Mpox disease Emergency Use Listing Procedure (EUL) for IVDs
Product: PortNAT Monkeypox Virus Assay
EUL Number: MPXV-13202-208-00
Outcome: Accepted.

The EUL process is intended to expedite the availability of in vitro diagnostics needed in public health emergency situations and to assist interested UN procurement agencies and Member States in determining the acceptability of using specific products in the context of a Public Health Emergency of International Concern (PHEIC), based on an essential set of available quality, safety, and performance data. The EUL procedure includes the following:

- Quality Management Systems Review and Plan for Post-Market Surveillance: a desktop review of the manufacturer's Quality Management System documentation and specific manufacturing documents.
- Product Dossier Review: assessment of the documentary evidence of safety and performance. This evaluation of limited scope is to verify critical analytical and performance characteristics.

The PortNAT Monkeypox Virus Assay, with product code U202031-20, CE-Mark regulatory version manufactured by Ustar Biotechnologies (Hangzhou) Ltd., Bldg 1, 2 & 4, 611 Dongguan Road, Binjiang District, 310053, Hangzhou, Zhejiang Province, PEOPLE'S REPUBLIC OF CHINA, was listed as eligible for WHO procurement on 13 May 2025.

Intended use:

According to the claim of intended use from Ustar Biotechnologies (Hangzhou) Ltd., Inc., *"The PortNAT Monkeypox Virus Test is an in vitro diagnostic test for the qualitative detection of the DNA of monkeypox virus clade I and clade II (including Ib) in lesion swabs specimens from individuals suspected of monkeypox virus infection by their healthcare provider. This product intended users are professional users with laboratory experience and non-laboratory professionals who received training on using the product. Testing with the PortNAT Monkeypox Virus Test and PortNAT Molecular Analyzer is optimally performed in laboratory settings. This product is used for the auxiliary diagnosis of monkeypox virus."*

Validated specimen type:
Human lesion swabs (of acute pustular or vesicular rash from individuals suspected of mpox) collected using Nylon flocked swabs by a healthcare provider.

Test kit contents:

Component	Number of tests and product code (20 T/kit, U202031-20)
Box A	
Cartridge-A	20
Swab	20
Zip-lock bag	20
Instructions for Use (IFU)	1
Box B	
Cartridge-B	20
IFU	1

Items required but not provided:

- PortNAT Molecular Analyzer （U300010）manufactured by Ustar Biotechnologies (Hangzhou) Ltd.（socket voltages: 100~240V）

Storage:
The reagents must be stored as follows:

- Box A at 2–37 °C, ≤+ 80% RH; until the expiration date provided on the label.
- Box B at 2–37 °C, ≤+ 80% RH; until the expiration date provided on the label.

Shelf-life upon manufacture:
The shelf-life is currently assigned 12 months dating.

Warnings/limitations:

Please refer to the IFU attached to this report.

Product dossier assessment

Ustar Biotechnologies (Hangzhou) Ltd. submitted a product dossier for the PortNAT Monkeypox Virus Assay in alignment with the Instructions and requirements for Emergency Use Listing (EUL) Submission: In vitro diagnostics detecting Monkeypox virus nucleic acid (PQDx_457). The WHO reviewed the information provided in the dossier.

The risk-benefit assessment conclusion was acceptable.

Quality Management Systems Review

To establish eligibility for WHO procurement, Ustar Biotechnologies (Hangzhou) Ltd. was asked to provide up-to-date information about the status of its quality management system.

Based on the WHO's review of the submitted quality management system documentation, Ustar Biotechnologies (Hangzhou) Ltd., Inc., provided sufficient information to fulfil the requirements described in the Instructions and requirements for EUL Submission: In vitro diagnostics detecting Monkeypox virus nucleic acid (PQDx_457).

The quality management system assessment conclusion was acceptable.

Plan for Post-Market Surveillance

Post-market surveillance, including monitoring all customer feedback, detecting and acting on adverse events, product problems, non-conforming goods and processes is a critical component of minimising the potential harm of an IVD listed for emergency use.

The following post-EUL activities are required to maintain the EUL status:
1. Notification to WHO of any planned changes to a prequalified product, in accordance with "*WHO procedure for changes to a WHO prequalified in vitro diagnostic" (document number PQDx_121*)[1]; and
2. Post-market surveillance activities, in accordance with "*WHO guidance on post-market surveillance of in vitro diagnostics" (ISBN 978 92 4 150921 3)*[2].

Ustar Biotechnologies (Hangzhou) Ltd. is also required to submit an annual report summarising sales data and all complaints. Certain complaints and changes to the product must be notified immediately to WHO, as per the above-mentioned documents. The sales data will serve as denominator data to guide the frequency of re-inspection.
The manufacturer has committed to ensuring that post-emergency use listing safety, quality, and performance monitoring activities are in place, which are in accordance with WHO guidance on post-market surveillance of in vitro diagnostics.

Scope and duration of procurement eligibility

The PortNAT Monkeypox Virus Assay, with product code U202031-20, manufactured by Ustar Biotechnologies (Hangzhou) Ltd., is eligible for WHO procurement for 12 months from the day of listing. The assay detects the monkeypox virus DNA clade I and clade II (including clade Ib). This listing does not infer that the product meets WHO prequalification requirements and does not mean that the product is listed as WHO-prequalified.

[1] https://iris.who.int/bitstream/handle/10665/251915/WHO-EMP-RHT-PQT-2016.01-eng.pdf;jsessionid=830C82950055325AF37A0A8302BE4623?sequence=1

[2] https://www.who.int/publications/i/item/9789240015319

As part of the ongoing requirements for listing as eligible for WHO procurement, Ustar Biotechnologies (Hangzhou) Ltd. must engage in post-market surveillance activities to ensure that the product continues to meet safety, quality, and performance requirements. Ustar Biotechnologies (Hangzhou) Ltd., Inc., is required to notify WHO of any complaints, including adverse events related to the use of the product, within 10 days.

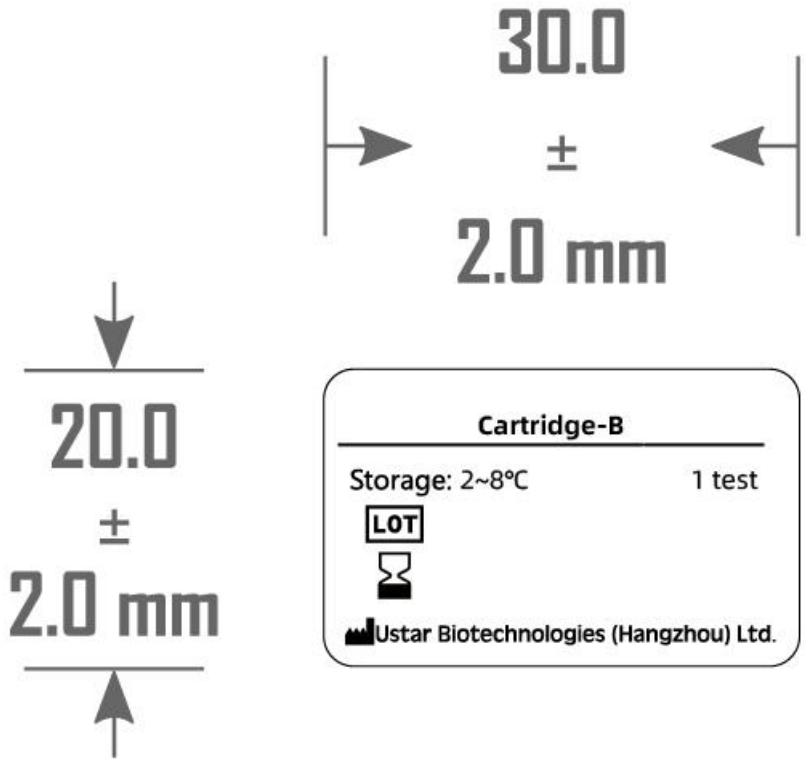
WHO reserves the right to rescind eligibility for WHO procurement if additional information on the safety, quality, and performance during post-market surveillance activities and if new data becomes available to WHO that changes the risk-benefit balance.

Labelling

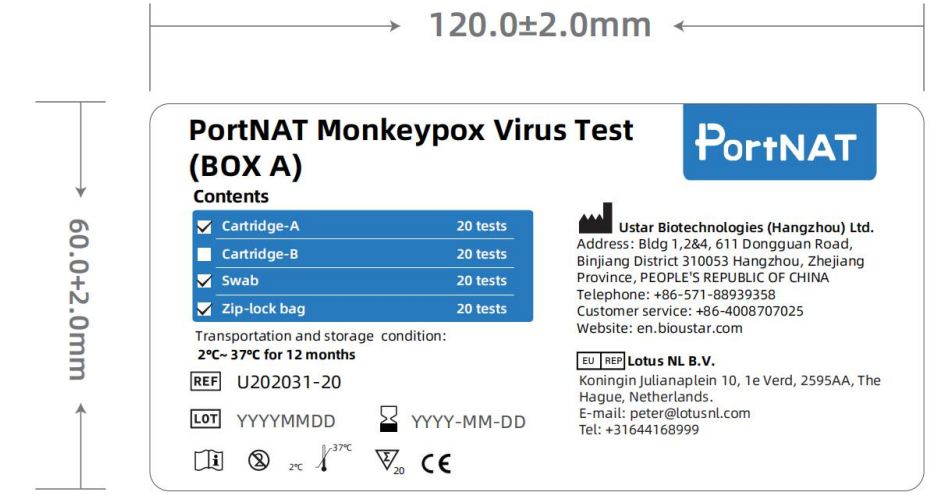
1. **Labels**
2. **Instructions for use**

1.0 Labels

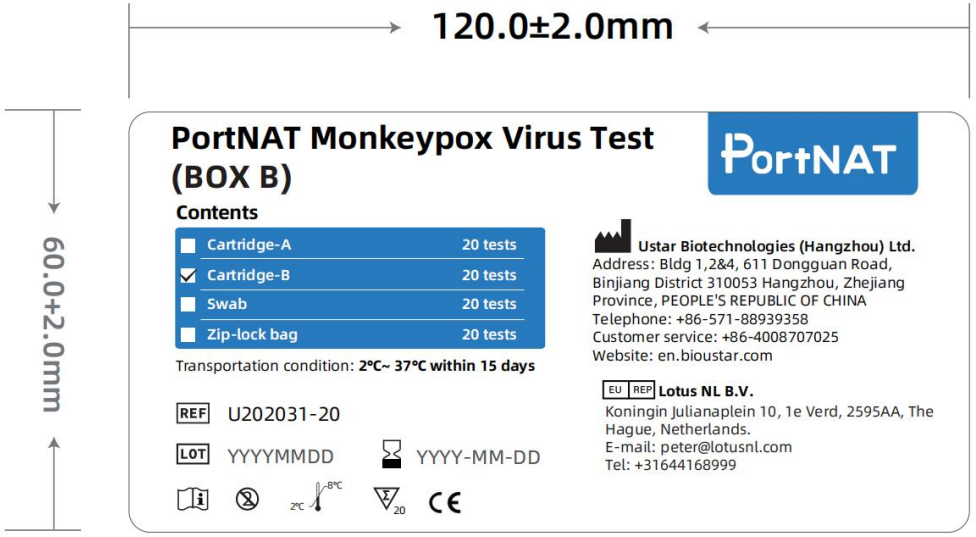
1.1 Label of Components



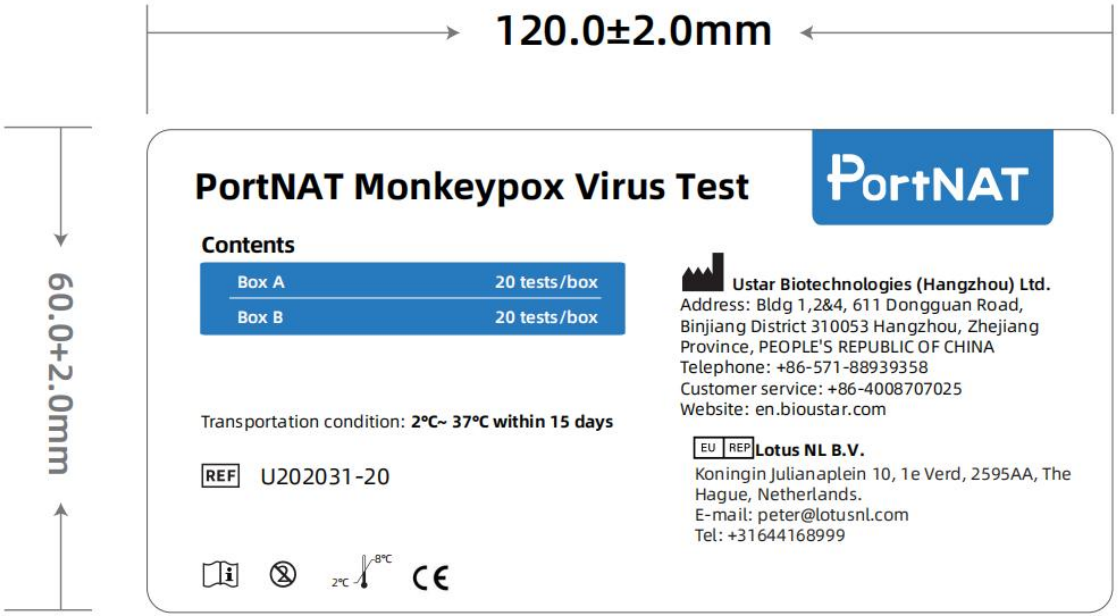
1.2 Label of Outer Package



BQ-MPXV3.5-001-ENG



1.3 Label of Shipping Package

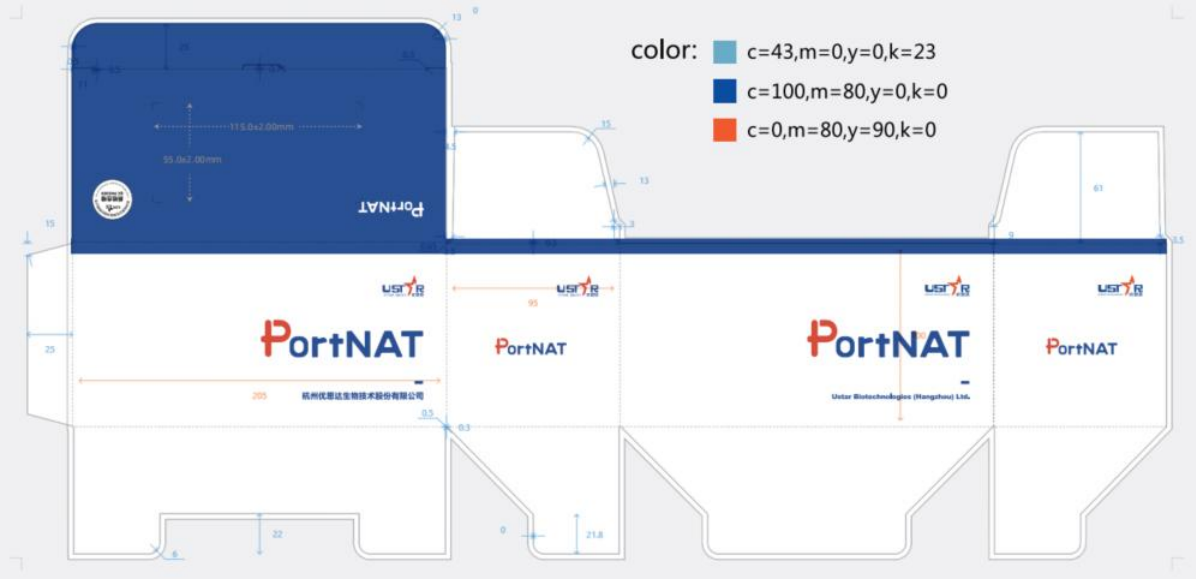


1.4 Label of QC Passed

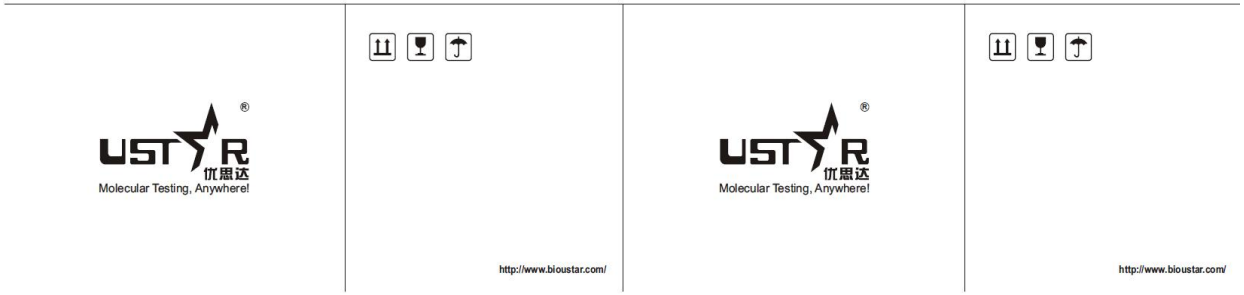
Square：35mm × 35 mm
Circle: 30mm × 30 mm

1.5 Outer Package

Size of outer package box: 205mm ×95mm×100mm



1.6. Shipping Package



2.0 Instructions for Use[3]

[3] English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages.

PortNAT Monkeypox Virus Test

Instructions for Use

1 PRODUCT NAME
PortNAT Monkeypox Virus Test

2 SPECIFICATION
Σ 20 REF U202031-20

3 INTENDED USE
The PortNAT Monkeypox Virus Test is an in vitro diagnostic test for the qualitative detection of the DNA of monkeypox virus clade I and clade II (including Ib) in lesion swabs specimens from individuals suspected of monkeypox virus infection by their healthcare provider. This product intended users are professional users with laboratory experience and non-laboratory professionals who received training on using the product. Testing with the PortNAT Monkeypox Virus Test and PortNAT Molecular Analyzer is optimally performed in laboratory settings. This product is used for the auxiliary diagnosis of monkeypox virus.

4 SUMMARY AND EXPLANATION
The PortNAT Monkeypox Virus Test is a qualitative test run on the PortNAT Molecular Analyzer for the detection of Monkeypox Virus (MPXV) DNA in lesion swabs specimens. Internal Endogenous Control (human β-actin gene) is included in the cartridge to monitor the test process.

5 MATERIALS PROVIDED

Box A:

S/N	Materials	Specification	Quantity	Main Components
1	Cartridge-A	1 pcs per test	20	Lysis buffer
2	Swab	1 swab per test	20	Flocked Swab
3	Zip-lock bag	1 bag per test	20	Plastic
4	Instructions for Use	1 pcs per box	1	/

Box B:

S/N	Materials	Specification	Quantity	Main Components
1	Cartridge-B	1 pcs per test	20	Amplification reagent
2	Instructions for Use	1 pcs per box	1	/

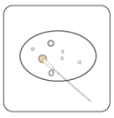
Note:
1. Do not mix the materials from different kit lots.
2. Materials required but not provided: PortNAT Molecular Analyzer （U300010） manufactured by Ustar Biotechnologies (Hangzhou) Ltd.（socket voltages: 100~240V）

6 WARNING AND PRECAUTIONS
6.1 This product contains no human-derived materials.
6.2 Please read this IFU carefully before use.
6.3 If positive and negative quality controls are needed, please contact the manufacturer.
6.4 This Assay is a disposable product.
6.5 The work table and required items should be regularly disinfected with 1% sodium hypochlorite, 75% alcohol or ultraviolet light.
6.6 Cartridge shall be using immediately once opening.
6.7 Do not take out the cartridge when running test.
6.8 Do not squeeze the middle and lower part of the Cartridge when operating.
6.9 Performance changes may happen due to various factors during the storage, transportation and use of reagents. For example, inappropriate storage and transportation, non-conformity of sample collection, processing and testing procedures. Please strictly follow the instructions. Due to the characteristics of the sample collection and virus infection, results may be false negative caused by insufficient sample volume. Other clinical diagnosis and treatment information should be considered for comprehensive determination. Perform retesting if necessary.
6.10 Pathogenic microorganisms, including hepatitis viruses and Human Immunodeficiency Virus, may be present in clinical specimens. Treat all biological specimens, including used cartridges, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be treated with standard precautions. Guidelines for specimen handling are available from the U.S. Center for Disease Control and Prevention and the Clinical and Laboratory Standards Institute[1][2].

7 PRINCIPLE OF THE PROCEDURE
The Cartridge is composed of plastic parts and is filled with lysis buffer and materials for DNA target amplification. The cartridge is divided into two main areas, which are separated by a plastic part. The lower area is the sample lysis area, which is filled with lysis buffer. The lysis buffer contains substances that lyse virus and prevent nucleic acid degradation, and is used to treat samples at a high temperature of 95 degrees. The upper area is the reaction area, which contains material for the amplification reaction, such as enzyme, primers and probes. These materials are dried onto a membrane using glassification technology. After the rod on the partition plastic part is broken, the lysis buffer enters the reaction area, redissolves the material on the membrane, and then performs amplification under heating conditions. The fluorescence signal generated during the amplification is detected by an optical system. And the test result is calculated based on the changes in the fluorescence signal.
The primers and probes are designed to carry out cross-priming amplification (CPA)[3], which can specifically and rapidly amplify the target DNA region at a constant temperature. The assay contains two amplification system to detect two different conserved regions of F3L-F4L gene of monkeypox virus. The reagent also contains an amplification system for the human β-actin gene as an internal control, which monitors the effectiveness of each step in sampling, sample processing, and amplification detection.

8 STORAGE AND HANDLING
- Storage: Box A at 2~37℃, ≤+ 80% RH; Box B at 2~8℃, ≤+ 80% RH.
- Shelf life: Box A 12months; Box B 12months.
- Transportation: at ambient temperature (2~37℃) within 15 days, allow brief periods at 40℃.
- Do not open a cartridge lid until you are ready to perform testing.
- Do not use reagents or cartridges that have passed the expiration date.
- Do not use a cartridge that has leaked.

9 SPECIMEN COLLECTION, TRANSPORT, AND STORAGE
This kit had been validated for testing lesion swabs specimens. Sample collection, transportation, and storage were performed completely according to the "Guidelines for Collecting and Handling Specimens for Mpox Testing" [4]from CDC.
9.1 Specimen Collection
Use a sterile swab to wipe the exudate with slight force for at least 3 times. The collected lesion swab samples could be stored in dry tube.



9.2 Specimen Storage
Dry swabs that are stored at 2-8℃ can be tested up to 7 days from collection. Dry swab that are stored frozen (- 20℃ or lower) can be tested up to 60 days from collection. Freeze and thaw no more than 3 times.
9.3 Specimen Transport
Ship specimens on dry ice, if available. Do not ship specimens between 25℃ and 40℃.

10 APPLICABLE INSTRUMENT
PortNAT Molecular Analyzer produced by Ustar Biotechnologies (Hangzhou) Ltd.The system could be run at 5~40℃ and 25~80% relative humidity.

11 PROCEDURE
Note: Please test in accordance with this IFU. Before start test, take Box B out from the 2-8℃ storage environment. If the sample is stored at -20℃ or below, take it out to 2~40 ℃ until completely thawed, then proceed with the test.

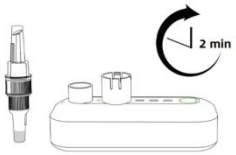
11.1 Open the kit, take out the cartridge, and place it on the table.

11.2. Open the Cartridge-A, dip the collected swab sample into the cartridge solution, stir the swab for 20 s, and make the sample fully elute in the solution.

11.3 Remove the swab and close the cartridge.

11.4 Insert the cartridge into the lysis module and hold the power button for 5 seconds, the lysis indicator light changes from green to blinking blue, indicating that the lysis begins.It will take about 5 minutes.

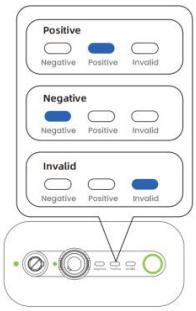
11.5 After lysis, the blue light turns green ,take-out the cartridge, and cool it down for 2 min at room temperature.



11.6 After cooling, break off the rod in its upper area. Turn the cartridge upside down, squeeze the bottom tube (soft) 3-5 times, so that all the liquid flows to the soft plastic part, and fully mix it with the pre-packed reaction reagents in it.

11.7 Insert the soft plastic part of the cartridge into amplification module of the analyzer. Press and hold the power button for 5 seconds, and the amplification indicator light changes from green to blinking blue,indicating that the amplification begins.It will take about 30 minutes.When the sample is positive, the amplification will be completed early.

11.8 After the amplification is complete, the power button turns green. Observe the test result in the display area.



12 INTERPRETATION OF RESULTS
Positive: The monkeypox virus (MPXV) DNA is detected in the sample.
Negtive: The monkeypox virus (MPXV) DNA is not detected in the sample.
Invalid: The monkeypox virus (MPXV) DNA and human β-actin gene is not detected in the sample.

13 Retest
If any of the following conditions occur, please retest with a new Cartridge.
Invalid results. Invalid results may be caused by improper sample collection/processing procedures, inhibition of test reagent, or expired products.
Invalid results. The test is terminated before the due time.
If an invalid result is obtained, please follow these steps:
Perform the negative control test on the same instrument while simultaneously diluting the sample threefold and testing it on a separate instrument. If the negative control is normal but the diluted sample remains invalid, proceed to resample.
If the resampling still produces an invalid result, contact the manufacturer's customer service for further assistance.

14 Quality Control
The kits contains human β-actin gene detecting system as an internal quality control. Internal quality control is intended to monitor failures in sample collection, sample processing, amplification reagents, and malfunctions of analyzers.

15 LIMITATIONS
15.1 The test results of this assay are for clinical reference only. The clinical diagnosis and treatment of patients should be considered in combination with their symptoms, signs, medical history, other laboratory tests and therapeutic effect.
15.2 The detection of Monkeypox Virus is contingent upon the viral load in the sample. False-negative results may occur due to patient-related factors (e.g., presence, type, and duration of symptoms), improper sample collection methods (e.g., inadequate collection, transportation, or handling), infection stage (e.g., samples collected too early or too late during the illness), and/or the presence of interfering substances.
15.3 Other unverified interference or amplification inhibitors may yield false negative results.
15.4 Mutations or other changes within the regions of the genomes covered by the primers and/or probes in the assay may result in false negative results.
15.5 False-positive results may arise from contamination during specimen preparation or handling, or cross-contamination among patient specimens.

16 PERFORMANCE CHARACTERISTICS
16.1 Analytical Sensitivity (Limit of Detection (LoD))
The limit of detection (LoD) of the PortNAT Monkeypox Virus Test is 200 copies/mL for MPXV.
16.2 Analytical Specificity
16.2.1 Cross-Reactivity
Potential cross-reactivity was assessed in silico by calculating the % homology of the genomic sequence of organisms including: Variola Virus, Vaccinia Virus, Cowpox Virus, Mousepox Virus, Molluscum Contagiosum Virus, Tana River Orthopoxvirus, Yaba Monkey Virus,Varicella-Zoster Virus, Rubella Virus, Herpes Simplex Virus-1/-2, Human Herpesvirus 6, Human Herpesvirus 7, Human Herpesvirus 8, Measles Virus, Enterovirus, Treponema Pallidum, Dengue Virus, Human Papillomavirus, Staphylococcus Aureus, Streptococcus Pyogenes, Candida Albicans, Enterococcus Faecalis, Propionibacterium Acnes, Diphtheroids, Pseudomonas Aeruginosa, Corynebacterium, Escherichia Coli, Mycoplasma Genitalium, Chlamydia Trachomatis. All organisms listed are predicted to not cross-react with this assay.

16.2.2 Exogenous and Endogenous Interfering Substances

Positive and negative samples were prepared in pooled negative sample and tested in the presence of potentially interfering substances including:Pooled negative matrix,Abrevea,Acyclovir,Albumin,Blood/EDTA,Mucin,Hydrocortisone cream,Benadryl cream/ointment,Carmex,Casein,Lanacane,KY Jelly,Douche,Neosporin,Female urine,Male urine,Feces,Seminal fluid,Zinc Oxide ointment,Vagisil cream,Cornstarch.All materials listed are not cross-react with this assay.
16.3 Clinical Performance
Performance characteristics of the PortNAT Monkeypox Virus Test were determined in a clinical study.The clinical sensitivity is 98.67%.The clinical specificity is 100%.

17 REFERENCE

1. Centers for Disease Control and Prevention. Biosafety in microbiological and biomedical laboratories. (refer to latest edition).
2. CLSI Publication M29. Protection of laboratory workers from occupationally acquired infections; Approved Guideline. (refer to latest edition).
3. Xu G, Hu L, Zhong H, et al. Cross priming amplification: mechanism and optimization for isothermal DNA amplification. Sci. Rep. 2012;2:246.
4. http:www.cdc.gov/poxvirus/mpox/clinicians/prep-collection-specimens.html

18 TABLE OF SYMBOLS

IVD	*In vitro* diagnostic medical device		Do not re-use
	Use-by date		Consult instructions for use
	Temperature limit		Manufacturer
EU REP	Authorized representative in the European Union	LOT	Batch code
	Keep away from sunlight		Keep dry
	Date of manufacture		Do not use if package is damaged
Σ	Contains sufficient for <*n*> tests		Biological risks
REF	Catalogue number	CE	CE Marking

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Tel: +31644168999

20 INSTRUCTION VERSION AND MODIFICATION DATE

Approved on April 19, 2022. Version: A0
Revised on August 15, 2024. Version: A1
Revised on February 08, 2025. Version: A2
Revised on May 06, 2025. Version: A3
Revised on May 12, 2025. Version: A4