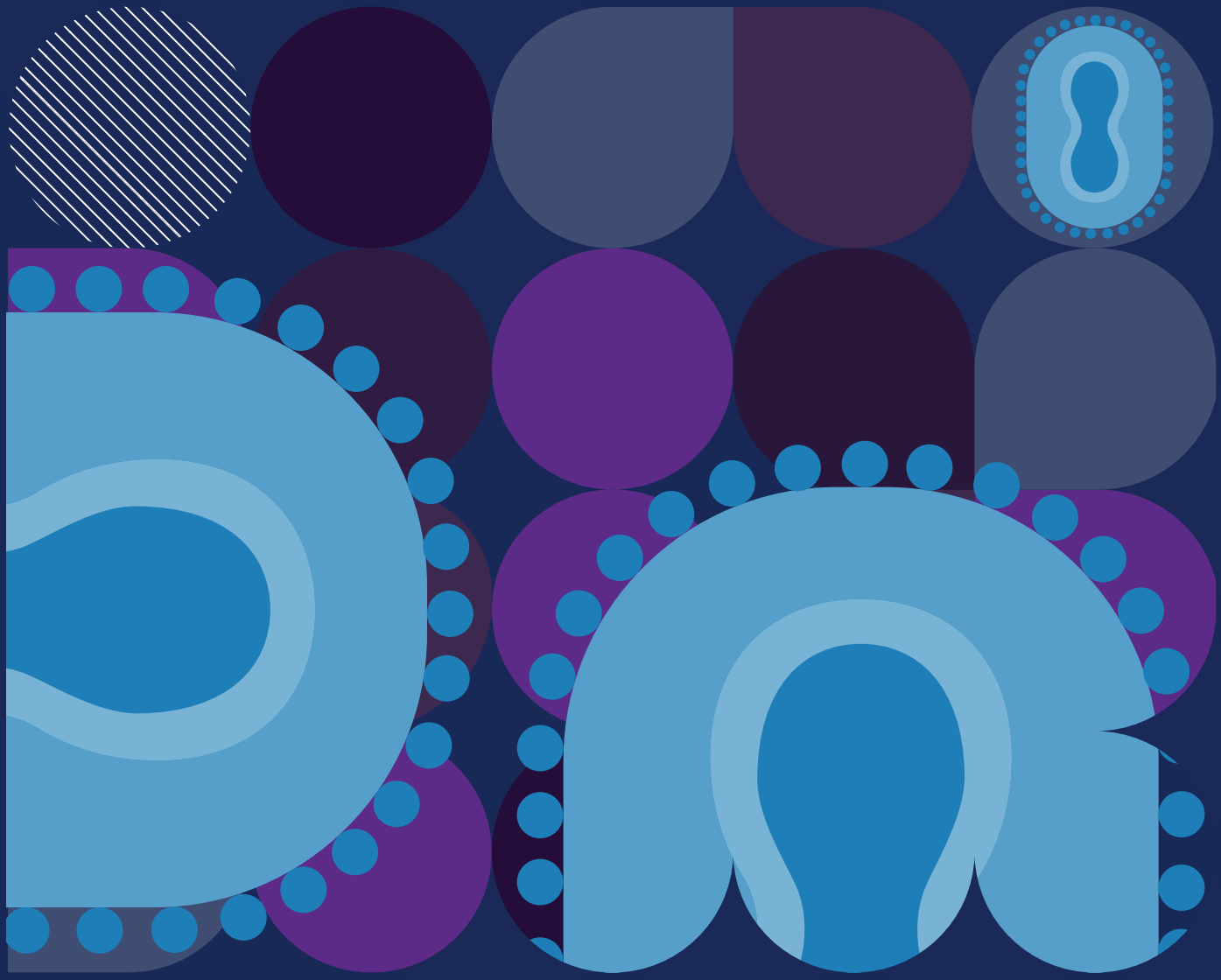


Target product profiles for tests used for **mpox (monkeypox) diagnosis**

World Health Organization

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Abbreviations

˚C	celsius
CPXV	cowpox virus
Ct	cycle threshold
DNA	deoxyribonucleic acid
EDL	essential diagnostics list
HSV	herpes simplex virus
IFU	instructions for use
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization
IVD	*in vitro* diagnostic
Kg	kilogram
LOD	limit of detection
ml	milliliter
mpox	disease caused by monkeypox virus, formerly known as monkeypox
MPXV	monkeypox virus
NAAT	nucleic acid amplification test
OPXV	orthopoxvirus
PCR	polymerase chain reaction
PFU	plaque forming units
PHEIC	public health emergency of international concern
POC	point of care
RDT	rapid diagnostic test
SAGE	strategic advisory group of experts
STI	sexually transmitted infection
TPP	target product profile
VACV	vaccinia virus
VZV	varicella zoster virus
WHO	World Health Organization

Contributors

These TPPs were developed according to a process based on the WHO document: *Target Product Profiles, Preferred Product Characteristics, and Target Regimen Profiles: Standard Procedure, version 1.03 dated 7 December 2021.*

External contributors with subject matter expertise:

First Name	Last Name	Institution	Country
Tamir	Abdelrahman	Laboratoire National de Santé	Luxembourg
Michael	Akanji	Heartland Alliance Nigeria	Nigeria
Patricia	Alvarez	The Oswaldo Cruz Foundation (Fiocruz)	Brazil
Laura	Bachmann	Centers for Disease Control and Prevention (CDC)	United States of America
Daniel	Bailey	UK Health Security Agency (UKHSA)	United Kingdom of Great Britain and Northern Ireland
Augusto	Bencke Geyer	Agência Nacional de Vigilância Sanitária (ANVISA)	Brazil
Konrad	Bradley	USAID	United States of America
Peter Valentine	Coyle	Hamad Medical Corporation	Qatar
Clarissa	Damaso	Universidade Federal do Rio de Janeiro	Brazil
Sheila	Govind	Medicines & Healthcare products Regulatory Agency (MHRA)	United Kingdom of Great Britain and Northern Ireland
Dirceu	Greco	Federal University of Minas Gerais	Brazil
Nagwa	Hasanin	Unicef	Switzerland
Christina	Hutson	CDC	United States of America
Nina	Lagerqvist	European Centre for Disease Prevention and Control (ECDC)	Sweden
Keletso	Makofane	Harvard T.H. Chan School of Public Health	United States of America
Michael	Messenger	FIND	Switzerland
Emmanuel	Nakoune	Institut Pasteur de Bangui	Central African Republic
Andreas	Nitsche	Robert Koch Institute	Germany
Richard	Njouom	Centre Pasteur in Cameroon	Cameroon
Pascale	Ondoa	African Society for Laboratory Medicine (ASLM)	Ethiopia
Nir	Paran	Israel Institute for Biological Research	Israel
Trevor	Peter	Clinton Health Access Initiative (CHAI)	United States of America

First Name	Last Name	Institution	Country
Lance	Presser	National Institute for Public Health and the Environment [Rijksinstituut voor Volksgezondheid en Milieu] (RIVM)	Netherlands
Kris	Roth	Food and Drug Administration (FDA)	United States of America
Jorge	Saavedra	AHF Global Public Health Institute	United States of America
Francis Amirtharaj	Selvaraj	Sheikh Khalifa Medical City	United Arab Emirates
David	Uleato	Defence Science and Technology Laboratory (DSTL)	United Kingdom of Great Britain and Northern Ireland
Juan Carlos Castro	Vargas	Sociedad Peruana de Enfermedades Infecciosas	Peru
Harry	Vennema	RIVM	Netherlands
Aurelia	Vessiere	FIND	Switzerland
Jacqueline	Weyer	The National Institute For Communicable Diseases Of South Africa (NICD)	South Africa
Toni	Whistler	Global Fund	Switzerland
Jason	Williams	USAID	United States of America
Deborah	Williamson	Victorian Infectious Diseases Reference Laboratory (VIDRL)	Australia
Penny	Wilson	MHRA	United Kingdom of Great Britain and Northern Ireland
Pragya	Yadav	National Institute of Virology (NIV) Pune	India

WHO headquarters and regional office contributors:

April Baller, Amal Barakat, Susie Braniff, Lisa Carter, Sébastien Cognat, Janet Diaz, Meg Doherty, Lionel Gresh, Belinda Herring, Ana Hoxha, Shilpa Iyer, Kaz Kojima, Krutika Kuppalli, Rosamund Lewis, Hibak Mahamed, Tamano Matsui, Jairo Andres Mendez Rico, Francis Moussy, Karen Nahapetyan, Dhamari Naidoo, Bernard Onoja, Mark D. Perkins, Irena Prat, Jamie Rylance, Jilian Sacks, Lisa Scheuermann, Andrew Seale, Nikola Sklenovska, Ute Ströher, Lorenzo Subissi, Max Tello, Lara Vajnov, and Adesola Yinka-Ogunleye.

Declaration of interests

External contributors completed a declaration of interest. The declaration of interest forms were reviewed, and no conflicts regarding the support of this document were identified.

Background

Since early May 2022, cases of mpox[1] (monkeypox) – caused by infection with monkeypox virus (MPXV) – have been reported from countries that have not previously reported cases and continue to be reported in West and Central African countries. This is the first time that several mpox (monkeypox) cases and clusters have been reported concurrently across multiple countries in widely disparate geographical areas. On 23 July 2022, mpox (monkeypox) was declared a public health emergency of international concern (PHEIC) by the WHO, accelerating the global response,[2] with the goal to stop the multi-country outbreak.[3]

WHO recommends testing individuals who meet the suspected case definition[4] for mpox (monkeypox) as soon as possible to confirm clinical diagnosis.[5,6] Laboratory confirmation currently is recommended using nucleic acid amplification tests (NAAT), such as real-time or conventional polymerase chain reaction (PCR), of lesion material (from skin or mucosal surfaces). In the absence of lesions, PCR can be done on a mucosal swab, e.g., an oropharyngeal, anal or rectal swab.[4] However, the interpretation of results from oropharyngeal, anal or rectal swabs in the absence of a lesion requires caution; while a positive result is indicative of MPXV infection, a negative result is not enough to exclude the infection.

Accurate diagnosis of MPXV infection in individuals who meet the current WHO definition of a suspected case is needed to guide rapid action for isolation and clinical care, including decisions on the need for contact tracing and antiviral treatments (as appropriate, including through monitored protocols) for test positive individuals, or preventive management and further investigation for test negative individuals, and to support monitoring of the impact of public health interventions. To achieve these objectives, tests need to be sensitive and specific enough to be used as the primary test for diagnosis.

Increased circulation of MPXV globally has increased demand for diagnostics, prompted rapid development of commercial kits, and driven expansion of networks of laboratories and health facilities offering diagnosis. However, a clear need for more simplified, automated and/or accessible assays remains, including those that can enable testing at decentralized sites outside the laboratory. In response, to increase access to quality-assured, accurate and affordable mpox (monkeypox) diagnosis, an expert consultation process has been initiated, resulting in the drafting of two target product profiles (TPPs):

1. Tests used for diagnosis within health care settings and laboratories (TPP1).

2. Tests used as an aid to diagnosis by detecting orthopoxvirus (OPXV) antigens, which are amenable to decentralized use, including in the community (TPP2).

Generally speaking, a TPP is a planning tool for the development of health products. The primary target audience of the TPPs are manufacturers, suppliers, and researchers developing new assays. Additionally, countries and agencies evaluating and/or selecting assays for procurement and use for mpox (monkeypox) testing across both urban and rural environments, especially in settings with constrained resources, may benefit from the criteria and information presented. The TPPs are intended as a strategic reference document for comparison and transparency. The criteria lay out some of the characteristics that are most relevant to inform the expeditious development of tests that address

1 https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease
2 https://www.who.int/europe/news/item/23-07-2022-who-director-general-declares-the-ongoing-monkeypox-outbreak-a-public-health-event-of-international-concern
3 https://www.who.int/publications/m/item/monkeypox-strategic-preparedness--readiness--and-response-plan-(sprp)
4 Surveillance, case investigation and contact tracing for monkeypox: interim guidance
5 Laboratory testing for the monkeypox virus: interim guidance
6 Clinical management and infection prevention and control for monkeypox: Interim rapid response guidance

the greatest and most urgent public health need according to WHO. As is the case with all WHO TPPs, it is recognized that access, equity, and affordability are integral parts of the innovation process and need to be considered at all stages, not just after a product is developed.

Definitions

The report of the third meeting of the WHO Strategic Advisory Group of Experts on In Vitro Diagnostics (SAGE IVD), and the WHO Essential Diagnostics List (EDL)[7], defines specific test purposes – which are based on definitions from the International Medical Device Regulators Forum (IMDRF[8]) – three of which aim to evaluate a patient's current state:

(i) **Screening tests.** Screening tests are used to determine the status of a disease, disorder or other physiological state in an asymptomatic individual. Depending on the nature of the condition and the targeted patient population, screening tests may be used routinely or may be restricted to "at risk" patients.

(ii) **Diagnostic tests.** Diagnostic tests are used to determine, verify or confirm a patient's clinical condition as a sole determinant. This type of testing also includes sole confirmatory assays (to verify results of previous testing) and sole exclusion assays (to rule out a particular condition).

(iii) **Aids to diagnosis.** Tests that are used as aids to diagnosis provide additional information to assist in the determination or verification of a patient's clinical status. The test is not the sole determinant.

Methods

The need for a TPP was assessed and confirmed in October 2022. A TPP expert group was established comprised of 36 leading scientists, experts, public health officials and regulators with due attention to geographical and gender representation (see external contributors). All expert group members first received a draft of the TPPs in November 2022. Comments were received in writing and then discussed over the course of three virtual meetings. Once there was agreement within the group, the draft TPPs were posted on the WHO website for a public consultation of 14 days in January 2023. Anyone could respond by completing a survey identifying themselves and listing their comments and suggested amendments. A total of 77 submissions across both TPPs were received, comprised of 27 full responses. The WHO secretariat reviewed all responses and revised the TPPs where appropriate and feasible. All received responses were shared with the expert group and the group provided their input in writing and through virtual consultation to then finalize the two TPPs. All experts reviewed the final versions prior to the WHO release of the current version 1 of the two TPPs.

[7] The selection and use of essential in vitro diagnostics – TRS 1031

[8] Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

TPP descriptions

Minimal vs preferred targets

The TPPs describe both (1) minimally acceptable and (2) preferred characteristics to define appropriate ranges. The minimal and preferred targets define a range within which each test can be differentiated from others that may result in certain tests being better suited for certain use cases or clinical contexts. Test products generally should meet all the minimal targets and ideally as many of the preferred targets as possible. Likewise, the preferred characteristics should not be considered as the maximum desirable characteristics; assays that exceed these characteristics are certainly of added value.

- **Minimal:** For a specific characteristic, "minimal" refers to the lowest acceptable output for that characteristic. A test that fails to meet a minimal requirement may still be acceptable in some situations.

- **Preferred:** For a specific characteristic, "preferred" provides an ideal target that is believed to be realistically achievable. Meeting the preferred target(s) will provide the greatest impact for the end-users. Developers would ideally design and develop their solutions to meet the preferred requirements for all characteristics.

Assumptions

Through expert consultation, it was noted that diagnosis of mpox (monkeypox) in humans is the current priority. Additional use cases for testing deserve exploration, including the value of an mpox (monkeypox) screening test (i.e., to test asymptomatic individuals), as well as serological assays to describe seroprevalence for better epidemiological understanding, but fall outside of the scope of the current TPPs.

Both TPPs are intended to support mpox (monkeypox) diagnosis to mitigate outbreaks, particularly in settings where there is ongoing human-to-human transmission of MPXV, and are accompanied by a universal cautionary note that positive test results do not rule out co-infection with other viruses, bacteria and/or parasites, and similarly that negative results do not preclude MPXV infection; all tests have limitations and results should always be considered in combination with other elements of clinical history, physical examination and epidemiological context. Results also should be contextualized based on sample type – whereby lesion material is the recommended sample type and negative results from other sample types should be interpreted with caution. Further, positive results should be interpreted in the local context including with an understanding of other OPXVs that may be circulating. These cautionary notes are particularly applicable for assays



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developed based on characteristics in TPP2, in which a positive result could be indicative of infection with a different OPXV, not only MPXV. At the current time, clinical management of mpox (monkeypox) is not dependent on distinguishing the virus clade, but given the increased severity of clade I, knowledge of clade could be valuable. Therefore, differentiation between MPXV clades is considered as a preferred not minimum characteristic.

Additionally, the scope of TPP2 is for assays that can detect antigens common across OPXV, as it is understood that this approach may be needed to achieve the level of sensitivity required but does not preclude the development of an assay that does, in fact, target MPXV protein(s) specifically. In developing TPP2, it was noted by the expert group that ***there is limited data on the kinetics of antigen expression and detection throughout the mpox (monkeypox) disease course and across sample types, therefore it is hoped that these TPPs also encourage additional clinical research to demonstrate the scientific validity and applicability of detection of OPXV/MPXV antigen(s).***

The importance of providing a differential diagnosis especially for individuals who present during the prodromal period is also noted, as mpox (monkeypox) symptoms may be overlapping with several other illnesses. It is also acknowledged that incorporating MPXV nucleic acid detection within a multi-pathogen panel test (i.e., one test that can detect multiple different pathogens, e.g. other causes of lesions) is of interest but necessitates additional complexity for assay design and development. Finally, when documented, transmission during sexual encounters has contributed to most cases during the current multi-country outbreak[9] and therefore considerations to integrate mpox (monkeypox) testing in the context of overall sexual health services is important. Currently, though, delineating a multi-pathogen panel test for sexually transmitted infections (STIs) is not in scope for these TPPs.

[9] https://worldhealthorg.shinyapps.io/mpx_global/#3_Detailed_case_data

Target product profile 1 (TPP1) description

Intended use: Tests used for mpox (monkeypox) diagnosis within health care settings and laboratories.

Characteristic	Minimal	Preferred	Comment(s)
Section 1: Scope			
Target use setting	Performed in laboratory settings.	1. Can be performed in laboratories within any health care facility level (1 – 4). 2. Performed at the point of care (POC) within a health care facility, e.g., in outpatient or STI clinics, in emergency units, or other settings near patient care, particularly in low resource settings.	POC refers to decentralized testing that can be performed by a non-lab trained health care professional and/or lay health worker[10] near a patient, and outside of a laboratory setting, where test results are generally made available during a single clinical encounter.
Target population	Individuals suspected of MPXV infection,[4] including children and adults.		
Target user / operator	Sample collected by laboratory personnel or non-lab trained health care professional[10] in health care facilities. Performed by trained laboratory personnel.	In addition to sample collection by laboratory personnel or non-lab trained health care professional in health care facilities, sample can be collected by lay health worker in the community, and/or directly by target population (recipients of care). Performed by trained laboratory personnel or any trained staff in health care facilities.	

[10] Non-lab trained health care professional could include: nurse, midwife, general practitioner/family physician, specialist physician; Lay health worker: Any person who performs functions related to health-care delivery and has been trained to deliver specific services but has not received a formal professional or paraprofessional certificate or tertiary education degree, e.g., community health worker, village health worker, treatment supporter https://www.who.int/publications/i/item/9789241504843

Characteristic	Minimal	Preferred	Comment(s)
Section 2: Assay Design			
Sample type	Dry lesion material (swabs of surface or exudate, or crusts) and those placed in transport media.	Lesion material (swabs of surface or exudate, or crusts) and in the absence of lesion material: mucosal swabs (i.e., oro/nasopharyngeal and/or anorectal). Note: this does NOT include saliva. Sample type compatible with self-/home-collection by target population.	When present, lesions are the preferred sample type. Research on compatibility and accuracy of sample types that can enable diagnosis in the prodromal period, such as mucosal swabs, saliva, urine, semen, and/or blood, is encouraged.
Target analyte	Two independent targets within gene(s) conserved across all known circulating MPXV clades (I and II), with at least one target that is MPXV specific.	Meets minimal criteria, with ability to distinguish between clades (I or II). *Optional:* compatible with a multi-pathogen panel assay (e.g., distinction of clade I and II in addition to alternative causes of lesions such as VZV or HSV).	The priority is for testing lesion material therefore if a multi-pathogen panel is being included then the focus should be on alternative causes of rash/lesions.
Test kit format	Nucleic acid amplification test (NAAT). If nucleic acid extraction is required, assay should be compatible with a range of standard extraction methods (but extraction reagents do not need to be included.) Supplier sells all required reagents for amplification and detection – preferably in one kit (sample collection and sample transport preservative, if applicable, do not need to be included.)	*Optional:* test does not require extraction prior to amplification/ detection. Assay in which reagents for sample preparation (including nucleic acid extraction, if applicable), amplification and detection are all included and used on a closed/ automated system, or as part of an instrument-free test.	Open or closed molecular systems are acceptable, as well as instrument-free assays. (Requirement for controls listed separately.)
Need for additional equipment	If nucleic acid extraction is required, compatible with automated workflows in wide use, without the need for additional proprietary extraction instrumentation. If PCR-based, assay compatible with off-the shelf equipment for amplification/detection, i.e., at least one of the most widely used thermocyclers.	A) If PCR-based, compatibility across multiple thermocyclers. B) None needed. For use on an automated instrument that runs integrated self-contained assay (i.e., extraction, amplification and detection in one device); the possibility for compatibility with an open, automated diagnostic instrument is encouraged as well as assays that do not require any instrumentation.	Open or closed molecular systems are acceptable, as well as instrument-free assays.

Characteristic	Minimal	Preferred	Comment(s)
Result output / interpretation	Qualitative detection (detected or not detected). If PCR-based, maximum cycle threshold (Ct) provided for interpretation as a positive result for each claimed thermocycler.	If PCR-based, operator access to Ct values and amplification curves.	
Time to results	For manual assays ≤ 2 hours [includes assay run time, excluding pre-analytical or extraction steps[11].] For automated assays in which sample preparation, extraction and amplification are fully integrated: ≤ 4 hours	≤ 1 hour [includes assay run time and extraction, excluding pre-analytical steps.]	
Quality control	Manufacturer states target region(s) of assay (i.e., name of gene(s) in instructions for use (IFU)).	In addition to noting target region(s) of assay, disclosure of specific target location(s) against the reference sequence, for example in the IFU or upon inquiry by end users for quality control purposes.	
	Endogenous internal control (i.e., sample adequacy control), positive control and negative control are provided in the kit or are sold separately (directly through the NAAT kit supplier). Note: If no nucleic acid extraction/purification step included, then an exogenous internal control is required.	Internal control for sample adequacy, reaction inhibition and extraction all included. If within an automated testing system, minimal control requirements are integrated.	
Biosafety / safety precautions	Standard sample collection safety precautions recommended. All materials are free of substances with a GHS classification of H340, H350[12] and H360 , minimal inclusion of any materials with other GHS classification H. The test can be performed under core biosafety requirements, similar to those previously referred to as biosafety level 2, with heightened control measures applied based on local risk assessment.	Tests that minimize the need for biosafety requirements i.e., sample collection/preparation includes buffer-based (non-heat) lysis and inactivation[13], or sample enters closed system.	

[11] Pre-analytical activities include those conducted prior to performing the patient test, e.g. verifying the clinician's order, properly identifying the patient, patient preparation and collection of the sample. NOTE: The ISO standard term is "preexamination," as per the Clinical and Laboratory Standards Institute (CLSI) Harmonized Terminology Database accessible here: https://htd.clsi.org/default.asp

[12] Global Harmonized System of Classification and Labelling of Chemicals: H350 may cause cancer; H340 may cause genetic defects; H360 may damage fertility of the unborn child.

[13] As a DNA virus, MPXV is very stable. Lysis buffer/media should have data to support ability to inactivate.

Characteristic	Minimal	Preferred	Comment(s)
Section 3: Assay Performance and Regulatory			
Analytical performance	1. Inclusivity: Able to detect clades I, IIa and IIb. 2. Limit of detection (LOD): determined using control material of defined quantity, equivalent to at least 1,000 genomic copies per ml of specimen. 3. Analytical specificity: - assay performance should not be impacted by common interfering substances - assay should not cross-react with other common human pathogens, especially those causing similar signs and symptoms as MPXV (e.g., VZV, HSV). - MPXV specific target(s), at least one per assay, should not cross-react with other closely-related human OPXV, e.g., Vaccinia virus (VACV), Cowpox virus (CPXV).		LOD is a quantitative measurement determined using control material of defined quantity. Example control materials for NAAT include synthetically derived nucleic acids in buffered solution, MPXV DNA and inactivated whole virus. Consequently, the type of material used for LOD assessment and the method for value assignment of that material's quantity should be included in any report on method LOD.
Clinical sensitivity	≥ 95% when using lesion material compared to a reference molecular method.	≥ 97% when using lesion material compared to a reference molecular method.	Performance targets should be met for lesion material and ideally should be demonstrated using prospective or retrospective (remnant) natural clinical samples. Samples should cover a range of clinically relevant viral loads, e.g., Ct equivalent 15-38 as per the reference method.
Clinical specificity	≥ 97% when using lesion material compared to a reference molecular method.	≥ 99% when using lesion material compared to a reference molecular method.	
Invalid/error rate	≤ 5%[14]		
Manufacturing / Regulatory approvals	ISO 13485:2016 compliant	ISO 13485:2016 compliant **AND** 1) WHO prequalification or WHO emergency use listing (as available) **AND/OR** 2) Authorization by a founding member of the Global Harmonization Task Force (Australia, Canada, European Union, Japan, United States of America)	

[14] This invalid/error rate target is set to ensure a comprehensive set of controls are incorporated.

Characteristic	Minimal	Preferred	Comment(s)
Section 4: Procedures and operational conditions			
Training needs	≤ 3 days	≤ 1 day with online modules	
Operating conditions	Operation between 10°C and 35°C at an altitude up to 2,500 meters.	Operation between 10°C and 40°C at an altitude up to 3,000 meters. Ability to tolerate low relative humidity to condensing humidity. Able to function in direct sunlight and low light; able to withstand dusty conditions.	
Maintenance needs	Where proprietary equipment used: Routine maintenance included in procurement contract with replacement option. Daily preventive maintenance and/or calibration can be performed by laboratory staff. Invalid and error results provided with suggested corrective actions. It is expected that if assay is intended for use on a third-party thermocycler that this instrument should already meet the minimal requirements.	Where proprietary equipment used: No maintenance required, swap out or replace ancillary device when needed. Weekly preventive maintenance can be performed by trained non-laboratory staff. No calibration needed or can be performed remotely by central lab or manufacturer.	
Sample transport / stability (pre-testing)	For lesion material, assay is compatible with dry and wet swab (in a range of transport media) to enable transport without cold chain ≤ 24 hours. If other sample types are claimed, compatible with one or more standard transport media to enable transport without cold chain ≤ 24 hours. Compatible with stored sample: at least 7 days at 2-8°C; ≥ 30 days at -20°C or lower.	Compatible with preparation (e.g., preservative and/or inactivation media) that stabilizes specimens for increased longevity without need for cold chain (i.e., > 24 hours).	
Sample and reagent preparation needs	Benchtop preparation, including reagent reconstitution (with possibility for sample inactivation) and transfer of sample.	All reagents are ready to use or automated on-board sample preparation within assay.	
Test kit transport and storage conditions	Temperature-controlled storage acceptable. 12 months, stable -20° to 4°C, 70% humidity; up to 2,500 meters altitude. Indicator of expiration included.	No requirement for temperature-controlled transport. 18-24 months, stable between 4-40°C (no cold chain required), 90% humidity; 3,000 meters altitude.	Real time stability data to support shelf-life requirements may not be available at the time of product release, but manufacturers should be challenged to meet targets that match what is realistic for supply chains in low- and middle-income countries.

Characteristic	Minimal	Preferred	Comment(s)
Test kit stability once opened / on-board stability (if applicable)	Reagents once thawed / opened, stable up to 24 hours refrigerated (2-8°C). Where reagents are loaded onto machine upon opening, up to 7 days.	Reagents once thawed / opened, stable up to 90 days refrigerated (2-8°C) or without need for cold storage. Where reagents are loaded onto machine upon opening, up to 90 days.	
Waste disposal	Standard biohazardous waste disposal or incineration; no high temperature incineration required.	Small environmental footprint; recyclable or compostable plastics for test cartridges and other materials after decontamination; no incineration required.	
Data export / remote connectivity	Remote export of data possible through USB.	Direct electronic data exportation via LAN or wirelessly (wifi or Bluetooth).	
Section 5: Price			
Test price	For kits inclusive of amplification/ detection only compatible with non-proprietary equipment: ≤ US$ 11 per reaction. For kits for use on closed/automated systems inclusive of sample preparation, amplification and detection: ≤ US$ 15 per reaction.	≤ US$ 5 per reaction	Price is for reaction kit from supplier (inclusive of amplification and detection, at minimum.)

Target product profile 2 (TPP2) description

Intended Use: Tests used as an aid to mpox (monkeypox) diagnosis by targeting orthopoxvirus antigen(s), that are amenable to decentralized use, including in the community.

Characteristic	Minimal	Preferred	Comment(s)
Section 1: Scope			
Target use setting	Performed outside of the laboratory setting, at the POC within a health care facility.	Performed outside of health care facilities, within the community, including rural environments, in low-resource settings.	POC refers to decentralized testing that is performed by a non-lab trained health care professional and/or lay health worker[10] near a patient, and outside of a laboratory setting, where test results are generally made available during a single clinical encounter. It is envisioned that this test would be most relevant in outbreak contexts in which there is known human-to-human transmission of MPXV.
Target population	Individuals suspected of MPXV infection[4], including children and adults.		
Target user / operator	Sample collected and test can be performed by non-lab trained health care professional[10] or laboratory personnel.	Sample collected by target population receiving the test (i.e. self/home-collection of sample), in addition to non-lab trained health care professional or lay health worker. Test performed by trained lay provider, health care worker or laboratory personnel.	
Section 2: Assay Design			
Sample type	Lesion material swabs (surface or exudate).	Lesion material swabs (surface or exudate) and in the absence of lesion material: mucosal swabs (i.e., oro/nasopharyngeal and/or anorectal) or saliva. Sample type compatible with self-/home-collection by target population. Compatible with samples preserved in third party media for retesting and quality control.	When present, lesions are the preferred sample type. Research on compatibility and accuracy of sample types that can enable diagnosis in the prodromal period, such as mucosal swabs, urine, semen, saliva and/or blood, is encouraged.
Target analyte	Highly conserved region of OPXV protein across all known MPXV clades (I and II).	Highly conserved region of MPXV protein, across all known clades.	Tests targeting detection of immunoglobulins (antibodies) are not acceptable.

Characteristic	Minimal	Preferred	Comment(s)
Test format	Immunoassay in lateral flow format, or equivalent.		
Test kit components	All materials for sample collection, preparation and test operation included. IFU include information on viral region(s) being targeted.	Consider inclusion of waste disposal materials within kit.	Note: Requirement for controls listed separately.
Need for additional equipment	Minimal, ancillary device, e.g., handheld or on desktop < 1 kg; battery or solar power operated; > 8 hours rechargeable battery life.	Device-free/disposable - no additional equipment required.	It is acknowledged that to achieve higher sensitivity a reader/device may be needed; as well that a reader/device may facilitate more uniform data capture and reporting. However, any device should be appropriate for target use setting.
Result output / interpretation	Qualitative (detected/not detected). Visual manual and/or reader (proprietary or non-proprietary smart phone application).	Visual manual and/or digital readout via smartphone application reader (ideally, non-proprietary) with connectivity.	
Time to results	≤ 40 minutes	≤ 20 minutes	It is expected that recipients of care will wait for results.
Result validity stability	≥ 15 minutes	≥ 2 hours	Longer results validity supports data recording/ reporting and quality control.
Quality control	Internal control (for sample flow/ migration) in an area or region within the individual testing device; positive control and negative control sold separately by supplier; calibration control for reader available, if applicable.	Positive control and negative (full process) control provided in the kit. Meets all other minimal requirements. Inclusion of integrated sample adequacy control is encouraged.	
Biosafety / safety precautions	Standard sample collection safety precautions recommended. All materials are free of components with a GHS classification of H340, H350, H360, minimal inclusion of any substances with other GHS classification H[11]. Tests/sample buffer minimizes the need for biosafety requirements e.g., sample preparation includes (non-heat-based) virus inactivation. Evidence of sample inactivation preferably included in IFU.		

Characteristic	Minimal	Preferred	Comment(s)
Section 3: Assay Performance and Regulatory			
Analytical performance	1. Inclusivity: Able to detect MPXV clades I, IIa and IIb. 2. LOD: determined using control material of defined quantity, equivalent to at least 10^6 PFU per ml of specimen. 3. Analytical specificity: - assay performance should not be impacted by common interfering substances - assay should not cross-react with other human non-OPXV, especially those causing similar signs and symptoms as MPXV (e.g., VZV, HSV). Cross reactivity with other OPXV is acceptable and should be clearly documented in IFU.	2. LOD: determined using control material of defined quantity, equivalent to at least 10^4 PFU per ml.	LOD is a quantitative measurement determined using control material of defined quantity[15]. Example control materials for protein-detection assays include purified protein in buffered solution to inactivated whole virus, among others. Consequently, the type of material used for LOD assessment and the method for value assignment of that material's quantity should be included in any report on method LOD. LOD targets have been set to reflect range of infectious virus titres reported in clinical samples and detectability in proof-of-concept studies.[16,17]
Clinical sensitivity	≥ 80% when using lesion material compared to a reference molecular method.	≥ 90% when using lesion material compared to a reference molecular method.	Performance targets should be met for lesion material and ideally should be demonstrated using prospective or retrospective (remnant) clinical samples. Samples should cover a range of clinically relevant viral loads, e.g., Ct equivalent 15-38 as per the reference method.
Clinical specificity	≥ 97% when using lesion material compared to a reference molecular method.	≥ 99% when using lesion material compared to a reference molecular method.	
Invalid / error rate	≤ 5%		

[15] It is acknowledged that there is a significant gap in availability of validated higher order reference material for antigen-detection assays and progress in this area is encouraged.

[16] https://doi.org/10.2807/1560-7917.ES.2022.27.35.2200636

[17] https://doi.org/10.1016/S1473-3099(22)00440-6

Characteristic	Minimal	Preferred	Comment(s)
Manufacturing / Regulatory approvals	ISO 13485:2016 compliant	ISO 13485:2016 compliant **AND** 1) WHO prequalification or WHO emergency use listing (as available) **AND/OR** 2) Authorization by a founding member of the Global Harmonization Task Force (Australia, Canada, European Union, Japan, USA)	
Section 4: Procedures and operational conditions			
Training needs	≤ 1 day using IFU and quick reference guide(s).	≤ 0.5 day with IFU and quick reference guide(s), including through smart phone application(s) to ensure ongoing compliance and up to date training.	
Operating conditions	15-35°C; 25-80% relative humidity; altitude up to 1,500 meters. If device required: ability to tolerate low relative humidity to condensing humidity. Able to function in direct sunlight and low light; able to withstand dusty conditions.	10-40°C; 25-90% relative humidity; up to 3,000 meters.	
Maintenance needs	None, swap out or replace ancillary device when needed.	None required, as instrument-free.	
Sample transport / stability (pre-testing)	Samples should be stable ≥ 30 minutes (not refrigerated, 10-35°C) before sample preparation/ test operation.	Test compatible with both dry and wet swab samples. Test compatible with samples that have been stored up to 3 hours (not refrigerated, 10-40°C) or ≤ 12 hours (refrigerated, 2-8°C). Ideally, test is compatible with samples preserved in media and frozen (-20°C) for retesting and quality control purposes.	As the preference is for the test to be operated at the POC, acceptable for sample to be used immediately, but compatibility with samples that have been refrigerated and/or frozen and with generic preservation media is encouraged for quality control and possible repeat or follow-up testing.
Sample and reagent preparation needs	Minimal pre-test processing required such as need for sample inactivation step and/or sample preparation/ transfer step (e.g., placement of swab in proprietary buffer and then addition to the test). Minimal reagent reconstitution acceptable without any requirement for precise measurement.	All reagents ready to use.	

Characteristic	Minimal	Preferred	Comment(s)
Need for precise volume	If autofill or graduated volume, markings should be on sample transfer device. If precise volumes of buffer are required, should be pre-aliquoted.	Not needed or limited to number of drops (note that addition of drops is not considered 'precise' volume requirement).	
Number of timed steps	≤ 3	1	
Specimen throughput	≥ 5 per hour, per operator	≥ 10 per hour, per operator	This throughput assumes operator can batch tests.
Test kit stability and storage conditions	12 months at 4-30°C but tolerates brief periods > 40°C; humidity up to 80%; any associated reader/ device must meet or exceed these requirements.	18-24 months at 4-40°C but tolerates freezing and brief periods > 45°C; any associated reader/device must meet or exceed these requirements.	Real time stability data to support shelf-life requirements may not be available at the time of product release, but manufacturers should be challenged to meet targets that match what is realistic for supply chains in low- and middle-income countries.
Stability of kit once opened	≥ 30 minutes for single use test after opening the pouch.	≥ 1 hour for single use test after opening the pouch.	
Waste disposal	Routine biohazard waste.	Small environmental footprint; recyclable or compostable plastics.	
Data export / remote connectivity	Not required.	Test is compatible with a reader that can either be a dedicated hardware instrument or an application that operates on a general-purpose mobile device. Detailed characteristics for such readers can be found at: https://www.who.int/publications/i/item/9789240067172.	
Price			
Test price	≤ US$ 5	≤ US$ 2.50	


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