INNOVA

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SARS-CoV-2 Antigen Rapid Qualitative Test
Risk Management Report

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1. Basis of Compilation

1.1 Referenced Standards

No.	Standard No.	Standard Title
1	EN ISO 14971:2012	Medical devices--Application of risk management to medical devices
2	EN 13641:2002	Elimination or reduction of risk of infection related to in vitro diagnostic reagents
3	EN 13612:2002/AC:2002	Performance evaluation of in vitro diagnostic medical devices
4	EN ISO 23640: 2015	In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents (ISO 23640:2011)
5	EN ISO 15223-1: 2016	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements
6	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)
7	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)

1.2 Related data

(1) Instruction for Use;

(2) Service condition in hospitals, customer complaint records;

(3) Design and development output file;

(4) Product inspection report.

2. Purpose and Scope

This is a report for the risk management of SARS-CoV-2 Antigen Rapid Qualitative Test, in which all possible hazards and the cause for each hazard are determined. Severity and occurrence probability of each hazards are estimated. When a risk is unacceptable, a control measurement is taken to reduce it. At the same time, the residual risk is evaluated. Finally, all residual risks shall be made as low as reasonably acceptable low enough to be acceptable.

3. Risk Management Team and Responsibility

Title	Name	Educational background	Responsibility
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

4. Product Description

4.1 Brief Introduction to the Product

SARS-CoV-2 belongs to the broad family of viruses known as coronaviruses. It is a positive-sense single-stranded RNA (+ssRNA) virus. Other coronaviruses are capable of causing illnesses ranging from the common cold to more severe diseases such as Middle East respiratory syndrome(MERS). It is the seventh known coronavirus to infect people, after 229E, NL63, OC43, HKU1, MERS-CoV, and the original SARS-CoV. Protein modeling experiments on the spike (S) protein of the virus suggest that it has sufficient affinity to the angiotensin converting enzyme 2 (ACE2) receptors of human cells to use them as a mechanism of cell entry. Studies have shown that SARS-CoV-2 has a higher affinity to human ACE2 than the original SARS virus strain. An atomic-level image of the S protein has been created using cryogenic electron microscopy.

SARS-CoV-2 infections cause COVID-19 disease. People who have confirmed COVID-19 have a range of symptoms, from people with little to no symptoms to people being severely sick and dying. Symptoms can include: fever, tiredness, and dry cough.. Some patients may have aches and pains, nasal congestion, runny nose, sore throat or diarrhea. These symptoms are usually mild and begin gradually. Some people become infected but don’ t develop any symptoms and don't feel unwell. Most people (about 80%) recover from the disease without needing special treatment. Around 1 out of every 6 people who gets COVID-19 becomes seriously ill and develops difficulty breathing. Older people, and those with underlying medical problems like high blood pressure, heart problems or diabetes, are more likely

to develop serious illness. About 2% of people with the disease have died. People with fever, cough and difficulty breathing should seek medical attention.

Human-to-human transmission of the virus has been confirmed and occurs primarily via respiratory droplets from coughs and sneezes within a range of about 6 feet (1.8m). Viral RNA has also been found in stool samplesfrom infected patients. It is possible that the virus can be infectious even during the incubation period, but this has not been proven, and the WHO stated on 1 February 2020 that "transmission from asymptomatic cases is likely not a major driver of transmission" at this time

4.2 Intended Use

The SARS-CoV-2 Antigen Rapid Qualitative Test is a colloidal gold immunochromatography intended for the qualitative detection of nucleocapsid antigens from SARS-CoV-2 in human nasal swabs, throat swabs, and sputum from individuals who are suspected of COVID-19 by their healthcare provider within the first five days of the onset of symptoms.

For in vitro diagnostic use only.

4.3 Test Principle

This reagent is based on colloidal gold immunochromatography assay.

During the test, sample extracts are applied to the test cartridges. If there were SARS-CoV-2 antigen in the extract, the antigen will bind to the SARS-CoV-2 monoclonal antibody. During lateral flow, the complex will move along the nitrocellulose membrane toward the end of the absorbent paper. When passing the test line (line T, coated with another SARS-CoV-2 monoclonal antibody) the complex is captured by SARS-CoV-2 antibody on test line resulting in coloring on line T; when passing the line C, colloidal gold-labeled goat anti-rabbit IgG is captured by control line (line C, coated with rabbit IgG) resulting in coloring on line C.

5. Identification of Intended Use and Characteristics Related to Safety

Questions that can be used to identify medical device characteristics that could impact on safety are described as follows:

No.	Question	Description
1	**What is the intended use and how is the medical device to be used?** Factors that should be considered include: — what is the medical device's role relative to - diagnosis, prevention, monitoring, treatment or alleviation of disease, - compensation for injury or handicap or - replacement or modification of anatomy, or control of conception? — what are the indications for use (e.g. patient population)? — does the medical device sustain or support life? is special intervention necessary in the case of failure of the medical device?	The test is intended for the qualitative detection of nucleocapsid antigens from SARS-CoV-2 in human nasal swabs, throat swabs, and sputum from individuals who are suspected of COVID-19 by their healthcare provider within the first five days of the onset of symptoms For in vitro diagnostic use only.
2	**Is the medical device intended to be in contact with the patient or other persons?** Factors that should be considered include the nature of the intended contact, i.e. surface contact, invasive contact, or implantation and, for each, the period and frequency of contact.	No
3	**What materials or components are utilized in the medical device or are used with, or are in contact with, the medical device?** Factors that should be considered include: compatibility with relevant substances; — compatibility with tissues or body fluids; — whether characteristics relevant to safety are known; — is the device manufactured utilizing materials of animal origin?	The SARS-CoV-2 Antigen Rapid Qualitative Test consists of goat anti-rabbit antibody, mouse anti-SARS-CoV-2 mAb, rabbit IgG antibody, colloidal gold, glass cellulose membrane, nitrocellulose filter, PS base, absorbent paper, among which the goat anti-rabbit antibody, mouse anti-SARS-CoV-2 mAb, rabbit IgG antibody are animal origin materials.
4	**Is energy delivered to or extracted from the patient?** Factors that should be considered include: — the type of energy transferred; — its control, quality, quantity, intensity and duration; whether energy levels are higher than those currently used for similar devices.	No

No.	Question	Description
5	**Are substances delivered to or extracted from the patient?** Factors that should be considered include — whether the substance is delivered or extracted; — whether it is a single substance or range of substances; — the maximum and minimum transfer rates and control thereof.	No
6	**Are biological materials processed by the medical device for subsequent re-use, transfusion or transplantation?** Factors that should be considered include the type of process and substance(s) processed (e.g. autotransfusion, dialysis, blood component or cell therapy processing).	No
7	**Is the medical device supplied sterile or intended to be sterilized by the user, or are other microbiological controls applicable?** Factors that should be considered include — whether the medical device is intended for single use or re-use packaging; — shelf-life issues; — limitation on the number of re-use cycles; — method of product sterilization; — the impact of other sterilization methods not intended by the manufacturer.	No
8	**Is the medical device intended to be routinely cleaned and disinfected by the user?** Factors that should be considered include the types of cleaning or disinfecting agents to be used and any limitations on the number of cleaning cycles. The design of the medical device can influence the effectiveness of routine cleaning and disinfection. In addition, consideration should be given to the effect of cleaning and disinfecting agents on the safety or performance of the device.	No
9	**Is the medical device intended to modify the patient environment?** Factors that should be considered include: temperature, humidity, atmospheric gas composition, pressure and light.	No
10	**Are measurements taken?** Factors that should be considered include the variables measured and the accuracy and the precision of the measurement results.	

No.	Question	Description
11	**Is the medical device interpretative?** Factors that should be considered include whether conclusions are presented by the medical device from input or acquired data, the algorithms used, and confidence limits. Special attention should be given to unintended applications of the data or algorithm.	No
12	**Is the medical device intended for use in conjunction with other medical devices, medicines or other medical technologies?** Factors that should be considered include identifying any other medical devices, medicines or other medical technologies that can be involved and the potential problems associated with such interactions, as well as patient compliance with the therapy.	No
13	**Are there unwanted outputs of energy or substances?** Energy-related factors that should be considered include noise and vibration, heat, radiation (including ionizing, non-ionizing, and ultraviolet/visible/infrared radiation), contact temperatures, leakage currents, and electric or magnetic fields. Substance-related factors that should be considered include substances used in manufacturing, cleaning or testing having unwanted physiological effects if they remain in the product. Other substance-related factors that should be considered include discharge of chemicals, waste products, and body fluids.	Chemical residue, waste products, and body fluids.
14	**Is the medical device susceptible to environmental influences?** Factors that should be considered include the operational, transport and storage environments. These include light, temperature, humidity, vibrations, spillage, susceptibility to variations in power and cooling supplies, and electromagnetic interference.	Yes, the device is susceptible to temperature. The test should be stored at 2 ~ 30°C.
15	**Does the medical device influence the environment?** Factors that should be considered include: — the effects on power and cooling supplies; — emission of toxic materials; — the generation of electromagnetic disturbance.	Yes, specimens, spent test cartridges, pipette tips, extraction tube and extraction solution should be treated as per local laws and regulations.

No.	Question	Description
16	**Are there essential consumables or accessories associated with the medical device? Are they reusable?** Factors that should be considered include specifications for such consumables or accessories and any restrictions placed upon users in their selection of these.	Yes, there are accessories, including transfer pipette set, swabs, specimen collection container, extraction tube and timer. These accessories are intended for single use only.
17	**Is maintenance or calibration necessary?** Factors that should be considered include: — whether maintenance or calibration are to be carried out by the operator or user or by a specialist; — are special substances or equipment necessary for proper maintenance or calibration?	No
18	**Does the medical device contain software?** Factors that should be considered include whether software is intended to be installed, verified, modified or exchanged by the operator or user or by a specialist.	No
19	**Does the medical device have a restricted shelf-life?** Factors that should be considered include labelling or indicators and the disposal of such medical devices when the expiration date is reached.	Yes, the shelf-life of SARS-CoV-2 Antigen Rapid Qualitative Test is 24 mouths, which is indicated in the IFU and label of the product.
20	**Are there any delayed or long-term use effects?** Factors that should be considered include ergonomic and cumulative effects. Examples could include pumps for saline that corrode over time, mechanical fatigue, loosening of straps and attachments, vibration effects, labels that wear or fall off, long term material degradation.	No
21	**To what mechanical forces will the medical device be subjected?** Factors that should be considered include whether the forces to which the medical device will be subjected under the control of the user or controlled by interaction with other persons.	No
22	**What determines the lifetime of the medical device?** Factors that should be considered include ageing and battery depletion.	Temperature determines the lifetime of the device.

No.	Question	Description
23	**Are the medical device and accessories intended for single use?** Factors that should be considered include: does the medical device self-destruct after use? Is it obvious that the device has been used?	Yes, for single use.
24	**Is safe decommissioning or disposal of the medical device necessary?** Factors that should be considered include the waste products that are generated during the disposal of the medical device itself. For example, does it contain toxic or hazardous material, or is the material recyclable?	Yes, the used device should be disposed of as biological waste.
25	**Does installation or use of the medical device require special training or special skills?** Factors that should be considered include the novelty of the medical device and the likely skill and training of the person installing the device.	Yes, it does.
26	**How will information for safe use be provided?** Factors that should be considered include: — whether information will be provided directly to the end user by the manufacturer or will it involve the participation of third parties such as installers, care providers, health care professionals or pharmacists and whether this will have implications for training; — commissioning and handing over to the end user and whether it is likely/possible that installation can be carried out by people without the necessary skills; — based on the expected life of the device, whether re-training or re-certification of operators or service personnel would be required.	Information for safe use is provided in IFU and label by the manufacturer to the end user directly. The technician should provide corresponding training to the relevant party.
27	**Will new manufacturing processes need to be established or introduced?** Factors that should be considered include new technology or a new scale of production.	No

No.	Question	Description
28	**Is successful application of the medical device critically dependent on human factors such as the user interface?**	No
29	**Does the medical device use an alarm system?** Factors that should be considered are the risk of false alarms, missing alarms, disconnected alarm systems, unreliable remote alarm systems, and the medical staff's possibility of understanding how the alarm system works.	No
30	**In what way(s) might the medical device be deliberately misused?** Factors that should be considered are incorrect use of connectors, disabling safety features or alarms, neglect of manufacturer's recommended maintenance.	No
31	**Does the medical device hold data critical to patient care?** Factors that should be considered include the consequence of the data being modified or corrupted.	No
32	**Is the medical device intended to be mobile or portable?** Factors that should be considered are the necessary grips, handles, wheels, brakes, mechanical stability and durability.	Yes, it is mobile.
33	**Does the use of the medical device depend on essential performance?** Factors that should be considered are, for example, the characteristics of the output of life-supporting devices or the operation of an alarm.	Yes, the use of the device is depended on analytical performance of the device.
34	Can the medical device be used with other devices of different lot number?	No, the test kit should be used with the solution of the same lot number.
35	Can the medical device be used with other SD cards of different lot number?	No, it can't.
36	Whether testing results of the device can be used as the only diagnosis basis by doctor?	No.

6. Hazard Identification

Using of the IVD instrument does not cause direct risks to patient or other personnel, because the examination is conducted in vitro. See the following table for known or foreseeable hazards related to the medical device.

Hazard	Biological and Chemical hazards	Applicable?	Explanation/examples
	Biological:		
E-1	Bacteria	Yes	Antibodies are animal origin materials so there could be carry over. Solution not sterilized. Other solutions sterilized
E-2	Viruses	Yes	Solution and other solutions not sterilized
E-3	Other agents (e.g. prions)	Yes	Solution and other solutions not sterilized
E-4	Re- or cross-infection	Yes	Solution and other solutions not sterilized
	Chemical:		
E-5	-Acids or alkalis	Yes	Product contain acids or alkalis.
E-6	-Residues	Yes	Antigens produced in bacteria. Solutions not sterilized. Raw material purity.
E-7	-Contaminates	Yes	Antigens produced in bacteria. Solutions not sterilized. Raw material purity.
E-8	-Additives or processing aids	Yes	Solution contains preservatives
E-9	-Cleaning, disinfecting or testing agents	No	Product does not require treatment prior to release. It is single use IVD.
E-10	-Degradation products	Yes	Reagents degradation over shelf-life
E-11	-Medical gasses	No	Product does not require or produce gas
E-12	-Anesthetic products	No	Product does not contain anesthetics
	Biocompatibility:		

Hazard	Biological and Chemical hazards	Applicable?	Explanation/examples
E-13	- Allergenicity / irritancy	No	
E-14	- Pyrogenicity[1]	No	
E-15	- Mutagenicity	No	
E-16	- Teratogenicity	No	
E-17	- Carcinogenicity	No	
E-18	Degradation	Yes	Product is not stable
E-19	Incorrect formulation (chemical composition)	Yes	Wrong formulation in the sample diluent. Wrong composition of assay Cartridge

Hazard	Operational hazards	Applicable?	Explanation/examples
	Function:		
E-20	Incorrect or inappropriate output or functionality	Yes	Device provides no result or incorrect result if malfunctioning
E-21	Incorrect measurement	Yes	Faint lines hard to interpret
E-22	Erroneous data transfer	No	/
E-23	Loss or deterioration of function	Yes	Product has a shelf life
	Use error:		
E-24	Attentional failure	Yes	User does not read the result within the time required and gets false result.
E-25	Memory failure	No	Not a machine, single use device
E-26	Rule-based failure	No	Not a machine, single use device
E-27	Knowledge-based failure	Yes	Product requires minimal training

Hazard	Operational hazards	Applicable?	Explanation/examples
E-28	Routine violation	Yes	User does not follow procedure
Hazard	Operational hazards	Applicable?	Explanation/examples
	Function:		
E-20	Incorrect or inappropriate output or functionality	Yes	Device provides no result or incorrect result if malfunctioning
E-21	Incorrect measurement	Yes	Faint lines hard to interpret
E-22	Erroneous data transfer	No	Do not transfer data
E-23	Loss or deterioration of function	Yes	Product has a shelf life
	Use error:		
E-24	Attentional failure	Yes	User does not read the result within the time required and gets false result.
E-25	Memory failure	No	Not a machine, single use device
E-26	Rule-based failure	No	Not a machine, single use device
E-27	Knowledge-based failure	Yes	Product requires minimal training
E-28	Routine violation	Yes	User does not follow procedure

Hazard	Information hazards	Applicable?	Explanation/examples
	Labeling:		
E-29	Incomplete instructions for use	Yes	IFU is not completed, missing sections
E-30	Inadequate description of performance characteristics	Yes	Information is not adequate or insufficient
E-31	Inadequate specification of intended use	Yes	Intended use is not justified based on the study result

Hazard	Information hazards	Applicable?	Explanation/examples
E-32	Inadequate disclosure of limitations	Yes	Not enough information about the test limitations provided
	Operating instructions:		
E-33	Inadequate specification of accessories to be used with the medical device	Yes	Transfer pipette set, specimen collection container be used with the product
E-34	Inadequate specification of pre-use checks	Yes	No mention of package inspection before open to use
E-35	Over-complicated operating instructions	Yes	Test procedure is not well written
	Warnings:		
E-36	Side effects	No	Product does not have side effects as it is an IVD
E-37	Hazards likely with re-use of single – use medical devices	Yes	If there is inadequate information on handling and discarding product
E-38	Specification of service and maintenance	No	Does not require service or maintenance

Annex H: Guidance on risk management for *in vitro* diagnostic medical devices: IVD-specific hazards

Hazard	IVD-specific hazards	Applicable?	Explanation
	H2.2: Identification of possible use errors:		
	H2.2.2: Possible use errors by laboratory personnel:		
H-1	Use of IVD with inappropriate calibrator, reagent, instrument or sample matrix	Yes	Not using sample diluent provided, substitute sample diluent. Use wrong sample matrix or wrong volume.
H-2	Attempt to optimize procedure to improve performance	Yes	Operator may change the sample volume, or sample diluent volume, or reading time
H-3	Abbreviation of examination procedure (taking shortcuts)	Yes	Reading result before the specified time
H-4	Neglect of instrument maintenance	No	Product requires no maintenance

Hazard	IVD-specific hazards	Applicable?	Explanation
H-5	Disabling or failing to enable safety features	No	Product has no safety features
H-6	Operation in adverse environmental conditions	Yes	Operating in environment with strong air flow, hot temperature
	H2.2.3: Possible use errors by healthcare providers:		
H-7	Use of results to screen a population for a disease when the procedure is intended for diagnosing the disease	Yes	Product is a screening test in aid of diagnosis of COVID-19, but is used as the single diagnosis tool
H-8	Use of results to diagnose a disease when the procedure is intended for monitoring a condition	Yes	Product is a screening test in aid of diagnosis of COVID-19, but is used as the single diagnosis tool
H-9	Use of IVD examination results for a new clinical application that is not claimed by the manufacturer	Yes	Intended use of the product is as a screening test in aid of diagnosis of COVID-19
	H.2.2.4: Possible use errors by patients in self-testing:		
H-10	Using insufficient volume of sample	No	Read the IFU carefully
H-11	Failure to insert a reagent module properly	No	Read the IFU carefully
H-12	Dividing reagent strips (e.g. to reduce cost)	No	Read the IFU carefully
H-13	Disabling or failing to enable safety features	No	Read the IFU carefully
H-14	Storing reagent in inappropriate conditions	No	Read the IFU carefully
	H.2.4: Identification of known & foreseeable hazards:		
	H.2.4.1: Hazards to the patient:		
H-15	Incorrect results	Yes	False negative or positive result
H-16	Delayed results	Yes	Test failure leads to need to repeat test
H-17	Incorrect information accompanying the result	Yes	Screening test result is directly reported to patient without further confirmation

Hazard	IVD-specific hazards	Applicable?	Explanation
	H.2.4.3: Identification of hazards in fault conditions:		
H-18	Within-batch inhomogeneity	Yes	Intra-lot result inconsistency
H-19	Batch-to-batch inconsistency	Yes	Lot to lot result inconsistency
H-20	Non-traceable calibrator value	No	No calibrators used
H-21	Non-commutable calibrator	No	No calibrators used in product
H-22	Non-specificity (e.g., interfering factors)	Yes	Interfering factors could affect test result
H-23	Sample or reagent carryover	Yes	User adds the wrong sample/solution volume and spills over
H-24	Measurement imprecision (instrument-related)	Yes	Test provides no result or incorrect result if malfunctioning
H-25	Stability failures	Yes	Wrong storage or transportation conditions leads to product failure
H-26	Unstable reagent	Yes	Cartridge or sample diluent is not stable, causing faulty result
H-27	Hardware/software failure	Yes	Cartridge not assembled leads to device failure.
H-28	Packaging failure	Yes	Pouch not sealed appropriately, leading to leakage
H-29	Incorrect patient name or identification number	Yes	Wrong patient ID is marked by operator
H-30	Incorrect birth date or age	No	No information of date of birth or age is required
H-31	Incorrect gender	No	No gender information is recorded or required
	H.2.4.4: Identifying hazards in normal use		
H-32	Imperfect discrimination between positive and negative samples: qualitative examination procedures exhibit inherent false negative and positive rates, caused in part by uncertainties determining suitable cut-off value	Yes	Incorrect reading time could lead to false positive or false negative

Hazard	IVD-specific hazards	Applicable?	Explanation
H-33	Uncertainty of measurement: state-of-the-art technology can limit the precision of quantitative IVD medical devices, such as glucose monitoring systems described in ISO 15197; if performance criteria requires 95% acceptance criteria, then up to 5 % of the individual results are allowed to fall outside the limit.	No	It is a simple, manual and qualitative test method.
H-34	Unexpected influence of other constituents (interfering factors) in the sample matrix: new drugs, biochemical metabolites, heterophilic antibodies and sample preparation materials can affect the performance characteristics of an IVD examination procedure	Yes	Unrecognized interference factors could interfere with the test result: false positive or false negative
H-35	Natural heterogeneity of the analyte: antibodies and other proteins in blood samples are mixtures of different isoforms; published performance characteristics of an IVD examination procedure might not apply to all components of the mixture	Yes	Test developed based on samples from one geographic region might not be reactive to those from different geographic regions due to strain difference of the pathogen

7. Risk evaluation Criteria

7.1 Severity of harm: grade by severity of possible harm that may cause

Severity	Designation	Description
Minimal	1	Slight or no effect to patients or users
Minor	2	No lasting effects
Moderate	3	Short-term effects, requiring medical action
Major	4	Severe lasting effects, requiring medical action

Critical	5	Life-threatening, loss of limb, threat to community

7.2 Probability of occurrence of harm: per probability of adverse event that happens (time/year)

Probability	Designation	Range
Frequent	5	$\geq 10^{-3}$
Probable	4	$< 10^{-3}$ and $\geq 10^{-4}$
Occasional	3	$< 10^{-4}$ and $\geq 10^{-5}$
Rare	2	$< 10^{-5}$ and $\geq 10^{-6}$
Improbable	1	$< 10^{-6}$

7.3 Criteria of risk acceptability

	SEVERITY				
PROBABILITY	Minimal	Minor	Moderate	Major	Critical
Frequent	**5**	**10**	**15**	**20**	**25**
Probable	**4**	**8**	**12**	**16**	**20**
Occasional	3	6	**9**	**12**	**15**
Rare	2	4	6	**8**	**10**
Improbable	1	2	3	4	5

7.4 Risk index table

RI >9: Unacceptable Risk Index (UNACC)
RI <10: Acceptable Risk Index (ACC)

7.5 Additional Criteria

(1) All risks must be taken into account; all risks have to be reduced as far as possible and that all risks combined, regardless of any "acceptability" assessment, need to be balanced, together with all other risks, against the benefit of the device; risks must be reduced "as far as possible" without there being room for economic considerations.

(2) The risk-benefit analysis for the individual risk and the overall risk-benefit analysis must be undertaken.

(3) All the “control options” must be applied if the first or the second control option has reduced the risk to an “acceptable level” (unless the additional control option(s) do(es) not improve the safety).

(4) "Information for safety" cannot be used as risk control measures. Accordingly, manufacturers should not attribute any additional risk reduction to the information given to the users.

(5) If the risk can’t be eliminated due to technical reason any longer, it can be regarded to be the lowest.

(6) Risk can be regarded acceptable after measures being taken to eliminate the risk low enough to conform with the standard or other standards.

8. Risk Evaluation and Control

P: Probability; S: Severity; RI: Risk index

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
Biological contamination:										
E-1: Bacteria	- Carryover from antigen production in bacteria - User handling - Solutions are not sterilized. - Raw material contamination	- User gets sick from contamination - Incorrect test result - Delay diagnosis & treatment	3	4	12	- Use non-pathogenic bacteria for antigen production - Clean manufacturing environment to avoid production contamination - Qualify raw material suppliers - Incoming QC testing	1	4	4	Residual risk is acceptable. Mitigation measures won’t bring additional risks.
E-2: Viruses										
E-3: Others (e.g. prions)										

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
						- Manufacturing and testing lab to follow GLP - Use antimicrobial agents in sample diluent solution				
E-4: Re- or cross-infection	- No for re-infection (product does not contact patient) - User failure to follow good laboratory practices for using and discarding product	- User gets sick from cross-contamination with infected samples	2	5	10	- Testing lab to follow GLP - Labeling design control for biohazards	1	5	5	Residual risk is acceptable. Mitigation measures won't bring additional risks.
Chemical toxicity:										
Exposure of airway, tissues, environment or property, e.g. to foreign materials:										
E-5: Acids or alkalis	- No for **E-9**, **E11, E-12** - Manufacturing handling - Solutions not sterilized. - Raw material contamination - Product degradation	- User gets sick from exposure to toxic chemicals	3	3	9	- Manufacturing and QC controls - Raw material/vendor controls - Labeling design for hazards - Line clearance procedures	1	3	3	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-6: Residues										
E-7: Contaminates										
E-8: Additives or processing aids										
E-9: Cleaning, disinfecting or testing agents		- Product failure - Incorrect test result - Delay diagnosis & treatment	2	4	8	- Manufacturing and QC controls - Validated manufacturing process - Raw material/vendor controls - Labeling design control for chemical hazards - Product stability studies	1	4	4	
E-10: Degradation products										
E-11: Medical gasses										
E-12: Anesthetic products										
Biocompatibility:										

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
E-13: Allergenicity / irritancy **E-14:** Pyrogenicity[2] **E-15:** Mutagenicity **E-16:** Teratogenicity **E-17:** Carcinogenicity	- N/A for patient, as product does not contact patient. Applicable for user (manufacturing or health care workers)	- User gets sick from hazardous product. Potential long-term health effects including death.	3	5	15	- Qualify raw material suppliers - Incoming QC testing - Manufacturing and testing lab to follow GLP - Labeling design control for biohazards	1	5	5	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-19: Degradation	- Poor design control - Errors in manufacturing process - Insufficient/wrong raw material specifications - Use of uncalibrated equipment - Improper shipping/storage - Use of expired products	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Raw material/vendor controls - Incoming raw material QC - Labeling design for hazards	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-20: Incorrect formulation (chemical composition)	- Poor design control - Errors in manufacturing process - Insufficient/wrong raw material specifications - Use of uncalibrated equipment	- Delayed or incorrect test result - Delay diagnosis & treatment	4	4	16	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Raw material/vendor controls - Incoming raw material QC	2	4	8	Residual risk is acceptable. Mitigation measures won't bring additional risks.
Function:										

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
E-20: Incorrect or inappropriate output or functionality	- Poor design control - Operator not following IFU - Improper shipping/storage - Use of expired products	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Testing lab to follow GLP - Labeling design (IFU)	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-21: Incorrect measurement	- Poor design control - Operator not following IFU - Improper shipping/storage - Use of expired products	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Testing lab to follow GLP - Labeling design (IFU)	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-22: Erroneous data transfer	- N/A: this product does not include any data transfer options									
E-23: Loss or deterioration of function	- Poor design control - Errors in manufacturing process - Insufficient/wrong raw material specifications - Use of uncalibrated equipment - Improper shipping/storage - Use of expired products	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Raw material/vendor controls - Incoming raw material QC - Labeling design for hazards	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
Use error:										

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
E-24: Attentional failure	- Operator not following instructions - Inadequate labeling - Wrong sample, wrong sample volume - Wrong reading time	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Testing lab to follow GLP - Labeling design control - Measuring device provided with product	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-25: Memory failure										
E-26: Rule-based failure										
E-27: Knowledge-based failure										
E-28: Routine violation										
Labeling:										
E-29: Incomplete instructions for use	- Poor design control - Inadequate labeling	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control - Product labeling design control	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-30: Inadequate description of performance characteristics										
E-31: Inadequate specification of intended use										
E-32: Inadequate disclosure of limitations										
Operating instructions:										

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
E-33: Inadequate specification of accessories to be used with the medical device	- Inadequate labeling	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control - Product labeling design control	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-34: Inadequate specification of pre-use checks	- Poor design control - Inadequate labeling	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control - Product labeling design control - Clear instructions for use	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-35: Over-complicated operating instructions	- Poor design control - Inadequate labeling	- Delayed or incorrect test result - Delay diagnosis & treatment	2	4	8	- Product labeling design control - Follow WHO TGS - Product verification and validation	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
Warnings:										
E-36: Side effects	- Poor design control - Inadequate labeling	- Delayed or incorrect test result - Delay diagnosis & treatment	2	4	8	- Product labeling design control - Confirmation of positive results by alternative method specified	1	4	4	Residual risk is acceptable. Mitigation measures won't bring

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
						- Product verification and validation				additional risks.
E-37: Hazards likely with re-use of single – use medical devices	- Inadequate information on handling and discarding product	- User gets sick from cross-infection with infected sample	2	5	10	- Product labeling design control - Following GLP practices for biohazards	1	5	5	Residual risk is acceptable. Mitigation measures won't bring additional risks.
E-38: Specification of service and maintenance	- N/A: no service or maintenance needed									
Hazard	**Cause of hazard or failure**	**Hazardous situation/harm**	**Risk evaluation**			**Risk control measures and mitigating factors**	**Residual risk evaluation**			**Acceptability or action**
			P	**S**	**RI**		**P**	**S**	**R**	
Possible use errors by laboratory personnel:										
H-1: Use of IVD with inappropriate calibrator, reagent, instrument or sample matrix	- Poor design control - Operator not following instructions (wrong sample specifications, wrong volume, wrong order…) - Inadequate labeling design - User failure to follow good laboratory practices (IFU not read)	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control (product robustness testing, clear product specifications) - Product labeling design control (IFU, using and discarding, hazards) - Testing lab to follow GLP	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-2: Attempt to optimize procedure to improve performance	- Untrained operator - Inadequate labeling design - User failure to follow good	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Product labeling design control (IFU, using and discarding, hazards)	1	4	4	Residual risk is acceptable. Mitigation

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
H-3: Abbreviation of examination procedure (taking shortcuts)	laboratory practices (IFU not read)					- Product robustness testing - Testing lab to follow GLP				measures won't bring additional risks.
H-4: Neglect of instrument maintenance	- N/A: no maintenance required									
H-5: Disabling or failing to enable safety features	- N/A: no safety measures to enable									
H-6: Operation in adverse environmental conditions	- Manufacturing errors - Inadequate shipping or storage - Operator not following instructions - Inadequate labeling design - Use of product outside environmental specifications	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Controlled manufacturing process - Product labeling design control (specified expiration date and environmental conditions) - Testing lab to follow GLP	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
Possible use errors by healthcare providers:										
H-7: Use of results to screen a population for a disease when the procedure is intended for diagnosing the disease	- Inadequate labeling design - IFU not read or ignored - User failure to follow good laboratory practices	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Product labeling design control - User to follow GLP	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-8: Use of results to diagnose a disease when the procedure is intended for monitoring	- Inadequate labeling design - IFU not read or ignored - User failure to follow good laboratory practices	- Test used to diagnose wrong disease - Delayed or incorrect test result - Wrong treatment	3	4	12	- Product labeling design control - User to follow GLP	1	4	4	Residual risk is acceptable. Mitigation measures

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
a condition										won't bring additional risks.
H-9: Use of IVD examination results for a new clinical application that is not claimed by the manufacturer	- Inadequate labeling design - IFU not read or ignored - User failure to follow good laboratory practices	- Test used to diagnose wrong disease - Delayed or incorrect test result - Wrong treatment	3	4	12	- Product labeling design control - User to follow GLP	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H.2.2.4: Possible use errors by patients in self-testing:										
H-10: Using insufficient volume of sample	- N/A: device not for self-testing									
H-11: Failure to insert a reagent module properly	- N/A: device not for self-testing									
H-12: Dividing reagent strips (e.g. to reduce cost)	- N/A: device not for self-testing									
H-13: Disabling or failing to enable safety features	- N/A: device not for self-testing									
H-14: Storing reagent in inappropriate conditions	- N/A: device not for self-testing									
H.2.4: Identification of known & foreseeable hazards										
H.2.4.1: Hazards to the patient										

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
H-15: Incorrect results	- Poor design control - Manufacturing process errors - Improper shipping and storage - Use of device past expiration - IFU not read or ignored - User failure to follow good laboratory practices	- Delayed or incorrect test result - Delayed diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Labeling design control - Device has a control line - Shipping simulation under stress conditions - Testing lab to follow GLP	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-16: Delayed results	- Poor design control - Manufacturing process errors - Improper shipping and storage - Use of device past expiration - IFU not read or ignored - User failure to follow good laboratory practices	- Delayed diagnosis & treatment	3	3	9	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Labeling design control	1	3	3	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-17: Incorrect information accompanying the result	- Test result reported to patient without further confirmation - Poor labeling design - User failure to follow good laboratory practices	- Delayed diagnosis & treatment	3	3	9	- Require confirmation of positive results with alternative method - Device has space for patient identification - Validated manufacturing process - Labeling design control - Testing lab to follow GLP	1	3	3	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H.2.4.3: Identification of hazards in fault conditions										

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
H-18: Within-batch inhomogeneity	- Incorrect mixing in manufacturing - Poor manufacturing process design - Uncalibrated equipment used - Reagent degradation over time	- High product variability - Inconsistency of test result - Delayed diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Calibrated equipment - Product verification and validation - Stability testing and specifications	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-19: Batch-to-batch inconsistency	- Poor manufacturing process design - Insufficient raw material specifications - Uncalibrated equipment used - Reagent degradation over time	- Lot to lot product variability - Inconsistency of test result - Delayed diagnosis & treatment	4	4	16	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Calibrated equipment - Product verification and validation - Stability testing and specifications	2	4	8	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-20: Non-traceable calibrator value	- N/A: no calibrators used									
H-21: Non-commutable calibrator	- N/A: no calibrators used									

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
H-22: Non-specificity (e.g., interfering factors)	- Poor design control (not enough substances tested) - Poor labeling design - Operator not following IFU - Using the wrong sample	- Delayed or incorrect test result - Delayed diagnosis & treatment	4	4	16	- Manufacture line clearance - Follow design control practices - Review literature and test enough interfering substances - Labeling design control - Testing lab to follow GLP	2	4	8	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-23: Sample or reagent carryover	- Uncalibrated equipment (pipette) - Poor design control (volume tolerances) - User not following instructions	- Reagent or sample spill, possible contamination - Delayed or incorrect test result - Delayed diagnosis & treatment	2	4	8	- Follow design control (establish volume tolerances) - Labeling design control - Testing lab to follow GLP	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-24: Measurement imprecision (instrument-related)	- Not enough tolerance for line intensity; time to read - User failure to follow good laboratory practices	- Delayed or incorrect test result - Delayed diagnosis & treatment	3	4	12	- Follow design control (establish product tolerances) - Labeling design control - Testing lab to follow GLP - Verification and validation	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-25: Stability failures (storage, transportation, in-use)	- Errors in manufacturing process - Insufficient/wrong raw material specifications - Raw material contamination - Improper shipping/storage - Poor design controls	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Raw material/vendor controls - Labeling design control (IFU)	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
						- Shipping simulation under stress conditions				
H-26: Unstable reagent	- Errors in manufacturing process - Insufficient/wrong raw material specifications - Raw material contamination - Improper shipping/storage - Poor design controls	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Raw material/vendor controls - Labeling design control (IFU) - Shipping simulation under stress conditions	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-27: Hardware/software failure	- Poor design control - Insufficient/wrong raw material specifications - Improper shipping	- Delayed or incorrect test result - Delay diagnosis & treatment	3	4	12	- Follow design control practices - Validated manufacturing process - Raw material/vendor controls - Labeling design control (IFU) - Shipping simulation under stress conditions	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
H-28: Packaging failure	- Pouch not sealed properly - Test cassette break - Poor design control	- Reagent spill - User injury from broken cassette	3	3	12	- Follow design control practices - Validated manufacturing process - Raw material/vendor controls - Labeling design control (IFU) - Shipping simulation under stress conditions	1	3	3	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-29: Incorrect patient name or identification number	- User failure to follow good laboratory practices - Poor labeling design - Poor design control	- Wrong patient diagnosed - Delay/wrong diagnosis and treatment	2	4	8	- Follow design control practices - Labeling design control - Testing lab to follow GLP - Patient ID to be written on device	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-30: Incorrect birth date or age	- N/A: No age information required									
H-31: Incorrect gender	- N/A: No gender information required									
H.2.4.4: Identifying hazards in normal use										

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
H-32: Imperfect discrimination between positive and negative samples: qualitative examination procedures exhibit inherent false negative and positive rates, caused in part by uncertainties determining suitable cut-off value	- Poor design control - Manufacturing process errors - Improper shipping and storage - Use of device past expiration - IFU not read or ignored - User failure to follow good laboratory practices	- Delayed or incorrect test result - Delayed diagnosis & treatment	3	4	12	- Follow design control practices - Manufacturing and QC controls - Validated manufacturing process - Labeling design control - Device has a control line - Shipping simulation under stress conditions - Testing lab to follow GLP	2	4	8	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-33: Uncertainty of measurement (as described in ISO 15197; if performance criteria require 95% acceptance criteria, then up to 5 % of the results are allowed to fall outside the limit.	- Not enough tolerance for line intensity; time to read - No QC specifications for product release - Variability of product performance	- Delayed or incorrect test result - Delayed diagnosis & treatment	3	4	12	- Follow design control (establish product tolerances) - Establish product QC specifications - Verification and validation (robustness/flex studies)	1	4	4	Residual risk is acceptable. Mitigation measures won't bring additional risks.

Hazard	Cause of hazard or failure	Hazardous situation/harm	Risk evaluation			Risk control measures and mitigating factors	Residual risk evaluation			Acceptability or action
			P	S	RI		P	S	RI	
H-34: Unexpected influence of other constituents (interfering factors) in the sample matrix: new drugs, biochemical metabolites, heterophilic antibodies and sample preparation materials can affect the performance characteristics of an IVD examination procedure	- Poor design control (not enough substances tested) - Poor labeling design - Operator not following IFU - Using the wrong sample - Not enough coverage of different populations (eg, sexes, ages, pregnancy status)	- Delayed or incorrect test result - Delayed diagnosis & treatment	4	4	16	- Manufacture line clearance - Follow design control practices - Review literature and test enough interfering substances - Labeling design control - Testing lab to follow GLP - Perform extensive testing of different populations (eg, sex, age, pregnancy status)	2	4	8	Residual risk is acceptable. Mitigation measures won't bring additional risks.
H-35: Natural heterogeneity of the analyte: antibodies and other proteins in blood samples are mixtures of different isoforms; published performance characteristics of an IVD examination procedure might not apply to all components of the mixture	- Poor design control - Not enough samples tested - Not enough geographical populations tested	- Delayed or incorrect test result - Delayed diagnosis & treatment	4	4	16	- Follow design control practices - Testing on extensive samples - Testing on different geographical populations - Labeling design control	2	4	8	Residual risk is acceptable. Mitigation measures won't bring additional risks.

9. Overall residual risks evaluation

Risks of hazard are reduced to the lowest level after implementation of risk control measures and no new risk is introduced. Besides, benefits of the medical device outweigh the overall residual risks, so the overall residual risks are acceptable. The residual risks should be included in the accompanying documents such as Instructions for Use are as follows:

No.	Residual risk description
1	This reagent is used for in vitro diagnosis only. Please do not use expired products.
2	All samples (including the remaining samples after testing), used reagents and waste should be treated as infectious materials.
3	The reagent is for single use. Once the pouch is opened, it should be used within 30 minutes to avoid test failure caused by the moisture absorption.
4	While using the test cartridge, vibration and electromagnetic environment should be avoided.
5	Lot number of solutions and test cartridges must be matched.

10. Evaluation on Production and Post-market Information

The post-production information will be collected after the product is marketed.

11. Conclusion

According to the analysis, evaluation and control of risks in full life-cycle of the device, all risks are acceptable. Therefore, the device is safe to be used.