Surveillance, case investigation and contact tracing for mpox

Interim guidance
27 November 2024

World Health Organization

Key points

- Since 2023, the Democratic Republic of the Congo has been experiencing a steady increase in mpox cases in both endemic and newly affected areas, and in early 2024, a new monkeypox virus (MPXV) strain, subclade Ib was identified. The continuing spread of mpox in the Democratic Republic of the Congo and the detection of subclade Ib in neighbouring countries led the WHO Director-General to declare mpox a Public Health Emergency of International Concern (PHEIC) on 14 August 2024. In addition, a multi-country outbreak of mpox, caused by MPXV clade IIb, has been ongoing since May 2022 with continuing transmission reported across all WHO regions.
- The primary goals of mpox surveillance, case investigation, and contact tracing are to detect and contain outbreaks and stop ongoing transmission, as well as to monitor and orient the epidemic response. This approach aims to protect people at risk of mpox in endemic and new settings while working towards eliminating human-to-human transmission.
- The specific objectives of surveillance and case investigation for mpox are to rapidly identify cases, clusters of cases, and sources of exposure in order to: provide optimal clinical care; isolate cases to prevent further transmission; identify and monitor contacts to recognize early signs of infection; identify risk groups for infection and for severe disease; protect frontline health workers; and tailor effective control and prevention measures.
- Key actions of outbreak response are to provide accurate information to people at risk; offer pre- and post-exposure vaccination to people at risk; stop further spread; and protect vulnerable individuals and frontline health workers.
- Clinicians should immediately report suspected mpox cases to relevant national public health authorities.
- Probable and confirmed cases of mpox should be reported to WHO through national IHR national focal points (NFPs) as early as possible, at least monthly, and with a minimum epidemiological dataset, in line with Article 6 of the International Health Regulations (IHR 2005) and the Standing recommendations extended by the Director General of WHO (August 2024). African countries experiences an upsurge in cases should report weekly on suspected, probable, and confirmed mpox cases according to national or WHO case definitions, in line with the mpox temporary recommendations (August 2024).
- All confirmed cases of clade Ib MPXV should be reported to WHO through IHR notification as soon as they are detected and confirmed.
- If mpox is suspected, case investigation should consist of a clinical examination of the patient in a well-ventilated room while using appropriate personal protective equipment (PPE), questioning the patient about possible sources of exposure, and safe collection and dispatch of specimens for laboratory testing.
- As soon as a suspected case is identified, contact identification and tracing should be initiated.
- Contacts of probable and confirmed cases should be monitored, or should self-monitor, daily for any sign or symptom for a period of 21 days from last contact with an infectious case or contaminated materials.
- Contacts do not require quarantine or exclusion from work during the contact monitoring period as long as they are symptom-free. WHO encourages contacts to rigorously practice hand hygiene and respiratory

etiquette, avoid contact with persons who are immunocompromised or pregnant and avoid sexual contact throughout the 21-day monitoring period. Non-essential travel is discouraged during this period.

Changes from earlier version

This is an updated version of the interim guidance on surveillance, case investigation and contact-tracing published on 20 March 2024.

In line with the International Health Regulations 2005 (IHR) and following the Emergency Committee for the upsurge of mpox on 14 August 2024, the WHO Director-General concurred with the Committee's advice that the surge of mpox cases in the Democratic Republic of the Congo (DRC) and other African countries constitutes a Public Health Emergency of International Concern (PHEIC) (1). In view of this, the WHO Director-General extended the Standing recommendations (2) for mpox issued in August 2023 (3) for one additional year to August 2025 and issued new Temporary recommendations to States Parties (4).

This interim guidance has been updated to reflect recent changes in reporting procedures, following the issuance of the temporary recommendations, the updated WHO mpox surveillance tools and includes the latest information available on the disease (5–7). The case definition for suspected cases has been updated to better reflect the clinical presentation observed in diverse settings. Definitions for probable and confirmed cases have been aligned with the latest WHO interim guidance on diagnostic testing and testing strategies for mpox (8), and the criterion of multiple sexual partners has been removed from the probable case definition. A new section on community-based surveillance for mpox has been added. Language describing respiratory transmission has been revised in line with the new proposed terminology for pathogens that transmit through the air (9). Additional details are provided on investigations following exposure to infected animals. The type of contacts through which human-to-human mpox transmission occurs, as well as the measures for mpox contacts, have been further framed and defined. This document also includes additional considerations for wastewater and environmental surveillance, with relevant considerations for African countries. Language throughout the document has been refined for clarity.

Introduction

This guidance serves to provide interim recommendations for surveillance, case investigation and contact tracing for mpox in the context of the ongoing multi-country outbreak (10) and new Public Health Emergency of international Concern (PHEIC) (1,4).

Mpox is an infectious disease caused by the monkeypox virus (MPXV). There are two distinct clades of the virus: clade I (with subclades Ia and Ib) and clade II (with subclades IIa and IIb) (5) Historically, clade I was found in Central Africa (Congo Basin) and clade II in West Africa (11), but a clade IIb-driven outbreak has been spreading globally since 2022through human-to-human transmission, especially via sexual contact (7) From 2022 the number of mpox cases has also increased and expanded in central Africa, especially in the Democratic Republic of the Congo (12–14), where cases are linked to both clade Ia and clade Ib MPXV (15–17).

The incubation period of mpox ranges from 2 to 21 days, with shorter or longer periods occasionally noted (5,18). During the 2022-24 multi-country outbreak, shorter incubation periods than previously reported have been observed (19–22) which could be due to differences in the virus strains, mode of transmission, methods of data collection, and patient demographics, among others. Typically, the prodromal phase of clinical illness lasts 1-5 days, during which time patients may experience fever, headache, back pain, myalgias, and lymphadenopathy. This is followed by a second phase which typically occurs after the fever subsides, with the appearance of skin and/or mucosal rash, which might include a single, multiple or numerous lesions. Typically, skin lesions progress through macules, papules, vesicles, and pustules, before crusting over and desquamating over a period of two to four weeks. During the clade IIb MPXV multi-country outbreak, patients presented with more mucosal lesions than previously described, often localized in the genital or perineal/perianal area, as well as in the mouth and on the eyes (23). Genital lesions were also

predominant among the first mpox cases due to clade Ib MPXV in the the Democratic Republic of the Congo which were linked to sexual contact transmission (17) Lesions may appear at different stages of progression, and rash can develop prior to typical prodromal or constitutional symptoms (such as fever or fatigue).

The infectious period of mpox can vary, but generally, patients are considered infectious from the time of symptom onset until skin lesions have crusted, the scabs have fallen off and a fresh layer of skin has formed underneath. Emerging and not conclusive evidence suggests possible pre-symptomatic transmission (21,24–27).

Human-to-human transmission of mpox can occur through contact with lesions and body fluids carrying the virus, respiratory particles, contaminated objects, and vertical transmission from mother to child. Contact with lesions and body fluids includes skin-to-skin, mucosa-to-mucosa, or mucosa-to-skin contact. Contact with infectious respiratory particles (IRP) occurs when IRPs are expelled into the air by the case, then directly deposited on the exposed mucosal surfaces (mouth, nose, or eyes) of another person, or when IRPs have travelled either short or long distances from the infectious person and are inhaled by a receiving person. This may include exposure to a case in close proximity, such as speaking, eating in front of each other, and other close proximity activities. It may also include aerosol-generating procedures performed on cases in healthcare settings. The distance and time over which this occurs may vary. Contact with contaminated objects (also described as fomite transmission) includes clothing, linen or any other object that has infectious skin particles coming from a mpox case. If shaken, these particles can disperse into the air and be inhaled or land on broken skin or mucosal membranes, and lead to transmission and infection (28). In addition, transmission has been shown to occur from contaminated needles in the healthcare setting or in tattoo facilities. During pregnancy, the virus can cross the placenta, causing intrauterine exposure of the fetus, complications such as fetal loss or stillbirth, and congenital infection of the infant (29,30).

While sexual transmission of mpox was not well understood before 2022, the epidemiology of the global IIb outbreak, detection of virus in semen and anal swabs of affected patients (23,31–34) have highlight sexual contact as an efficient way for the virus to spread between individuals (7,12,15,35–39).

Most individuals with mpox outside Africa, predominantly affected by clade IIb MPXV, have not experienced severe disease (7,22,23,32,40) although many have developed complications and/or required hospitalization for management of severe pain (7,22,23). Persons with immune suppression, due to immunosuppressive treatments, untreated or inadequately managed HIV infection or other medical conditions, are at higher risk of severe mpox disease and death (35,41–43). The highest mpox mortality continues to be reported in the Democratic Republic of the Congo, mostly in endemic settings (14).

The overall goal of surveillance, case investigation and contact tracing is to detect new outbreaks and stop transmission in order to contain the multiple ongoing outbreaks, protect people at risk in endemic and new settings, and make progress towards elimination of human-to-human transmission.

Monkeypox virus in animals

Although the ongoing global mpox outbreak to clade IIb MPXV is sustained exclusively through human-to-human transmission, and at the time of writing clade Ib MPXV is spreading without evidence of zoonotic exposure, mpox remains a zoonosis. There are regions on the African continent where the virus has been found in wild animals (44–46), and sporadic transmission from animals to humans continues to occur, notably in East, Central and West Africa. Genomic sequencing of the circulating viral strain in most endemic regions of the Democratic Republic of the Congo, the Central African Republic, and the Republic of Congo suggest multiple zoonotic introductions of clade Ia MPXV followed by human-to-human transmission (47–51). When transmission from an animal to a person is suspected, it is important to collect information on the exposure (including type of contact and animal species) as part of the case investigation, and collaborate with animal health (agriculture and wildlife) authorities for further investigation (6). Surveillance of MPXV in animal populations is beyond the scope of this document. Basic considerations for investigations of zoonotic sources and sampling animals for investigation purposes are outlined under the section

Investigating exposure to an infected animal. Countries are encouraged to report confirmed cases of MPXV infection in animals to the World Organisation for Animal Health (WOAH) with all relevant animal health information as described in Article 1.1.5 of the Terrestrial Animal Health Code (52), via the country's disease notification focal points and the WOAH Delegate.

Surveillance case definitions

The case definitions may be reviewed as more evidence becomes available.

Suspected case:

i) A person presenting with an acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions on the face, palms of hands and feet, genital area (penis, scrotum, vulva), perianal area, mouth or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

AND

for which the following common causes of acute rash or skin lesions do not fully explain the clinical picture: varicella zoster, scabies, herpes zoster, measles, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (e.g., to plants); and any other locally relevant common causes of papular or vesicular rash.

N.B. It is not necessary to obtain negative laboratory results for listed common causes of rash illness in order to classify a case as suspected. Further, if suspicion of mpox or MPXV infection is high due to either history and/or clinical presentation or possible exposure to a case, the identification of an alternate pathogen which causes rash illness should not preclude testing for MPXV, as co-infections have been identified.

OR

ii) A person who is a contact of a probable or confirmed mpox case in the 21 days before the onset of signs or symptoms, and who presents with any of the following: acute onset of fever (>38.5°C), headache, myalgia (muscle pain/body aches), back pain, profound weakness, or fatigue, WITHOUT lesions.

Probable case:

A person presenting with an acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions on the face, palms of hands and feet, genital area (penis, scrotum, vulva), perianal area, mouth or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

AND

has an epidemiological link[1] to a probable or confirmed case of mpox in the 21 days before symptom onset.

Confirmed case:

A person who meets either of the following laboratory criteria:

i) Detection of monkeypox virus (MPXV) DNA by real-time polymerase chain reaction (PCR) and/or sequencing.

OR

ii) Detection of orthopoxvirus (OPXV) DNA by PCR in settings where:

- An mpox outbreak has been confirmed through MPXV-specific PCR or sequencing;

[1] Please see below definition of a contact.

AND

- no other orthopoxviruses are known to circulate in human populations.

For further guidance on testing please refer to Diagnostic testing and testing strategies for mpox: interim guidance (8).

Discarded case:

A suspected or probable case for which laboratory testing of lesion fluid, skin specimens or crusts by PCR and/or sequencing is negative for MPXV or OPXV in an mpox outbreak setting.

Of NOTE: A retrospectively detected probable case for which lesion testing can no longer be adequately performed (i.e., after the crusts fall off) and no other specimen is found PCR-positive, would remain classified as a probable case. A suspected or probable case should not be discarded based on a negative result from an oropharyngeal, anal or rectal swab or from a blood test alone

These case definitions were developed with a view to balance the importance of detecting cases and interrupting chains of transmission, while avoiding an overly sensitive definition that would overburden public health, diagnostic and treatment resources.

Public health authorities should maintain a high degree of vigilance for the possibility of mpox outbreaks in congregate settings such as camps for people who are displaced, educational, residential, or correctional facilities and/or in relation to events, gatherings and venues where people may be at risk through different types of exposure. Clinicians should maintain a high index of suspicion for mpox among health workers, sex workers and other key populations including gay men, bisexual men, other men who have sex with men, and transgender individuals and all close contacts of mpox cases.

Public health authorities may adapt these case definitions to suit local circumstances while aiming to maintain international comparability and continuity as much as possible. All efforts should be made to avoid unnecessary stigmatization of individuals and communities potentially affected by mpox.

These definitions are for surveillance purposes and should not be used to guide clinical management. WHO interim guidance for clinical management and infection prevention and control for mpox has been published separately (28).

MPXV reinfection – Case definitions

The duration of immunity following primary MPXV infection and protection against reinfection were not known prior to the Clade IIb-related outbreak and understanding remains limited (53). A few case reports and case series have presented instances where individuals previously diagnosed with PCR-confirmed MPXV infection developed the disease and tested PCR-positive for MPXV for a second time (54–62). It is currently unclear whether these episodes represent new infections following clinical recovery and the apparent clearance of the virus, a recrudescence of a latent prior infection, or lack of complete viral clearance. Genetic analysis identifying specific viral variants may distinguish a reinfection from recrudescent infection. However, in practice, genomic sequencing is not commonly performed due to limited capacity for genomic sequencing analysis in certain settings, technical constraints stemming from the possible low viral load in subsequent mpox episodes, and difficulties in sequence data interpretation for reinfection determination due to generally slow viral mutation (58,59,62).

A lack of consensus on the definition of MPXV reinfection complicates the comparison of reported cases and the compilation of evidence to reach a better understanding to accurately characterize the burden, natural history, clinical characteristics and capacity for onward transmission associated with MPXV reinfection (53).

Additionally, where access to MPXV PCR testing is constrained, clinically compatible mpox cases that meet national case definitions may remain classified as suspected; in this situation the ability to confirm reinfection is hindered by the absence of documented history of a prior probable or confirmed mpox episode.

Here we propose definitions for suspected, probable, and confirmed MPXV reinfection for surveillance purposes. These aim to assist clinicians, researchers, and public health officials by standardizing the reporting of MPXV reinfections across public health jurisdictions and countries.

Given the emerging evidence, these definitions assume a pragmatic and implementation-oriented approach. The aim is to allow flexibility of use in diverse settings, depending on diagnostic capacity, while aiming for standardized reporting and better understanding of MPXV reinfections. These definitions are provisional and subject to refinement as more knowledge is gained about mpox immunity and infection protection.

Four main elements were considered for these definitions:

I. A current confirmed mpox diagnosis;
II. A documented history of a previous mpox episode, either as a suspected, probable, or confirmed case (WHO mpox case definition);
III. A temporal gap of at least three months between two episodes (60,63);
IV. Exclusion of continuous infection, as verified by the full clinical resolution of the previous mpox episode. Clinical resolution includes complete disappearance of all signs and symptoms related to the previous episode of mpox, such as fever, headache, muscle aches, backpain, swollen lymph nodes, skin and/or mucosal lesions, or systemic symptoms (eg pulmonary disease), except for long-term sequelae (e.g., blindness, scarring, depigmentation).

Suspected mpox reinfection

- A person who currently meets the criteria for a confirmed case of mpox

AND

- Has a documented history of a previous episode of mpox, as a suspected, probable or confirmed case.
- It is unclear if the person presented full clinical resolution of the previous episode.

Probable mpox reinfection

- A person who currently meets the criteria for a confirmed case of mpox

AND

- Has a documented history of a previous episode of mpox, as a probable or confirmed case.
- Full clinical resolution of the previous mpox episode occurred.
- The time between the resolution of the first episode and the onset of new symptoms is less than three months.

Confirmed mpox reinfection

i) A person who currently meets the criteria for a confirmed case of mpox

AND

- Has a documented history of a previous episode of mpox, as a confirmed case.
- Full clinical resolution of signs and symptoms (as defined for suspect case above) of the previous mpox episode occurred.
- The time between the resolution of the first episode and the onset of new symptoms is three months or more.
- When possible, strain differentiation is undertaken using genetic sequencing.

OR

ii) Has a probable mpox reinfection (as described above) with significant strain differentiation between the two MPXV infections (e.g. different lineage and descendant lineages) using genetic sequencing.

If enough MPXV DNA is detected during a subsequent mpox episode, every effort should be made to sequence it to confirm reinfection if there is sequence data from the first episode for comparison.

Considerations for mpox reinfection in immunosuppressed patients

Mpox disease progression may differ in immunocompromised patients, who may experience prolonged viral persistence and varied clinical manifestations due to impaired viral clearance (64). Persons who are immunocompromised include those who have cancer or immunodeficiency, who are on active treatment with immunosuppressive agents or are transplant recipients. They also include people living with HIV with a current CD4 cell count of <200 cells µl.

Some immunocompromised individuals have been shown in case series to have severe disseminated forms of mpox including organ involvement. The illness can be prolonged (2-3 months) (60,63). Therefore, in these patients there is less certainty about the potential for latency and the three-month time limit may not be appropriate.

Consequently, when applying these definitions to immunosuppressed patients, a more individualized approach, considering each patient's immune status, clinical presentation, and epidemiological risk factors, is recommended to assess the likelihood of reinfection or recrudescence accurately.

Definition of mpox death for surveillance purposes

A mpox death for surveillance purposes is defined as a death in a probable or confirmed mpox case unless the alternative cause of death is trauma.

In the endemic setting where access to laboratory confirmation of mpox is limited, this definition includes deaths among persons with suspected (clinically compatible) mpox, which are to be considered suspected mpox deaths. The diagnosis for mpox can also be confirmed after the death has occurred if there is sufficient lesion material to perform PCR testing. There should be no period of complete recovery between the illness and death for the death to be recorded as a mpox death.

Most persons with mpox who died have had a co-existing health condition, and mpox may not fully explain the outcome for the case. Nevertheless, for surveillance purposes, it is important to count and report all cases that die with mpox to improve understanding of the full spectrum of disease. Although some countries undertake detailed medical investigations to decide on the most likely cause of death and may not rule the case a 'mpox death', WHO reiterates the importance of reporting *all* deaths among mpox cases.

Surveillance

The key objectives of surveillance and case investigation for mpox are to rapidly identify cases and clusters of cases as well as the sources of exposure in order to: provide optimal clinical care; isolate cases to prevent further transmission; identify and monitor contacts to recognize early signs of infection; identify risk groups for infection and for severe disease; protect frontline health workers; and tailor effective control and prevention measures.

In all non-endemic countries, one case of mpox should be considered an outbreak. Because of the public health risks associated with a single case of mpox, clinicians should report suspected cases immediately to national or local public health authorities according to the case definitions above or nationally tailored case definitions, regardless of whether they are also exploring other potential diagnoses. Probable and confirmed cases of mpox should be reported to WHO

through national IHR NFPs as early as possible, at least monthly, including a minimum dataset of epidemiologically relevant information, in line with Article 6 of the International Health Regulations (IHR 2005) and the Temporary recommendations together with the extended Standing recommendations for mpox (August 2024) (2,3). Countries in Africa experiencing the upsurge of mpox cases should report to WHO the number of suspected, probable and confirmed mpox cases that meet the national or WHO case definition on a weekly basis.

Elements to consider in order to evaluate and describe an outbreak of mpox include the following:

- **Baseline number of cases**: expected average number of cases in time based on historical data.
- **Exceeding the baseline**: context-specific thresholds to define a significant exceedance
- **Localized increases**: unexpected rise in cases in a specific city, province or region.
- **Cases linked to a gathering, event or activity**: especially population movements in areas with outbreaks or gatherings with international participation or activities involving sexual contact, including use of commercial sex venues.
- **Changes in disease dynamics**: appearance of new risk factors and/or modes of transmission; a shift in the demographic distribution of reported cases; changes in the severity of disease or the case fatality.
- **Monitoring of viral evolution** to identify signatures of potential adaptation to human-to-human transmission as well as mutations that may have an impact on the effectiveness of medical countermeasures such as diagnostics, therapeutics or vaccines.
- **Vulnerability of affected population**: age, prior exposure, underlying medical conditions.
- **Public health response**: capacity to respond and contain the outbreak and prevent further spread.
- **Availability of countermeasures**: access to diagnostics, vaccines, basic clinical care, specific therapeutics.

Public health authorities and clinicians should be on alert for signals related to patients presenting with mpox. It is important to note that patients may present to various community and other health facility settings including but not limited to primary care, fever clinics, sexual health services, infectious disease units, obstetrics and gynaecology, emergency departments, and dermatology clinics. Guidance for clinical management, infection prevention and control, and the safe collection of samples for confirmatory testing should therefore be disseminated widely (28,65). In countries detecting cases of mpox, epidemiological and transmission patterns should be investigated wherever possible in order to tailor response activities.

At local and national level, countries should systematically document the number of suspected cases reported, the number of suspected cases which are tested, and the number of confirmed cases among those tested.

Indicators for monitoring the quality of mpox surveillance should be selected in accordance with the established objectives of surveillance in each context. These will likely include but not be limited to:

1. Timeliness of receipt of case reports at each administrative level.
2. Completeness of receipt of case reports at each administrative level.
3. Proportion of suspected outbreaks (alerts) investigated.
4. Proportion of suspected cases with laboratory testing performed.
5. Time from specimen collection to receipt of specimens in the laboratory.
6. Time from receipt of specimens in the laboratory to provision of results to appropriate authorities.
7. Proportion of confirmed and probable cases with complete demographic information
8. Proportion of confirmed and probable cases with complete clinical and risk factor information.
9. Proportion of suspected, probable and confirmed cases with a known epidemiological link with a previous probable or confirmed case.

For each indicator selected, a target appropriate to the context should be set and compliance against this standard monitored. These targets will complement others on preparedness and outbreak response performance to meet policy goals and document progress towards elimination of human-to-human transmission of mpox (66).

Mpox community-based surveillance

Community-based surveillance (CBS), defined as "*the systematic detection and reporting of events of public health significance within a community by community members, volunteers, or other non-professionals*", can be a critical component of the mpox outbreak response. CBS is particularly valuable in areas with limited access to healthcare services, where mpox transmission may occur in underserved populations, both in endemic and newly affected regions. CBS enhances early detection of mpox cases, reduces the time between symptom onset and linkage to health services, and supports monitoring of events or identification of potential risks within the community. CBS complements indicator-based surveillance by engaging community members in actively identifying cases or potential cases. This collaboration increases the capacity to detect diseases like mpox, especially in remote or high-risk areas.

Mpox cases identified through CBS should be considered alerts requiring investigation to validate them as suspected mpox cases. These cases must undergo further assessment and testing for confirmation. Since CBS is often conducted by non-health professionals, broad case definitions can be applied to identify alerts more effectively.

Mpox community alert definition for community-based surveillance

An individual presenting with a skin rash OR one or more sores, especially in sensitive areas, such as:

- Face, hands or feet
- Genitals or around the anus
- In or around the mouth

Rashes or sores may vary in appearance and can include spots, fluid-filled blisters, pus-filled blisters, or scabs.

To implement CBS for mpox effectively, it is crucial to engage and train community members, ensuring they are equipped to recognize and report mpox community alert to the healthcare system. CBS for mpox must be closely integrated with formal health systems for case investigation, validation, and timely response, as well as with pre-existing CBS systems monitoring other conditions. Clear communication protocols, risk communication, and data collection mechanisms are essential to ensure efficient coordination. Flexibility in adapting CBS to local contexts, adequate resources, and ongoing monitoring are key for sustainability and ensuring the system's effectiveness in identifying and managing mpox outbreaks.

Indications for mpox testing

Any individual meeting the definition for a suspected or probable case should be offered PCR testing for mpox, where resources allow. In the case of limited resources, contacts of a confirmed case that develop lesions can be considered probable cases and thus testing can be deprioritised. Testing should continue to be offered for the following groups, to prioritise depending on local epidemiology: young children (particularly those under five), those with particularly severe unusual clinical presentation of mpox, those at risk of particularly severe disease (e.g. immunocompromised, people living with HIV), those from a new geographical area or area not currently under surveillance, those with no epidemiological link to other confirmed cases and health care workers (65).

In the absence of skin or mucosal lesions, PCR can be done on an oropharyngeal swab; anal or rectal swab can be done in case of exposure history. However, such specimen types may provide less sensitive results and the interpretation of their results requires caution: while a positive result of an oropharyngeal, anal or rectal swab is indicative of mpox, a negative result is not enough to exclude MPXV infection. PCR testing of blood is not recommended for surveillance and diagnosis of mpox, as MPXV viremia is likely to occur early in the course of infection and has a short duration, thus false negative test results are to be expected (65). Blood specimens are generally not useful for diagnosis of acute illness unless this is taken to rule out other infections.

Due to the range of conditions that cause skin and mucosal rashes, it can be challenging to differentiate mpox solely based on the skin and mucosal clinical presentation, particularly in the early stages of rash, for cases with an atypical

presentation, or for cases linked to sexual transmission which may not match classic descriptions of mpox rash. The decision to test should be based on clinical and epidemiological factors, linked to assessing the likelihood of infection. When clinical suspicion for mpox is high due to history, clinical presentation and/or atypical response to syndromic management of sexually transmitted infections, the identification of an alternate pathogen that causes rash illness should not preclude testing for mpox, as coinfections have been identified. Given the epidemiological characteristics observed in mpox outbreaks, criteria such as having had contact with a person with mpox, being a health worker, being a man who has sex with men, being a sex worker or otherwise reporting having multiple sex partners in the previous three weeks, can all be suggestive of the need to test for mpox.

Where children or adolescents may be at risk of mpox infection, particularly but not exclusively in areas where mpox is endemic and continues to occur, or areas newly affected where cases occur among children, the differential diagnosis for rash and fever illness should include mpox and investigation should be initiated. For countries with animal-to-human transmission, epidemiological criteria to test for mpox include known or presumed contact with wild animals (dead or alive) and/or contact with sick animals in the 21 days before the onset of symptoms.

For study purposes, countries can retrospectively expand their testing to residuals of specimens collected from patients presenting for sexually transmitted infection (STI) screening and/or with symptoms suggestive of mpox. Prospectively, STI testing (e.g. HIV, syphilis) of patients positive for Mpox is recommended (65).

Serological tests for OPXV antibodies can be appropriately used in an outbreak investigation or research setting but their results are to be interpreted with caution, since they most often cannot distinguish between immunity due to mpox or another orthopoxvirus-related infection or immunity generated by prior smallpox or mpox vaccination. WHO recommends that serology testing should be restricted to reference laboratories for research use until further evidence is available.

For detailed laboratory guidance on differential diagnosis of mpox cases and testing strategies in different settings, please refer to the latest WHO interim guidance on Guidance on Diagnostic testing and testing strategies for mpox (8).

Reporting

WHO has updated and re-published the mpox Case Reporting Form (CRF)(6) which constitutes the minimum data countries are requested to report to the respective WHO Regional Office, and includes the following information:

- Record ID
- Reporting Country
- Date of notification
- Case classification
- Age, sex, gender, sexual behavior
- Occupation, sex worker, health worker
- Living in an internally displaced people's (IDP) or refugee camp
- Medical history (pregnancy, immunosuppression, HIV status, previous mpox infection)
- Vaccination history (smallpox and mpox)
- Clinical signs or symptoms
- Date of onset of first symptoms
- Hospital admission
- Intensive care unit (ICU) admission
- Complications
- Epidemiological link with a known mpox case (in the 21 days before onset of illness)
- Recent travel history (in the 21 days before onset of illness)
- Contact with animals (in the 21 days before onset of illness)

- Mode of transmission
- Collected sample
- Diagnostic test performed
- Clade and genomic characterization (if available)
- Outcome status at time of reporting

The number of variables to report to WHO has been expanded in order to better describe the new outbreaks caused by clade Ib, as outlined in PHEIC temporary recommendations (4).

Case investigation

Close physical contact, including sexual contact, with a person who has mpox or may have mpox during the infectious period of the latter, is the most significant risk factor for MPXV infection. If mpox is suspected, the investigation should consist of:

(i) clinical examination of the patient, using appropriate infection prevention and control (IPC) measures as reported in the specific guidance (28).

(ii) enquiring about possible sources of exposure and the presence of similar illnesses among the patient's contacts or in their community prior to diagnosis of mpox, to identify the source (backward contact tracing).

(iii) Identifying all possible individuals with whom the suspected case had contact from the beginning of symptoms until all lesions are healed, to put in place control measures and reduce onward transmission (forward contact tracing).

(iv) safe collection and dispatch of specimens for mpox diagnostic testing and laboratory examination (8).

In addition to the minimum dataset (CRF), WHO has published the mpox Case investigation form (CIF) (6) designed as a tool for Member States and researchers to conduct in-depth epidemiological investigation of suspected, probable and confirmed cases of mpox, as well as their contacts, either prospectively or retrospectively. The full form is meant for in-country use and the data are not required to be reported to WHO.

Exposure investigation should cover the period of 21 days prior to symptom onset. Laboratory confirmation of suspected cases is important but should not delay implementation of public health actions.

Cases found by retrospective active search may no longer have the clinical symptoms of mpox (i.e., they have recovered from acute illness) but may exhibit marks on the skin such as depigmentation or scarring or other sequelae. A contact identified retrospectively who exhibits signs or reports a history compatible with mpox and otherwise meets the case definition can be classified as a probable case. It is important to collect epidemiological information and where feasible identify other contacts for retrospectively identified cases in addition to active ones. Retrospective cases cannot be laboratory confirmed; however, in the context of special studies, serum from retrospectively identified cases can be collected and tested for OPXV IgM and/or IgG antibodies to assess exposure or immunity or aid in their classification as a probable case if necessary. Please refer to the WHO guidance on testing for MPXV for more details on serology testing (65).

Samples taken from persons with suspected mpox should be safely handled by trained staff working in suitably equipped laboratories. National and international regulations on transport of infectious substances should be strictly followed during sample packaging and transportation. Careful planning is required to consider national laboratory testing capacity. Clinical laboratories should be informed, in advance, of samples to be submitted from persons with suspected or confirmed mpox, so that they can minimise risk to laboratory workers and, where appropriate, safely perform laboratory tests that are essential for clinical care. For more details, please refer to the WHO interim guidance on laboratory testing for MPXV (65).

Any patient with suspected mpox should be isolated during the presumed and known infectious periods, that is during the prodromal and rash stages of the illness, respectively.

Investigating exposure to an infected animal

The monkeypox virus was first identified in 1958 in non-human primates (67) (now known to be susceptible as a spillover host), and cases of human mpox have been described in the Democratic Republic of the Congo since 1970 (68). Although recent mpox outbreaks have been characterized by extensive human-to-human transmission, in countries where MPXV is endemic in wildlife population, the proportion of human cases that can be attributed to zoonotic transmission is unknown, but likely to play an important role in mpox outbreaks (47).

Routes of infection include direct contact with an infected animal (cuddling, bites, scratches, etc.), their body fluids, or potentially their faeces. Mpox might also be contracted through handling, preparation or consumption of insufficiently processed products (e.g., meat, hides) from wild animals. MPXV infection has been reported in a wide range of mammal species such as monkeys, squirrels, dormice, and pouched rats; most of these were sampled in captive animals. Neither the animal reservoir(s), which maintain the virus in nature, nor the full range of potential intermediate animal hosts, which could play a role in animal-to-human transmission, are known. Therefore, it is critical to investigate human cases for potential exposure to MPXV-infected animals, to conduct animal investigations to prevent further introductions of the virus into the human population, and to provide useful insights to reduce future spillover risks. Further investigations and studies are needed to understand the relative proportion (compared to human-to-human transmission) and risk factors for zoonotic transmission. Investigations and studies involving animals should always be performed jointly with the animal health sector.

When human exposure to an infected animal or animal products is suspected, it is important to collect information during the case investigation on the animal species (preferably the exact species, for example by using species keys or collecting samples for DNA barcoding) with which the case came into contact, the time and place of the contact, the types and frequency of contact, information on whether the animal was caught alive or found dead, and whether the animal presented any signs of illness (6). Investigations regarding animal exposures are difficult because of the high frequency of animal-human contact in endemic areas, and because of several weeks passing between exposure and investigations (due to the incubation period and delays in identification and notification). For this reason, exposure investigations should be conducted as soon as possible after a case has been identified.

WHO has included a specific section on animal exposure on the mpox CIF (6). The standardized data collection for animal exposure will allow animal and health authorities to more easily compile and compare this information in order to better quantify animal exposure risk. This is particularly important for countries in East, Central and West Africa, and will also be useful for any situation or context in which zoonotic transmission or exposure to infected animals is considered a possibility.

Should exposure through an animal be the most likely route of transmission, and should the suspected animal, parts of the animal or animals held /living in close proximity still be available, adequate samples should be collected by a professional trained for sampling animals (e.g., wildlife biologists, lab technicians, or wildlife veterinarians).

In areas with no known viral circulation in animals, human infection presents a risk of spillback transmission (also known as reverse zoonosis), which involves transmission of a pathogen from humans to animals (including pets, wildlife, and peridomestic species) (69). Spillback transmission might lead to the establishment of new reservoir host populations, making the virus endemic to these regions. In such a situation, prevention and control of the global health emergency will be complicated, both for humans and animals, because the disease will become established in the region. Monkeypox virus could be spread from humans to animals via direct (e.g., hugging pets) or indirect contact (e.g., a rodent coming into contact with soiled bedsheets). In addition to posing a public health threat, introduction of monkeypox virus in a naïve animal population could pose a threat to local biodiversity, for example in endangered

great apes. Aside from preventing contact between animals and infectious humans (or contaminated materials such as sheets and linens), Member States should consider environmental and animal surveillance in areas where contaminated materials are not being properly disposed of.

Contact tracing

Contact tracing is a key public health measure to control the spread of infectious pathogens such as MPXV. It allows to identify individual exposed to mpox, monitor their health status, implement infection prevention measures and detect early infection in order to interrupt chains of transmission. Where vaccination is available, it also allows to identify individuals that can be targeting for post exposure prophylaxis.

Mpox cases should be interviewed as soon as possible to elicit the names and contact information of all potential contacts and identify events, gatherings, venues or places visited where contact with other people may have occurred. Contacts of cases should be notified within 24 hours of identification and advised to monitor their health status and seek medical care if they develop symptoms.

In the current context, as soon as a suspected case is identified, contact identification and contact tracing should be initiated, while further investigation of the source case is ongoing to determine if the case can be classified as probable or confirmed; in the event that a case is classified as discarded (i.e., no longer considered a suspected or probable case), contact tracing may be adapted to the new circumstances (e.g. for contact notification for another sexually transmitted infection) or stopped if no longer required.

Definition of a contact

A contact is defined as a person who has been exposed to a suspected, probable or confirmed mpox case during the infectious period of the latter. Exposure can happen through:

1. **Direct contact**
    - skin-to-skin, skin-to-mucosal or mouth-to-mucosal physical contact
    - Examples: touching, hugging, kissing, intimate oral or other sexual contact
2. **Indirect contact**
    - contact with items contaminated by the case, such as clothing or bedding
    - This includes handling contaminated materials like laundry and cleaning rooms
3. **Non-physical contact**
    - close and prolonged conversation with a symptomatic mpox case, especially if they have visible mpox ulcers
    - talking near such a person increases the risk of exposure to infectious respiratory particles (IRP) expelled through the mouth
4. **Mother-to-child contact (vertical transmission)**
    - Transmission can occur during pregnancy through the placenta or during delivery

The above also apply for health workers potentially exposed in the absence of proper use of appropriate personal protective equipment (PPE) (28).

Household members living with a mpox case may present multiple potential exposures (direct, indirect, non-physical).

The infectious period for mpox is the period beginning with the onset of the index case's first symptoms, or if relevant up to two days before the onset, and ending when their skin lesions have crusted, the scabs have fallen off and a fresh layer of skin has formed underneath. In the absence of symptoms, a person with a positive PCR test for mpox, for example from an oropharyngeal or anal swab, should also be considered a confirmed case and infectious and contact-tracing should be initiated as outlined here.

Contact identification and notification

Once an mpox case has been detected, they can be prompted to identify contacts across several contexts, including household, sexual contacts, workplace, school/nursery, healthcare (including laboratory exposure), houses of worship, social gatherings, prison, refugee camps, festivals, personal service settings (tattoo or massaging parlours), and any other recalled events, locations or interactions. Attendance lists, passenger manifests, or other methods such as web or mobile applications can be used to identify contacts at events, gatherings, during travel or on conveyances such as flights or cruise ships.

Any patient or other person exposed to contaminated materials from a patient/person with mpox in the health care or other congregate setting or venue should be considered a contact even in the absence of direct contact with the case.
In settings where zoonotic transmission occurs, community contacts for point source exposure may include other persons hunting, selling, handling, preparing or consuming the bushmeat meal at the same time.

Individuals may be reluctant or unable to provide contact information for all contacts, especially for sexual contacts. To overcome this challenge, public health authorities conducting contact tracing should encourage cases to directly notify their contacts and provide them with advice on how best to do this. Research in sexually transmitted infections has shown that activities such as partner notification, i.e., voluntarily notifying a partner that they have been exposed to an infection, can yield good contact tracing results (70). Cases should be offered adequate counselling on how to notify their contact, the recommendations for the contact's movement and activities, and referral information about health providers who can support the contact with information, or in case of symptoms, with health services. If possible, all information should also be provided in written form (e.g., leaflets, cards, links to webpages, or QR codes) to avoid misinterpretation.

Organizers of events or managers of venues or community settings from which mpox cases have been identified and for which direct contact occurs frequently, may also be involved in contact notification. Examples for such venues are saunas, bathhouses, nightclubs, cruise ships, commercial sex venues or personal service settings such as tattoo or massage parlours. If a confirmed mpox case reports having attended an event or a venue where close physical contact took place during the infectious period, but is unable to identify all possible contacts, public health authorities should liaise with the event organizers to send a general notification to all participants about the potential risk of exposure. Also, in this case all relevant information about mpox, including referral to health services in case of relevant symptoms, should be provided together with the notification.

Summarizing, once contacts have been identified, they should be informed of their exposure, their risk of developing infection, the symptoms of mpox, when symptoms may appear and testing options.

Contact monitoring

The objective of health monitoring for contacts is to identify and diagnose the illness of a contact person as early as possible in order to receive treatment and put in place measures to prevent further spread.

Contacts should be monitored, or should self-monitor, daily for the onset of signs or symptoms for a period of 21 days from the last contact with the mpox case or their contaminated materials (or up to two days before the onset of symptoms if feasible and appropriate). Signs and symptoms of concern include headache, fever, chills, sore throat, myalgia, malaise, fatigue, rash, and lymphadenopathy. Contacts should monitor their temperature twice daily irrespective of symptoms.

Options for monitoring by public health authorities are dependent on available resources. Health monitoring of contacts can be passive, active, or direct. In passive monitoring, the identified contact is provided with information on mpox sing and symptoms to monitor, and they themselves or a care giver (e.g. parents) checks on a daily basis and contact public health authorities if signs or symptoms develop. Active monitoring involves dedicated and trained public

health officials that actively reached out to the contact person (e.g. once a day) whether such signs or symptoms have appeared. Direct monitoring is a variation of active monitoring in which dedicated personnel examines the presence or absence of indicative signs and symptoms either personal visit and examination or via video call. Combinations of the three approaches are also possible.

Measures for mpox contacts

During the 21-days after last contact, contact persons should:

- Regularly practice hand hygiene and respiratory etiquette.
- Avoid sexual contact
- Avoid physical contact with persons who are immunocompromised or pregnant.
- Minimize close contact with children, while keeping the overall health and wellbeing of children as the primary consideration and avoid contact if any symptom appears.
- Avoid contact with animals, including pets.
- As a precautionary measure, should not donate blood, cells, tissue, organs, breast milk, or semen.

Asymptomatic contacts who adequately and regularly monitor their status can continue routine daily activities such as going to work and attending school (i.e., no quarantine is necessary).

Management of symptomatic contacts who become cases

A contact who develops prodromal symptoms or lymphadenopathy should be isolated and closely examined as a suspected case for signs of rash. In absence of skin or mucosal lesions, PCR can be done on an oropharyngeal, anal or rectal swab. However, the interpretation of results from oropharyngeal, anal or rectal swabs requires caution; while a positive result is indicative of mpox, a negative result is not enough to exclude infection. A contact with a positive PCR test from an oropharyngeal, anal or rectal swab is to be considered a confirmed case, while if it is negative the contact needs to actively monitor for signs of rash for the next five days.

A contact who develops skin or mucosal lesions should be isolated and evaluated as a probable case, and a specimen from the lesions should be collected for laboratory analysis to test for mpox. If no rash develops, the contact can return to temperature monitoring for the remainder of the 21 days.

The following individuals should consider avoiding undertaking any travel, including international travel, until they are determined to no longer constitute a public health risk for others: any individual with signs and symptoms compatible with MPXV infection; anyone being considered as a suspected, probable, or confirmed case of mpox by jurisdictional health authorities; anyone who has been identified as a contact of a mpox case and, therefore, is subject to health monitoring. Exemptions include any individual who needs to undertake travel to seek urgent medical care or flee from life-threatening situations, such as conflict or natural disasters; and contacts for whom pre-departure arrangements to ensure the continuity of health monitoring are agreed upon by sub-national health authorities concerned, or, in the case of international travel, by national health authorities. Cross-border workers who are identified as contacts of a mpox case can continue their routine daily activities provided that health monitoring is duly coordinated by the jurisdictional health authorities from both/all sides of the border (71).

Monitoring exposed health workers

In order to avoid transmission in the health care or other congregate setting, it is critically important to ensure that infection prevention and control measures be in place (28). Any health worker who has cared for a person with probable or confirmed mpox or worked with a relevant laboratory specimen should be alert to the development of symptoms that could suggest mpox, especially within the 21-day period after the last date of contact, if there has been a known or suspected breach in IPC precautions. WHO recommends that any health worker with an occupational exposure to an mpox case or MPXV should notify infection control, occupational health, and public health authorities to receive an assessment and develop a management plan for the exposure and potential infection (28).

Health workers who have occupational exposure to patients with mpox or possibly contaminated materials (such as by a needlestick or other percutaneous sharps injury, fomites or contact with a case while not wearing appropriate PPE or a breach of PPE) should follow national infection control guidance. Such contacts do not need to be excluded from work duty if asymptomatic, but should actively monitor for symptoms, for 21 days following the exposure; conversely, they should not work with vulnerable patients during this period. Prior to reporting for work each day, the health worker should be interviewed regarding evidence of any relevant signs or symptoms as above.

Where vaccines are available, post-exposure vaccination within four days of exposure (or up to 14 days in the absence of symptoms) is recommended for health workers, including laboratory personnel, who come in contact with a case or potentially infectious material without use of appropriate PPE. For more details on vaccines and immunization for mpox, please consult the specific guidance (72).

Travel-related contact tracing

Public health officials should work with transportation authorities, conveyance and points of entry operators, and other national health authorities to facilitate international contact tracing, when required, during travel or upon return, in order to assess potential risk of exposure and to identify contacts (passengers and others) who may have had exposure to a case while travelling. If a probable or confirmed case is identified on board a conveyance, point of entry and conveyance operators should follow the advice provided by public health authorities. A case-by-case, context-specific risk assessment should be conducted taking into consideration the specific characteristics accordingly to the type of travel, point of entry (airport, port or ground crossing) and conveyance (such as aircraft, ship, train or truck), as well as evidence on the modes of transmission of the virus.

In the context of air travel, the Passenger Health Locator Form should be used (73). If a suspect or confirmed case is identified on board an aircraft, the guidelines of the International Air Transport Association (IATA) for cabin crew on a suspected communicable disease can be used (74). These state that travellers seated in the same row, two rows in front and two rows behind the sick traveller, as well as the cabin crew who served the case, should be contacted to assess the risk of exposure and monitoring requirements. Nonetheless, in the context of mpox, a case-by-case risk assessment should be conducted taking into account the evidence on modes of transmission. Any passenger or crew team member who did not report physical contact with a symptomatic case and was not seated in the aforementioned rows should not be considered a mpox contact.

For themed events or gatherings such as cruises with many passengers on board and where they have frequent close physical contact including sexual contact, and social interactions in spaces here predetermined seats may not be assigned, it may be difficult to identify contacts of a case identified on board, as many people may have been exposed. If a person with mpox reports having attended an event or a venue where close physical contact took place during the infectious period, but is unable to identify all possible contacts, public health authorities should liaise with the event organizers or cruise operators to send a general notification to all participants about the risk of possible exposure. The detected cases should be encouraged to inform directly their close and sexual contacts considering the cases may not be willing to share contact details of their close contacts in particular sexual contacts.

In specific settings such as travel by river boat with many passengers on board or in and around ground crossings bordering countries experiencing an upsurge in cases of mpox, there may be an additional risk of exposure to MPXV through sale, preparation and consumption of bushmeat. Wherever there is a high risk of transmission of mpox to travellers, organizers or point of entry authorities may consider applying risk-based screening measures for mpox, such as administering a short health questionnaire, and providing further information on mpox to passengers before they disembark. All relevant information about mpox, including referral to health care, should be provided together with the notification. Given the lack of scientific evidence available on the effectiveness of syndromic entry and exit screening for epidemic-prone diseases, data on the effectiveness, cost-effectiveness and impact of such measures should be collected to the extent possible (75).

More specific evaluations for each scenario need to be assessed on a case-by-case basis by national and local health authorities.

Monitoring and evaluation of contact tracing quality

Indicators for monitoring the quality of mpox contact tracing include:

1. Proportion of mpox cases with identified contacts
2. Average number of contacts reported per mpox case
3. Proportion of identified contacts with complete monitoring information
4. Proportion of cases coming from a contact tracing list.

For each indicator selected, a target appropriate to the context should be set and compliance against this standard monitored.

Wastewater and environmental surveillance for mpox

Wastewater and environmental surveillance (WES) has been shown to assist in public health decision-making for a number of public health threats – most notably for polio, typhoid, COVID-19 and antimicrobial resistance (76). WES provides cost-effective, geographic and population-level data that are useful when they reveal information not available from clinical data when testing and treatment services are not available, or are not accessed by symptomatic individuals, and/or individuals are asymptomatic or presymptomatic (77). Further WES may provide more timely data ahead of clinical reports. As such it may provide early warning of emergence, re-emergence. Additionally, genomic analysis may be used cost-effectively to identify which subclades are present, similar to the WES application for SARS-CoV-2 variants. Banking of samples allows retrospective analysis to be performed (77). Information from WES can be integrated into geographically targeted risk communication for communities.

Monkeypox viral DNA has been detected in urine, faeces, saliva, skin and mucosal lesions as well as semen samples of confirmed mpox cases in different countries, including in discarded condoms (33,78–80). Live (replication competent) MPXV has been isolated from skin and mucosal lesions, semen, genital and rectal swabs. The concentration and persistence of virus or viral DNA shedding from the different sites vary based on the duration of the infection, and although no clear description of these dynamics is currently available, studies show that viral shedding can occur in the absence of symptoms and last up to 16 days from onset of symptoms (33).

The virus present in mucosal and skin lesions can be released into wastewater during teeth brushing, hand washing, showers or baths, and from urine and faeces via toilets. Since the start of the multi-country outbreak in 2022, several countries integrated MPXV DNA monitoring as part of multi-target wastewater surveillance programs (81) and results have been reported from multiple countries demonstrating its technical and operational feasibility to detect presence of cases complementing case-based surveillance (82). An analysis of empirical data from the large national program in the United States of America estimated a weekly sensitivity of 32%, 49% and 77% for detecting respectively 1, 5 and 15 mpox cases in wastewater samples that represent thousands to millions of persons with high positive and negative predictive values (62 and 80% respectively) (83). A modelling study estimated that wastewater surveillance could feasibly detect seven infections out of 100 000 people at US wastewater treatment plants(84). To date, most evidence is derived from clade IIb and in sewered settings. Studies in South-East Asia in non-sewered settings demonstrated wastewater mpox detection in the absence of reported clinical cases (85).

While replication competent MPXV has been shown to persist in wastewater (83), there is no known case of mpox contracted from contact with contaminated wastewater, standard precautions for handling wastewater are recommended including the use of personal protective equipment.

WES could be a complementary monitoring approach to strengthen surveillance which are contextually relevant, such as early detection of mpox or new clade incursion, the extent of geographic spread and/or identification of circulating clades. Further analysis of MPXV DNA data obtained from wastewater monitoring in relation to local epidemiological reports is needed to further validate the routine use of wastewater and environmental surveillance for mpox for clade I in both sewered and non-sewered settings (81). Additionally, where mpox vaccination is underway with vaccinia virus

vaccines, as well as in areas with zoonotic OPXV, selecting MPXV-specific PCR assays rather than generic OPXV assays would be essential.

WHO encourages countries to support research to clarify possible objectives, approaches, methods, and challenges for wastewater and environmental surveillance for mpox in different contexts. WHO also encourages innovative approaches to environmental surveillance which may be particularly useful in large cities, in specific work settings where population movements are significant, or locations where surveillance may be suboptimal, or contacts cannot be traced. Respect for dignity and human rights must always be foundational for any approach considered.

If WES is implemented, indicators for monitoring should be identified and may include aspects such as sampling coverage, completeness and timeliness, laboratory quality control measures, and timeliness of reporting results with health authority.

Data collection and sharing

In order to facilitate data collection following the updated requested minimum dataset of the case reporting form, WHO has prepared a macro-enabled Microsoft Excel form (CRF data collection tool) is available on the webpage; however, any reporting format agreed with the respective Regional Office may be used.

WHO has also implemented the in-depth case investigation form in the Go.Data platform (86) to facilitate local capture, analysis, and/or sharing of the relevant data. Countries that are using Go.Data can upload the mpox CIF and directly use it to collect case-based data for their mpox cases. The Go.Data mpox outbreak template and associated metadata description can be obtained upon request by emailing godata@who.int, and technical support for implementation is available from WHO.

Analysis of transmission chains and network visualization have been used in past outbreaks to identify clusters, understand patterns of exposure, and quantify viral transmission across different settings. In the context of the multi-country mpox outbreak, understanding patterns of transmission has been critical to finding effective control measures and will allow for further characterization of modes of transmission including, in future, determining where multiple introductions (human or zoonotic) continue to occur.

Data collected in a harmonized way through the WHO case investigation form (6) can also be collated across multiple countries in a collaborative effort, increasing the sample size and allowing for more robust analyses.

WHO will use case-based surveillance data only in aggregate and only for its own products, including external peer reviewed publications, to better understand and explain the epidemiology of the mpox outbreak for the benefit of all countries. Data will not be shared with external third parties. Any subnational analysis presented in WHO external products will be agreed with the country.

Methods

The recommendations in this guidance are based on the inputs of expert contributors (see below) and a literature search conducted by WHO, focusing on case definitions, transmission routes, contact tracing and mpox epidemiology, as well as guidance previously developed for other mpox outbreaks. WHO also monitors established and emerging literature about MPXV clade distribution, animal infections, human reinfections and use of wastewater surveillance for mpox.

Plans for updating

WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any important factors change, WHO will issue a further update. Otherwise, this interim guidance will expire one year after the date of publication.

Acknowledgments

The initial version of this guidance was developed through the contributions of an expert group from the WHO secretariat in headquarters and regional offices, in consultation with the Strategic and Technical Advisory Group on Infectious Hazards (STAG-IH) and clinical and laboratory experts in Portugal, Spain, Sweden, the United Kingdom, and the United States of America. Additional contributions have been provided by colleagues from the United States Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC). Updates have been developed with contributions from experts working in the mpox Incident Management Team for WHO headquarters and WHO regional offices, experts from the Africa Centres for Disease Control and Prevention (CDC), the United States Centers for Disease Control and Prevention (CDC), the European Centre for Disease Prevention and Control (ECDC), the United Kingdom, the World Animal Health Organization (WOAH) and Food and Agriculture Organization (FAO); and continues to be informed by other interim guidance published and updated by WHO for this response

References

1. World Health Organization (WHO). WHO Director-General declares mpox outbreak a public health emergency of international concern [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.who.int/news/item/14-08-2024-who-director-general-declares-mpox-outbreak-a-public-health-emergency-of-international-concern
2. World Health Organization (WHO). Extension of the standing recommendations for mpox issued by the Director-General of the World health organization (WHO) in accordance with the International Health Regulations (2005) (IHR) [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.who.int/publications/m/item/extension-of-the-standing-recommendations-for-mpox-issued-by-the-DG-of-the-WHO-in-accordance-with-the-IHR-2005-21082024
3. World Health Organization (WHO). Standing recommendations for mpox issued by the Director-General of the World Health Organization (WHO) in accordance with the International Health Regulations (2005) (IHR) [Internet]. 2023 [cited 2023 Dec 27]. Available from: https://www.who.int/publications/m/item/standing-recommendations-for-mpox-issued-by-the-director-general-of-the-world-health-organization-(who)-in-accordance-with-the-international-health-regulations-(2005)-(ihr)
4. World Health Organization (WHO). First meeting of the International Health Regulations (2005) Emergency Committee regarding the upsurge of mpox 2024 [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.who.int/news/item/19-08-2024-first-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-upsurge-of-mpox-2024
5. World Health Organization (WHO). Mpox fact-sheet [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.who.int/news-room/fact-sheets/detail/mpox
6. World Health Organization (WHO). Mpox Case Investigation Form (CIF) and minimum dataset Case Reporting Form (CRF) [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.who.int/publications/m/item/monkeypox-minimum-dataset-case-reporting-form-(crf)
7. World Health Organization (WHO). 2022-24 Mpox (Monkeypox) Outbreak: Global Trends [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://worldhealthorg.shinyapps.io/mpx_global/
8. World Health Organization (WHO). Diagnostic testing for the monkeypox virus (MPXV): interim guidance, 10 May 2024 [Internet]. 2024 [cited 2024 Jul 4]. Available from: https://www.who.int/publications/i/item/WHO-MPX-Laboratory-2024.1
9. World Health Organization (WHO). Global technical consultation report on proposed terminology for pathogens that transmit through the air [Internet]. 2024 [cited 2024 Oct 11]. Available from: https://www.who.int/publications/m/item/global-technical-consultation-report-on-proposed-terminology-for-pathogens-that-transmit-through-the-air
10. World Health Organization (WHO). Mpox [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.who.int/health-topics/mpox#tab=tab_1
11. World Health Organization. Monkeypox: experts give virus variants new names [Internet]. 2022 [cited 2023 Feb 16]. Available from: https://www.who.int/news/item/12-08-2022-monkeypox--experts-give-virus-variants-new-names
12. World Health Organization (WHO). Disease Outbreak News - Mpox (monkeypox)- Democratic Republic of the Congo [Internet]. 2023 [cited 2024 Jan 8]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON493
13. World Health Organization (WHO), Government of the Democratic Republic of the Congo. La variole simienne (monkeypox) en République démocratique du Congo: Évaluation de la situation Rapport de mission conjointe (22 novembre – 12 décembre 2023) - Democratic Republic of the Congo | ReliefWeb [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://reliefweb.int/report/democratic-republic-congo/la-variole-simienne-monkeypox-en-republique-democratique-du-congo-evaluation-de-la-situation-rapport-de-mission-conjointe-22-novembre-12-decembre-2023

14. World Health Organization (WHO). Disease Outbreak News - Mpox - Democratic Republic of the Congo [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON522
15. Masirika LM, Udahemuka JC, Schuele L, Ndishimye P, Otani S, Mbiribindi JB, et al. Ongoing mpox outbreak in Kamituga, South Kivu province, associated with monkeypox virus of a novel Clade I sub-lineage, Democratic Republic of the Congo, 2024. Eurosurveillance [Internet]. 2024 Mar 14 [cited 2024 Jul 1];29(11):2400106. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2024.29.11.2400106
16. Masirika LM, Kumar A, Dutt M, Ostadgavahi AT, Hewins B, Nadine MB, et al. Complete Genome Sequencing, Annotation, and Mutational Profiling of the Novel Clade I Human Mpox Virus, Kamituga Strain. J Infect Dev Ctries [Internet]. 2024 Apr 1 [cited 2024 Sep 29];18(4):600–8. Available from: https://pubmed.ncbi.nlm.nih.gov/38728644/
17. Vakaniaki EH, Kacita C, Kinganda-Lusamaki E, O'Toole Á, Wawina-Bokalanga T, Mukadi-Bamuleka D, et al. Sustained Human Outbreak of a New MPXV Clade I Lineage in the Eastern Democratic Republic of the Congo. Nature Medicine 2024 [Internet]. 2024 Jun 13 [cited 2024 Jul 1];1–1. Available from: https://www.nature.com/articles/s41591-024-03130-3
18. Ponce L, Linton NM, Toh WH, Cheng HY, Thompson RN, Akhmetzhanov AR, et al. Incubation Period and Serial Interval of Mpox in 2022 Global Outbreak Compared with Historical Estimates - Volume 30, Number 6—June 2024 - Emerging Infectious Diseases journal - CDC. Emerg Infect Dis [Internet]. 2024 Jun 1 [cited 2024 Sep 9];30(6). Available from: https://wwwnc.cdc.gov/eid/article/30/6/23-1095_article
19. Kröger ST, Lehmann MC, Treutlein M, Fiethe A, Kossow A, Küfer-Weiß A, et al. Monkeypox outbreak 2022–an overview of all cases reported to the Cologne Health Department. 2022;
20. Guzzetta G, Mammone A, Ferraro F, Caraglia A, Rapiti A, Marziano V, et al. Early Estimates of Monkeypox Incubation Period, Generation Time, and Reproduction Number, Italy, May-June 2022. Emerg Infect Dis. 2022;28(10).
21. Madewell ZJ, Charniga K, Masters NB, Asher J, Fahrenwald L, Still W, et al. Serial Interval and Incubation Period Estimates of Monkeypox Virus Infection in 12 Jurisdictions, United States, May–August 2022 - Volume 29, Number 4—April 2023 - Emerging Infectious Diseases journal - CDC. Emerg Infect Dis [Internet]. 2023 Apr 1 [cited 2024 Sep 29];29(4):818–21. Available from: https://wwwnc.cdc.gov/eid/article/29/4/22-1622_article
22. Tarín-Vicente EJ, Alemany A, Agud-Dios M, Ubals M, Suñer C, Antón A, et al. Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study. Lancet [Internet]. 2022 Aug 8 [cited 2022 Aug 17];0(0). Available from: http://www.ncbi.nlm.nih.gov/pubmed/35952705
23. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox Virus Infection in Humans across 16 Countries - April-June 2022. N Engl J Med [Internet]. 2022 Jul 21 [cited 2022 Aug 17]; Available from: http://www.ncbi.nlm.nih.gov/pubmed/35866746
24. Miura F, Backer JA, van Rijckevorsel G, Bavalia R, Raven S, Petrignani M, et al. Time Scales of Human Mpox Transmission in The Netherlands. J Infect Dis [Internet]. 2024 Mar 14 [cited 2024 Sep 29];229(3):800–4. Available from: https://dx.doi.org/10.1093/infdis/jiad091
25. Ward T, Christie R, Paton RS, Cumming F, Overton CE. Transmission dynamics of monkeypox in the United Kingdom: contact tracing study. BMJ [Internet]. 2022 Nov 2 [cited 2022 Dec 14];379:e073153. Available from: https://www.bmj.com/content/379/bmj-2022-073153
26. Brosius I, Dijck C Van, Coppens J, Vandenhove L, Bangwen E, Vanroye F, et al. Presymptomatic viral shedding in high-risk mpox contacts: A prospective cohort study. J Med Virol [Internet]. 2023 May 1 [cited 2024 Feb 8];95(5):e28769. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.28769
27. Ferré VM, Bachelard A, Zaidi M, Armand-Lefevre L, Descamps D, Charpentier C, et al. Detection of Monkeypox Virus in Anorectal Swabs From Asymptomatic Men Who Have Sex With Men in a Sexually Transmitted Infection Screening Program in Paris, France. Ann Intern Med [Internet]. 2022 Oct 1 [cited 2024 Jul 4];175(10):1491–2. Available from: https://pubmed.ncbi.nlm.nih.gov/35969863/

28. World Health Organization (WHO). Clinical management and infection prevention and control for monkeypox: Interim rapid response guidance, 10 June 2022 [Internet]. 2022 [cited 2022 Jun 21]. Available from: https://www.who.int/publications/i/item/WHO-MPX-Clinical-and-IPC-2022.1
29. Mbala PK, Huggins JW, Riu-Rovira T, Ahuka SM, Mulembakani P, Rimoin AW, et al. Maternal and Fetal Outcomes Among Pregnant Women With Human Monkeypox Infection in the Democratic Republic of Congo. J Infect Dis [Internet]. 2017 Nov 1 [cited 2022 Jun 22];216(7):824–8. Available from: https://pubmed.ncbi.nlm.nih.gov/29029147/
30. Murhula Masirika L, Claude Udahemuka J, Schuele L, Nieuwenhuijse DF, Ndishimye P, Boter M, et al. Mapping and sequencing of cases from an ongoing outbreak of Clade Ib monkeypox virus in South Kivu, Eastern Democratic Republic of the Congo between September 2023 to June 2024. medRxiv [Internet]. 2024 Sep 19 [cited 2024 Sep 29];2024.09.18.24313835. Available from: https://www.medrxiv.org/content/10.1101/2024.09.18.24313835v1
31. Antinori A, Mazzotta V, Vita S, Carletti F, Tacconi D, Lapini LE, et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill [Internet]. 2022 Jun 2 [cited 2022 Jun 22];27(22):2200421. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35656836
32. Noe S, Zange S, Seilmaier M, Antwerpen MH, Fenzi T, Schneider J, et al. Clinical and virological features of rst human Monkeypox cases in Germany. [cited 2022 Jun 23]; Available from: https://doi.org/10.21203/rs.3.rs-1725831/v1
33. Peiró-Mestres A, Fuertes I, Camprubí-Ferrer D, Marcos MÁ, Vilella A, Navarro M, et al. Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022. Euro Surveill [Internet]. 2022 Jul 14 [cited 2022 Aug 17];27(28):2200503. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35837964
34. Brosius I, Dijck C van, Coppens J, Vandenhove L, Bangwen E, Vanroye F, et al. Pre- and asymptomatic viral shedding in high-risk contacts of monkeypox cases: a prospective cohort study. medRxiv [Internet]. 2022 Nov 27 [cited 2022 Dec 14];2022.11.23.22282505. Available from: https://www.medrxiv.org/content/10.1101/2022.11.23.22282505v1
35. Laurenson-Schafer H, Sklenovská N, Hoxha A, et al. Description of the first global outbreak of mpox: an analysis of global surveillance data. Lancet Global Health 2023 (in press).
36. Zayat N, Huang S, Wafai J, Philadelphia M. Monkeypox Virus Infection in 22-Year-Old Woman after Sexual Intercourse, New York, USA. Emerg Infect Dis [Internet]. 2023 Jan 1 [cited 2024 Sep 30];29(1):222. Available from: /pmc/articles/PMC9796209/
37. Portela-Dias J, Sereno S, Falcão-Reis I, Rasteiro C. Monkeypox infection with localized genital lesions in women. Am J Obstet Gynecol. 2022 Dec 1;227(6):906.
38. Kibungu EM, Vakaniaki EH, Kinganda-Lusamaki E, Kalonji-Mukendi T, Pukuta E, Hoff NA, et al. Clade I–Associated Mpox Cases Associated with Sexual Contact, the Democratic Republic of the Congo. Emerg Infect Dis [Internet]. 2024 Jan 1 [cited 2024 Jun 7];30(1):172. Available from: /pmc/articles/PMC10756366/
39. Vakaniaki EH, Kinganda-Lusamaki E, Merritt S, Kasongo F, Malembi E, Lunyanga L, et al. Presumed Transmission of 2 Distinct Monkeypox Virus Variants from Central African Republic to Democratic Republic of the Congo - Volume 30, Number 10—October 2024 - Emerging Infectious Diseases journal - CDC. Emerg Infect Dis [Internet]. 2024 Oct [cited 2024 Oct 15];30(10). Available from: https://wwwnc.cdc.gov/eid/article/30/10/24-1118_article
40. European Centre for Disease Prevention and Control (ECDC), WHO Regional Office for Europe (WHO). Joint ECDC-WHO Regional Office for Europe Mpox Surveillance Bulletin [Internet]. [cited 2024 Feb 8]. Available from: https://monkeypoxreport.ecdc.europa.eu/
41. Miller MJ, Cash-Goldwasser S, Marx GE, Schrodt CA, Kimball A, Padgett K, et al. Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022. MMWR Morb Mortal Wkly Rep

[Internet]. 2022 Nov 4 [cited 2022 Dec 14];71(44):1412–7. Available from: https://www.cdc.gov/mmwr/volumes/71/wr/mm7144e1.htm
42. Yinka-Ogunleye A, Dalhat M, Akinpelu A, Aruna O, Garba F, Ahmad A, et al. Monkeypox Risk and Mortality Associated with HIV Infection: A National Case Control Study in Nigeria. SSRN Electronic Journal [Internet]. 2022 Jul 28 [cited 2022 Dec 14]; Available from: https://papers.ssrn.com/abstract=4172063
43. Mitjà O, Alemany A, Marks M, Lezama Mora JI, Rodríguez-Aldama JC, Torres Silva MS, et al. Mpox in people with advanced HIV infection: a global case series. Lancet [Internet]. 2023 Mar 18 [cited 2023 Aug 31];401(10380):939–49. Available from: https://pubmed.ncbi.nlm.nih.gov/36828001/
44. Khodakevich L, Jezek Z, Kinzanzka K. Isolation of monkeypox virus from wild squirrel infected in nature. Lancet [Internet]. 1986 Jan 11 [cited 2024 Jan 10];1(8472):98–9. Available from: https://pubmed.ncbi.nlm.nih.gov/2867342/
45. Radonić A, Metzger S, Dabrowski PW, Couacy-Hymann E, Schuenadel L, Kurth A, et al. Fatal Monkeypox in Wild-Living Sooty Mangabey, Côte d'Ivoire, 2012. Emerg Infect Dis [Internet]. 2014 [cited 2024 Jan 10];20(6):1009. Available from: /pmc/articles/PMC4036778/
46. Patrono L V., Pléh K, Samuni L, Ulrich M, Röthemeier C, Sachse A, et al. Monkeypox virus emergence in wild chimpanzees reveals distinct clinical outcomes and viral diversity. Nat Microbiol [Internet]. 2020 Jul 1 [cited 2024 Jan 10];5(7):955–65. Available from: https://pubmed.ncbi.nlm.nih.gov/32341480/
47. Kinganda-Lusamaki E, Amuri-Aziza A, Fernandez N, Makangara-Cigolo JC, Pratt C, Vakaniaki EH, et al. Clade I Mpox virus genomic diversity in the Democratic Republic of the Congo, 2018 - 2024: Predominance of Zoonotic Transmission. medRxiv [Internet]. 2024 Aug 14 [cited 2024 Aug 22];2024.08.13.24311951. Available from: https://www.medrxiv.org/content/10.1101/2024.08.13.24311951v1
48. Vakaniaki EH, Kinganda-Lusamaki E, Merritt S, Kasongo F, Malembi E, Lunyanga L, et al. Documented transboundary transmission of mpox between the Central African Republic and the Democratic Republic of the Congo. medRxiv [Internet]. 2024 Aug 14 [cited 2024 Aug 25];2024.08.13.24311555. Available from: https://www.medrxiv.org/content/10.1101/2024.08.13.24311555v1
49. Yinda KC, Koukouikila-Koussounda F, Mayengue PI, Elenga GR, Greene B, Ochwoto M, et al. Likely cross-border introductions of MPXV Clade I into the Republic of the Congo from the Democratic Republic of the Congo. medRxiv [Internet]. 2024 Aug 21 [cited 2024 Aug 25];2024.08.21.24312265. Available from: https://www.medrxiv.org/content/10.1101/2024.08.21.24312265v1
50. Wawina-Bokalanga T, Akil-Bandali P, Kinganda-Lusamaki E, Lokilo E, Jansen D, Amuri-Aziza A, et al. Co-circulation of monkeypox virus subclades Ia and Ib in Kinshasa Province, Democratic Republic of the Congo, July to August 2024. Eurosurveillance [Internet]. 2024 Sep 19 [cited 2024 Sep 20];29(38):2400592. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2024.29.38.2400592
51. APOBEC3 deaminase editing supports human-to-human transmission in escalating Mpox outbreaks of both Clade Ia and Ib in Kinshasa, Democratic Republic of the Congo, July-September 2024 - MPXV / Evolution - Virological [Internet]. 2022 [cited 2024 Oct 30]. Available from: https://virological.org/t/apobec3-deaminase-editing-supports-human-to-human-transmission-in-escalating-mpox-outbreaks-of-both-clade-ia-and-ib-in-kinshasa-democratic-republic-of-the-congo-july-september-2024/982
52. World Organization for Animal Health (WOAH). Terrestrial Code Online Access - WOAH - World Organisation for Animal Health [Internet]. [cited 2022 Dec 14]. Available from: https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/
53. Musumeci SJLLKOSAC. Mpox reinfection: a literature review. Authorea. 2023 Aug 23;
54. Zeggagh J, Ferraris O, Salmona M, Tarantola A, Molina JM, Delaugerre C. Second clinical episode of hMPX virus in a man having sex with men. Vol. 401, The Lancet. 2023.
55. Rocha SQ, Fonsi M, Tancredi MV, Alencar HDR de, Abbud A, da Silva MH. Monkeypox in a Couple Living with HIV: Relapse or Reinfection? AIDS Res Hum Retroviruses. 2023;
56. Golden J, Harryman L, Crofts M, Muir P, Donati M, Gillett S, et al. Case of apparent mpox reinfection. Sex Transm Infect. 2023;99(4).

57. Musumeci S, Najjar I, El Amari EB, Schibler M, Jacquerioz F, Yerly S, et al. A Case of Mpox Reinfection. Clinical Infectious Diseases. 2023;77(1).
58. The Lancet Infectious Diseases. A tale of potential mpox reinfection. Vol. 23, The Lancet Infectious Diseases. 2023.
59. Raccagni AR, Canetti D, Mileto D, Tamburini AM, Candela C, Albarello L, et al. Two individuals with potential monkeypox virus reinfection. Vol. 23, The Lancet Infectious Diseases. 2023.
60. Hazra A, Zucker J, Bell E, Flores J, Gordon L, Mitjà O, et al. Mpox in people with past infection or a complete vaccination course: a global case series. Lancet Infect Dis. 2023;
61. Ogoina D, Oru Oru I, Yinka-Ogunleye A, Ihekweazu C, Ndodo N, Aruna O. Case Report: Recurrent Mpox in a Healthcare Worker in Nigeria. Am J Trop Med Hyg. 2023;
62. Álvarez-López P, Borras-Bermejo B, López Pérez L, Antón A, Piñana M, García-Pérez J, et al. Suspected case of monkeypox reinfection versus reactivation in a immunocompetent patient, Barcelona, 2022. Int J STD AIDS. 2023;34(9).
63. Suñer C, Ubals M, Tarín-Vicente EJ, Mendoza A, Alemany A, Hernández-Rodríguez Á, et al. Viral dynamics in patients with monkeypox infection: a prospective cohort study in Spain. Lancet Infect Dis. 2023;23(4).
64. Barnes AH, Smith C, Dash A, Shishido AA. Mpox: Special Considerations in the Immunocompromised Host. Curr Treat Options Infect Dis. 2023;14(4).
65. World Health Organization (WHO). Diagnostic testing and testing strategies for mpox: interim guidance, 12 November 2024 [Internet]. 2024 [cited 2024 Nov 18]. Available from: https://iris.who.int/handle/10665/379547
66. World Health Organization (WHO). Strategic framework for enhancing prevention and control of mpox 2024-2027. World Health Organization [Internet]. 2024 May 24 [cited 2024 Sep 30]; Available from: https://iris.who.int/bitstream/handle/10665/376839/9789240092907-eng.pdf?sequence=1
67. McConnell SJ, Herman YF, Mattson DE, Erickson L. Monkey Pox Disease in Irradiated Cynomologous Monkeys. Nature 1962 195:4846 [Internet]. 1962 [cited 2023 Dec 18];195(4846):1128–9. Available from: https://www.nature.com/articles/1951128a0
68. Breman JG, Kalisa-Ruti, Steniowski M V., Zanotto E, Gromyko AI, Arita I. Human monkeypox, 1970-79. Bull World Health Organ [Internet]. 1980 [cited 2023 Dec 18];58(2):165. Available from: /pmc/articles/PMC2395797/?report=abstract
69. World Organisation for Animal Health (WOAH). Risk Guidance on Reducing Spillback of Mpox (Monkeypox) Virus from Humans to Wildlife, Pet Animals, and Other Animals [Internet]. 2022 [cited 2024 Oct 6]. Available from: https://www.woah.org/app/uploads/2022/12/woah-mpox-guidelines-en.pdf
70. Trelle S, Shang A, Nartey L, Cassell JA, Low N. Improved effectiveness of partner notification for patients with sexually transmitted infections: systematic review. BMJ [Internet]. 2007 Feb 15 [cited 2022 Jun 21];334(7589):354. Available from: https://www.bmj.com/content/334/7589/354
71. World Health Organization (WHO). Second meeting of the International Health Regulations (2005) (IHR) Emergency Committee regarding the multi-country outbreak of monkeypox [Internet]. 2022 [cited 2022 Aug 17]. Available from: https://www.who.int/news/item/23-07-2022-second-meeting-of-the-international-health-regulations-(2005)-(ihr)-emergency-committee-regarding-the-multi-country-outbreak-of-monkeypox
72. World Health Organization (WHO). Vaccines and immunization for monkeypox: Interim guidance, 16 November 2022 [Internet]. 2022 [cited 2022 Dec 21]. Available from: https://www.who.int/publications/i/item/WHO-MPX-Immunization
73. ICAO. APPENDIX 13. PUBLIC HEALTH PASSENGER LOCATOR FORM [Internet]. 2022 [cited 2024 Oct 1]. Available from: https://www.icao.int/Security/FAL/ANNEX9/PublishingImages/Pages/Publications/Annex%209%20Appendix%2013%20Public%20Health%20Passenger%20Locator%20Form-1.pdf

74. IATA. Suspected Communicable Disease - Guidelines for passenger agents [Internet]. 2017 [cited 2024 Oct 1]. Available from: https://www.iata.org/contentassets/f1163430bba94512a583eb6d6b24aa56/health-guideline-pax-agents.pdf
75. World Health Organization (WHO). Syndromic entry and exit screening for epidemic-prone diseases of travellers at ground crossings: evidence review and a call for research [Internet]. 2024 [cited 2024 Oct 1]. Available from: https://iris.who.int/handle/10665/376764
76. Parkins MD, Lee BE, Acosta N, Bautista M, Hubert CRJ, Hrudey SE, et al. Wastewater-based surveillance as a tool for public health action: SARS-CoV-2 and beyond. Clin Microbiol Rev [Internet]. 2024 Mar 1 [cited 2024 Oct 1];37(1). Available from: https://journals.asm.org/doi/10.1128/cmr.00103-22
77. World Health Organization (WHO). Environmental surveillance for SARS-CoV-2 to complement other public health surveillance [Internet]. 2023 [cited 2024 Oct 1]. Available from: https://www.who.int/publications/i/item/9789240080638
78. Moschese D, Pozza G, Mileto D, Giacomelli A, Cutrera M, Cossu MV, et al. Isolation of viable monkeypox virus from anal and urethral swabs, Italy, May to July 2022. Eurosurveillance. 2022;27(36).
79. Palich R, Burrel S, Monsel G, Nouchi A, Bleibtreu A, Seang S, et al. Viral loads in clinical samples of men with monkeypox virus infection: a French case series. Lancet Infect Dis. 2023;23(1).
80. Wannigama DL, Amarasiri M, Phattharapornjaroen P, Hurst C, Modchang C, Besa JJ V., et al. Community-based mpox and sexually transmitted disease surveillance using discarded condoms in the global south. Lancet Infect Dis [Internet]. 2024 Oct 1 [cited 2024 Oct 7];24(10):e610–3. Available from: http://www.thelancet.com/article/S1473309924005140/fulltext
81. Tiwari A, Adhikari S, Kaya D, Islam MA, Malla B, Sherchan SP, et al. Monkeypox outbreak: Wastewater and environmental surveillance perspective. Science of The Total Environment. 2023 Jan 15;856:159166.
82. Islam MA, Kumar R, Sharma P, Zhang S, Bhattacharya P, Tiwari A. Wastewater-Based Surveillance of Mpox (Monkeypox): An Early Surveillance Tool for Detecting Hotspots. Curr Pollut Rep [Internet]. 2024 Jun 1 [cited 2024 Oct 1];10(2):312–25. Available from: https://link.springer.com/article/10.1007/s40726-024-00299-6
83. Adams C, Kirby AE, Bias M, Riser A, Wong KK, Mercante JW, et al. Detecting Mpox Cases Through Wastewater Surveillance — United States, August 2022–May 2023. MMWR Morb Mortal Wkly Rep [Internet]. 2024 Jan 18 [cited 2024 Feb 8];73(2):37–43. Available from: https://www.cdc.gov/mmwr/volumes/73/wr/mm7302a3.htm
84. Chen W, Bibby K. Model-Based Theoretical Evaluation of the Feasibility of Using Wastewater-Based Epidemiology to Monitor Monkeypox. Environ Sci Technol Lett [Internet]. 2022 Sep 13 [cited 2022 Dec 14];9(9):772–8. Available from: https://pubs.acs.org/doi/abs/10.1021/acs.estlett.2c00496
85. Wannigama DL, Amarasiri M, Phattharapornjaroen P, Hurst C, Modchang C, Chadsuthi S, et al. Tracing the transmission of mpox through wastewater surveillance in Southeast Asia. J Travel Med [Internet]. 2023 Jul 1 [cited 2024 Oct 1];30(5). Available from: https://pubmed.ncbi.nlm.nih.gov/37462504/
86. Global Outbreak Alert and Response Network (GOARN). Go.Data [Internet]. [cited 2022 Jun 23]. Available from: https://extranet.who.int/goarn/godata

Suggested citation. Surveillance, case investigation and contact tracing for mpox: interim guidance, 27 November 2024. Geneva: World Health Organization; 2024. https://doi.org/10.2471/B09169