Risk Management Report

Name:Novel Coronavirus (COVID-19) Antigen Test Kit (Colloidal Gold)

No.: 303036

Drafter: 5.1.2e

Date: 2021.01.24

Reviewer 5.1.2e

Date: 2021.01.29

Approver 5.1.2e

Date: 2021.01.29

Part I: Risk Management Plan

1.Scope:

Description of product: Novel Coronavirus (COVID-19) Antigen Test Kit (Colloidal Gold) is an IVD product. It is intended for the qualitative detection of antigen (N-protein) of SARS-CoV-2 from Nasal specimens.

The immune colloidal gold technique is used in the assay to detect antigens (N-protein) of COVID-19. The reagent binding pad is coated with anti-SARS-CoV-2 monoclonal antibodies which is labeled with colloidal gold marker, respectively. A nitrocellulose membrane in test area of a strip is coated with anti-SARS-CoV-2 antibodies. The quality control area within the nitrocellulose membrane is coated with goat anti-mouse IgG antibodies. When testing, the antibodies against COVID-19 form immuno-complexes with the antigen(N-protein) of the virus in the specimen to be tested. As a result of chromatography, immuno-complexes move along the membrane and will be captured by the anti-SARS-CoV-2 antibodies coated in the test area to form a visible line with red color (T line). The free colloidal gold marker or immune complexes continue to move forward and specifically bind to the goat anti-mouse antibody coated in the quality control area to form a visible line (C line). If the specimen does not contain the antigen of COVID-19, no test line will show, only quality control line (C line) will appear.

This product contains the following components

Device:

Test device: There are two different packages with 1 or 5 or 25 test cassettes containing immobilized anti-SARS-CoV-2 antibodies labeled which is labeled with colloidal gold, anti-SARS-CoV-2 monoclonal antibodies, goat anti-mouse IgG antibodies as a control.

Swabs: 1 or 5 or 25 Pcs

Prepackaged extraction buffer: 350 μ L per vial. 1 or 5 or 25 vials, respectively.

This risk management plan mainly refers to the planning of risk management activities of the product during its entire life cycle (including design and development, product realization, final outage and disposal phase) as required by EN ISO14971:2012. As the product is already on the market, the risk management focuses on the production process, the stage before production and post-marketing risk. We'll also carried post-marketing risk management once a year according to product quality and customer feedback.

2.Assignment of responsibility and authority

2.1 The general manager provides appropriate resources for risk management and assumes leadership responsibility for risk management. Ensure that the personnel assigned to risk management, implementation and evaluation work are trained and qualified and that the risk management practitioners have appropriate knowledge and experience. Be responsible for the approval of risk management reports.

2.2 The R&D department shall be responsible for the risk management activities in the process of product design and development, and forms relevant records of risk analysis, risk assessment, risk control and comprehensive residual risk analysis and assessment.

2.3 The quality department, sales department, production department and other relevant departments

shall be responsible for analyzing all known and foreseeable hazards from the perspective of product realization, as well as the collection of production and post-marketing information, and timely feedback to the R&D department for risk assessment, and carry out a new round of risk management activities if necessary.

2.4 The R&D department and members of the review panel shall regularly review the results of risk management activities and are responsible for their correctness and effectiveness.

2.5 The quality department shall be responsible for the collation of all risk management documents.

2.6 The risk management panel includes:

Panel leader: 5.1.2e

Members 5.1.2e

5.1.2e

3.Risk analysis

3.1 The R &D department and the person in charge of quality shall be responsible for the analysis of the intended use and identifying possible errors, general manager and the person in charge of quality shall be responsible for the identification and safety features. And the person in charge quality shall be responsible for collecting the analytical results of relevant departments and classifying all of the identified risks in accordance with the requirements of the No.16 Decree and The appendix of EN ISO 14971:2012, then organize all departments to carry out risk assessment and analysis of risk control measures. Meanwhile, compile the above contents into the corresponding tables.

3.2 Risk analysis includes:

1）An error condition that can lead to a potential source of harm and the risk it poses

2）Analyze possible error situations and the risks they pose

4.Risk evaluation

4.1The panel members analyze the occurrence probability and severity of the hazard judged by the risk analysis, and finally determined the acceptability of the risk according to the risk acceptability criteria determined by the plan, and kept the evaluation records.

4.2The following are the acceptable risk criteria determined for the risk management, in which the severity of damage is qualitatively analyzed, the probability of damage is semi-quantitatively analyzed, and the risk acceptability criteria are represented by S, O, D matrix.

RE	Risk Evaluation
S	Severity (9 –very severe, 0 –not severe). very severe means may cased many people death.
O	Occurrence (9 –often, 0 –never). Often mean may happened 1/10, or more.
D	Detection (9 –impossible to detect before risk occurs, 0 –will be certainly detected before risk occurs)

RL	Risk Level = Severity × Occurrence × Detection 1-9: Neglectable risk, no further actions; 9-24: Moderate: minimal risk, preventive action recommended; 25-48: Moderate risk, preventive action required; >48: Risk is usually not acceptable
RRM	Risk Reduction Measure
NH	New hazard generated (no/ yes - if yes, then number of new hazard indicated)
ALOR	Acceptable Level of Risk

4.3 After the risk analysis and risk assessment process to judge all the risks of the products are feasible measures should be taken down to the acceptable area, when the risks are judged as unacceptable, should collect relevant data and documents to risk/benefit analysis of risk, if the benefit is greater than the risk, the risk is still acceptable, if the risk is greater than the benefit, design should give up.

4.4 For hazard situations where the probability of damage cannot be estimated, a list of possible consequences of the hazard should be prepared for risk assessment and risk control. Panel members shall adopt a reasonably feasible mitigation method to reduce the risk to a reasonably feasible minimum level, and carry out risk/benefit analysis for the risk that cannot be reduced. If the benefit exceeds the risk, the risk is acceptable; otherwise, the risk is unacceptable.

4.5 In the acceptable area, the risk is very low, but control measures to reduce the risk should also be taken proactively.

4.6 It can be judged as acceptable when benefits are greater than risks

5.Risk control

5.1 Feasible measures should also be taken to minimize risks judged to be acceptable.

5.2 For risks judged to be unacceptable, each department shall cooperate with the technical department to analyze the risk control plan from the following aspects in R&D phase, and identify one or more risk control measures to reduce the risk to an acceptable level.

1）To obtain inherent safety by design methods

- To eliminate specific hazards;
- To reduce the probability of damage
- To reduce the severity of the damage

2）Protective measures in the product itself or during manufacturing.

3）Safety information

- Warnings and instructions are given in the accompanying documentation
- Restrict the use or environment of medical devices
- Train operators

5.3 Control the manufacturing process during the pilot production or production phase, such as using

HACCP technology.（Hazard analysis and critical control points）

5.4 If it is determined by the program analysis that the required risk reduction is not feasible, each department shall collect relevant data for risk/benefit analysis of the remaining risks. If the data and literature collected by the review do not support that the benefits outweigh the risks, the design shall be abandoned.

5.5 Each department shall ensure that one or more risks arising from the identified hazard situation are taken into account to ensure the integrity of risk control.

5.6 During or after the implementation of the risk control plan, the implementation effect shall be verified to determine the adaptability and effectiveness of the control measures. Any remaining risks shall be evaluated using the risk acceptability criteria of section 4 of the plan and further risk control measures should be taken for those judged unacceptable. If control measures are not feasible, relevant data and literature should be collected and reviewed for risk/benefit analysis of residual risks. If the benefit outweighs the risk, the residual risk is still acceptable;otherwise, it is unacceptable. For residual risks judged to be acceptable, the sales department shall cooperate with the technical department to determine which residual risks shall be disclosed according to the guidelines in the Annex of EN ISO 14971:2012. At the same time, It shall be analyzed that whether the implementation of the control measures will cause one or more new risks or whether there is an impact on the risk assessment before the adoption of the measures; If necessary, the risk analysis, risk assessment and risk control shall be conducted again and the results of the activities taken shall be recorded.

6.Verification requirements for risk management activities

6.1 Verify that whether the risk management plan has been properly implemented

Members of the review panel shall be responsible for verifying the implementation of the risk management plan and reviewing the records of risk analysis, risk assessment, risk control, etc. in the form of risk management documents to ensure that the risk management activities planned by the risk management plan have been properly implemented.

6.2 Verification of the effectiveness of risk management activities

The review panel can verify the implementation effect of risk management by collecting clinical data and production and post-production information to ensure the effectiveness of risk management activities.

7.Review requirements of risk management activities

7.1 Member of Review panel

Reviewer	Department	Title
5.1.2e	Operation	General Manager
	Operation	Technical Vice General Manager
	Operation	Management Representative
	R&D	Manager
	Sales	Manager

5.1.2e	Marketing	Manager
	Production	Manager
	Materials Control	Manager
	Quality	Supervisor
	Production	Supervisor
	Quality	QC

7.2 The members of the review panel shall be responsible for the correctness and validity of the review results.

7.3 Every members of the review panel review the information related to product safety by using < control procedure of user feedback and after-sales service> and<control procedure of quality accident and adverse event report> to provide a basis for the comprehensive residual risk assessment.

7.4 Review the product design and development, trial production, production and after sales according to the following safety related information

1）Whether there is a previously unknown hazard;

2）Whether an estimated risk (one or more) caused by a hazard is no longer acceptable

3）Whether other aspects of the initial evaluation have failed

4）Whether the comprehensive residual risk of the product has been reduced to an acceptable level or judged to be acceptable by risk/benefit analysis.

7.5 Product production and post-marketing information acquisition methods shall be reviewed Maintain review records to verify that each element of the risk management plan has been properly implemented at a specific life-cycle stage of the product.

8.Comprehensive residual risk analysis

8.1 After all risk control measures have been implemented and verified, each department shall consider whether all the comprehensive residual risks caused by the product are acceptable in accordance with the criteria in section 4 of the plan. If the judgment is unacceptable, each department shall collect and review relevant data and literature in order to determine whether the medical benefits of the intended use exceed the comprehensive residual risk. If the above evidences support the conclusion that the medical benefits exceed the comprehensive residual risks, the comprehensive residual risks are acceptable .Otherwise, the composite residual risk is still unacceptable.

8.2 Each department can evaluate the comprehensive residual risk by referring to the following methods

1）Event tree analysis: a joint study of individual risks to determine whether the comprehensive residual risk is acceptable;

2）Fault tree analysis: the same damage may be caused by different probability of the harm situation, the method can be derived the combined probability of the damage;

3）Comprehensive review of individual risk control measures: the risk control measures that are appropriate for a single risk may have conflicting requirements;

4）Review of warnings: a single warning may provide risk reduction, but too many warnings may reduce the effectiveness of warnings;

5）Review of operating instructions: review of all operating instructions of the product may result in inconsistent information or difficulty in compliance;

6）Comparison of risk:The collated individual residual risks are compared one by one with the risks of similar existing products considering different usage situations, especially the latest adverse events.

8.3 Each department shall determine which comprehensive residual risks shall be published in accordance with YY/ t0316:2016 Appendix J, and shall keep records of the evaluation results of the comprehensive residual risks.

9.Risk management report

Prior to the commercial sale of the product, each department shall cooperate with the technical department to complete the review of the risk management process. The review requirements are set forth in article 7 of the plan. The final result of the review shall be presented in the form of a risk management report.

Risk Analysis Report

Identification of qualitative and quantitative characteristics (acc.to EN ISO 14971:2012,cl. 4.2)

Questions	Answer
C.2.1 What is the intended use and how is the medical device to be used?	The LYHER® Novel Corona virus (COVID-19) Antigen Te st Kit (Colloidal Gold) is an in vitro immunoass assay. The assay is for the direct and qualitative detection of SARS-CoV-2 nucleoprotei n antigens from Nasal swab specimens. The kit is for in vitro diagnostic use. For no professional use.
C.2.2 Is the medical device intended to be implanted?	NO.
C.2.3 Is the medical device intended to be in contact with the patient or other persons?	Yes, The product not in contact with the surface of the body intact skin
C.2.4 What materials or components are utilized in the medical device or are used with, or are in contact with, the medical device?	See Instruction for User
C.2.5 Is energy delivered to or extracted from the patient?	NO.
C.2.6 Are substances delivered to or extracted from the patient?	NO.
C.2.7 Are biological materials processed by the medical device for subsequent re-use, transfusion or transplantation?	NO.

C.2.8 Is the medical device supplied sterile or intended to be sterilized by the user, or are other microbiological controls applicable?	YES.
C.2.9 Is the medical device intended to be routinely cleaned and disinfected by the user?	NO.
C.2.10 Is the medical device intended to modify the patient environment?	NO.
C.2.11 Are measurements taken?	NO.
C.2.12 Is the medical device interpretative?	NO.
C.2.13 Is the medical device intended for use in conjunction with other medical devices, medicines or other medical technologies?	NO.
C.2.14 Are there unwanted outputs of energy or substances?	NO.
C.2.15 Is the medical device susceptible to environmental influences?	Yes.Store in a dry place at 2-30 ℃, protected from humidity.
C.2.16 Does the medical device influence the environment?	NO.
C.2.17 Are there essential consumables or accessories associated with the medical device?	NO.
C.2.18 Is maintenance or calibration necessary?	NO.
C.2.19 Does the medical device contain software?	NO.
C.2.20 Does the medical device have a restricted shelf-life?	18 months.
C.2.21 Are there any delayed or long-term use effects?	NO.
C.2.22 To what mechanical forces will the medical device be subjected?	NO.
C.2.23 What determines the lifetime of the medical device?	NO.

C.2.24 Is the medical device intended for single use?	YES, single use
C.2.25 Is safe decommissioning or disposal of the medical device necessary?	NO.
C.2.26 Does installation or use of the medical device require special training or special skills?	Yes.
C.2.27 How will information for safe use be provided?	Manual.
C.2.28 Will new manufacturing processes need to be established or introduced?	NO.
C.2.29 Is successful application of the medical device critically dependent on human factors such as the user interface? C.2.29.1 Can the user interface design features contribute to use error?	NO.
C.2.29.2 Is the medical device used in an environment where distractions can cause use error?	NO.
C.2.29.3 Does the medical device have connecting parts or accessories?	NO.
C.2.29.4 Does the medical device have a control interface?	NO.
C.2.29.5 Does the medical device display information?	NO.
C.2.29.6 Is the medical device controlled by a menu?	NO.
C.2.29.7 Will the medical device be used by persons with special needs?	NO.
C.2.29.8 Can the user interface be used to initiate user actions?	NO.
C.2.30 Does the medical device use an alarm system?	NO.
C.2.31 In what way(s) might the medical device be deliberately misused?	NO.
C.2.32 Does the medical device hold data critical to patient care?	NO.
C.2.33 Is the medical device intended to be mobile or portable?	YES. portable
C.2.34 Does the use of the medical device depend on essential performance?	NO.
Letters in the first column refer to EN ISO 14971:2012, cl. 4.2	

No	Hazard General	Identify hazards	Risk Evaluation S	O	D	RL	Risk Reduction Measure	Evidence	NH	ALOR
D2.	**Energy Hazards**									
1	Electricity	N/A								
2	Heat	N/A								
3	Mechanical force	N/A								
4	Ionizing radiation	N/A								
5	Non Ionizing radiation	N/A								
6	Electromagnetic fields									
7	Moving parts	N/A								
8	Suspended masses	N/A								
9	Patient support device failure	N/A								
10	Pressure(vessel rupture)	N/A								
11	Acoustic pressure	N/A								
12	Vibration	N/A								
13	Magnetic fields(e.g. MRI)	N/A								
D3.	**Biological hazards**									
1	Bio-contamination	The product may be contaminated if the package is damaged.	2	3	1	6	Single use and package control	Instruction		Acc
2	Bio-incompatibility	The product may cause the user uncomfortable if the material is not OK	2	4	1	8	Choose raw materials of fabrics with qualified biological properties	See test report of swabs.		Acc
3	Incorrect formulation(chemical composition)	The product may cause the user uncomfortable if the material is not OK	2	3	1	6	Choose safe chemical raw material in recognize to ensure that the ingredients are accurate.	See test report of swabs, and MSDS of swab.		Acc

No	Hazard General	Identify hazards	Risk Evaluation S	O	D	RL	Risk Reduction Measure	Evidence	NH	ALOR
4	Toxicity	The product may cause the user uncomfortable if the material is not OK	2	4	1	8	Choose raw materials of fabrics with cyto toxicity meeting the requirements	See test report report of swabs.		Acc
5	Allergenicity	N/A								
6	Mutagenicity	N/A								
7	Oncogenicity	N/A								
8	Teratogenicity	N/A								
9	Carcinogenicity	N/A								
10	Re-and/or cross-infection	The product is single use product and could not be re used.	2	3	2	12	Ensure that the products are for single use shall be shown on the instruction of use and labels.	Instruction of use and Labels		Acc
11	Pyrogenicity	The product may cause the user uncomfortable if the material is not OK	2	3	1	6	Ensure that microb content in the production environment meets the requirements.	The swab is required to produced in 10000 grade clean area, and sterilized when finished.		Acc
12	Inability to maintain hygienic safety	The product may cause the user uncomfortable if the material is not OK	2	3	2	12	Ensure that microb content in the production environment meets the requirements.	The swab is required to produced in 10000 grade clean area, and sterilized when finished.		Acc
13	Degradation	N/A								

No	Hazard General	Identify hazards	Risk Evaluation S	O	D	RL	Risk Reduction Measure	Evidence	NH	ALOR
D4.	**Environmental hazards and contributory factors**									
1.	Electromagnetic fields	N/A								
2.	Inadequate supply of power or coolant	N/A								
3.	Susceptibility to electromagnetic interference	N/A								
4.	Emissions of electromagnetic interference	N/A								
5.	Inadequate supply of power or coolant	N/A								
6.	Inadequate supply of coolant	N/A								
7.	Storage or operation outside prescribed environmental conditions	N/A								
8.	Incompatibility with other devices	N/A								
9.	Accidental mechanical damage	N/A								
10.	Contamination due to waste products and /or device disposal	N/A								

No	Hazard General	Identify hazards	Risk Evaluation S	O	D	RL	Risk Reduction Measure	Evidence	NH	ALOR
D5. Hazards resulting from incorrect output of energy and substances										
1.	Electricity	NA								
2.	Radiation	NA								
3.	Volume	NA								
4.	Pressure	NA								
5.	supply of medical gases	NA								
6.	supply of anaesthetic agents	NA								
D6. Hazards related to the use of the device and contributory factors										
1	Inadequate labeling	The inadequate labeling may cause misuse	2	2	1	4	Strengthen amending the label for warning	Refer to label		Acc
2	Inadequate operating instructions	The inadequate operating instructions may cause misuse	2	2	1	4	Strengthen amending the operating instructions	See instruction of use		Acc
2.1	Inadequate specification of accessories	NA								
2.2	Inadequate specification of pre-use checks	The device may be damaged	2	2	1	4	To strengthen pre-use checks	See instruction of use		Acc
2.3	Over-complicated operating instructions	NA								
2.4	Inadequate specification of service and maintenance	NA								
3	Use by unskilled/untrained personnel	The device may be damaged	2	3	1	6	To strengthen training	See instruction of use		Acc

No	Hazard General	Identify hazards	Risk Evaluation S	O	D	RL	Risk Reduction Measure	Evidence	NH	ALOR
4	Reasonably foreseeable misuse	NA								
5	Insufficient warning of side effects	The device has no side effects								
6	Inadequate warning of hazards likely with re-use of single use devices	NA								
7	Incorrect measurement and other metrological aspects	NA								
8	Incompatibility with consumables/accessories/other devices	NA								
9	Sharp side	NA								
D7. Complicated operation										
1	Mistakes and judgement errors	NA								
2	Lapses and cognitive recall errors	NA								
3	Slips and blunders (mental or physical)	NA								

No	Hazard General	Identify hazards	Risk Evaluation S	O	D	RL	Risk Reduction Measure	Evidence	NH	ALOR
4	Violation or abbreviation of instructions, procedures, etc.,	NA								
5	Complex or confusing control system	NA								
6	Ambiguous or unclear device state	NA								
7	0Ambiguous or unclear presentation of settings, measurements or other information	NA								
8	Mispresentation of results	NA								
9	Insufficient visibility, audibility or tactility	NA								
10	Poor mapping of controls to action, or of displayed information to actual state	NA								
11	Controversial modes or mappings as compared to existing equipment	NA								

No	Hazard General	Identify hazards	Risk Evaluation S	O	D	RL	Risk Reduction Measure	Evidence	NH	ALOR
D8. Hazards arising from functional failure, maintenance and ageing										
1	Erroneous data transfer	NA								
2	Lack of , or inadequate specification for maintenance including inadequate specification of post maintenance functional checks	The device may not work well if lack of inadequate post maintenance or functional checks	2	1	3	6	Strengthen post maintenance and functional checks	See instruction of use		ACC
3	Inadequate maintenance	The lifetime of the device may be reduced	1	2	2	4	Strengthen management	See instruction of use		ACC
4	Lack of adequate determination of end of device life	NA								
5	Loss of mechanical integrity	NA								
6	Inadequate packaging(contamination and /or deterioration of the device)	The lifetime of the device may be reduced	3	2	1	6				Acc
7	Re-use and / or Improper re-use	NA								
8	Deterioration in function (e.g. gradual occlusion of fluid/gas path, or change in resistance to flow, electrical conductivity) as a result of repeated use.	NA								

B2. Additional hazards to in vitro diagnostic medical devices										
1	Batch inhomogeneity, batch-to-batch inconsistency	Leading to product traceability or customer complaints	4	2	1	8	Strengthen batch management and supervision	See Lot number management regulations		ACC
2	Common interfering factors	Affect product quality and reduce product functions	3	2	1	6	Control and strengthen the control of interference factors	See instruction of use		ACC
3	Carry-over effects	NA								
4	Specimen identification errors	Lead to misuse and customer complaints	3	2	1	6	Strengthen product identification control	See instruction of use		ACC
5	Stability problems (in storage, in shipping, in use, after first opening of the container)	Affect product quality and reduce product functions	2	2	2	8	Strengthen product quality inspection and transportation control	See Design and development program files		ACC
6	Problems related to taking, preparation and stability of speciments	Reduce the functional effect of the product	3	2	2	12	Increase product quality inspection and product stability analysis control	See stability study report		ACC
7	Inadequate specification of prerequisites	Lead to misuse	3	2	2	12	Complete product manual	See instruction of use		ACC
8	Inadequate test characteristics	Lead to product quality substandard	4	2	2	16	Strengthen product quality control and arrange products for full inspection	See test report		ACC

Conclusion:

According to the analysis of the risk, all the risk has been identified and the risks which are none accepted have been controlled by measure taken by the manufacturer. In one word, the risk has been managed accordingly.

The above products are analyzed according to EN ISO14971: 2016. The analysis is objective and the conclusion is valid. Through security risk control, the risk level of the product is reduced, and all items are within acceptable ranges. In summary, all risks of the product have been reduced to acceptable levels through risk control measures, and no additional risks have been generated during the period. The benefits of the product outweigh the risks, so it can be seen that using the product is safe and reliable. Through prior security risk analysis and preventive measures, we have reduced hazards to acceptable levels throughout the development phase. After the product reaches the user, precautionary measures such as the user's qualification will be notified with warning statements in the instruction manual to minimize harm. The product will be continuously improved from user feedback in future use to minimize risks.