Risk Management Report

COVID-19 Antigen Detection Reagent

(Colloidal Gold method)

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1 Introduction

The document is a risk management report for COVID-19 Antigen Test Kit (colloidal gold method), which evaluates the entire potential hazard (source). Estimate the probability and severity levels of all types of risk. If the risk is unacceptable, a risk mitigation approach should be taken and the remaining risk should be assessed after the risk control approach has been adopted. Finally, keep all residual risk at an acceptable level.

2 Purpose

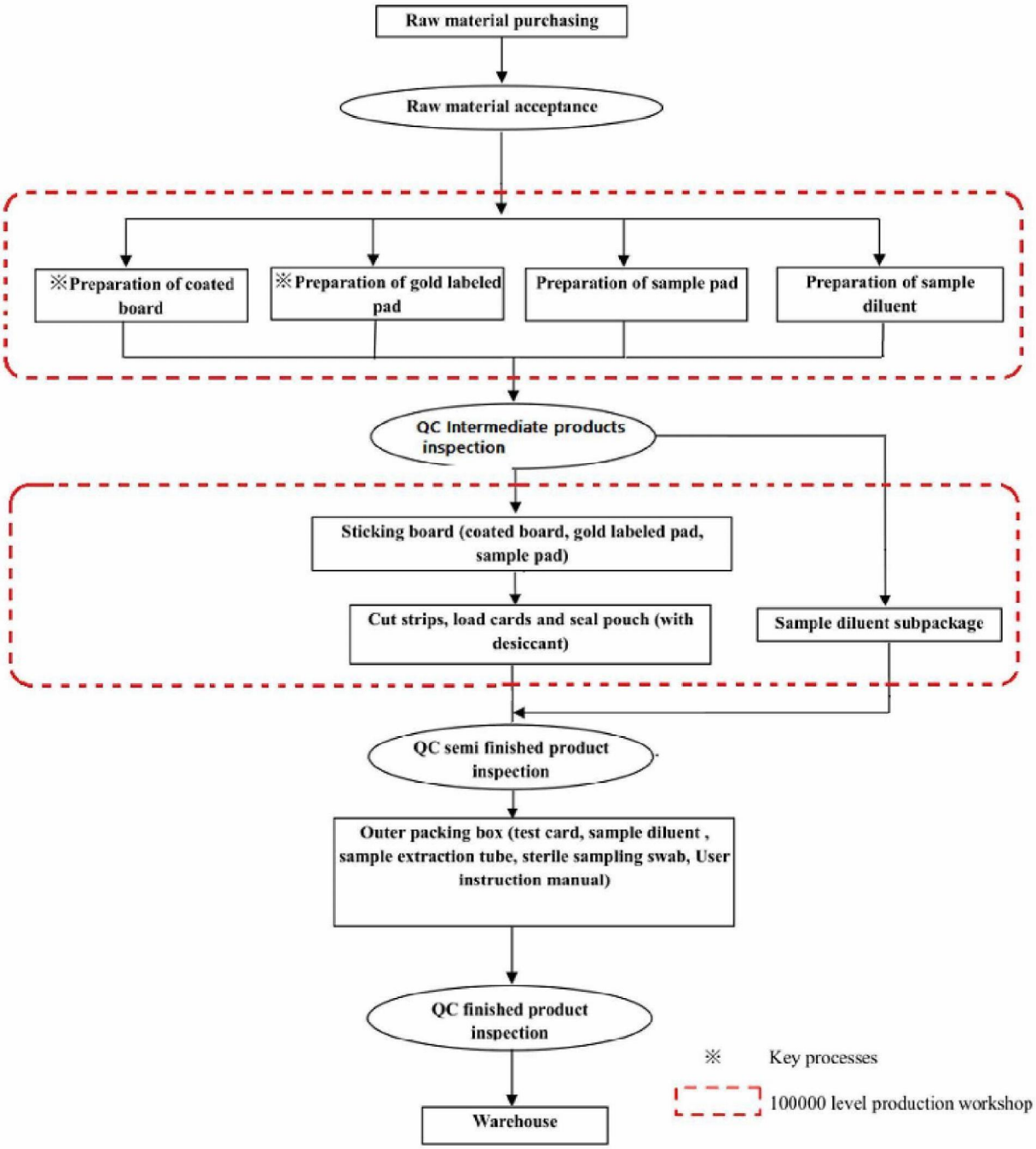
The purpose of the review of risk management is based on will be COVID-19 Antigen Test Kit (colloidal gold method) in pre-market risk management activities in each stage of the overall evaluation, to ensure that risk management plan has been completed successfully, and through to the product risk analysis, risk evaluation and risk control, as well as the comprehensive residual risk acceptability evaluation, confirmed that the product has the risk of management, and control in the acceptable range.

3 Basic information of the product

3.1 Detailed description of product configuration

The test kit consists of test card, sample diluent, sterile sampling swab.

3.2 Production process



3.3 Functional principle

The kit is immunochromatographic and uses double-antibody sandwich method to detect COVID-19 antigen. During detection, the treated specimens are loaded into the sample wells of the test card. When the concentration of COVID-19 antigen in specimen is higher than the minimum detection limit, the viral antigen will form complexes with labeled antibodies first. Under chromatography, the complexes move forward along the nitrocellulose membrane till captured by pre-coated monoclonal antibody of COVID-19 in detection zone on nitrocellulose film (T) to form a pink/purple reaction line on the detection zone, at this point the result is positive; conversely, if there is no viral antigen or the concentration of antigen in specimen is below the minimum detection limit, no pink/purple reaction line appears in the detection zone, at this point the result is negative. Regardless of whether the sample contains viral antigens or not, a pink/purple reaction line will appear in the quality control zone (C), the pink/purple reaction line that appears in the quality control zone (C) is the criterion for determining if the chromatography process is normal.

3.4 Intended use

This kit is only used for the in vitro qualitative detection of COVID-19 antigen from human nasal swab specimens.

This kit is intended for self-use by laypeople (self-tests) for the detection of COVID-19 antigen.

This kit is suitable for the auxiliary diagnosis of COVID-19, the results are for clinical reference only and cannot be used as the sole basis for diagnosis and exclusion decision. The clinical diagnosis and treatment of patients should be considered in combination with their symptoms/signs, medical history, other laboratory tests and treatment responses.

Positive test result needs to be further confirmed, negative result does not preclude COVID-19 infection.

3.5 Applicable environment

For self-testing use.

3.6 Product classification

According to DIRECTIVE 98/79/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 October 1998 on in vitro diagnostic medical devices, COVID-19 Antigen Test Kit (colloidal gold method) is not in the coverage of List A and List B of Annex II, it belongs to self-testing IVDs

4 Reference standards and other reference information

NO.	Document NO	Document name
1.	Directive 98/79/EC	Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices
2.	EN ISO 14971:2012	Medical devices. Application of risk management to medical devices
3.	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions and general requirements (ISO 18113-1:2009)
4.	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use (ISO 18113-2:2009)
5.	EN 13641:2002	Elimination or reduction of risk of infection related to in vitro diagnostic reagents
6.	EN 13612:2002/AC: 2002	Performance Evaluation Summary & Device Description of in vitro diagnostic medical devices
7.	EN ISO 23640:2015	In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents

Risk management team

Department	Duties	Responsibilities
5.1.2e	5.1.2e	General responsibility for risk management, allocation of resources and deployment of personnel, organizational review
Management representative	Team member	System formulation and management of the risk management process
Technology Department	Team member	Risk analysis in the process of product design and development
Production Department	Team member	Risk analysis in the production process
Quality Control Department	Team member	Responsible for reviewing risk analysis during product inspection, storage and transportation
Sale Department	Team member	Risk analysis of product sales process and customer feedback
Registration Department	Team member	Collection of relevant regulations

5 Risk acceptance criteria

5.1 Injury severity criteria

grade	Code	Definition of system risk (example)

Catastrophic	S4	Incorrect operation of the test results in the opposite result, leading to the death of the patient's medication errors
Serious	S3	The kit may not be carried out as required during production, transportation, and storage. The kit may fail and the test result may not be obtained; or the result may be biased, leading to a diagnostic error
Mild	S2	The kit contains substances that are harmful to the user, and the inspector is burned by the chemical substance or has an allergic reaction
Ignorable	S1	Inconvenience or temporary discomfort

5.2 Probability level of injury

grade	code	Frequency (annual)
often	P5	$\geq 10^{-3}$
sometimes	P4	$10^{-4} \leq P < 10^{-3}$
occasional	P3	$10^{-5} \leq P < 10^{-4}$
seldom	P2	$10^{-6} \leq P < 10^{-5}$
very few	P1	$< 10^{-6}$

Remarks: When the product is initially developed, the defect rate may be difficult to define. It can be described qualitatively. When there is relevant data, it can be defined by quantitative data. If possible, use quantitative data to describe it.

5.3 Risk evaluation criteria

Severity / Probability		Ignorable	general	serious	Catastrophic
		S1	S2	S3	S4
often	P6				
sometimes	P5				
Very likely	P4	R1			
occasional	P3		R13	R2、R15、R16	
seldom	P2	R5	R4、R12	R9、R10、R17、R18	R3、R6、R11
Very few	P1	R14		R7	R8

Acceptable risk, denoted by A

Reasonably practicable risk reduction, expressed by ALARP;

The unacceptable risk is denoted by N.

6 Completion of the risk management plan

Through inspection of relevant risk management documents, it is believed that the risk management plan of the COVID-19 Antigen Test Kit (colloidal gold method) has been implemented.

7 Results and analysis of risk management

As shown in the risk management table, the risk index for each hazard has been reduced to an acceptable range.

The following two tables show the changes in the number of hazard projects before and after the control measures are taken. We can conclude that the risk of each hazard has been reduced to an acceptable range.

Before taking measures:

code	Source of risk	Foreseeable events and event sequences	Dangerous situation	Possible injury	Risk level		
					Severity	Probability	level
R1	Chemical or biological hazard (source) (Operational waste)	Samples, used test cards and other wastes are not disinfected or not handled according to relevant regulations	Waste that has not been disinfected or not handled according to relevant regulations flows into the environment	Environmental pollution	S3	P3	AL ARP
R2	Operational hazard (source) (Loss or deterioration)	The kit has not been stored and transported under the prescribed conditions, resulting in loss of function or deterioration of performance	Self-testing people make a judgement based on the test result	Patients receive unnecessary medical treatment or do not receive due medical treatment	S4	P2	AL ARP
R3	Operational hazard (source) (Expiration period of kit)	Use expired products for testing	Self-testing people make a judgement based on the test result	Patients receive unnecessary medical treatment or do not receive due medical treatment	S2	P2	AL ARP
R4	Operational hazard (source) (Use error)	• Mix reagents with different batches • The test steps did not follow the instructions • Use inappropriate samples	Self-testing people make a judgement based on the test result	Patients receive unnecessary medical treatment or do not receive due medical treatment	S4	P2	AL ARP
R5	Operational hazard (source) (Over-range use)	Failure to follow the instructions to interpret the result	Wrong test result	Patients receive unnecessary medical treatment or do not receive due medical treatment	S3	P1	AL ARP
R6	Operational hazard (source) (reuse)	The reagents used are reused	Wrong test result	Patients receive unnecessary medical treatment or do not receive due medical treatment	S4	P1	AL ARP
R7	Operational hazard (source)	Too much sample added	Self-testing people make a judgement	Patients receive unnecessary	S3	P2	AL ARP

code	Source of risk	Foreseeable events and event sequences	Dangerous situation	Possible injury	Risk level		
					Severity	Probability	level
	(Incorrect measurement)		based on the test result	medical treatment or do not receive due medical treatment			
R8	Operational hazard (source) (Unevenness within the batch)	• The dosing equipment is not suitable • Scribing pad equipment is not suitable • Unable to control the deviation of scribing pad equipment	Some product test results are wrong	Patients receive unnecessary medical treatment or do not receive due medical treatment	S3	P2	AL ARP
R9	Operational hazard (source) (Unevenness between batches)	• Difference in stability of raw material suppliers • Difference in dosing operation • Unsuitable storage conditions • Scribing pad equipment is not suitable • The deviation of the liner spray pad is uncontrollable • Incorrect recipe	Some product test results are wrong	Patients receive unnecessary medical treatment or do not receive due medical treatment	S4	P2	AL ARP
R10	Chemical or biological hazard (source) (Non-specific)	• Uncontrollable contamination during the dosing process • The sample contains interfering substances	Wrong test result	Patients receive unnecessary medical treatment or do not receive due medical treatment	S2	P2	AL ARP
R11	Operational hazard (source) (Inaccurate measurement)	• Changes in the use environment • Deviation of sample collection	There is a deviation in the test results, self-testing people make a wrong judgement	Patients receive unnecessary medical treatment or do not receive due medical treatment	S2	P3	AL ARP
R12	Operational hazard (source) (Stability failure)	• Excessive acceptable reagent transportation and storage conditions • The cycle of the transportation process exceeds the acceptable range	No test results	Delayed treatment	S1	P1	A
R13	False negatives	Wrong test result	Self-testing people	The patient did not	S3	P2	AL

code	Source of risk	Foreseeable events and event sequences	Dangerous situation	Possible injury	Risk level		
					Severity	Probability	level
	inherent in the detection system		use test results as the sole basis	receive due medical treatment			ARP
R14	Chemical or biological hazard (source) (Effects of interfering substances on sample testing)	Wrong test result	Self-testing people use test results as the sole basis	Patients receive unnecessary medical treatment or do not receive due medical treatment	S3	P2	AL ARP
R15	Energy hazard (source) (power failure)	Raw material storage environment is out of control; environmental monitoring equipment fails	Use of unqualified raw materials into production	Product failed	S4	P1	AL ARP
R16	Operational hazard (source) (Production personnel training is not in place)	Unqualified production personnel were placed on the production line	Incorrect liquid distribution; wrong line drawing; wrong board attachment; wrong strip cutting; wrong card loading	Produced substandard products	S3	P2	AL ARP
R17	Operational hazard (source)	There are sharp objects in the membrane environment	The membrane is damaged	Product failed	S3	P1	AL ARP
R18	Operational hazard (source) (Inspector does not measure correctly)	Incoming materials, semi-finished products, process inspection, finished product inspection did not operate according to regulations	The inspection items are not qualified; Unqualified products for inspection	Delayed production of raw material returns; Product failed	S3	P1	AL ARP
R19	Operational hazard (source) (Improper storage and transportation)	Improper packaging;Temperature and humidity are not within the agreed range;Improper anti-leaching measures	Weted or damaged by high temperature during storage and transportation	Kit failure	S4	P1	AL ARP

After taking measures:

code	Source of risk	Risk control measures	Risk assessment after taking measures			Whether new risks arise	Verification conclusion
			Severity	Probability	Risk level		
R1	Chemical or biological hazard (source) (Operational waste)	The instructions give a reminder that the disposal of operating waste must comply with the relevant regulations.	S2	P1	A	no	accord

code	Source of risk	Risk control measures	Risk assessment after taking measures			Whether new risks arise	Verification conclusion
			Severity	Probability	Risk level		
R2	Operational hazard (source) (Loss or deterioration)	Study the validity period of each component, determine the storage environment requirements and validity period, and clearly mark on the label and instruction manual, and use the symbols and terms that conform to the accord national standard	S1	P1	A	No	accord
R3	Operational hazard (source) (Expiration period of kit)	The instructions and labels clearly indicate the expiration date of the kit and each component, and indicate that products beyond the expiration date cannot be used.	S1	P1	A	No	accord
R4	Operational hazard (source) (Use error)	• The instructions clearly indicate that different batches of reagents should not be mixed • Specify sample requirements	S1	P1	A	No	accord
R5	Operational hazard (source) (Over-range use)	The instructions indicate this risk, and the inspection results are for reference only. Verify compliance with the instructions and evaluate the usability of the instructions.	S1	P1	A	No	accord
R6	Operational hazard (source) (reuse)	• The instruction clearly states that it cannot be reused	S1	P1	A	No	accord
R7	Operational hazard (source) (Incorrect measurement)	• In the manual, clearly indicate the sample requirements, operating procedures, operating environment requirements,. • In the instruction manual, the reasons for possible false negatives are noted, and prompt attention to negative results.	S1	P1	A	No	accord
R8	Operational hazard (source) (Unevenness within the batch)	• Regular inspection of production and inspection equipment. • SOP is established for each process, and it is reviewed by a designated person during operation. • Control the number of microorganisms in the production environment and regularly check. • Establish a quality inspection system, find unqualified products and correct them in time to prevent unqualified products from flowing to the market.	S1	P1	A	No	accord
R9	Operational hazard (source) (Unevenness between batches)	• Strengthen supplier management, evaluate and screen the safety of raw materials, and require suppliers to provide proof of conformity for each batch of raw materials. • Train production personnel, establish SOP for each process, and review by special personnel during operation. • Monitor the storage environment and generate an alarm message when it exceeds the standard.	S1	P1	A	No	accord

code	Source of risk	Risk control measures	Risk assessment after taking measures			Whether new risks arise	Verification conclusion
			Severity	Probability	Risk level		
		• Regular inspection of production and inspection equipment. • Establish a quality inspection system, find unqualified products and correct them in time to prevent unqualified products from flowing to the market.					
R10	Chemical or biological hazard (source) (Non-specific)	• SOP is established for each process, and it is reviewed by a special person during operation; the site is cleared in time after each production. • Control the number of microorganisms in the production environment and regularly check. • Establish a quality inspection system, find unqualified products and correct them in time to prevent unqualified products from flowing to the market.	S1	P1	A	No	accord
R11	Operational hazard (source) (Inaccurate measurement)	In the manual, clearly indicate the sample requirements, operating procedures, operating environment requirements.	S1	P1	A	No	accord
R13	False negatives inherent in the detection system	The instructions clearly state that false negatives may occur. And verified by clinical trials before registration.	S2	P1	A	No	accord
R14	Chemical or biological hazard (source) (Effects of interfering substances on sample testing)	Carry out an interference test to verify potential interferences and mark them in the instructions.	S2	P1	A	No	accord
R15	Energy hazard (source) (power failure)	Check the monitoring equipment regularly and be equipped with spare motors	S1	P1	A	No	accord
R16	Operational hazard (source) (Production personnel training is not in place)	• The production operator is trained and passed the examination, and the training is irregular • SOP is established for each process, and it is reviewed by a designated person during operation.	S1	P1	A	No	accord
R17	Operational hazard (source)	• Clear the site in time after each production. • Before entering the workshop, the production staff should dress strictly according to the regulations to avoid exposing nails, jewelry and other sharp objects or entering the workshop	S1	P1	A	No	accord
R18	Operational hazard (source) (Inspector does not measure correctly)	• Establish a quality inspection SOP, train quality inspection personnel, and only then pass the practice before they are qualified.	S1	P1	A	No	accord

code	Source of risk	Risk control measures	Risk assessment after taking measures			Whether new risks arise	Verification conclusion
			Severity	Probability	Risk level		
		• A second person reviews the inspection process and finds the unqualified operation corrected in time					
R19	Operational hazard (source) (Improper storage and transportation)	Establish SOP for packaging, storage and transportation, comply with SOP implementation	S1	P1	A	No	accord

Due to the above measures, all remaining risks are acceptable according to the risk acceptance criteria.

A risk assessment of a COVID-19 Antigen Test Kit (colloidal gold method) has been carried out on all known or foreseeable risks related to the design, manufacture, storage and intended use of the product for consideration. Risk mitigation, as specified in the risk control document, should implement and fully indicate all potential risks related to the design, manufacture, storage and use of the product. According to the data provided by the risk management document, the clinical manifestations and clinical applications of similar products or other forms of therapy that are currently feasible are also considered. The product is expected to work fully according to its intended use.

8 Post-marketing Information collection

Type of information	method of obtaining	Get frequency	Responsible department
Changes in regulations (eg standards), clinical evaluation reports	Reports issued by websites, related institutions and clinical institutions	Real-time, at the end of clinical trials	Registration Department
Adverse events, quality accidents (including inside and outside the company)	Website, related institutions, related products "Quality Accident Investigation and Processing Record" "Suspicious Questionnaire for Feedback of Adverse Events of Medical Devices"	Outside the company: real time Inside the company: when a quality accident occurs; when an adverse event occurs	Quality Control Department Sales Department
Notice / Recall (including inside and outside the company)	According to the notice recall process	Outside the company: real time Inside the company: when a notice / recall occurs	Technology Department Quality Control Department Sales Department
Supervision and random inspection by regulatory authorities	Supervision spot check report	Outside the company: Collected in real time on the website of the relevant regulatory authority Inside the company: real time	Quality Control Department
Customer return (customer complain)	Related Products "Customer Satisfaction Survey Form"	When a customer complaint occurs	Quality Control

information		When you ask customers about the product satisfaction survey quarterly	Department Sales Department
Quality of purchased products	Relevant products "Supplier Survey Form", related raw and auxiliary materials inspection report	When the incoming inspection fails	Quality Control Department
Design changes	Design change review	When introducing new risks and starting a new risk management process	Technology Department Quality Control Department
Problems with the manufacturing process	related records	When the product has quality problems or when the production process changes	Quality Control Department
Product inspection results and retained sample products	Product inspection failed, related inspection report	Summarize quality information such as product inspections every month	Quality Control Department
Monitoring results of product storage process (including validation of validity period and product storage), performance report of similar products	Stability experiment records, websites, related institutions	Abnormal and real-time results of product stability experiments	Quality Control Department

9 Residual risk estimation

No additional risks related to the design, manufacture, storage and intended use of the product were found. The risk-benefit ratio is acceptable.