test result directly determine the medical decision / treatment? ---Are there other available test as a alternative , such as in a central laboratory if equipment in the care area doesnot work.		
H.2.5.4.4 What's the possibility that the physician will take action or fail to take action on the results? ---Whether the IVD device is a major determinant of a serious situation such as a malignancy or a life-threatening infection. ---Is the IVD medical device intended for blood transfusion, transplantation, or other medical use that may infect the recipient with the disease? ---Are IVD medical devices intended for monitoring important human functions, the mistake or delay may cause death or permanent damage to patients?	/	/
H.2.5.4.5 How much is the possibility that doctors will take (not take) measures to cause or contribute to harm to patients? ---Is the measure irreversible, such as surgical removal or abortion? ---To what extent can be reversed? ---To what extent are the measures likely to harm the patient? ---To what extent failure to take action result in death or injury? ---What physiological condition will affect the possibility of injury?	Incorrect test results can cause varying degrees of health harm to users.	E11
H.2.5.4.6 What is the severity of the harm caused? ---death? ---Life-threatening injuries? ---shorten the anticipated life time?	Incorrect test results can cause varying degrees of health harm to users.	E11

Question	Feature judgment	Danger (source) identification
---Unrecoverable deterioration in health? ---Permanent damage? ---Permanent damage to human function or structure? ---Injuries that require medical intervention to prevent serious injuries? ---Recoverable deterioration in health? ---Minor physical damage? ---Temporary injuries that do not require medical intervention? ---Temporary discomfort?		
H.2.5.5 Risk information for IVD medical devices		
H.2.5.5.1 Database of adverse event The alert procedures of the medical device collects data from manufacturers or end users including examples of adverse effects of incorrect or delayed IVD test results. Manufacturers evaluate reports of similar IVD medical devices to find information suitable for their medical device to help identify hazards (sources) or related trends that were not previously recognized. However, caution is required when drawing conclusions from individual reports. The information in adverse event database is unverified, and a single report may include incomplete, incorrect, or misleading information.	Tracking Adverse Events	E11
H.2.5.5.2 Consensus survey Parkes et al. Describe a systematic survey of medical inputs of patient risk. After Clarke et al used graphical modeling, they built an "error grid." Parkes et al. Can also be used for other measures.	/	/
H.2.5.5.3 Interview with physicians One traditional method of obtaining medical input of patient risk is to interview a practitioner to determine (1) How they use IVD to check the results (2) Are they able to recognize incorrect results (3) What measures will they take for a specific result (4) What are the consequences of improper medical measures? When more subjective than the Parkes	Interview doctors	E11

Question	Feature judgment	Danger (source) identification
survey method, an interview strategy can be conceived to help draw the degree of deviation or imprecision that may put patients at risk.		
The depth of the risk assessment should be proportional to the severity of the possible injury. The risk of each incorrect result identified to be dangerous should be evaluated.	/	/
H.4.1 General The severity on patient's injury is determined by the medical intervention (or insufficiency of medical intervention) triggered by the IVD test result. The influence ability of the manufacture on the damage severity depends on different IVD tests. If the medical intervention depends on the report values (such as the concentration of detecting glucose, electrolyte, treatment medicine or some enzyme), and the injury severity can be reduced by taking the risk control measures of limiting level of deviation, inaccuracy or interference. If all of the results are positive or negative, the injury severity cannot be reduced by the manufacturer. The patient risk caused by the IVD test result generally can be reduced by reducing the occurrence probability. Activities to reduce the risk of incorrect results shall be prioritized according to the levels specified in 6.2. as for the IVD medical devices: a) It should try to reduce the occurrence probability of the incorrect results by designing the solid safety. To ensure the results meet the requirements of the medical devices, the relevant performance properties (such as analysis or diagnosis specificity, accuracy or precision) should be improved. b) If it is not feasible by designing the solid safety, adopt protective measures to reduce the probability that the incorrect results are reported to the user. The preferred method is the self-test of the device or the quality control program provided by the device. c) If the protective measure is not feasible, it should provide safety information to the user, such as the specific instruction, warning or other information	a) The inherent safety of the design is used to reduce the probability of incorrect results; in order to ensure that the results meet the requirements of IVD medical devices, the related performance characteristics need to be improved. b) If it is not feasible to design with inherent safety, take protective measures to reduce the probability of incorrect results being reported to the doctor or user. The preferred method is to test by the IVD device itself or the quality control program provided by the IVD device.	E11

Question	Feature judgment	Danger (source) identification
for avoiding the dangerous environment. Notice 1.: the test method anticipated to be used beyond the device (such as the quality control test recommended by the laboratory or the confirmative test made by the doctor) is considered as the safety information but not the protective measure.		
H.4.2 Analysis of scheme		
H.4.2.1 Achieving inherent safety with design methods If the requirements of the medical device cannot be satisfied consistently, the design of the IVD medical device can be modified to avoid the incorrect clinical result, such as by improving the following applicable contents: --precision of the measurement system; --accuracy of the calibrator value; --analysis specificity of IVD reagent (such as better antibody); --test limit or quantity limit of test program; --device reliability (such as the prevention of forged results); --differentiation of positive and negative samples; --automation of program procedures of easy-occurrence mistakes; --authentication of positive samples (such as the bar code); --Convenience of use (E.g. Outcomes identified by human factors research).Similarly, the production process can be improved so as to produce the IVD medical devices which do not generate the incorrect clinical results (i.e., don't meet the requirements of medical devices). The Hazard(source) Analysis and Critical Control Point method can help to judge the steps of the production process to prevent unqualified products from being generated. --over-high difference of reagents of different batches; --device components which cause false results; --the calibrator values exceed the deviation specification;	Convenience of use; Control materials to meet life cycle requirements;	/

Question	Feature judgment	Danger (source) identification
--the control material, calibrator or reagent don't meet the declared shelf life.		
H.4.2.2 Protective measures If improving the design of the IVD device is not feasible, additional control measures can be taken to test the conditions which may cause incorrect results, such as: --check the completeness of the sample to test the unacceptable samples (such as hematolysis); --remove the foam (if there is a level sensor on the sample instrument) or fiber coagulation in the sample; --check the self-carried sensor and software so as to check adverse system conditions (such as incorrect temperature, drift of spectrophotometer, suction device blocked); --built-in reference standards for testing invalid calibrator, reagent or device; --prevent the alarming of incorrect results and false information or algorithm; --use the feasible algorithm to judge the impossible results. If the improvement in the manufacturing process is not feasible, additional process control or more strict codes can be taken to prevent unqualified products from being released, such as: --check if the raw materials delivered to the factory meets the quality requirements; --use the process test to detect the unqualified components; --reference materials for the recalling of the measurement of the calibration instrument; --performance features relating to the user's requirements; --final release check.	Prevent incorrect results from being reminded; Use the feasible algorithm to judge the impossible result; Take the following measures for the unqualified products. Check if the raw materials delivered to the factory meets the quality requirements; --use the process test to detect the unqualified components; --performance features relating to the user's requirements; --final release check.	/
H.4.2.3 Security Information **H.4.2.3.1 Performance features** The responsible person for the laboratory and the healthcare provider should understand relevant performance features to judge if the IVD medical device is applicable.	Carry out the trials of performance estimation.	E3 E11

Question	Feature judgment	Danger (source) identification
The information is provided by the manufacturer. Disclose the residual risk and ensure the correct explanation of the tested results by estimating the performance properties of known judgment points of the medical devices, such as: --analysis specificity (such as interference or cross substance); --percent of accuracy (i.e., the acceptable deviation); --precision; --detection limit or quantitative limit; --accuracy (combination of precision and percent of accuracy); --diagnosis sensitivity (Fragment of the truly positive results of the confirmed patients with diseases); --diagnosis specificity (Fragment of the truly negative results of the confirmed patients without diseases);		
H.4.2.3.2 Prevent the information of the incorrect result The instruction of use, process restrictions and environment regulations must be helpful for the user to prevent incorrect results, such as: --sample collection, storage and preparation requirements; --known interference substances --Confirmed measurement range; --warning on the incorrect usage which may cause incorrect results; --limit to specific patient crowd; --warning to the improper clinical condition or improper sample type; --correct cleaning method; --preventive maintenance program and maintenance cycle; --storage condition and shelf life of the reagent.	The instruction for use, process restrictions and environmental regulations prevent incorrect results: Sample collection, storage and preparation requirements; Tips for incorrect usage that may cause incorrect results; Storage condition and shelf life of the reagent.	E11
H.4.2.3.3 Enables detection of incorrect results Other information and suggestions helpful for reducing the incorrect results (hazard(source)) should be provided, such as: ---detect the control program which causes the	/	/

Question	Feature judgment	Danger (source) identification
status of incorrect results; ---the acceptable installation program used for confirming performance; ---system adaptability guidelines for identifying the invalid HPLC (high-performance liquid-phase chromatograph) or GC (gas-phase chromatograph).		
H.4.2.3.4 Training and user qualification The manufacturer can provide training to avoid false use. The training material applicable to continuing education can be provided to the user IVD medical devices. To some significant IVD medical devices (such as the oral anticoagulation monitoring system for home use)	User training	E11
H.4.2.4 Designated safety information Many countries have the regulations require the information which should be provided by the manufacturer. It is the risk control measures explaining the possible false use and other potential hazard(source) of the IVD medical device. At the case of validity verified, obeying the applicable regulations or standards can be used as the evidence that the risk caused by specific false use has been controlled.	Requirements on obeying the applicable regulations or standards for the laboratory environments, recycling standards of medical waste liquid, etc.	E11
H.4.2.5 Warnings, precautions and restrictions Only sufficient disclosure or obviously knowing the consequence of not obeying, clear warning, instruction or reverse indications are the effective risk control measures to the IVD medical device for professional use, for example, an IVD medical device is anticipated to used for testing serum and plasma samples but not urine. If the instruction doesn't mention the whole blood, serum ad plasma samples, some laboratories may use the device to test whole blood, serum and plasma samples, particularly the advanced IVD medical device can be used for testing the whole blood, serum and plasma samples. If it doesn't indicate the program cannot meet the demand of testing the whole blood, serum and plasma samples, the sample test will be a foreseeable false use.	Strictly operate as per the instruction.	E10 E11

Question	Feature judgment	Danger (source) identification
Similarly, the test results can be used for the medical applications beyond the anticipated application of the manufacturer. The manufacturer should estimate the risks generated by these applications, and consider to use similar devices for trial, similar use environments of the other devices and the possibility of the use. The manufacturer may need to provide proper warning, prevention measures and limits to the user to reduce the risk.		
H.4.2.6 Standards of IVD medical devices International standards, state standards, regulations and regulative directive documents may be applied to the IVD medical devices of some types. Obeying the recognized product standards, rules and the guidelines of solid safety and prevention measures and safety information can be used for the requirements of specified design and check, and the qualified property can be used as the evidence of risk control, such as O15197, ISO 17593, ISO19001 and ISO 18113-1.	International standards, national standards, regulations and management guideline documents are applicable.	E11
H.4.3 Verify the effectiveness of risk control The implementation and effectiveness of the risk control measures (including safety information) should be verified. The verification depends on the risk to be controlled. Where appropriate, this verification should include a prospective review of the information available for IVD medical devices with similar risk controls. Prospective investigations may be required to verify the effectiveness of risk control for the severity of the injury or a high probability of occurrence. For example, studies of human factors can assess the extent to which users understand and comply with warnings and instructions, and verify the effectiveness of the safety information provided. This can include human factors such as the size of the printed font, reading level, and appropriate prominent warning messages. Assumptions about the validity of security information should be used with caution. When estimating the risk reduction caused by specific	The review of customer complaint documents can be used as an effective verification for the risk of injury severity or low probability of occurrence. For risks with a high severity of injury or a high probability of occurrence, prospective studies are performed to verify the effectiveness of risk control. Assumptions about security information should be made with caution. When estimating the reduction in risk from the information provided by the manufacturer, consider the following limitations: Laboratory certification requirements, regulations, and enforcement requirements are not the same worldwide; quality control	/

Question	Feature judgment	Danger (source) identification
information provided by the manufacturer, the following limitations should be considered: ---Laboratory accreditation requirements, regulations and compulsions are different around the world; the practice of quality control and quality assurance is also very different; ---The instruction provided with the professional IVD medical device is anticipated to be used for the laboratory. Information about contraindicated use, interference drugs, and other information about the use of IVD test results may not be delivered to the doctor who arranged the test.	and quality assurance measures vary widely.	
H.5.1 External performance monitoring IVD manufacturers can often provide external data to monitor the performance of certain aspects of IVD medical devices; where applicable (for example): ---Adverse event reports; ---Complaints about incorrect results, misidentified samples, and instrument reliability; ---Internal quality control data of the laboratory; ---Interlaboratory Quality Evaluation System (EQAS), also known as competency assessment; ---Performance evaluations performed by independent laboratories, usually published in scientific literature.	/	/
H.5.2 Internal performance monitoring Manufacturers can also obtain data in routine operation that can be used to monitor certain performance characteristics under controlled conditions. These sources include: ---Process monitoring; ---Stability monitoring; ---calibrator assignment; ---Accept inspection; ---Equipment reliability testing; ---Confirmation activities;	/	/

Appendix E

Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold)
Initial Hazard (Source) Analysis (PHA)

No.	Hazard(Source) Type	Foreseeable examples and sequences	Hazard(Source) situations	Consequences or injuries	Analysis of initial risk control plan
E1	Biological or chemical hazard (source)	Product components contain pathogens Chemical composition contains toxicity	pathogens and toxic materials are in contact with users	Poisoning, irritation and other symptoms harm the user's health and endanger the user's life in severe cases	Purchase control Monitoring and quality control
E2	Biological or chemical hazard (source)	1 product components contain pathogens 2 Chemical composition contains toxicity 3 Insufficient composition	Pathogens and toxic materials are in contact with the user, the test is not accurate	Symptoms such as poisoning, irritation and allergies harm patients 'health, and endanger patients' lives in severe cases. Insufficient composition causes experimental results to be inaccurate, making medical staff make mistakes in judgment, delaying or aggravating conditions	Purchase control Production control
E3	Information hazard (Source)	1 Failure to operate in accordance with the requirements specified in the instructions 2 No line appears on the position of the	User misuse / product failure mode	Causes inaccurate experimental results, makes medical staff make misjudgments, delays or	Instruction provides detailed information

		quality control line (C line), the test is invalid		worsens the condition	
E4	Biological or chemical hazard (source)	Failure to protect the product in accordance with transportation and storage requirements, cause the product produce bacterial or active ingredient lose efficacy.	Medical worker used invalid product	The test is inaccurate, which is a medical staff's judgment error, delaying or aggravating the condition	Considering product storage standards when designing the product
E5	Biological hazard (source)	Products should be sterilized after use	Harmful microorganisms pollute the environment	Hazard (source) environment through harmful microorganisms	Considering product instruction when designing
E6	Biological hazard (source)	Products beyond their shelf life	Invalid product used in test	The test is inaccurate, which is a medical staff's judgment error, delaying or aggravating the condition	Consider product logo when designing. Expired products are clearly labelelld
E7	Biological or chemical hazard (source)	Before the expiry date of the label, the packaging material is damaged or the ambient temperature cannot meet the requirements, which will cause the aging of the effective ingredients of the product and cause the product performance to decline.	Invalid product used in test	The test is inaccurate, which is a medical staff's judgment error, delaying or aggravating the condition	Consider product logo when designing. Expired products are clearly labelelld
E8	Biological hazard (source)	Improper use of the product, cross-contamination	User uses contaminated product	Inaccurate test results delay patient's condition	Consider relevant requirements when designing product identification
E9	Biological or chemical	The product is not treated as medical	Toxic and harmful	Cause human infection	Improper disposal as medical

	hazard (source)	waste after use	substances affect the environment	(sometimes over a large area), or environmental damage	waste can affect the environment
E10	Operational hazard (Source)	Product users have not been trained and use the product improperly	Affect product use	Inaccurate test results may delay treatment	Instruction provides detailed information
E11	Information hazard (Source)	Product identification does not meet requirements	Use of non-conforming product or improper use of product	Inaccurate test results may delay treatment	Instruction provides detailed information

6.4 Risk List and its Evaluation, Assessment and Control Process

Table 1. Meaning of abbreviated words

Abbreviated symbol	Meaning
S	severity (1 - 5)
O	occurrence probability(1 – 5)
RL	Risk class(1 – 25)
NH	Does a new hazard(source) occurs, if yes, write out the hazard number.
ALOR	Is the risk can be accepted?

Table 2 List of product risks

No.	Harm		Risk assessment			Measures of risk reduction	Evidence of measure implementation	ALOR			NH
	Concrete danger type	Explain the possible harm in detail	S	O	RL			S	O	RL	
Production process											
1	Contamination of chemical reagent	1.Harm to the producer 2.Influence the product quality	2	2	4	1.Management of workshop 2.Regulation of production operation 3.Training the production personnel	Training record	2	1	2	NO
2	Harm caused by production equipment	1.Harm to the producer 2.Influence the product quality	3	1	3	1.Management system of production equipment 2.Operation regulations of production equipment 3.Training the production personnel	Training record	3	1	3	NO

3	The raw material doesn't meet the use requirements	1.Incorrect test results	2	2	4	1.Establish the supplier assessment system and strictly carry it out; 2.Carry out the quality check strictly according to the bio-activity raw material and training the personnel of quality test; 3.The raw materials should be stored, distributed and used strictly as required.	Refer to the supplier assessment material and purchase order	2	1	2	NO
4	The label doesn't meet the requirement	1.Invalid product is used in trial	2	2	4	1.Produce strictly according to the preparation standard operation regulation; 2.Reinforce the operator's technical operation training and check.	Refer to the training and check records of operating personnel	2	1	2	NO
5	Biological contamination	1.Harm the operator's safety	2	3	6	1.Use the new-born calf serum or the extracted new albumin to replace the common serum.	Preparation process and record	3	1	3	NO
6	Incorrect formula	1.The kit cannot be used.	3	2	6	1.Use different containers for different components; 2.Reinforce the technical operating training and check of the operating personnel.	Preparation process and record	2	1	2	NO
7	Batch unevenness and inconsistency among batches	1.influence the user's use 2.Influence the product result	4	2	8	1.Produce and test strictly according to the approved quality standard, and ensure the error is in the allowed range.	Records of customer complaints	4	1	4	NO
Test process											
8	Sample contamination	1.Incorrect results of product test	4	2	8	1.Check operating regulations 2.Reinforce the technical training and check of the operating personnel.	Training records	4	1	4	NO

9	Failure of test device	1.Inaccurate test results	3	1	3	1.Standard operating regulation of test instrument 2.Periodic maintenance standard of test instrument	Periodic calibration record of device	3	1	3	NO
10	False operation	1.Inaccurate test results 2.Cause the loss of control on the quality of raw and auxiliary materials, semi-finished product and finished products	3	2	6	1.Standard operation regulation of test 2.Train the test personnel	Training record	3	1	3	NO
Trial operation											
11	Sanitary safety cannot b kept	1.Harm the user's safety	3	2	6	1.Dealt by the user by an unified manner	The site is clean.	2	1	2	NO
12	Degradation	1.Invalid product	3	2	6	1.The user should pay attention to the storage method and valid period of the reagent.	Use in the valid period of the reagent.	2	1	2	NO
13	Storage or operation deviates from the anticipated environment condition	1.Inaccurate test result	3	3	9	1.The environment temperature requirements for the storage and use of the reagent are indicated in the instruction.	Correct storage and use.	2	1	2	NO
14	Accidental device damage	1.The product cannot be used	3	1	3	1.Tailor make the inner and outer package, and the interior package should be mainly made of plastic.	See the inner and outer package of the kit.	2	1	2	NO
15	Pollution of waste and disposal of medical devices.	1..Cause environment pollution	3	2	6	1.The user timely remove the waste and dispose according to relevant rules.	Dispose as medical rubbish, and the site is clean without pollution.	3	1	3	NO
16	Negligence and mistake (spiritual or physical)	1.Incorrect test result 2.Harm the user safety	3	2	6	1.Train the user, and reduce the negligence.	On-site operation and training record	3	1	3	NO
17	Violate or cut the instruction, procedure, etc.	1.Incorrect test results	2	2	4	1.Train the user and assess the training result.	Onsite operation and training records.	2	1	2	NO

18	Insufficient proper decision for terminating the service life of the medical device.	1.Incorrect test result	3	2	6	1.Train the user.	Onsite operating and training record	3	1	3	NO
19	Improper package	1.Influence the product performance 1.Invalid test result	3	2	6	1.Package strictly according to the package document, and QA is in charge of package check before being delivered.	Distribution record	3	1	3	NO
20	Reuse and/or improper reuse	1.Incorrect test result	3	3	9	1.Indicate the placement time and storage condition of the specimen in the instruction.	Refer to the instruction	3	1	3	NO
21	Invalid product is used	1.Incorrect test result	3	2	6	1.The user should store and use strictly according to the method ruled by the instruction.	Instruction, onsite storage condition.	3	1	3	NO
22	Unclear product mark or false mark	1.Incorrect test result	2	2	4	1.The user should mark and number all of the specimen.	Prompts of the instruction	2	1	2	NO
23	Operate by untrained or unskillful personnel	1.Incorrect test result	3	3	9	1.Reinforce training. The factory can appoint the engineer to train in the customer site and direct the operation as well as periodically carry out information feedback to the user and timely finds the user's operating problems.	Training record	2	1	2	NO
24	The specimen is not disposed or stored as required by the instruction	1.invalid product	2	2	4	1.Use the reagent in the valid period, and the received specimen should be immediately stored in the refrigerator. 2.The residual specimen after analysis should also be stored in the refrigerator immediately.	Storage condition of reagent	2	1	2	NO

25	The operator doesn't dispose the sample to be tested as required by the laboratory.	1.Harm the operator's safety	2	2	4	1.Dispose all of the specimen as the potential infection source. Strictly obey all rules for disposing the biological products, and all of the necessary protective measures must be taken.	Disposal process of sample	2	1	2	NO
Biological or chemical harm											
26	Low stability of the selected raw material	1.Incorrect test result，the judgment is influenced. 2.Unstable reagent performance	3	4	12	1.Clearly specify the material when the supplier is selected; 2.Test assessment reports should be issued for incoming inspection.	See the suppliyer assessment material and purchase contract.	3	1	3	NO
Information harm											
27	Uncompleted or false instruction information	1.Relevant models are not made clear in the instruction; 2.The sample type in use in not clear. 3.Notices are not clear.	2	2	4	1.The instruction information is completed and clearly marked.	Refer to the instruction.	2	1	2	NO
28	Storage temperature and transportation condition are not indicated in the package mark and instruction.	1.Invalid product 2.Poor reagent performance	2	2	4	1.Storage temperature and transportation condition are clear in the package mark and the instruction.	Refer to the package mark.	2	1	2	NO

6.5 Risk Control Integrity Review Record

Product life cycle stages	Review content	Review records	Review Date	Review results			
				conforming	Defective	nonconforming	Not applicable
Design and development planning and design development input stage	After reviewing the project's intended use (function, performance and safety requirements), applicable legal and regulatory requirements, market research and other documents, whether the project meets market requirements, whether the development of the project is targeted, whether the quality is guaranteed, and the design And development plans are reasonable and applicable.	See: 1.Design and development review report (input phase)	2020.04.02	√			

Design and development review and design development verification stage (before trial production)	Through analysis and comparison of the research and development process of the project's functions, performance indicators, technical parameters, and applicability analysis of the standards or regulations based on it, it is verified whether the project meets the input requirements and whether a small amount of trial production can be made.	See: 1. Design and Development Review Report (Performance Review)	2020.04.08	√			
Design and development review and design development verification stage (after trial production)	Through inspection and confirmation of the performance indicators and technical parameters of the trial production products, and according to the applicability analysis of standards or regulations, it is verified whether the process and operation of the project meet the input requirements.	See: 1. Design and Development Review Report (Process Verification stage) 2. Design and development verification report 3. Risk analysis report	2020.04.14	√			

Design and development output review and design and development validation stage	Through the confirmation of the relevant input documents, the technical procedure documents and quality standard documents formed after the output, and the clinical trial analysis, whether the process and operation of the project meet the standard requirements, and whether it has strong feasibility and effectiveness.	See: 1. Design and development review report (confirmation stage)	2021.2.3	√			
Production and post-production risk assessment	Through strict control of the product's market analysis, product safety-related issues, etc., if the product can be controlled to a harmless level, and if potentially unacceptable risks during the clinical use of the product, and if it is safe for the user.						

6.6 Comprehensive Assessment Records of Residual Risks

After the risk problems are improved, all of the foreseeable risks are in the acceptable range.

Risk	Risk nature	Before improvement	After improvement
1-4	Wide acceptable area	12	28
5-12	Reasonable and feasible reduction area	15	0
13-25	Forbidden area	1	0

The assessment team carry out the comprehensive analysis to all residual risks. Considering the effects of all residual risks, he assessment result is the comprehensive residual risk of the product is acceptable. Specific evaluation aspects as below:

(1) Are there conflicting requirements for risk control of individual risks?

Conclusion: No contradictions have been found in the existing risk control.

(2) Are there too many warning reviews (including warnings)?

Conclusion: The warnings are clear and in compliance with the regulations.

(3) Review of the instruction (including whether there are any contradictions and whether it is difficult to comply)

Conclusion: The product instruction complies with the notification of the guidelines for the preparation of in vitro diagnostic reagent manuals (No. 17 of 2014) and the requirements of product-specific safety standards. The descriptions of relevant product safety aspects are clear and easy to understand, and easy for users to read.

(4) Clinical verification

Conclusion: At present, a small number of clinical samples have been verified. Due to the particularity of the epidemic situation, it is necessary to collect clinical application data of the product at more than three clinical medical institutions.

(5) Expert conclusions

Conclusion: After analyzing the above aspects and fully communicating with the clinical application experts, the risk management review team unanimously evaluated that the comprehensive residual risk of this product is acceptable.

6.7 Requirements for production and post-production information and risk management

For the method of production and post-production information risk evaluation, please refer to the <Table of Summary Methods of Production and Post-production Information> in <Risk Management Control Procedures>.

The review team evaluated the suitability and effectiveness of the <Table of Summary Methods of Production and Post-production Information>, and concluded that the method is appropriate and effective. The production and post-production information of Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold) can be obtained in this method.

The person in charge of risk management of this project manages the obtained production and post-production information. When necessary, the risk management team should carry out activities to implement dynamic risk management.

6.8 Comparison of risk analysis between Laymen Use and Medical Use

(1) The home self-test is slower than the professional's understanding of the product and the acceptance speed of the use method, but the operation and interpretation method of this product is relatively simple, which can meet the acceptable range of the home self-test.

(2) For professional use, professionals can better control the dripping method and volume of samples. The instructions also give solutions to abnormal situations, which are suitable for home use.

(3) If the patient encounters a positive result, the patient cannot take the most effective measures to resolve their psychological worries and seek medical attention in the shortest time. It is recommended that the patient wear a mask after discovering the problem, do a good job of protection, and go to the nearest fever clinic for further examination or call the local epidemic prevention department for consultation.

(4) To prevent misunderstanding of the intend purpose and the complete testing process the instructions for use and the description on the packaging were change for the layperson.

7 Assessment Opinions:

The result of the risk management process has met the required objective, and the comprehensive residual risk is acceptable. What's more, the Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold) is the in-vitro diagnosis reagent and mainly comprises of Test Cassette and Sample extraction buffer. If the user operates as per the instruction in the trial process, the product will be safe and effective.

8 Assessment Conclusion

After assessing the Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold) the risk management assessment team believes:

--The risk management plan has been properly carried out;

--The comprehensive residual risk is acceptable;

--Appropriate methods are available to obtain relevant production and post-production information;

All remaining risks of the products Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold) are within the acceptable range of risk acceptance criteria.

Agree to approve the application for registration of the Novel Coronavirus 2019-nCoV Antigen Test (Colloidal Gold).