DRAFT FOR PUBLIC CONSULTATION

Target Product Profiles for tests used for mpox diagnosis

Table of Contents

List of Abbreviations 2

Background 3

Definitions 4

TPP Descriptions 4

Minimal vs Preferred Targets 4

Assumptions 5

TPP 1 6

TPP 2 14

List of 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
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

Background

Since early May 2022, cases of mpox[1] – 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 cases and clusters have been reported concurrently across multiple countries in widely disparate geographical areas. On 23 July 2022, mpox 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 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 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, that are amenable to decentralized use, including in the community (TPP2).

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 testing across both urban and rural environments, especially in settings with constrained resources, may benefit

[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

from the criteria and information presented. The criteria lay out some of the characteristics that are most relevant to inform the expeditious development of tests that address the greatest and most urgent public health need. 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.

TPP Descriptions

Minimal vs Preferred Targets

The TPPs describe both (1) minimally acceptable and (2) preferred characteristics to define appropriate ranges. 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.

- 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. The preferred characteristics should not be considered as the maximum desirable characteristics; assays that exceed these characteristics are certainly of value.

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.

[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

Assumptions

Through expert consultation, it was noted that diagnosis of mpox in humans is the current priority. Additional use cases for testing deserve exploration, including the value of an mpox 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 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 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 is not dependent on distinguishing the virus clade, therefore neither TPP is intended to differentiate between MPXV clades.

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 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 symptoms may be overlapping with several other illnesses. It is therefore acknowledged that incorporating MPXV nucleic acid detection within a multi-pathogen panel test (i.e., one test that can detect multiple different pathogens) is of interest but given the complexities of development is not the priority at this time. As well, when documented, transmission during sexual encounters has contributed to most cases during the current multi-country outbreak[9] and therefore considerations to integrate mpox 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

TPP 1

Intended use: Tests used for mpox 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 is performed by a minimally trained healthcare professional 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,* including children and adults		
Target user / operator	Sample collected by laboratory personnel or trained staff in health care facilities. Performed by trained laboratory personnel.	In addition to sample collection by laboratory personnel or trained staff in health care facilities, sample can be collected by trained staff 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.	
Section 2: Assay Design			
Sample type	Lesion material (swabs of surface or exudate, or crusts).	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).	When present, lesions are the preferred sample type.

Characteristic	Minimal	Preferred	Comment(s)
		Sample type compatible with self-/home-collection by target population.	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 gene targets 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., alternative causes of skin 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 dermal 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.)	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.)

Characteristic	Minimal	Preferred	Comment(s)
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, with cycle threshold (Ct) range for interpretation as a positive result provided for each claimed thermocycler. 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.
Result output / interpretation	Qualitative detection (detected or not detected).	If PCR-based, operator access to Ct values and amplification curves.	
Time to results	≤ 5 hours [includes assay run time, excluding pre-analytical steps.]	≤ 1 hour [includes assay run time, excluding pre-analytical steps.]	
Quality control	Manufacturer provides target region(s) of assay (i.e., name of gene(s) and target location(s) against the reference sequence) in instructions for use (IFU). 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. Meets minimal requirements with controls integrated within the automated testing system.	

Characteristic	Minimal	Preferred	Comment(s)
Biosafety / safety precautions	Standard sample collection safety precautions recommended. All materials are free of substances with a GHS classification of H340, H350 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[‡], or sample enters closed system.	
Section 3: Assay Performance and Regulatory			
Analytical performance	1. Inclusivity: Able to detect clades I, IIa and IIb. 2. Analytical sensitivity/limit of detection (LOD): determined using control material of defined quantity, equivalent to at least 1,000 genomic copies per ml or an input volume of less than 5 genomic copies per reaction. 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		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.

Characteristic	Minimal	Preferred	Comment(s)
	closely-related human OPXV, e.g.,Vaccinia virus (VACV), Cowpox virus (CPXV).		
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%		
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	≤ 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	

Characteristic	Minimal	Preferred	Comment(s)
		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 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.	

Characteristic	Minimal	Preferred	Comment(s)
Test kit stability and storage conditions	12 months, stable -20° to 4°C, 70% humidity; up to 2,500 meters altitude.	18-24 months, stable between 4-40°C (no cold chain required), 90% humidity; 3,000 meters altitude; indicator of instability or expiration included. Preference for temperature-stable/lyophilized reagents without the requirement for temperature-controlled shipment.	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	Single use reagents once thawed / opened, up to 24 hours refrigerated (2-8°C).	Up to 90 days refrigerated (2-8°C) or without need for cold storage.	
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.)

TPP 2

Intended Use: Tests used as an aid to mpox 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 minimally trained healthcare professional 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,* including children and adults.		
Target user / operator	Sample collected and test performed by trained health care worker or laboratory personnel.	Sample collected by target population receiving the test (i.e. self/home-collection of sample), in addition to trained health care or community worker. Test performed by trained lay provider, health care worker or laboratory personnel.	
Section 2: Assay Design			

Characteristic	Minimal	Preferred	Comment(s)
Sample type	Lesion material swabs (surface or exudate).	Lesion material (surface, exudate swabs or crusts) 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.
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.

Characteristic	Minimal	Preferred	Comment(s)
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[†]. 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.		
Section 3: Assay Performance and Regulatory			
Analytical performance	1. Inclusivity: Able to detect MPXV clades I, IIa and IIb.		LOD is a quantitative measurement determined using control material of

Characteristic	Minimal	Preferred	Comment(s)
	2. Analytical sensitivity/LOD: determined using control material of defined quantity. equivalent to at least 10^6 PFU per ml. 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. Analytical sensitivity/LOD: determined using control material of defined quantity. equivalent to at least 10^4 PFU per ml	defined quantity. 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.[§,**]
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

Characteristic	Minimal	Preferred	Comment(s)
Clinical specificity	≥ 97% when using lesion material compared to a reference molecular method.	≥ 99% when using lesion material compared to a reference molecular method.	samples.-Samples should cover a range of clinically relevant viral loads, e.g., Ct equivalent 15-38 as per the reference method.
Invalid / error rate	≤ 5%		
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.	

Characteristic	Minimal	Preferred	Comment(s)
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.	
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.

Characteristic	Minimal	Preferred	Comment(s)
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 for device-free/reader-independent tests; If device-based: remote export of data possible.	Test is compatible with readers and other non-proprietary data capture devices or applications; If device-based: internal memory to store results even if power cut and with the ability to report to country health information management systems using an onboard unique identifier or other personal data protection safeguard, linking the test to the user (e.g., QR codes, 2-D barcoding.)	
Price			
Test price	≤ US$ 5	≤ US$ 2.50	

[*] Surveillance, case investigation and contact tracing for monkeypox: interim guidance
[†] 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.
[‡] As a DNA virus, MPXV is very stable. Lysis buffer/media should have data to support ability to inactivate.
[§] https://doi.org/10.2807/1560-7917.ES.2022.27.35.2200636
[**] https://doi.org/10.1016/S1473-3099(22)00440-6