Monkeypox Virus Nucleic Acid Detection Kit (PCR-Fluorescence Probing)

Summary of Safety and Performance

Version: V03

	Name	Position	Signature	Date
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Manufacturer's reference number for the SSP: SF1210HSJ-1-SSP

1. Device identification and general information

1.1. Device name(s)

Monkeypox Virus Nucleic Acid Detection Kit (PCR-Fluorescence Probing)

1.2. Manufacturer's name and address

Manufacturer's name: Shanghai BioGerm Medical Technology Co., Ltd.

Manufacturer's address: Building 3, No. 1588 Huhang Road, Fengxian District, 201401 Shanghai, PEOPLE'S REPUBLIC OF CHINA

1.3. Manufacturer's single registration number (SRN)

CN-MF-000018164

1.4. Basic UDI-DI

6974677692537K9

1.5. European Medical Device Nomenclature (EMDN) description / text

Code: W0105040599

Description: VIROLOGY - NA REAGENTS - OTHER

1.6. Risk class of device

Class C

1.7. Year when the device was first CE-marked under Regulation (EU) 2017/746 covering the device

Expected to be launched in 2025

1.8. Authorised representative if applicable; name and the SRN

Name: MedUnion S.L.

Address: Carrer de Tapioles, 33, 2-1, 08004, Barcelona, Spain

SRN: ES-AR-000019366

1.9. NB's name (the NB that will validate the SSP) and the NB's single identification number

Name: TÜV SÜD Product Service GmbH

NB's single identification number: 0123

2. Intended purpose and other indications

2.1. Intended purpose (elements in Annex II 1.1 (c))

This kit is intended for in vitro qualitative detection of DNA from monkeypox virus (clade I/II) in lesion exudate swab samples of suspected monkeypox cases.

Results are for the identification of monkeypox virus (clade I/II) DNA, however, the assay does not distinguish between clade I and clade II. Positive results are indicative of the presence of monkeypox virus (clade I/II) DNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Negative results obtained with this device do not preclude MPXV (clade I/II) infection and should not be used as the sole basis for treatment or other patient management decisions. Negative results must be

combined with clinical observations, patient history, and epidemiological information.

The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

For in vitro diagnostic use only. For professional lab use.

2.2. Indication(s) and target population(s)

Indication(s): Suspected monkeypox cases

Target Population(s): suspected monkeypox cases.

2.3. Limitations and/or contra-indications (e.g. relevant interferences, cross-reactions)

Limitations:

1. The test results of this kit 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 treatment response.
2. If the sample is cross-contaminated during transportation and processing, it may lead to false positive results.
3. Contamination of the experimental environment with aerosols, such as PCR products, may lead to false positive results.
4. Contamination of consumables and equipment used in the 4. experimental process may lead to false positive results.
5. Improper sample collection, transportation and storage, and improper reagent transportation, storage and configuration may affect the detection results, potentially leading to false negative results.
6. A false negative result may result from a variation in the sequence of the target to be tested or a sequence change for other reasons.
7. Other unvalidated interferences or PCR inhibitors may result in false negative results.

Contra-indications:

Cross-reactivity: No cross-reactivity was observed with Measles virus (1.6×10^4 $TCID_{50}$/mL), Rubella virus (1.6×10^5 $TCID_{50}$/mL), Varicella-herpes zoster virus (1.55×10^3 $TCID_{50}$/mL), Herpes simplex virus-1 (8.9×10^5 $TCID_{50}$/mL), Herpes simplex virus -2 (1.6×10^6 $TCID_{50}$/mL), Volepox virus (2.2×10^7 PFU/mL), Molluscum contagiosum virus (34.1 ng/mL), Tanapox virus ($10^{3.25}$ $TCID_{50}$/mL), Yaba monkey tumor virus (2×10^4 $TCID_{50}$/mL), Human herpesvirus 7 (5.7×10^4 $TCID_{50}$/mL), Human herpesvirus 8 (4.17×10^4 $TCID_{50}$/mL, enterovirus (1.51×10^5 $TCID_{50}$/mL), Dengue virus (1.6×10^7 $TCID_{50}$/mL), SARS-CoV-2 (6.45×10^5 $TCID_{50}$/mL), Mousepox Virus ($5\times10^{4.5}$ $TCID_{50}$/mL), Staphylococcus aureus (8.35×10^8 CFU/mL), Staphylococcus Epidermidis (6.07×10^8 CFU/mL), Streptococcus pyogenes (9.6×10^7 CFU/mL), Pseudomonas aeruginosa (7.07×10^8 CFU/mL), Trichomonas Vaginalis (2.11×10^6 cells/mL), Candida albicans (8.4×10^6 CFU/mL) and human DNA (11.1 ng/μL).

Interfering substance: Mucin (0.5 mg/mL), bilirubin (0.1 mg/mL), hemoglobin (2 μg/mL), Histamine hydrochloride (1.0 mg/mL), loratadine (0.050 μg/mL), cetirizine (0.5 pg/mL), Levofloxacin (5 mg/mL), azithromycin (0.25 mg/mL), paracetamol (32.5 μg/mL), acetaminophen (250 μg/mL), aspirin (0.405 μg/mL), tobramycin (2.5 μg/mL) and Vitamin A (3 mg/L) did not have a significant impact on the test results of the kit.

Competitive interference substances: human immunodeficiency virus (1.16×10^4 $TCID_{50}$/mL) and SARS-CoV-2 (6.45×10^5 $TCID_{50}$/mL) did not have a significant impact on the test results of the kit.

3. Device description

3.1. Description of the device, including the conditions to use the device (e.g. laboratory, near-patient testing)

The Monkeypox Virus Nucleic Acid Detection Kit (PCR-Fluorescence Probing) is intended for in vitro qualitative detection of DNA from monkeypox virus (clade I/II) in lesion exudate swab samples of suspected monkeypox cases.

Results are for the identification of monkeypox virus (clade I/II) DNA, however, the assay does not distinguish between clade I and clade II. Positive results are indicative of the presence of monkeypox

virus (clade I/II) DNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Negative results obtained with this device do not preclude MPXV (clade I/II) infection and should not be used as the sole basis for treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

The kit should be professional lab use only.

3.2. In case the device is a kit, description of the components (including regulatory status of components, for example, IVDs, medical devices and any Basic UDI-DIs)

Components Name	Composition	Regulatory Status of Components	Specification	
			25 tests/kit	50 tests/kit
MPXV nucleic acid reaction solution	Buffer, dNTP Mix, DNA polymerase, UDG, primers and probes of target gene and internal gene	IVDs	250 μL×1 tube	500 μL×1 tube
Positive control MPXV	10^5~10^6 copies/mL Monkeypox virus fake virus and RNase P fake virus	IVDs	500 μL×1 tube	500 μL×1 tube
Negative control	Normal saline	IVDs	500 μL×1 tube	500 μL×1 tube

3.3. A reference to previous generation(s) or variants if such exists, and a description of the differences

Previous Generation(S):

The Monkeypox Virus Nucleic Acid Detection Kit (PCR-Fluorescence Probing) is the first generation of this kind product. It is applying for an IVDR CE certificate.

Variants:

The product has two package specifications. The detail information is listed in the below table.

Kit Component	Specification/Volume /Quantity	
	IS-FZ-064-25-CE	IS-FZ-064-50-CE
	25 Tests/Kit	50 Tests/Kit
MPXV nucleic acid reaction solution	250 μL×1 tube	500 μL×1 tube
Positive control MPXV	500 μL×1 tube	500 μL×1 tube
Negative control	500 μL×1 tube	500 μL×1 tube

3.4. Description of any accessories which are intended to be used in combination with the device

No.	Accessories Name	Supplier required/ Other requirements	If IVD MD, list the certificate number	Model or REF information
1	1.5 mL centrifuge tube	DNase/RNase free	NA	/
2	0.2 mL PCR tube or strip	DNase/RNase free	NA	/
3	Pipettes	Specifications: 10 μL, 200 μL and 1000 μL; DNase/RNase free	NA	/
4	Pipette tips	Specifications: 10 μL, 200 μL and 1000 μL; DNase/RNase free	NA	/

3.5. Description of any other devices and products which are intended to be used in combination with the device

No.	Equipment Name	Supplier required/ Other requirements	If IVD MD, list the certificate number	Model or REF information
1	Real-time PCR System	Shanghai Hongshi Medical Technology Co., Ltd.	IVD, certificate No.: DE/CA05/IvD-238321-1948-00	SLAN® -96S Instrument

No.	Equipment Name	Supplier required/ Other requirements	If IVD MD, list the certificate number	Model or REF information
2	Automatic Nucleic Acid Purification Instrument	Shanghai BioGerm Medical Technology Co., Ltd.	IVD, certificate No.: YFXM-2021-014-EDOC	BG-Flex-32
3	Sterile polyester or nylon swab	No need to specify manufacturer	MD	/
4	Universal Transport UTM	Copan Italia S.p.A.	IVD, certificate No.: None	/
5	Sampling tube with 3.5 mL normal saline	No need to specify manufacturer	IVD	/
6	Nucleic acid extraction and purification kit	Shanghai BioGerm Medical Technology Co., Ltd.	IVD, certificate No.: SF1180tqj-EDCR-003	TQ-BG-003-96B-96 TQ-BG-003-96D-96

4. Reference to any harmonised standards and CS applied

	Document Title
Common specification(s)	NA
Guidance on PMPF	NA
Harmonized standard(s)	EN ISO 13485:2016+A11:2021 Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)
	EN 13612:2002 Performance evaluation of *In vitro* diagnostic medical devices EN 13612:2002/AC:2002
	EN 13641:2002 Elimination or reduction of risk of infection related to *In vitro* diagnostic reagents
	EN ISO 14971: 2019 Medical devices - Application of risk management to

	medical devices
	ISO 15223-1 2021 Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1 General requirements
	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)
	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)
	EN ISO 23640:2015 *In vitro* diagnostic medical devices - Evaluation of stability of *In vitro* diagnostic reagents (ISO 23640:2011)
	IEC 62366-1: 2015 Medical device- part 1: Application of usability engineering to medical devices

5. Risks and warnings

5.1. Residual risks and undesirable effects

- The test results of this kit 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 treatment response.
- A false negative result may result from a variation in the sequence of the target to be tested or a sequence change for other reasons.
- Other unvalidated interferences or PCR inhibitors may result in false negative results.

5.2. Warnings and precautions

- Before testing, read this instruction carefully and operate in strict accordance with the instruction.
- This kit is an in vitro diagnostic reagent, and the operation requires certain professionalism, and

the operator should be trained professionally.

- The experimental operation must be strictly divided, and the instruments, equipment, consumables and work clothes used in each area must be dedicated, and shall not be cross-used to avoid pollution.
- Each component should be melted at room temperature before use, fully shaken and mixed, and used after instant centrifugation.
- Bubbles should be avoided when the reaction liquid is divided into different parts, and attention should be paid to check whether the reaction tube is tightly covered before loading the machine.
- After the experiment, the table should be cleaned in time and disinfected with 10% sodium hypochlorite, 75% alcohol and ultraviolet lamp.
- The test samples involved in the kit and used product should be regarded as infectious, and all laboratory operations should comply with the corresponding stipulation.
- Various factors may cause performance changes during storage, transportation, and use of reagents, such as improper storage, transportation, and non-standard sample collection, sample processing, and testing. Please strictly follow the instructions. Due to the characteristics of sample collection process such as swabs and pathogen infection process, there may be false negative results caused by insufficient sample size, etc., which should be comprehensively judged based on other clinical diagnosis and treatment information, and retest when necessary.
- The collected specimens and used product are processed according to local regulations.
- Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or you are established.
- Before EUDAMED's official launch, obtain the summary of safety and performance (SSP) from the manufacturer at the following address: https://www.bio-germ.com/en/products-solutions/molecular-detection-products/nucleic-acid-amplification-detection-kits/data_271.html
- Biological specimens, transfer devices and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These

materials may exhibit characteristics of chemical hazardous waste requiring specific disposal. If country or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO (World Health Organization) medical waste handling and disposal guidelines.

5.3. Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN), if applicable

None

6. Summary of performance evaluation and post-market performance follow-up (PMPF)

6.1. Summary of scientific validity of the device

The scientific validity study was supported for the scientific and validity of the Monkeypox Virus Nucleic Acid Detection Kit (PCR-Fluorescence Probing) claimed by BioGerm as following:
Through reviewing relevant information on the scientific validity of devices measuring the same analyte or marker, article review and consensus expert opinions/positions from relevant professional associations, it demonstrates that F3L is a conserved gene of monkeypox virus and monkeypox RT-PCR kit developed based on the F3L gene has been successfully commercialized and has been proven to have good clinical performance for detect monkeypox virus. Lesion exudate is considered the best sample for detecting monkeypox virus. Therefore, the Monkeypox Virus Nucleic Acid Detection Kit (PCR-Fluorescence Probing) by lesion exudate is considered as scientific and validity for auxiliary diagnosis of suspected monkeypox cases and other persons requiring diagnosis.

6.2. Summary of performance data from the equivalent device, if applicable

Not Applicable

6.3. Summary of performance data from conducted studies of the device prior to CE-marking

Characteristics	Specifications/ Claims
Limit of Detection	200 copies/mL for both clade I and clade II.
Analytical Reactivity	Inclusivity (In Silico Analysis): Inclusivity was demonstrated by analyzing the MPXV primer and probe of this kit binding the regions in clade Ia, clade Ib, clade IIa and clade IIb MPXV genomes reported in GISAID database as of August 19, 2024 including 7916 full-length genomic sequences (314 Clade I sequences and 7602 Clade II sequences). It showed that this kit can detect all analyzed MPXV isolates. Exclusivity (In Silico Analysis): Exclusivity was demonstrated by analyzing the MPXV primer and probe of this kit for possible cross-reactivity with 15,474 Variola virus sequences, 9,571 Vaccinia virus sequences and 10,223 Cowpoxvirus sequences reported in GISAID database as of August 19, 2024. It predicted that this kit doesn't have cross-react with Variola virus, Vaccinia virus and Cowpoxvirus.
Precision	The coincidence rates of precision samples were not less than 95% and CV of Ct values for precision samples were not more than 5.0%.
Analytical specificity: Interference	Mucin (0.5 mg/mL), bilirubin (0.1 mg/mL), hemoglobin (2 μg/mL), Histamine hydrochloride (1.0 mg/mL), loratadine (0.050 μg/mL), cetirizine (0.5 pg/mL), Levofloxacin (5 mg/mL), azithromycin (0.25 mg/mL), paracetamol (32.5 μg/mL), acetaminophen (250 μg/mL), aspirin (0.405 μg/mL), tobramycin (2.5 μg/mL) and Vitamin A (3 mg/L) did not have a significant impact on the test results of the kit. human immunodeficiency virus (1.16×10^4 $TCID_{50}$/mL) and SARS-CoV-2 (6.45×10^5 $TCID_{50}$/mL) did not have a significant impact on the test results of the kit.
Analytical specificity: Cross-reactivity	No cross-reactivity was observed with Measles virus (1.6×10^4 $TCID_{50}$/mL), Rubella virus (1.6×10^5 $TCID_{50}$/mL), Varicella-herpes zoster virus (1.55×10^3 $TCID_{50}$/mL), Herpes simplex virus 1 (8.9×10^5 $TCID_{50}$/mL), Herpes simplex virus 2 (1.6×10^6 $TCID_{50}$/mL), Volepox virus (2.2×10^7 PFU/mL), Molluscum contagiosum virus (34.1 ng/mL), Tanapox virus ($10^{3.25}$ $TCID_{50}$/mL), Yaba monkey tumor virus (2×10^4 $TCID_{50}$/mL), Human herpesvirus 7 (5.7×10^4 $TCID_{50}$/mL), Human herpesvirus 8 (4.17×10^4 $TCID_{50}$/mL), enterovirus (1.51×10^5 $TCID_{50}$/mL), Dengue virus (1.6×10^7 $TCID_{50}$/mL), SARS-CoV-2 (6.45×10^5 $TCID_{50}$/mL), Mousepox Virus ($5\times10^{4.5}$ $TCID_{50}$/mL), Staphylococcus aureus (8.35×10^8 CFU/mL), Staphylococcus Epidermidis (6.07×10^8 CFU/mL), Streptococcus pyogenes (9.6×10^7 CFU/mL), Pseudomonas aeruginosa (7.07×10^8 CFU/mL), Trichomonas Vaginalis (2.11×10^6 cells/mL), Candida albicans (8.4×10^6 CFU/mL) and human DNA (11.1μg/mL).
Metrological traceability of calibrator and control material	This product is a qualitative reagent. It isn't including the calibrator, but include a positive control and a negative control.

Characteristics	Specifications/ Claims
Diagnostic Sensitivity	99.71% (95%CI: 98.40% ~ 99.95%)
Diagnostic Specificity	98.08% (95%CI: 96.39% ~98.99%)

6.4. Summary of performance data from other sources, if applicable

Not Applicable

6.5. An overall summary of the performance and safety

From the performance evidence gathered, the Monkeypox Virus Nucleic Acid Detection Kit (PCR-Fluorescence Probing) can be concluded that it is safe and effective, little risk and in according with GSPRs of IVDR Annex I.

Summarizing the conclusions of the Scientific Validity Report, Analytical Performance Report and Clinical Performance Report, the Monkeypox Virus Nucleic Acid Detection Kit (PCR-Fluorescence Probing) is demonstrated to qualify as the State of the Art of this kind of the device and be safe and effective for the intended purpose claimed in IFU.

Residual risks and uncertain or unanswered questions will be traced by PMS.

6.6. Ongoing or planned post-market performance follow-up

The currently valid PMPF plan has 4 PMPF activities, including evaluation of complaint data, customer feedback surveys, evaluation of adverse events and advisory notices and scientific literature review including monitoring the new variant of the monkeypox virus. PMPF report would be implemented a year after PMPF plan approved and would be updated every two years.

7. Metrological traceability of assigned values

7.1. Explanation of the unit of measurement, if applicable

Not Applicable

7.2. Identification of applied reference materials and/or reference measurement procedures of higher order used by the manufacturer for the calibration of the device

Not Applicable

8. Suggested profile and training for users

The following table below details the required experience, education and training of the intended user(s):

No.	Kinds of the intended user(s)	Requirement for the Experience and Education	Trains
01	Laboratory Professional	Education: college degree;	PCR Operation trains; PCR Laboratory SOP;

9. Revision history

SSP revision number	Date issued	Change description	Revision validated by the Notified Body
V01	2024/8/23	First release	□ Yes Validation language: English √ No (only applicable for class C (IVDR, Article 48 (7)) for which the SSP is not yet validated by the NB)
V02	2024/9/24	1. Changed in Intended Purpose 2. Changed description in target population. 3. Changed in description of the device in section 3 4. More detailed description of accessories which are intended to be used in combination with the device 5. Added warning and precaution	□ Yes Validation language: English √ No (only applicable for class C (IVDR, Article 48 (7)) for which the SSP is not yet validated by the NB)

		6. More detailed on Summary of performance evaluation and post-market performance follow-up (PMPF)	
V03	2025/02/20	1. Revise the intended purpose in Section 2.1 and 3.1; 2. Revise the Target Population in Section 2.2 3. Revise the certificate information of Automatic Nucleic Acid Purification Instrument, Universal Transport UTM and Nucleic acid extraction and purification kit in Section 3.5; 4. Revise the concentration unit of Molluscum contagiosum virus in Section 2.3 and 6.3; 5. Revise the description of the claim for scientific validity in Section 6.1; 6. Revise the clinical performance in Section 6.3;	☑ Yes Validation language: English □ No (only applicable for class C (IVDR, Article 48 (7)) for which the SSP is not yet validated by the NB)