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Quality Assessment Requirements for Severe Acute Respiratory Syndrome Coronavirus 2(SARS-CoV-2) Nucleic Acid Detection Kit

新型冠状病毒核酸检测试剂盒质量评价要求

(征求意见稿)

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FOREWORD

SAC/TC 136, Clinical Laboratory Testing and Invitro Diagnostic Test Systems is in charge of this English translation, the Chinese original shall be considered authoritative.

This document is drafted in accordance with the rules given in GB/T 1.1-2020 *Directives for standardization - Part 1: Rules for the structure and drafting of standardizing documents.*

Please note that some contents in this document might refer to some patents. The issuing authority of this document is not responsible for identifying such patents.

This document was proposed by National Medical Products Administration.

This document was prepared by SAC/TC 136.

Quality Assessment Requirements for Severe Acute Respiratory Syndrome Coronavirus 2(SARS-CoV-2) Nucleic Acid Detection Kit

1. Scope

This document specifies the requirements for quality assessment, test method, labeling, instructions for use, package, transportation, and storage of nucleic acid detection kit for SARS-CoV-2.

This document is applicable to assess the kit on the basis of nucleic acid amplification test for qualitative detection of SARS-CoV-2 in specimens from oropharyngeal swabs, nasopharyngeal swabs, bronchoalveolar lavage fluid (BALF), sputum, respiratory tract washings, aspirated fluid, or other respiratory secretions.

Note: Nucleic acid amplification methods include polymerase Chain reaction (PCR) technology and isothermal nucleic acid amplification technology, etc.

2. Normative References

The following documents are indispensable for application of this document. For dated references, only the edition cited is applied. For undated references, the latest edition of the referenced document (including all amendments) was applied.

GB/T 191 *Packaging - Pictorial Marking for Handling of Goods*

GB/T 29791.2 *In Vitro Diagnostic Medical Devices - Information Supplied by the Manufacturer (Labelling) - Part 2: In Vitro Diagnostic Reagents for Professional Use*

3. Terms and Definitions

No terms or definitions need to be defined in this document.

4. Quality Assessment Requirements

4.1 Appearance

The appearance should meet but not be limited to the following requirements:

a) All components of the kit should be completely included without any leakage for liquid.

b) Packaging labels in Chinese should be legible and free from wearing.

4.2 Nucleic Acid Extraction and Purification

The performance of nucleic acid extraction and purification should meet the following requirements:

a) For kits with components for nucleic acid extraction and purification, the manufacturer should have appropriate requirements for performance of nucleic acid extraction and validate them. Such as efficiency, purity, integrity, etc.

b) For kits without components for nucleic acid extraction, the manufacturer should specify or designate the extraction kit, and verify the nucleic acid extraction and purification functions.

c) For kits performing detection following lysis or release of nucleic acid without extraction and purification, the manufacturer should verify the potential interference of nucleic acid lysis or release function on enzymes in the kits.

4.3 Internal reference and/or Internal Control

The manufacturer should establish appropriate quality assurance procedures for the test results of kits, according to the characteristics of its product process, reasonably setting internal reference or internal Control, which should be manipulated in the test procedures just as testing samples.

4.4 Limit of Detection (LOD)

The kit should be validated by National Reference Panel sensitivity samples or standardized references. The testing results of National Reference Panel sensitivity samples S1~S3 should be positive. The standardized references testing results requirements should not be less than those of the National Reference Panel sensitivity standards.

Serial dilutions of positive samples should be developed when preparing the standardized references including the LOD sample.

Note: See Appendix A for information on the National Reference Panel sensitivity sample in this document.

4.5 Coincidence Rate of Positive References

The kit should be positive when testing the National Reference Panel positive samples or standardized positive references.

Standardized positive references should include specimens from different sources with virus at different concentrations or titrations.

Note: See Appendix A for information on National Reference Panel positive samples in this document.

4.6 Coincidence Rate of Negative References

The kit should be negative when testing the National Reference Panel negative samples or standardized negative references.

Standardized negative references should include related respiratory pathogens such as coronaviruses (HKU1, OC43, NL63, 229E), SARS-CoV (pseudovirus is applicable), MERS-CoV (pseudovirus is applicable), influenza virus, parainfluenza virus, RSV and adenovirus.

Note: See Appendix A for information on the National Reference Panel negative samples in this document.

4.7 Repeatability

The kit should be validated by the National Reference Panel precision samples or standardized references in the following requirements.

a) For kits reporting Ct value, the precision references should be tested in 10 replicates per sample with positive results and variation coefficient (%CV) of the Ct value not exceeding 5.0%.

b) For kits not reporting Ct value, the precision references should be tested in 10 replicates per sample with positive results.

Standardized references should include samples with SARS-CoV-2 at LOD and intermediate positive levels.

Note: See Appendix A for information on the National Reference Panel precision sample in this document.

4.8 Stability

The kit should be validated using the following methods.

a) Shelf life stability: The manufacturer should specify the shelf life of the kit. Under the storage conditions claimed by the manufacturer, the kits near expiration should be used to perform the test in 4.4~4.7, the results should meet the corresponding requirements.

b) Thermal stability test: Test 4.4~4.7 under the thermal stability test conditions specified by the manufacturer, and the results should meet the corresponding requirements.

Note 1: Thermal stability test results should not be used directly to determine the shelf life of the kit unless the derivation formula used is based on extensive stability study data.

Note 2: Any combination of a) and b) methods can be selected depending on the product characteristics, but the method selected should be capable of validating the stability of the product to ensure that the performance meets the standard requirements during the shelf life.

5. Test Method

5.1 Appearance

Inspect components of the kit through visual examination with normal or corrected visual acuity under natural light.

5.2 Nucleic Acid Extraction and Purification

Validate using the method provided by the manufacturer.

5.3 Internal reference and/ Internal Control

Validate using the method provided by the manufacturer.

5.4 Limit of Detection (LOD)

National Reference Panel sensitivity sample or standardized references should be tested according to the instructions for Use provided by manufacturer.

The National Reference Panel sensitivity sample(S) should be serially diluted 3 times with RNase/DNase free water, labeled 1:9, 1:27, 1:81, 1:243, 1:729, 1:2187, 1:6561, 1:19683, 1:59049 and 1:177147 as S1~S10 respectively. Test the diluted samples with the kit according to the Instructions for Use after nucleic acid extraction.

5.5 Coincidence Rate of Positive References

National Reference Panel positive samples or standardized positive references should be tested by the kit according to the Instructions for Use.

National Reference Panel positive samples P1~P6 should be tested after nucleic acid extraction according to the kit instructions. P7 should be detected directly as nucleic acid extract.

5.6 Coincidence Rate of Negative References

National Reference Panel negative samples or standardized references should be tested according to the Instructions for Use.

National Reference Panel negative samples N1~N2 should be tested after nucleic acid extraction according to the kit instructions.

5.7 Repeatability

According to Instruction for Use, the National Reference Panel precision sample or standardized references should be tested in 10 replicates for each sample.

The National National Reference Panel precision sample R should be diluted with RNase/DNase free water (1:20) and tested after nucleic acid extraction according to the Instructions for Use.

5.8 Stability

5.8.1 Shelf Life Stability

Under the storage conditions specified by the manufacturer, the kits near expiration should be tested according to methods 5.4~5.7.

5.8.2 Thermal Stability Test

Under the condition of thermal stability test specified by the manufacturer, the kits within the shelf life should be

tested according to methods 5.4~5.7.

6. Labels and Instructions for Use

In compliance with the provisions in GB/T 29791.2.

7. Packing, Transportation and Storage

7.1 Packing

Packing - pictorial marking for handling of goods should meet the requirement of GB/T 191. The packing container should be well sealed, complete, and free from leakage and damage.

7.2 Transportation

Detection kits should be shipped according to the manufacturer’ s requirements. During transportation, they should be protected from moisture, excessive pressure, direct sunlight rain and snow, contact with acidic and alkaline substances, and damage to the internal and external packaging.

7.3 Storage

The kits should be stored under the conditions specified by the manufacturer.

Appendix A

(Informative)

Information on National Reference Panel for 2019-nCoV (SARS-CoV-2) Nucleic Acids Detection Kit

A.1 Description

This appendix provides information on the applicable National Reference Panel in Chapter 4 of this document, which are National Reference Panel for 2019-nCoV (SARS-CoV-2) Nucleic Acids Detection Kit (Reference No. 370099)".

A.2 Usage

Materials for the National Reference Panel include cultures of respiratory pathogen, specimen of throat swabs, pseudo-viruses, and plasmids, which are applicable to the quality assessment of nucleic acids detection kits in specimens of pharyngeal swabs, nasal swabs, sputum, BALF, etc. Applicable methods include but are not limited to fluorescence PCR, isothermal amplification, hybrid capture immunofluorescence assay, RNA capture probe, sequencing and CRISPR. The standards cannot be used for traceability.

A.3 Specification and Components

The specification and components of National Reference Panel are shown in Table A.1.

Table A.1 Specification and Composition of National Standards

Type	No.	Specimens	Size
Positive	P1	virus culture isolate	0.5 mL/vial
	P2	throat swab	0.5 mL/vial
	P3	virus culture isolate	0.5 mL/vial
	P4	throat swab	0.5 mL/vial
	P5	throat swab	0.5 mL/vial
	P6	throat swab	0.5 mL/vial
	P7	plasmid (N full-length gene)	0.1 mL/vial
Negative	N1	legionella pneumophila	0.5 mL/vial
	N2	klebsiella pneumoniae	0.5 mL/vial
	N3	streptococcus pneumoniae	0.5 mL/vial
	N4	haemophilus influenzae	0.5 mL/vial
	N5	Ad type 3	0.5 mL/vial
	N6	mycoplasma pneumoniae	0.5 mL/vial
	N7	chlamydia pneumoniae	0.5 mL/vial
	N8	influenza virus B	0.5 mL/vial
	N9	RSVA	0.5 mL/vial
	N10	bordetella pertussis	0.5 mL/vial
	N11	CoV-OC43	0.5 mL/vial
	N12	CoV-NL63	0.5 mL/vial
	N13	CoV-HKU-1	0.5 mL/vial

	N14	CoV-229E	0.5 mL/vial
	N15	AIV-H7N9	0.5 mL/vial
	N16	AIV-H5N1	0.5 mL/vial
	N17	influenza B virus (Victoria)	0.5 mL/vial
	N18	influenza A H1N1 (2009) virus	0.5 mL/vial
	N19	influenza A H3N2 virus	0.5 mL/vial
	N20	EB virus	0.5 mL/vial
	N21	MERS pseudovirus (ORF1ab+N+ part of RdRp gene)	0.5 mL/vial
	N22	Simulated negative swab samples	0.5 mL/vial
Sensitivity	S	Virus culture isolate	0.5 mL/vial
Precision	R	Virus culture isolate	0.5 mL/vial

A.4 Nominal Property Value

The concentration of sensitivity sample S (stock solution) was 3×10^5 copies/mL quantified by combination method of digital PCR.

S cannot be used for traceability.

A.5 Precaution

The current version of the specification for National Reference Panel can be viewed and downloaded from the website of the distributors of the National Reference Standards. Part of the specification might be modified in some batches, please refer to the specification in the package of National Reference Panel for detailed information.

References

[1] YY0466-2003 Medical Devices - Symbols to be used with Medical device labels, labeling and information to be supplied

[2] YY/T1182-2020 Nucleic acids amplification test reagents (kits)

[3] Registration Technology Review Points of Covid-2019 Nucleic Acid Test Reagent